Journal of Inclusion Phenomena and Macrocyclic Chemistry **42:** 169–186, 2002.

Review Article

Azacalixarenes: Synthesis, Complexation, and Structures *

HIROYUKI TAKEMURA
Department of Chemistry, Faculty of Science, Kyushu University, Ropponmatsu 4-2-1, Chuo-ku, Fukuoka, 810-8560 Japan

(Received: 31 August 2001; in final form: 22 October 2001)

Key words: azacalixarene, azacyclophane, calixarene, host–guest complex

Abstract

Azacalixarenes, which have various *N*-bound side arms, were synthesized in a one-pot manner in satisfactory yields. Their structures in the solid and solution were elucidated by the NMR spectroscopic method and X-ray crystallographic analyses. Some of them complexed with metal ions (alkali metal, lanthanide, and uranyl ions) under neutral conditions. By the functionalization of the side arms, a wide variety of applications is expected.

Introduction

Formation of azacalix structures

Azacalixarenes, which are generated by the insertion of nitrogen atoms into the bridging methylene unit of the calixarene structure, have several isomers based on the position of the nitrogen atoms and the ring size. Figure 1 shows examples of azacalix[3]arenes and azacalix[4]arenes. Among these, compounds **3**, **4**, **5**, and **7** were synthesized by us. Azacalixarenes can be easily synthesized by heating bis(hydroxymethyl)phenol derivatives and benzylamines in refluxing toluene or xylene for 3 days (Scheme 1) [1]. The desired cyclic compounds are obtained selectively in moderate to high yields. The choice of non-polar solvents is essential in this reaction because the template effect by OH···OH, OH···N hydrogen bonds play an important role in the cyclization [1a]. Thus, the high dilution technique is not required in this reaction. Several reports support this phenomenon; i.e., a phenol cyclic trimer was observed in supersonic jets [2]. Generally, condensation reactions between alcohol and amines require drastic reaction conditions and catalysts [3]. However, in the case of hydroxymethylphenols, C–N bond formation occurs under relatively mild conditions. The reaction is not a simple dehydration reaction but seems to be a kind of Mannich reaction via quinonemethides as shown in Scheme 2 because absence of the phenolic OH group allows no reaction; i.e., 1,3-bis(hydroxymethyl)-5-*tert*-butylbenzene and benzylamine do not react at all under similar conditions. Analogous azacalixarenes, containing **8**, were synthesized in a different manner [4].

The nomenclature of the azacalixarenes often gives long names; thus, we can use abbreviated names based on the number of phenols and the number of carbon and nitrogen atoms which connect the phenol units [5]. Therefore, hexahomotriazacalix[3]arene (for example, compound **3**), tetrahomodiazacalix[4]arene **5**, and dihomoazacalix[4]arene **4** can be abbreviated as triaza[3.3.3], diaza[3.1.3.1], and aza[3.1.1.1], respectively (in this case, substituents on the *para* position of the phenol and nitrogen atoms are ignored). We use this nomenclature system throughout this review. However, the homoazacalix[n]arene name system is sometimes more convenient; therefore, we use that system in some cases.

Synthesis, structures, and application

Synthesis of azacalixarenes with various N-bound side arms

Because functional groups can be introduced into three sites of azacalixarenes (aromatic ring, phenolic oxygen atom, and nitrogen atom), further functionalization and application can be expected. Firstly, we tried to introduce various side arms starting from hydroxymethylphenols and benzylamines. The results are summarized in Tables 1 and 2. The reaction product between phenol derivatives and alkyl amines is a viscous oil and cyclic products were not isolated. Reactions with aromatic amines; (e.g., aniline or toluidine) afforded resinous products: condensation occurred but no cyclic compounds were found. The reaction with toluenesulfonamide gave calix[n]arenes but not the desired azacalixarene. Thus, the reaction with sulfamine, 4-(aminomethyl)benzenesulfonamide, afforded cyclic compound **5h** in satisfactory yield (48.1%). Along with this compound, *N*-(4-aminosulfonyl)benzyl-[3.1.1.1] **4d** was obtained as a by-product (7.6%). As described below, degradation and recombination of bis(hydroxymethyl)phenol oligomers **10** or **11** often occurs under higher temperatures (higher than the boiling point of toluene). On the other hand, very high yields were obtained in the case of the reaction with picolylamines. Especially in the case of **3g**, **5c** and

* Supplementary Data relating to this article are deposited with the British Library as Supplementary Publication No. SUP 82293 (11 pages).

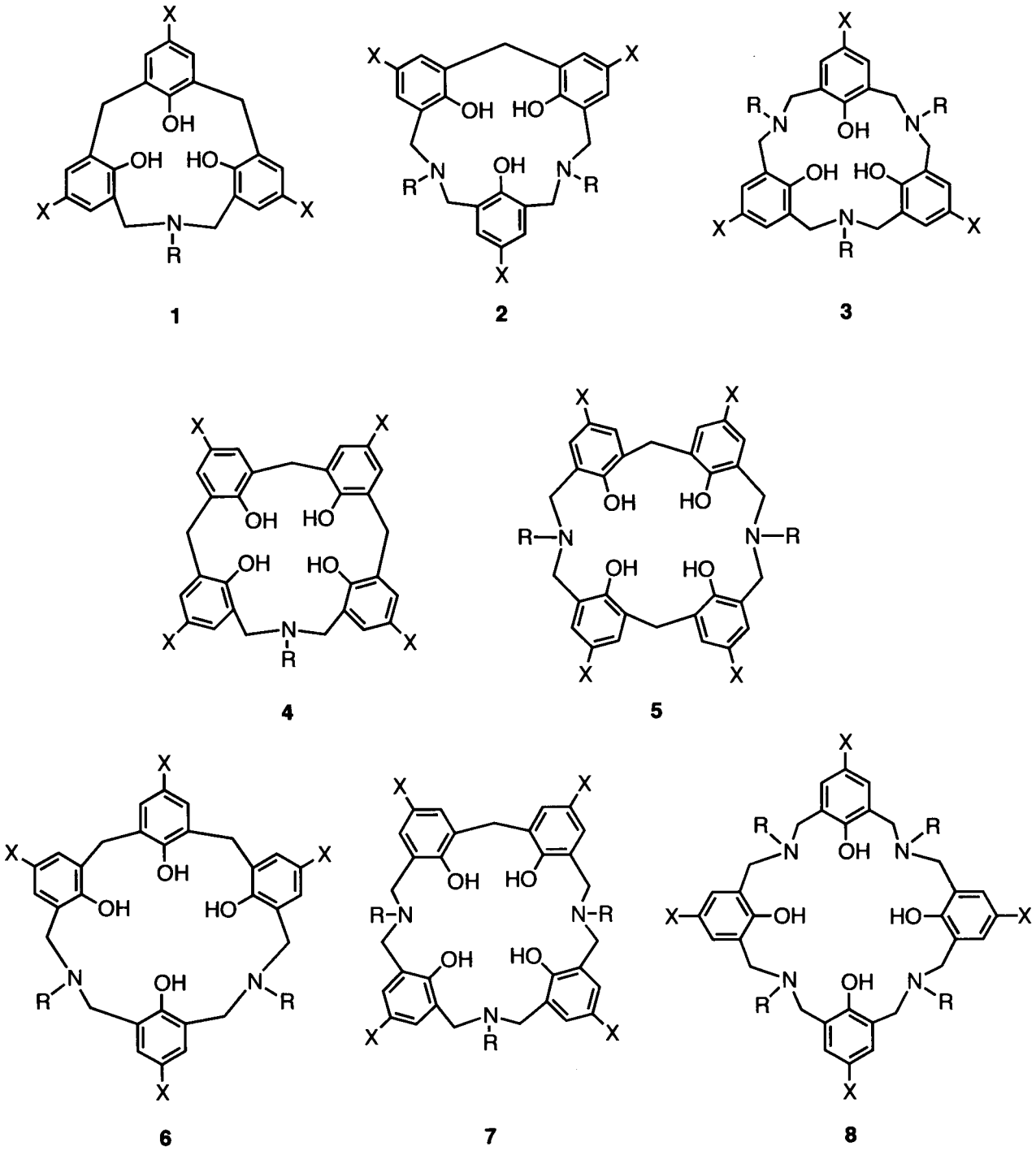
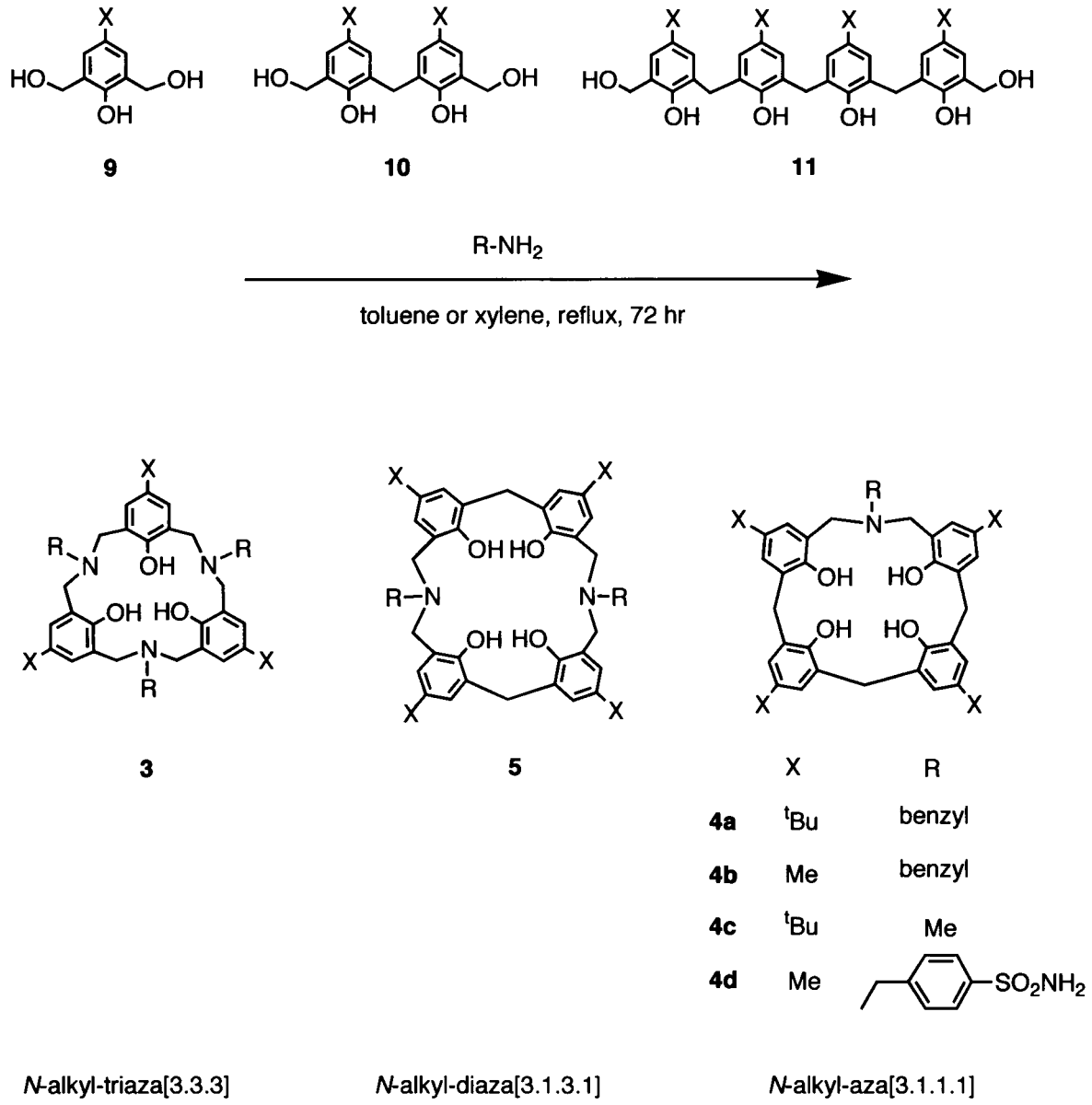


Figure 1. Structures of $(aza)_n$calix[3]arenes and $(aza)_n$calix[4]arenes.

5d, almost all of the products are the desired cyclic compounds. By using *p*-xylylenediamine as a nitrogen source, a concave molecule **13**, in which the four aromatic rings accommodate the bridged *p*-xylylene unit (Scheme 3), was obtained. Similarly, meta-bridged compound **14a** was also generated. Interestingly, by starting with the phenol trimer **12**, unexpected compound **14b** was obtained in higher yield than the desired compound **15**, and the yields were considerably lower than that of the *p*-xylyl derivative [6]. In this case, degradation and recombination of the phenol units occur.

Functional groups on the *para* position of phenols affect the cyclization. Although the reaction proceeds well with alkyl groups (methyl or *tert*-butyl) in toluene, the *para*-chloro derivative requires higher temperatures; thus the reaction was carried out in refluxing xylene. The reaction of *p*-chloro-2,6-bis(hydroxymethyl)phenol **9** (X = Cl) with benzylamine in toluene gave acyclic product **16** which was an intermediate of **3c** (Scheme 4). This intermediate cyclized in refluxing xylene. Other *para* substituted phenols, 2,6-bis(hydroxymethyl)-4-(2-hydroxyethyl)- and 2,6-bis(hydroxymethyl)-4-(ethoxycarbonylmethyl)phenols,

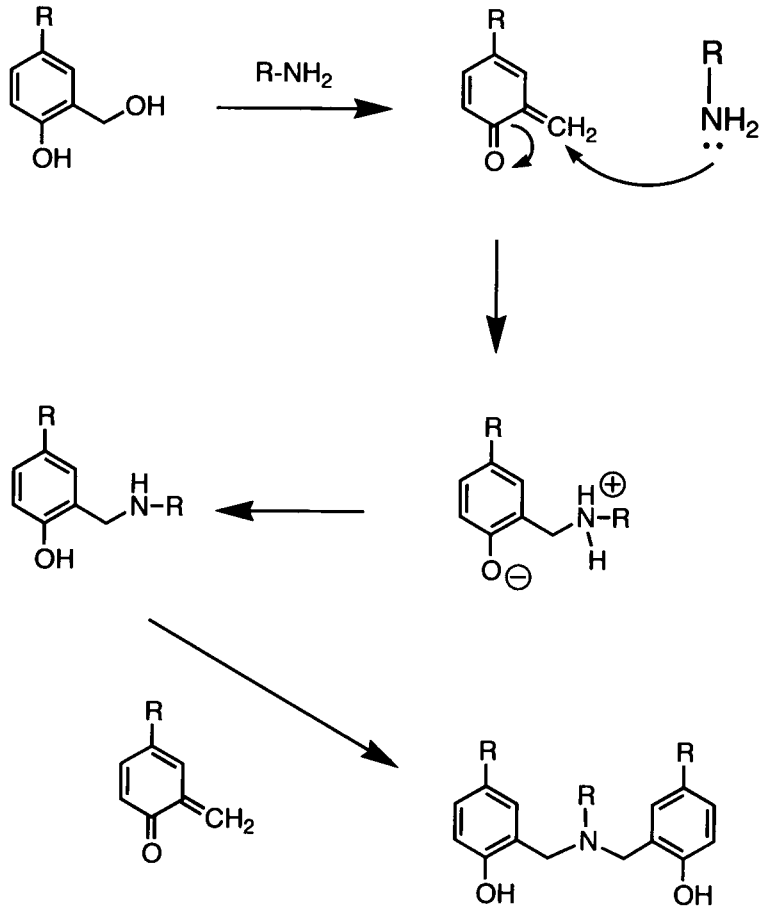


Scheme 1. Synthesis of azacalix[n]arenes **3**, **4**, and **5**.

gave complex mixtures, but cyclic products (compounds **3d** and **3e**) were not isolated. The reaction between propargylamine and 4-methyl-2,6-bis(hydroxymethyl)phenol gave only polymeric products. On the contrary, propargyl side arms could be easily introduced into the diaza[3.1.3.1] structure. The reasons for this difference in the reactions are so far not clear.

As previously reported, the conformation of *N*-benzyl-aza[3.1.1.1] in solution was determined by means of the VT-NMR technique [1c]. However, in this case, the signals of the benzyl and aromatic protons of the cyclic skeleton overlapped with those of the side arms. Therefore, detailed studies could not be accomplished. In order to overcome this problem, we had to develop a synthetic method for *N*-methyl derivatives (Scheme 5). This was achieved by employing methylamine; the method is also applicable for the synthesis of *N*-methyl-diaza[3.1.3.1] **5k** as described below, but not applicable for the synthesis of *N*-methyl-triaza[3.3.3].

Heating an aqueous solution of *p-tert*-butylphenol, formaldehyde, methylamine, and KOH at 50–55 °C for 48 h yielded a yellow sticky mass. This is a precursor of the cyclic products. The precursor was heated in refluxing xylene for another 48 h, and a resinous material, which contained macrocyclic compounds, was obtained [7]. Each compound, **4c**, **7**, and **17**, was easily separated from the reaction mixture by column chromatography on silica gel. Small amounts of other azacalix[n]arenes were also isolated, but the structures could not be identified. Calix[6]arene, calix[8]arene and hexahomotrioxacalix[3]arene were obtained as by-products. In some cases, *N*-methyl-tetraaza[3.3.3.3] was isolated. The yields of **4c**, **7**, and **17** were low (**4c**, 15%; **7**, 2.8%; **17**, 1.5%), but the advantage of this reaction is in avoiding the synthesis of intermediate linear bis(hydroxymethyl)phenol oligomers. In particular, compound **7** is difficult to synthesize even by the stepwise method.



Scheme 2. Reaction of hydroxymethylphenol and amine.

Synthesis of the smallest member, aza[3.1.1] **19**, was attempted by using the dibromide **18** and toluenesulfonamide [8]. However, the cyclic compound thus isolated was *N*,*N*′-ditosyl-diaza[3.1.1.3.1.1] **20** (17. 3% yield) as shown in Scheme 6.

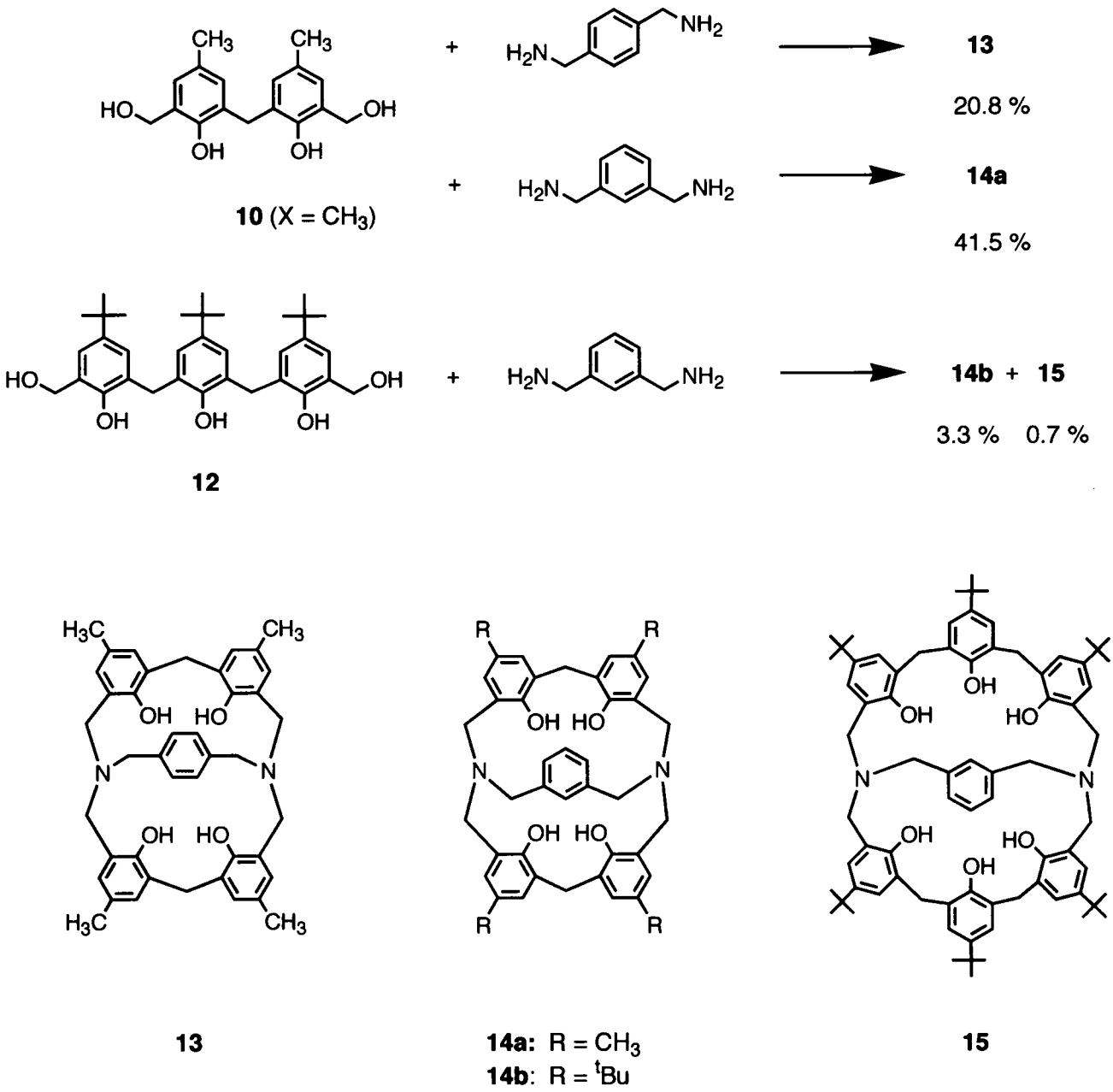
Structures of azacalixarenes

Conformation of azacalixarenes in solution

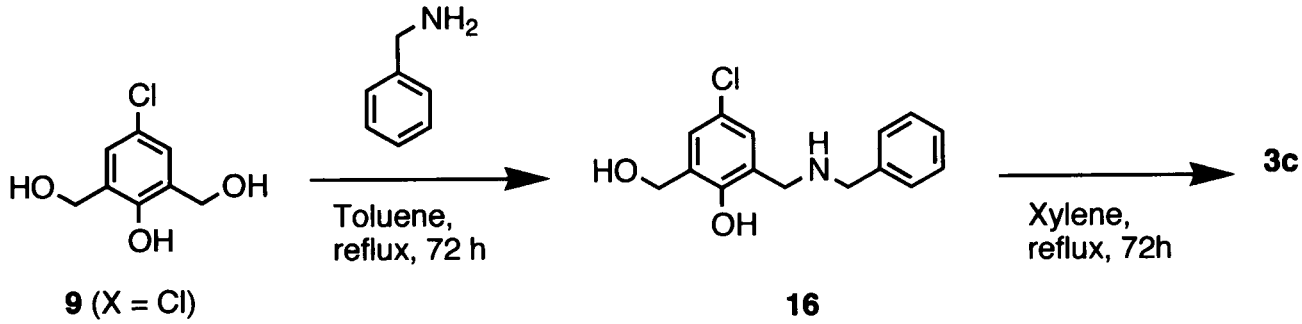
The most interesting target for conformational analysis in solution is aza[3.1.1.1] because it has the most similar skeleton to calix[4]arene. The triaza[3.3.3] series are too flexible to observe the spectral changes by NMR spectroscopy. In the case of *N*-benzyl-diaza[3.1.3.1] **4a**, the $\Delta G^{\ddagger}$ of the aromatic ring inversion was estimated to be 14.4 kcal mol^{-1} in $CDCl_3$ [1b]. Conformational analysis of aza[3.1.1.1] was restudied using the *N*-methyl derivative (**4c**: X = ^{t}Bu, R = Me) because the spectra of *N*-benzyl-aza[3.1.1.1] **4a** showed a complex pattern at low temperatures [9]. By the VT-NMR (^{1}H and ^{13}C) method [10], two conformers of **4c** were detected at low temperatures. Consequently, judging from the ^{1}H and ^{13}C NMR spectral data and the results of decoupling experiments, the major conformer of **4c** is "cone" and the minor conformer is "1,4-alternate" as shown in Figure 2. From the intensity of each signal, the ratio of the "cone" and "1,4-alternate" conformers is estimated to be 3.2 : 1.0 at −40 °C. The *N*-Me signals of **4c** appeared as two singlets below 0 °C and the ratio is equal to that of methylene or aromatic protons; thus the splitting of the *N*-Me signal is synchronized to the aromatic ring inversion. The ΔG^{0} (273 K) between two states (**4c**$_{major}$/**4c**$_{minor}$) is estimated to be ca. 0.88 kcal/mol, based on the ratio of *N*-Me signal intensities and also those of the methylenes. In the "cone" conformer, the energy barriers ($\Delta G^{\ddagger}$) of inversion of aromatic rings, –CH_2–*Ar*–CH_2– and –*Ar*–CH_2–N–, are estimated to be 16.8 kcal/mol and 16.5 kcal/mol in DMSO-d_6, respectively. The later value could not be estimated in the case of *N*-benzyl-*p*-*tert*-butyl-aza[3.1.1.1] **4a** [1c]. Analogously, the cone conformation of **7** was confirmed and the $\Delta G^{\ddagger}$ of the inversion of the aromatic rings is estimated to be 14.6 kcal/mol in $CDCl_3$. The conformation of *N*-benzyl-aza[3.1.1.1] (**4a** and **4b**) in the crystal is "cone" as discussed below. The energetic barrier of the aromatic ring inversion is larger than the corresponding calixarenes [1b]. In spite of the enlargement of the ring by the insertion of the nitrogen atoms, the molecule is more rigid compared to the calixarenes. This is attributed to the contribution of the nitrogen atoms to the conformational rigidity due to the OH···N···O hydrogen bond array.

Crystalline structures

Hampton et al. reported an alternative synthesis of triazacalix[3.3.3] with ethylglycine side arm and its crystallographic analysis [11]. It has a shallow saucer-like structure, and the side arms are standing perpendicularly on the nitrogen atoms. As expected, phenolic OH protons form a cyclic

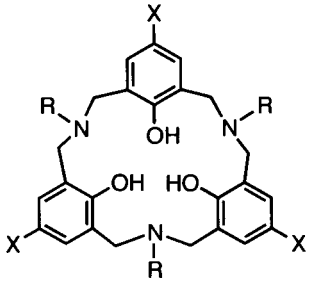


Scheme 3. Synthetic scheme and structures of *N*,*N*′-xylylene-bridged azacalixarenes.

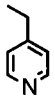


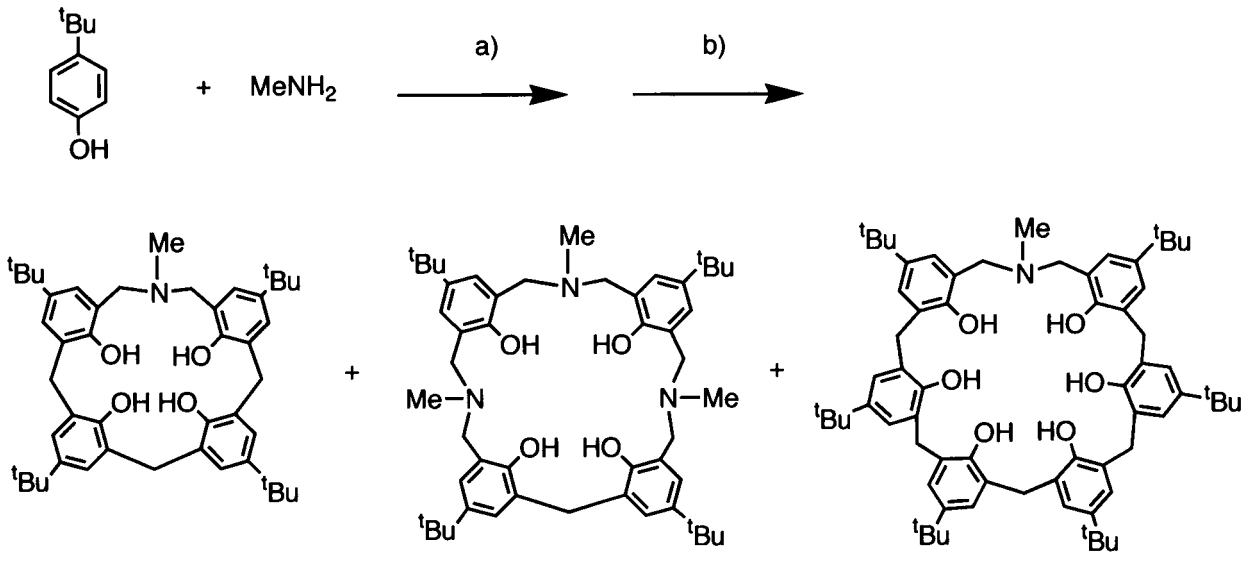
Scheme 4. Formation of acyclic intermediate **16**.

Table 1. Structures and yields of triaza[3.3.3] derivatives



3

	R	X	Yield(%)
a		Me	38
b		Br	36
c		Cl	37
d		CH_2CH_2OH	—
e		CH_2COOEt	—
f		Me	29
g		Cl	96
h		Cl	43
i		Br	—
j		Br	36
k		Me	—
l		Me	53



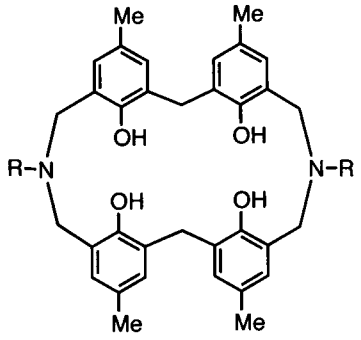
4c X = ^{t}Bu, R = Me — 15 %

7 X = ^{t}Bu, R = Me — 2.8 %

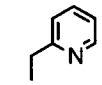
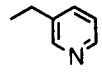
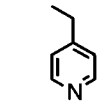
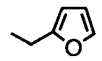
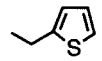
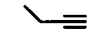
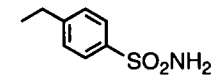
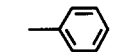
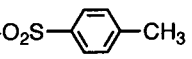
17 — 1.5 %

Scheme 5. Synthesis of *N*-Me-azacalixarenes. (a) Formalin, KOH at 50–55 °C for 48 h. (b) Xylene, reflux for 48 h.

Table 2. Structures and yields of diaza[3.1.3.1] derivatives



5

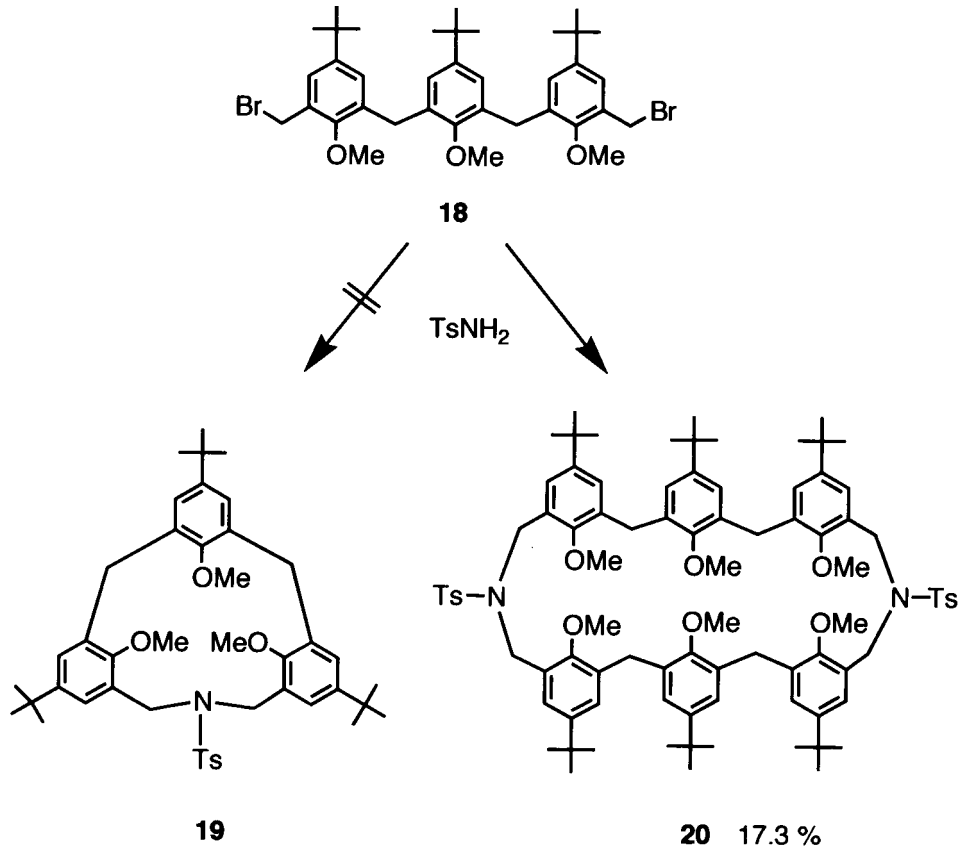
	R	Yield (%)
a		58.3
b		30.9
c		81.1
d		87.8
e		28.1
f		35.8
g		38.4
h		48.1*
i		—
j		—
k	-CH_3	see Scheme 7

array of OH···N···OH··· hydrogen bonds. On the other hand, we also elucidated the crystal structures of *N*-benzyl-triaza[3.3.3] **3c** and *N*-benzyl-diaza[3.1.3.1] **5a** (Figure 3) [12]. They have a shallow saucer-shaped structure; also, a cyclic array of OH···N···OH··· hydrogen bonds was observed. In the case of the structure of *N*-benzyl-triaza[3.3.3] **3c**, in contrast to Hampton's case, two benzyl side arms were placed at the lower side of the molecule and another one protruded above the cavity. On the other hand, trimethoxy derivative **21** has a very different structure, in which two aromatic rings are almost parallel and form a deep and close cavity as shown in Figure 3. The *p*-xylylene-bridged azacalixarene **13** also has a saucer-like structure and an OH···N···OH··· hydrogen bond array (Figure 4).

Interestingly, an inclusion complex was obtained by recrystallization of *p*-Me-*N*-benzyl-aza[3.1.1.1] **4b** from DMF. It has a capsule-like dimeric structure with two DMF molecules encapsulated in the cavity (Figure 5). Some interaction between a DMF molecule and the host **4b** is anticipated, but from the crystallographic structure, a reasonable interaction like CH···π is not apparent [13]. As previously reported, recrystallization of *p-tert*-butyl-*N*-benzyl-aza[3.1.1.1] **4a** from a DMF/DMSO mixture gave adduct **4a**·DMF [1c]. Interestingly, in contrast to **4b**·DMF, the crystallographic analysis of **4a**·DMF showed that a DMF molecule is not included in the cavity, but is placed outside of the molecule (Figure 4). *N*-benzyl-aza[3.1.1.1] has a cone conformation and a relatively deep cavity, and the side arm is placed at the lower side of the molecule.

Hydrogen bonds in the cyclic structures

As previously described, the azacalix[4]arene series form strong intramolecular hydrogen bonds both in solution and in the solid state: the IR and the NMR spectra show characteristic spectral features of these hydrogen bonds [1]. Calix[4]arene shows a clear and a relatively sharp OH vibra-



Scheme 6. An attempted synthesis of an aza[3.1.1] derivative.

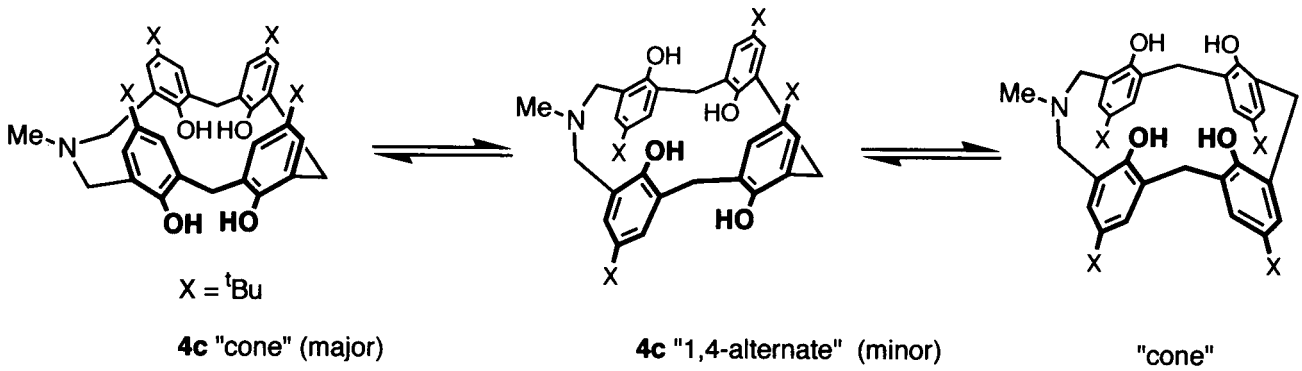


Figure 2. Conformational changes of *N*-Me-aza[3.1.1.1].

tional mode at 3160 cm^{-1}. On the contrary, azacalixarenes have very broad and strong absorption in the range of 2700–3000 cm^{-1}. The ^{1}H-NMR spectra of *N*-benzyl-aza[3.1.1.1] at low temperatures showed that OH peaks split into a multiplet at 17.1 $\sim$ 12.5 ppm [1c]. The protons exchange between the O and N atoms with sufficient rates at room temperatures, but at low temperatures, the protons localize and hydrogen bonds are fixed. The specific features of the OH signal of azacalixarenes are its broadness both in the ^{1}H and IR spectra, while calix[n]arenes generally show clear and sharp signals. Such strong hydrogen bonds and broadness result from the participation of nitrogen atoms in the cyclic hydrogen bond array.

As shown in Figure 6, azacalix[n]arenes show temperature-dependent OH signals in the ^{1}H NMR. The OH signals of *N*-methyl-[3.1.1.1] **4c** and *N*-methyl-[3.3.3.1] **7** appear as broad peaks at 11.8 ppm and 11.2 ppm (in $CDCl_3$, 25 °C), respectively. On the other hand, *N*-methyl-[3.1.1.1.1.1] **17** shows four broad singlets at 12.4, 13.8, 15.3, and 16.4 ppm, even at 25 °C. This is the first case in the azacalixarene series that shows a multiplet of OH signals at room temperature. The *p*-xylylene-bridged compounds **13** and **14** show two OH signals of equal intensity at low temperatures. The signal at lower field corresponds to OH···N, and the signal at higher field corresponds to OH···OH protons. This characterization is based on the crystallographic structure of **13** in which the O···O and O···N distances are 2.80 and 2.69 Å, respectively. The localization energies were estimated by the VT-NMR method as 10.8 and 11.2 kcal mol^{-1} for **13** and **14b**, respectively [6].

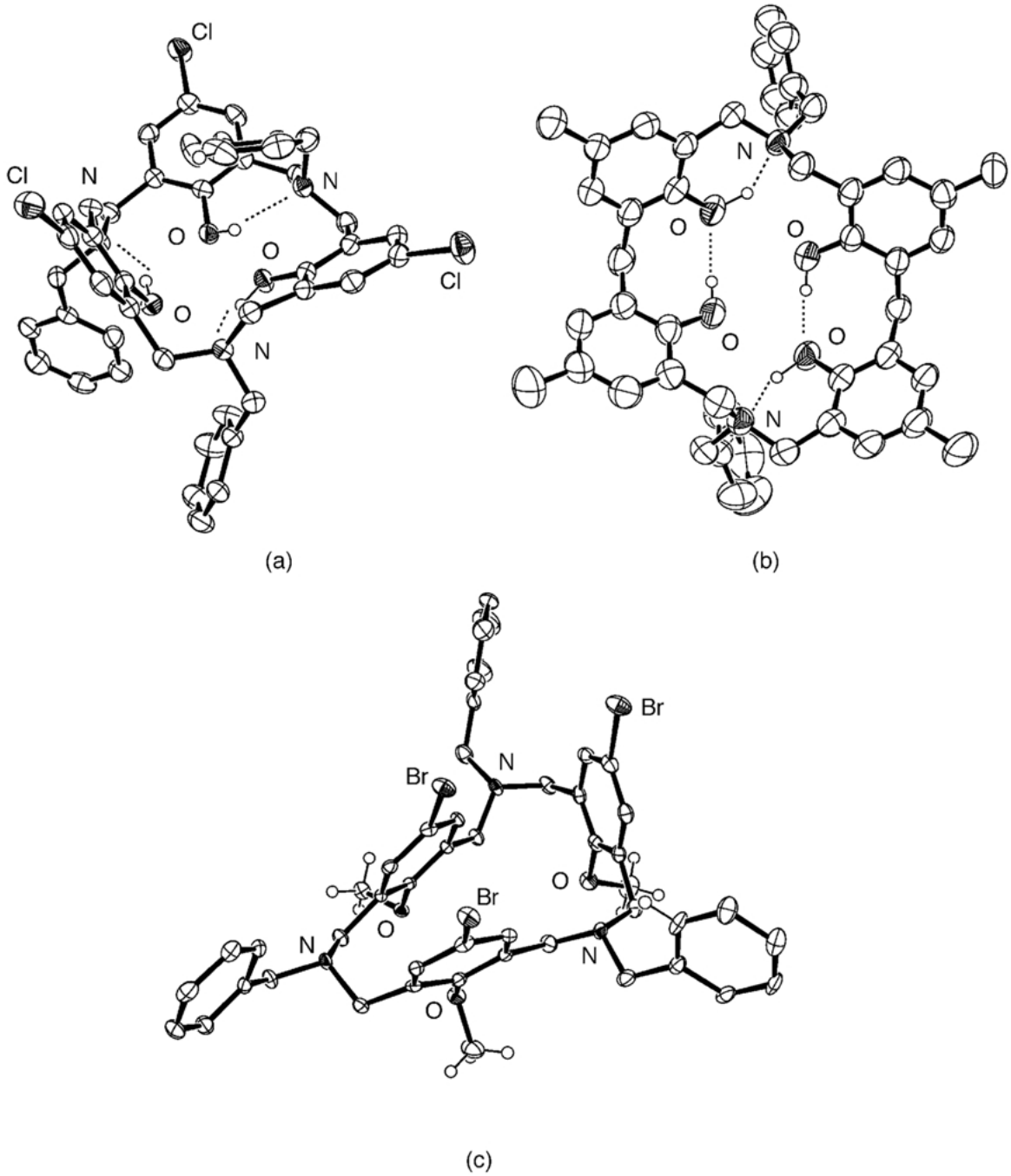


Figure 3. Molecular structures of (a) *N*-benzyl-triaza[3.3.3] **3c**, (b) *N*-benzyl-diaza[3.1.3.1] **5a**, and (c) *N*-benzyl-trimethoxytriaza[3.3.3] **21**.

Metal complexes of the azacalixarenes

The triaza[3.3.3] **3a** extracted UO_2^{2+} efficiently even in the presence of a high concentration of NaCl [1a]. The extraction ability has a high pH-dependency; uranyl ion is most effectively extracted in the neutral region. Since azacalixarenes have nitrogen atoms as a base, they form metal complexes under neutral conditions. Lanthanide extraction experiments were carried out by using *N*-(2-picolyl)-triaza[3.3.3] **3f** as a ligand in order to investigate the metal selectivities among lanthanide ions. In the previous report, we showed that ligand **3f** extracted alkali metal ions efficiently, but the selectivity was very poor because of the flexibility of the picolyl side arms [1c]. Also in the case of lanthanide ions, extraction occurred very efficiently, but here also, selectivities are not observed. However, the extraction is very sensitive to the pH of the aqueous phase. In the actual experimental conditions, the pH of each lanthanide solution is subtly different, and the result of the extraction showed that the distribution ratios do not reflect the selectivity among the metal ions, but it is the function of the pH of the solution. Figure 7 shows the results of the extraction experiment, and we can easily recognize the pH-dependence of the distribution ratio, D(%). This phenomenon is strongly re-

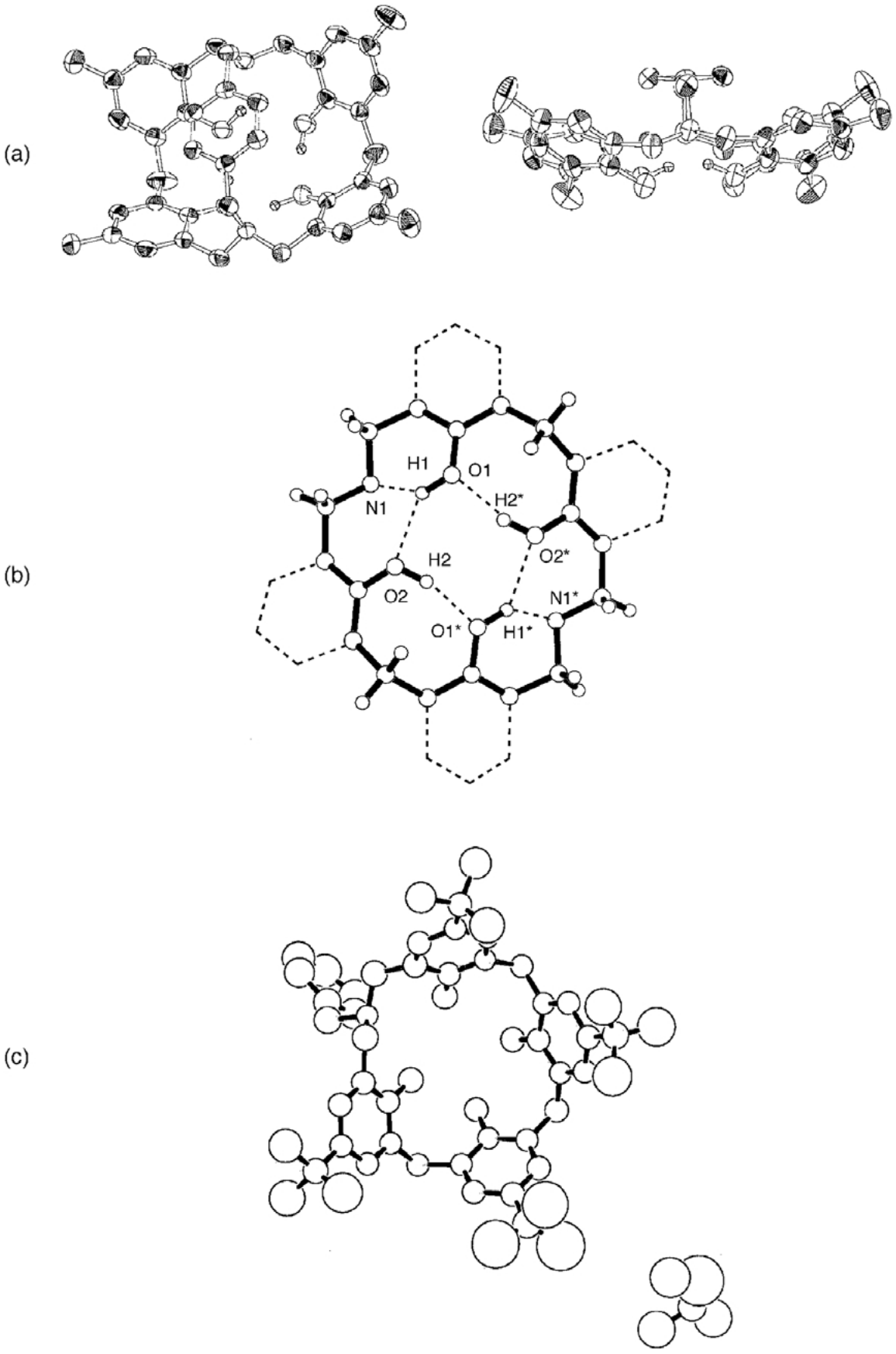


Figure 4. (a) Crystal structure of **13**. (b) Hydrogen bond network in the cavity of **13** (Aromatic rings are omitted for clarity. Dashed lines show the aromatic moiety). (c) Crystal structure of **4a** · DMF.

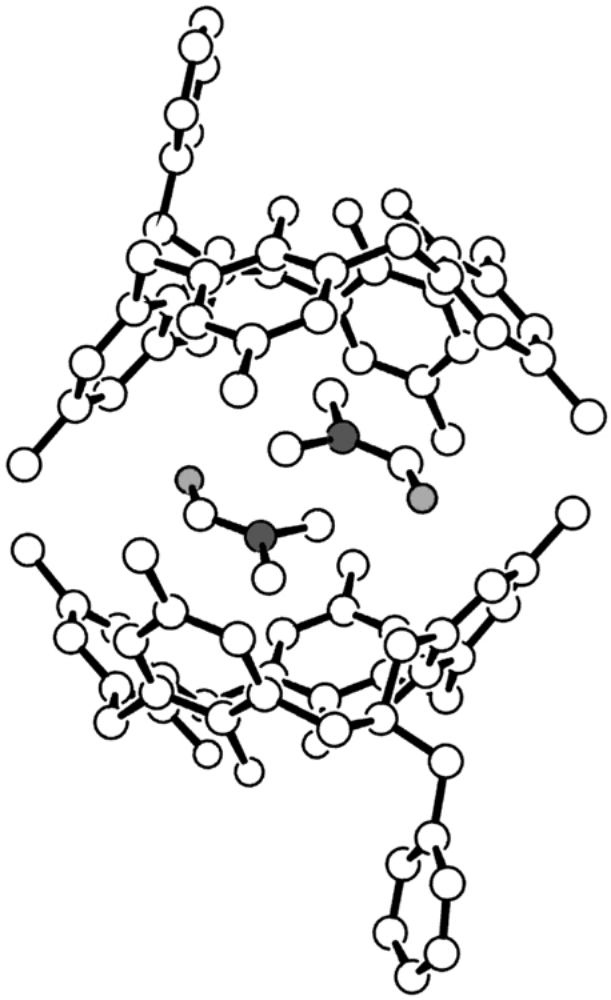


Figure 5. Molecular structure of the capsule-like dimer 2 · DMF ⊂ 2 · **4b**.

lated to the pKa of the azacalixarene, namely the equilibrium between $OH\cdots N \leftrightarrow O^{-}\cdots HN^{+}$.

Thuéry et al. prepared UO_2^{2+}, Nd^{3+}, and Yb^{3+} complexes of azacalixarenes (**3c** and **5a**) without using any bases and succeeded in obtaining complexes suitable for crystallographic analyses (Figure 8) [12]. Interestingly, in the crystal structures, OH protons are not located on the oxygen atoms but are transferred to nitrogen atoms and form intramolecular zwitter-ionic structures. The metal ions are placed out of the plane of the $O\cdots NH^{+}\cdots O\cdots$ linkage: this is ascribed to the $NH^{+}\cdots M^{+}$ repulsion. A review by Thuéry *et al.* described the complexes of *f*-element ions of oxa- and azacalixarenes [14].

Application

Azacalix betaine

Since azacalixarenes have nitrogen and oxygen atoms in the cyclic structure and if nitrogen atoms have a positive charge, generation of an intramolecular betaine compound is expected by the dissociation of OH protons similar to the metal complexes described above [15]. At first, we tried to make a betaine starting from *p*-Br-*N*-benzyl-triaza[3.3.3] **3b**. After protecting the phenolic OH groups by methoxy groups, nitrogen atoms were quaternarized by methyl triflate. However, in this case, the ammonium methyl groups were removed under the deprotection conditions for the methoxy group. Other protecting groups (–OAc, $–CH_2–OCH_3$, $–CH_2CH_2–OCH_3$) were attempted, but quaternarization did not proceed in these cases. Steric hindrance between the benzyl side arms and the protecting groups seemed to be a severe problem in these cases. Therefore, the *N*-methyl side arms are the best choice in order to make a betaine precursor. However, attempted synthesis of *N*-methyl-triaza[3.3.3] was unfruitful.

On the contrary, *N*-methyl-diaza[3.1.3.1] **5k** was easily synthesized by the reaction between bisphenol **10** and aq. CH_3NH_2 as shown in Scheme 7. Heating an excess of aqueous methylamine (>10 eq.) with bisphenol **10** (X = CH_3) in ethanol at 80 °C for 24 h yielded the precursor of the cyclic product. Heating the precursor in refluxing toluene for 48 h afforded compound **5k** in 44% yield. When using aq. $MeNH_2$ in a stoichiometric amount or less than 5 molar excess, azaoxa[3.1.3.1] **22** and diaza[3.1.3.1] **5k** were obtained in 23% and 28.6% yield, respectively. The phenolic OH groups were protected by acetyl groups and then nitrogen atoms were quaternarized by methyl triflate. After that, the acetyl groups were removed by aq. HCl and quaternarized azacalixarene **23** was obtained.

Treatment of **23** with a weak base, $NaHCO_3$, afforded the desired betaine $\mathbf{23}^{2-}$ in almost quantitative yield. pH-metric titration was carried out in order to estimate the pKa values of each phenolic OH group. Since compound **23** was insoluble in water, the measurement was performed in methanol. As a result, $pK_1 = 4.50$, $pK_2 = 6.17$, $pK_3 = 11.88$, and $pK_4 = 12.01$ were obtained. Under the same conditions, the pKa values of the reference compound, 2,2′-methylenebis(4-methyl)phenol were estimated to be $pK_1 = 10.48$ and $pK_2 = 11.68$. Because of charge repulsion, pK_1 and pK_2 of **23** are significantly shifted to the acidic region, but pK_3 and pK_4 are in the basic region. The distribution of each species is calculated and shown in Figure 9. The desired betaine species predominates in the weakly basic region (pH = 8 ∼ 10).

Prospect in the future

Functionalization of the picolyl side arm – construction of a molecular capsule and a rotor

Azacalixarenes can be expected as building blocks for a supramolecular system. Utilization of the side arms is the core of the application for this purpose. The connection of two azacalixarenes by alkylation of a picolyl side group may afford a hemi-capsule molecule such as compound **24**. However, contrary to the expectation, reaction between *N*-(4-picolyl)-diaza[3.1.3.1] **5d** and *p*-xylylene dibromide produced intramolecularly-bridged compound **25** (Scheme 8). The crystal structure has not been clarified as yet, but it is expected that the *p*-xylene unit is placed at the lower side of the molecule because the ^{1}H NMR signal of the bridged *p*-xylylene unit appears at a normal region in contrast to the high-field-shifted signal of the concave compound **13**. By using the *N*-picolyl-[3.3.3] system, cage compound **26**, hemi-capsule **27**, and **28** are expected (Scheme 9).

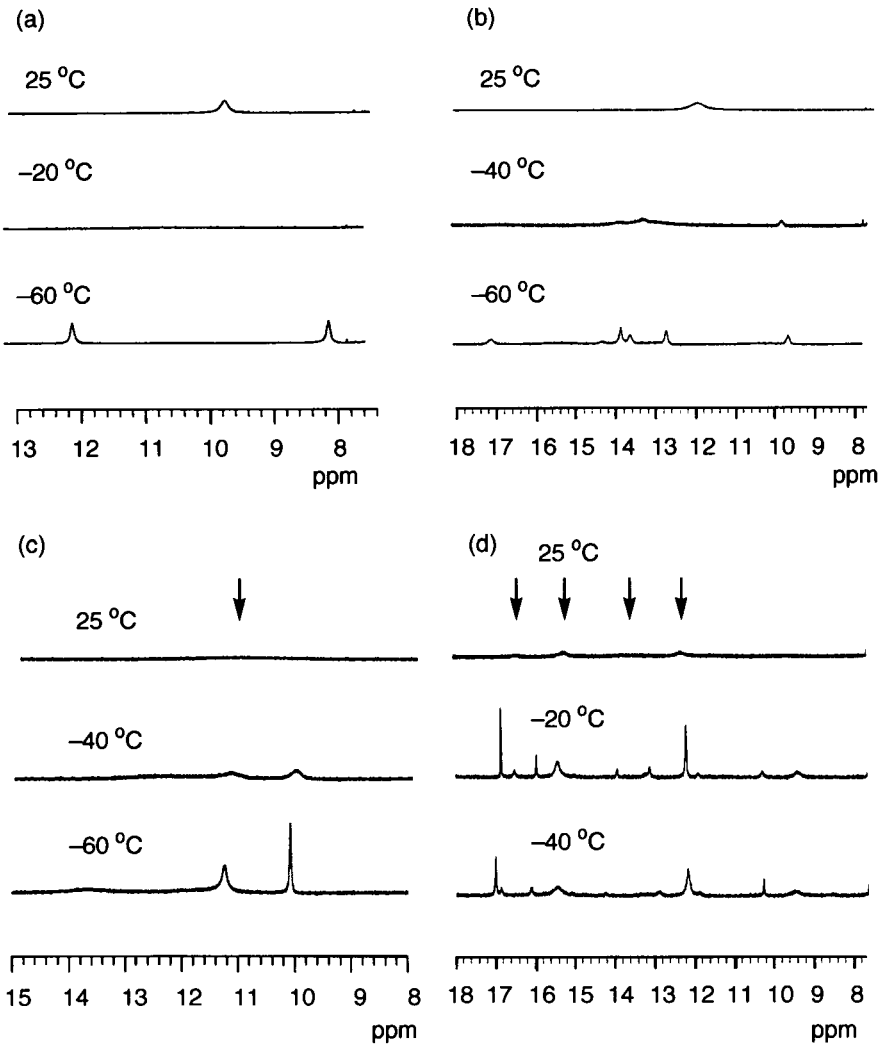


Figure 6. Phenolic OH proton signal patterns at various temperatures. (a) compound **13** (CD_2Cl_2), (b) compound **4c** ($CDCl_3$), (c) compound **7** ($CDCl_3$), and (d) compound **17** ($CDCl_3$). → shows the position of the peaks.

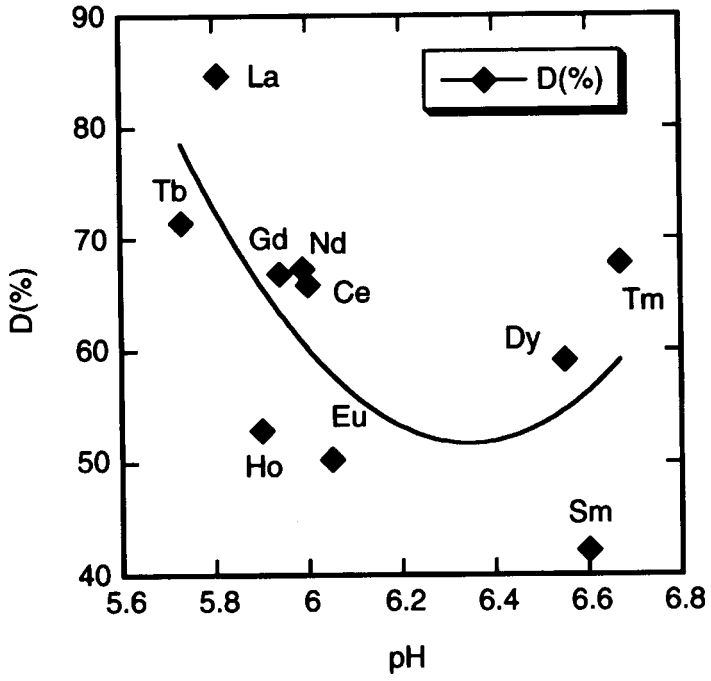


Figure 7. The pH-dependence of lanthanide ion extraction using **3f** as a ligand.

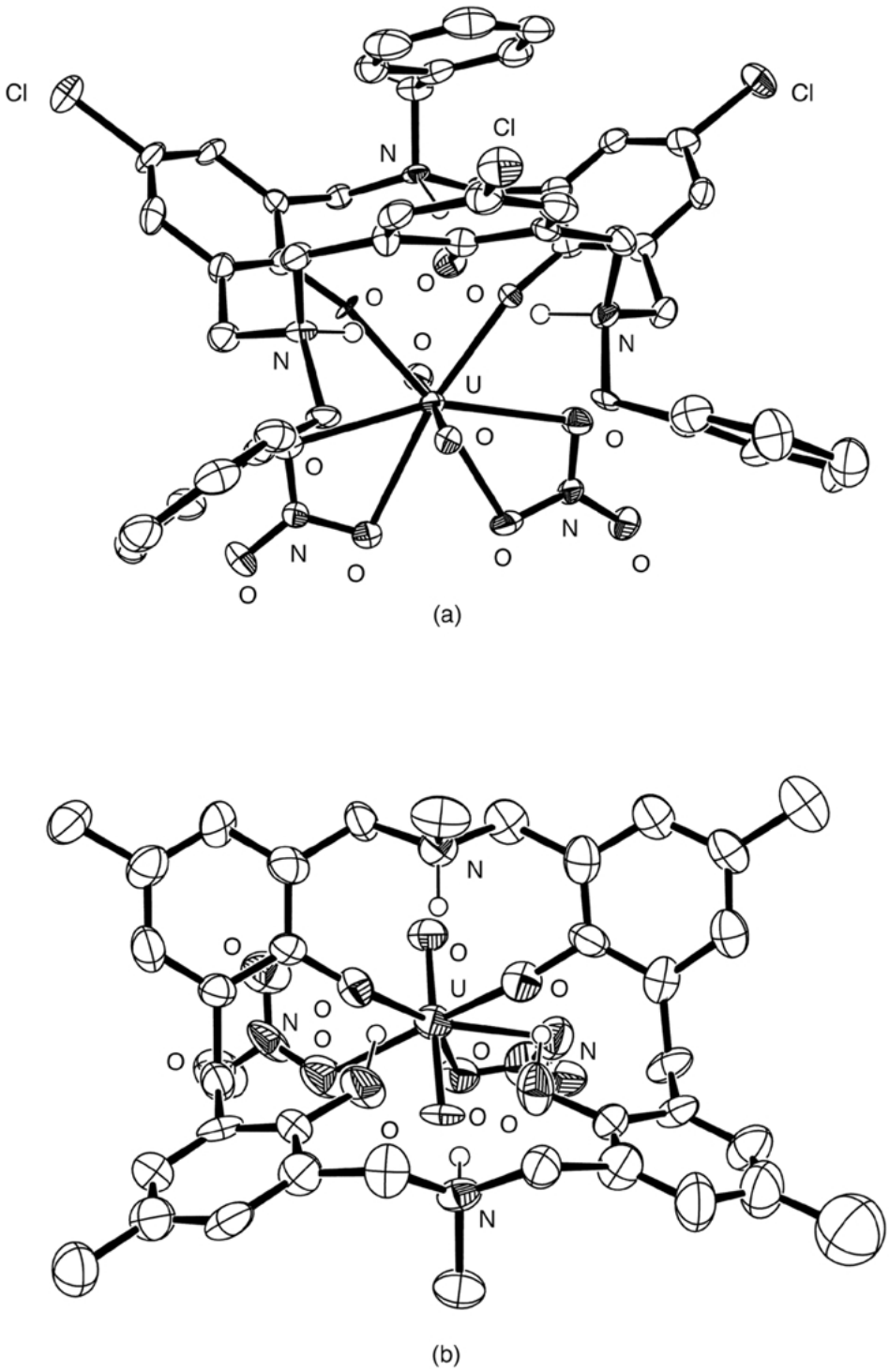
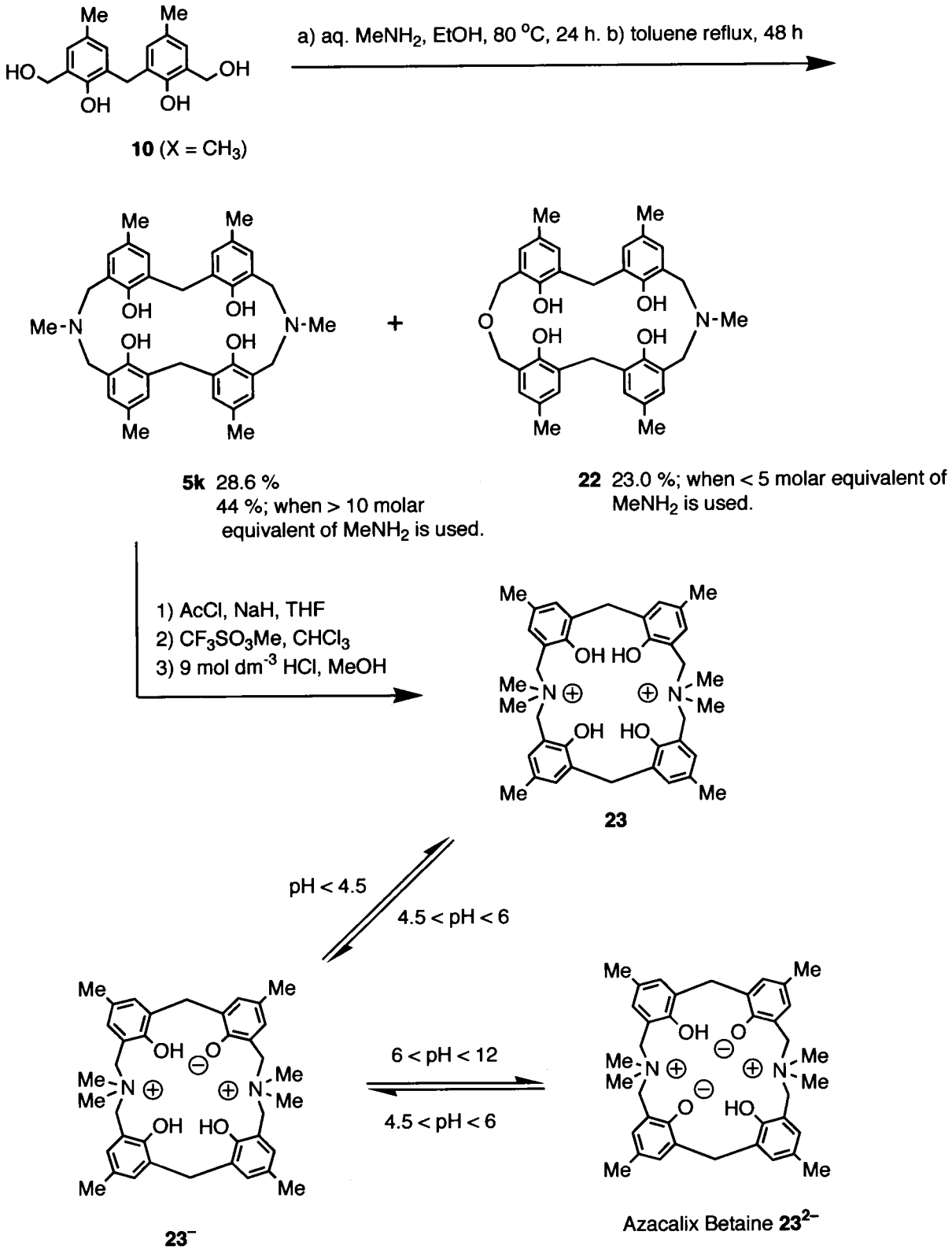


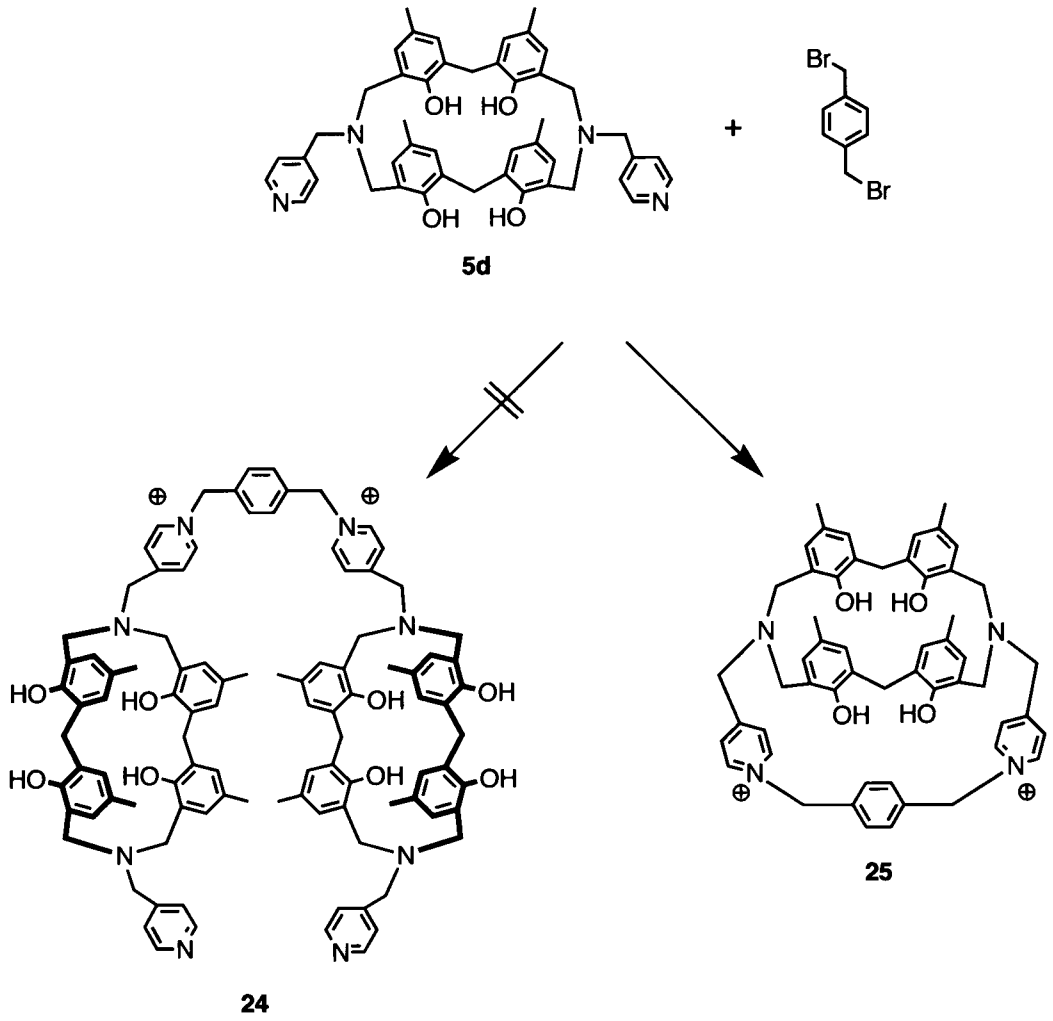
Figure 8. Crystallographic structures of (a) $UO_2^{2+} \subset$ **3c** and (b) $UO_2^{2+} \subset$ **5a** (Phenyl side arms of (b) are omitted for clarity).

The *N*-picolyl side arms can be used as a ligating unit and formation of metal-induced supramolecular structures can be expected by the complexation with metal ions (**29A** $\leftrightarrow$ **29A**′ and **30A** $\leftrightarrow$ **30A**′). The molecular gear **32** is expected by connection of two concave molecule, **31** which is a derivative of compound **14**. Introduction of the phenanthroline or bipyridine side arms into the azacalix[3.1.1.1.1] structure will provide a unique host system, which can encapsulate a guest molecule by addition of metal ions and release the guest by removing the metal ions as shown in Scheme 10. The system can be applied for the encapsulation of gaseous molecules or unstable chemical species and their transfers (the species can be removed at any time we want by removing the metal ions with CN^- or H_2S).

Conclusively, the specific feature of azacalixarenes arises from the presence of nitrogen atoms and side arms. Mak-



Scheme 7. Synthesis of azacalix betaine via *N*-Me-diaza[3.1.3.1].



Scheme 8. Reaction between **5d** and *p*-xylylene dibromide.

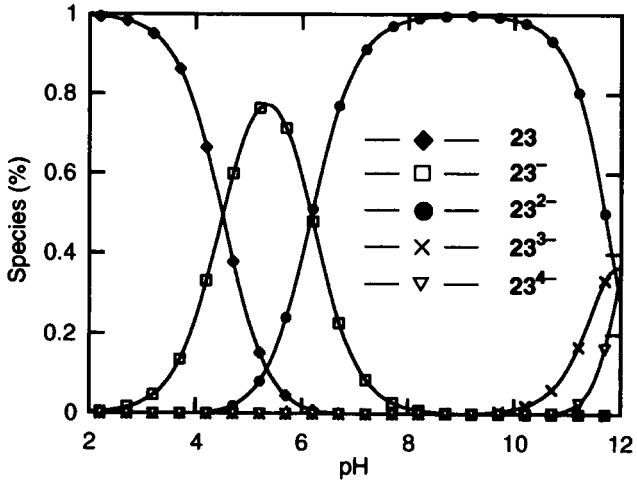


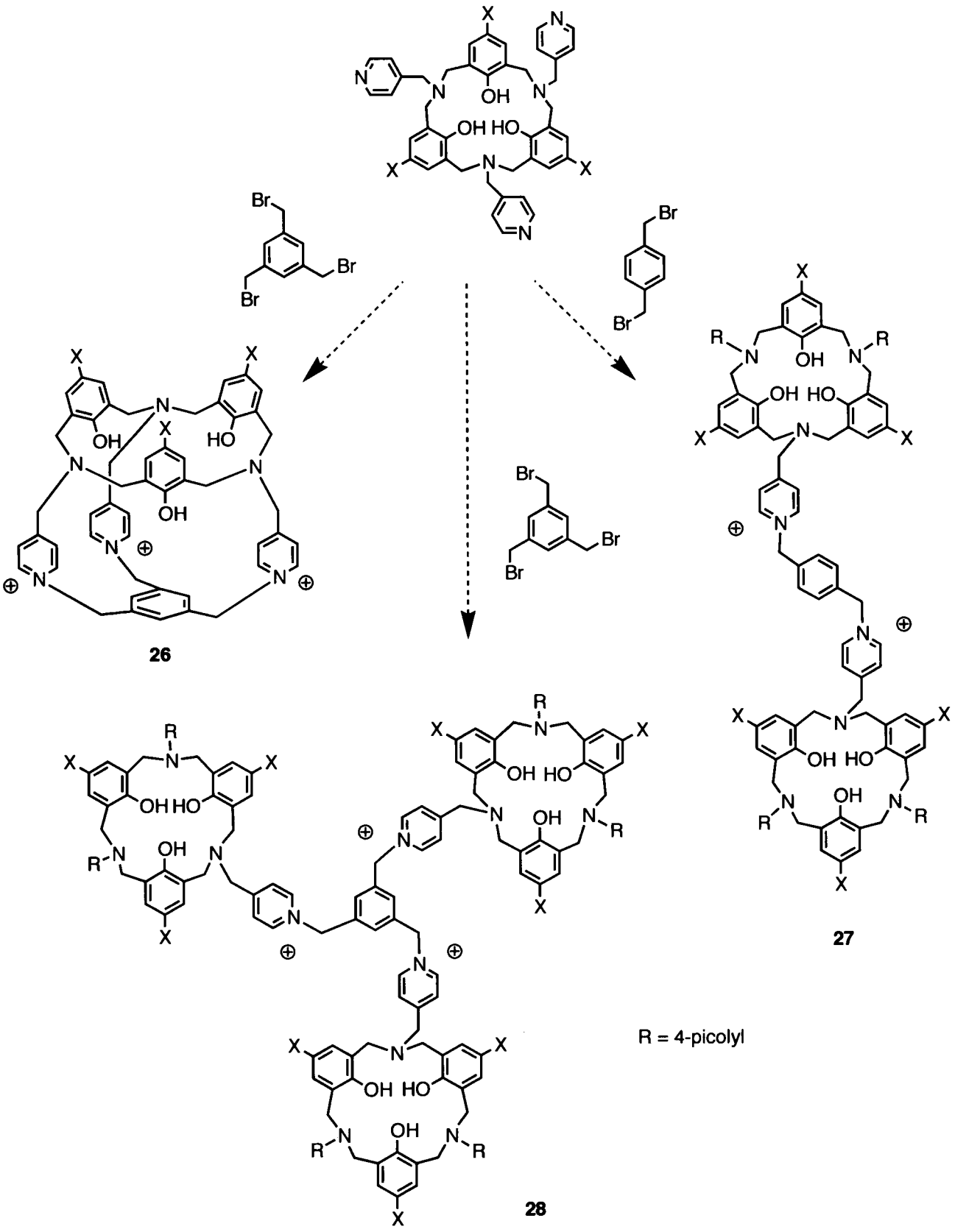
Figure 9. Distribution of proton-dissociated species of **23**.

ing further sophisticated molecules, metal ligating system, chiral molecules, etc. will start from the manipulation of the side arms.

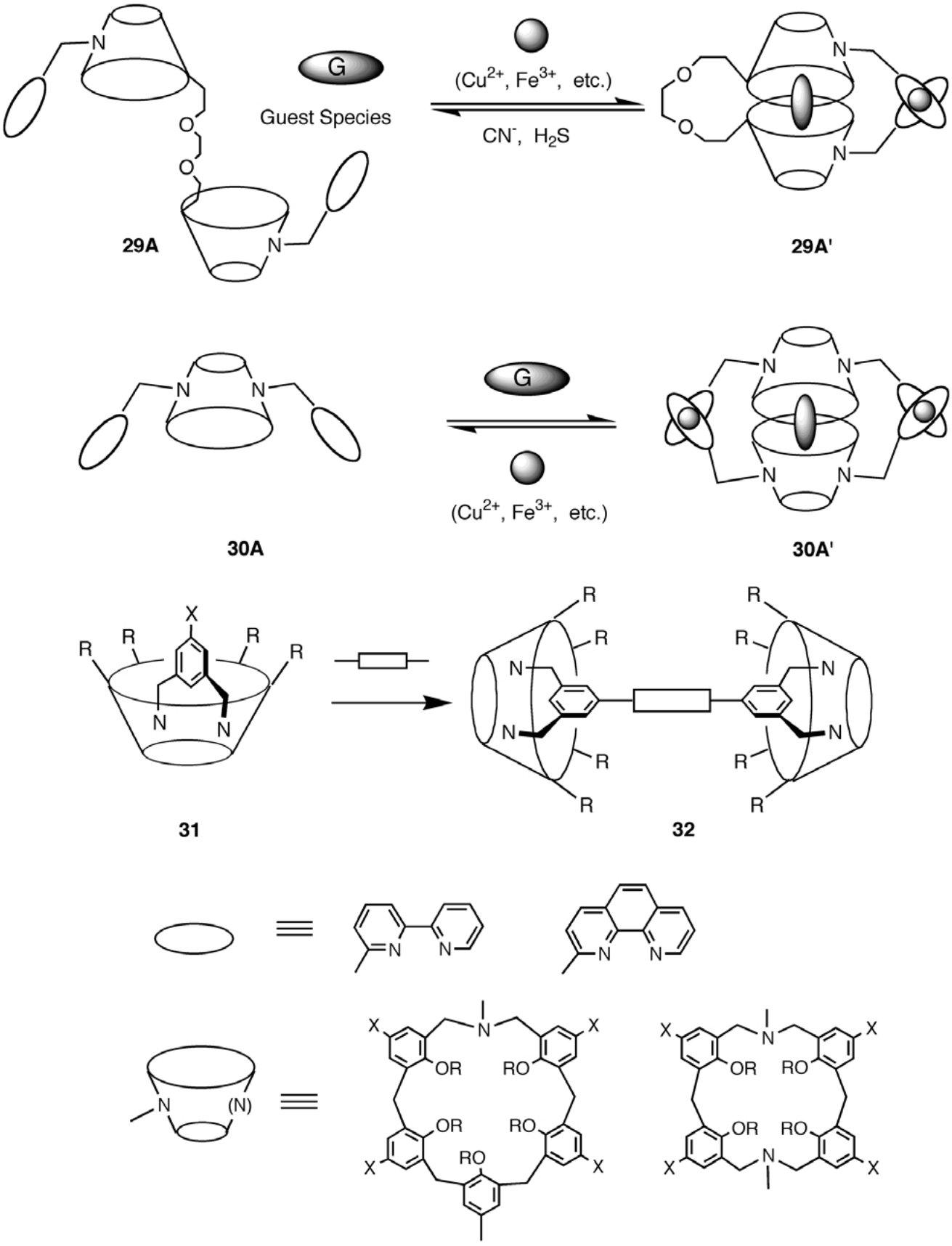
Acknowledgements

The author is grateful to Professor Emeritus Takahiko Inazu and Professor Jacques Vicens (ECPM, Laboratoire de Chimie des Interactions Moléculaires Spécifiques (CNRS UMR 7512), 25 rue Becquerel, 67087 Strasbourg, France) for encouragement of this work. The author also thanks Dr. Pierre Thuéry (CEA/Saclay, SCM (CNRS URA 331), Bât. 125, 91191 Gif-sur-Yvette, France) and Dr. Mikio Yasutake (Institute for Fundamental Research of Organic Chemistry, Kyushu University Hakozaki 6-10-1, Higashi-ku, Fukuoka 812-8581 Japan) for X-ray crystallographic analyses, and Dr. Hirokazu Miura (Toyota National College of Technology General Education, Eisei-cho 2-1, Toyota, Aichi, 471-8525 Japan) for collaboration.

Supporting information available: The liquid–liquid extraction method, the procedure for compounds **4c**, **7** and **17**, physical data of the compounds, and the results of X-ray crystallographic analyses of compound **21** and the DMF complex of **4b** have been deposited with the British Library at Boston Spa, Wetherby, West Yorkshire, U.K., as Supplementary Publication No. SUP 82293 (11 pages).



Scheme 9. Attempted syntheses of cage compound **26** and hemicapsule molecules **27** and **28**.



Scheme 10. Construction of azacalix-based capsules and rotax.

References

1. (a) H. Takemura, K. Yoshimura, I.U. Khan, T. Shinmyozu, and T. Inazu: *Tetrahedron Lett.* **33**, 5775 (1992). (b) I.U. Khan, H. Takemura, M. Suenaga, T. Shinmyozu, and T. Inazu: *J. Org. Chem.* **58**, 3158 (1993). (c) H. Takemura, T. Shinmyozu, H. Miura, I.U. Khan, and T. Inazu: *J. Incl. Phenom.* **19**, 193 (1994). (d) H. Takemura, T. Shinmyozu, and T. Inazu: *Coord. Chem. Rev.* **156**, 183 (1996).
2. T. Ebata, T. Watanabe, and N. Mikami: *J. Phys. Chem.* **99**, 5761 (1995) and references therein.
3. (a) S. Murahashi, K. Kondo, and T. Hakata: *Tetrahedron Lett.* **23**, 229 (1982). (b) R.C. Bernotas and R.V. Cube: *Tetrahedron Lett.* **32**, 161 (1991). (c) Y. Watanabe, Y. Tsuji, and Y. Ohsugi: *Tetrahedron Lett.* **22**, 2667 (1981).
4. (a) K. Niikura and E.V. Anslyn: *J. Chem. Soc., Perkin Trans. 2* 2769 (1999). (b) M.J. Grannas, B.F. Hoskins, and R. Robson: *Inorg. Chem.* **33**, 1071 (1994). (c) M.J. Grannas, B.F. Hoskins, and R. Robson: *J. Chem. Soc., Chem. Commun.* 1644 (1990). (d) K. Ito, A. Kida, Y. Ohba, and T. Sone: *Chem. Lett.* 1221 (1998). (e) K. Ito, Y. Ohba, and T. Sone: *Chem. Lett.* 783 (1996). (f) K. Ito, Y. Ohba, and T. Sone: *Chem. Lett.* 183 (1996). (g) B. Masci: *Calixarenes 2001*, in Z. Asfari, V. Böhmer, J. Harrowfield, and J. Vicens (eds.), Kluwer Academic Publishers (2001), pp. 235–249.
5. (a) F. Vögtle and P. Neumann: *Tetrahedron* **26**, 5847 (1970). (b) B. Masci, M. Finelli, and M. Varrone: *Chem. Eur. J.* **4**, 2018 (1998).
6. H. Takemura, K. Tani, H. Miura, G. Wen, T. Shinmyozu, and T. Inazu: *Supramol. Chem.* **11**, 83 (1999).
7. The procedure is described in the supporting information.
8. H. Takemura, M. Suenaga, K. Sakai, H. Kawachi, T. Shinmyozu, Y. Miyahara, and T. Inazu: *J. Incl. Phenom.* **2**, 207 (1984).
9. H. Miura: Thesis, 1997, Kyushu University.
10. C.D. Gutsche and L.J. Bauer: *J. Am. Chem. Soc.* **107**, 6052 (1985).
11. P.D. Hampton, W. Tong, S. Wu, and E.N. Duesler: *J. Chem. Soc., Perkin Trans. 2* 1127 (1996).
12. (a) P. Thuéry, M. Nierlich, J. Vicens, and H. Takemura: *J. Chem. Soc. Dalton Trans.* 279 (2000). (b) P. Thuéry, M. Nierlich, J. Vicens, B. Masci, and H. Takemura: *Eur. J. Inorg. Chem.* 637 (2001). (c) P. Thuéry, M. Nierlich, J. Vicens, and H. Takemura: *Polyhedron* **19**, 2673 (2000).
13. (a) J.C. Ma and D.A. Dougherty: *Chem. Rev.* **97**, 1303 (1997). (b) D.A. Dougherty: *Science* **271**, 163 (1996). (c) K. Murayama and K. Aoki: *J. Chem. Soc. Chem. Commun.* 607 (1998).
14. P. Thuéry, M. Nierlich, J. Harrowfield, and M. Ogden: *Calixarenes 2001*, in Z. Asfari, V. Böhmer, J. Harrowfield, and J. Vicens (eds.), Kluwer Academic Publishers (2001), pp. 561–582.
15. H. Takemura, Y. Kozima, and T. Inazu: *Tetrahedron Lett.* **40**, 6431 (1999).