Accounts

Armed Cyclen Receptors: From Three Dimensional Cation Recognition to Supramolecular Architecture

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The concept and examples of armed cyclens are described and some of their recent applications in molecular recognition and supramolecular chemistry are explained. Armed cyclens are characterized by a parent tetraamine ring and functionalized sidearms. They can act as three-dimensional ligands for octadentate metal complexation. They exhibit comparable log K values for Na^+ complexation to bicyclic cryptands, though they have flexible, open-chained structures. Since the resulting octacoordinate metal complexes have quadruple helicated structures, they can work as unique building blocks having C_4 symmetry for chiral supramolecular architecture. Cholesterol-armed cyclen typically formed a self-aggregate with the integrated chirality in aqueous solution, in which asymmetrically helicated cyclen complexes were arrayed on a supramolecular scale. The self-aggregate had asymmetrically ordered domains, in which achiral organic anions and racemic metal complexes were nicely accommodated in stereo-controlled fashions. Since the armed cyclens have broad structural variations, they are applicable as specific receptors for cation recognition at the molecular level and also as building blocks for supramolecular architecture.

A number of molecular recognition systems are involved in highly efficient and selective biological processes.[1,2] They are composed of biopolymers, metal complexes, receptors and other organic/inorganic components. The molecular recognition phenomena based on 1:1 complexation are frequently observed in ionophore–metal cation, enzyme–substrate, and antigen–antibody systems. High-order recognition phenomena via n:m complexation are also known in nature. When several receptors are highly arrayed on two- and three-dimensional scales, they can work cooperatively in supramolecular environments. Some proteosomes are typical examples, forming unique quarternary structures and acting as multienzymes:[3] seven of the protein subunits assemble into one ring and four of these rings collectively form the cylindrical or barrel-shaped complex. Such highly organized functional units result in great enzymatic efficiency.

The molecular recognition operates well in artificial systems which offer selective and efficient processes. A variety of macrocycles were reported to offer specific 1:1 recognition which mediated enzyme-mimetic catalysis and membrane transport.[4–6] These artificial receptor systems have advantages over complex biological ones such as facile synthesis, high physical stability and wide structural variation. Several useful strategies have already been established for design of the specific receptors for 1:1 recognition. As schematically illustrated in Fig. 1, there are three combinations of recognition processes at the molecular level (Fig. 1). Upgrade of these recognition processes to the supramolecular level has been investigated. We highlight below the receptor functions of "armed cyclens" for metal encapsulation at the molecular level and their applications as building blocks for supramolecular architecture (see Fig. 1[C]).

Several kinds of supramolecular systems were derived from metal complexes, which had highly ordered structures and unusual functions.[7–12] Since the metal complexes have well-defined coordination topology, high thermodynamic stability and inert kinetics, they can act as effective building blocks for supramolecular arrangements of functional units. The helicated metal complexes with one or more coordinating ligands have attracted much attention.[13–18] In addition to various metal complexes with 2,2-bipyridine derivatives, several designed ligands **1–4** were recently reported to offer triple helicates upon metal complexation (Fig. 2). Their optically active isomers, Δ- and Λ-types, were sometimes separated when chiral ligands were incorporated. Such helicates are further expected to act as building blocks for supramolecular architecture exhibiting integrated chirality and unique reactivity. When a large number of functional metal complexes are arrayed in a highly ordered fashion, these components can be concentrated, compartmentalized, organized, and localized in solution state or in solid state.

This account describes the design, synthesis, and functionalization of "armed cyclens", which are recognized as three dimensional ligands for some metal cations via 1:1 complexation. Although various macrocyclic receptors have already been developed,[19] we focus on the aremed cyclens here for several reasons: (1) They form encapsulated complexes with specific met-

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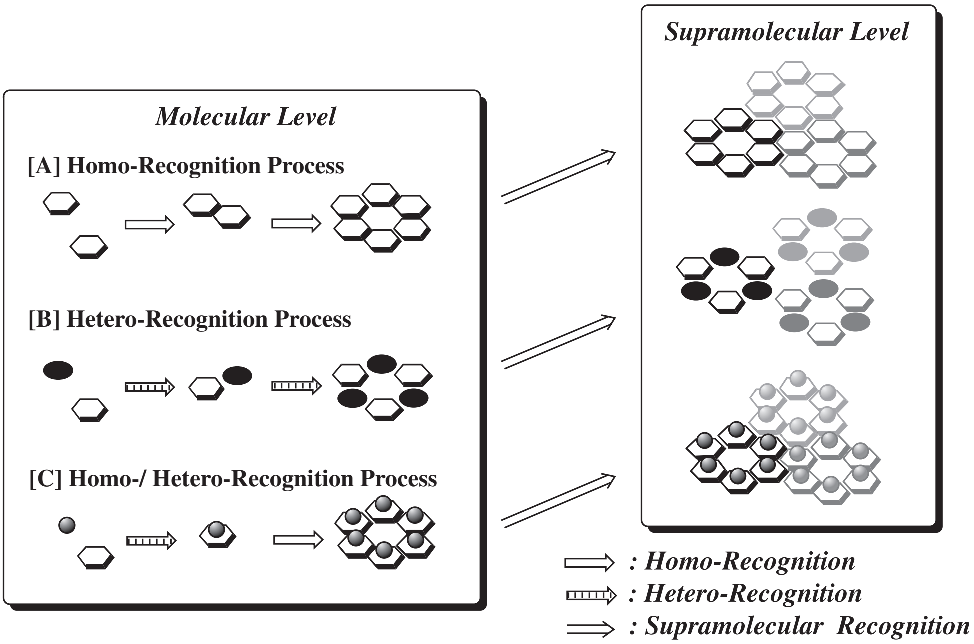

Fig. 1. Molecular recognition toward supramolecular architecture.

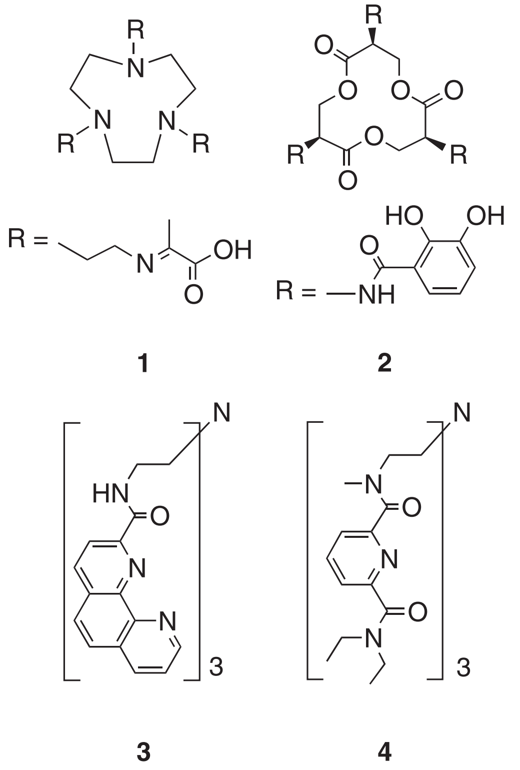

Fig. 2. Typical examples of ligands for triple metal helicates.

al cations; (2) This 1:1 recognition process can be tuned by structural optimization of the ligand; (3) They have quadruple helicated structures upon octadentate complexation; (4) They act as useful building blocks for self-aggregation when amphiphilic moieties are introduced on their sidearms; and (5) The resulting self-aggregates offer integrated chirality on a supramolecular scale. Therefore, a family of armed cyclens is expected to exhibit sophisticated functions via self-aggregation; such functions are impossible at the molecular level.

1. Armed Cyclens for Cation Recognition

(1) Strategy for Cation Recognition. 1,4,7,10-Tetraazacyclododecane **5**, cyclen, is widely used as a macrocyclic ligand; its derivatives complexed with various transition metal cations and exhibited interesting features.[20,21] The attachment of a coordinating sidearm often modified the stability of the complexes via macroring–sidearm cooperativity. Since the cyclen ring usually adopts a “square” conformation upon metal complexation, the arm-functionalization can organize the topology appropriate for octadentate complexation with alkali metal and lanthanide ions.[20]

The armed cyclens with four ligating sidearms can use varying numbers of sidearms to form stable metal complexes. These complexes exhibit different coordination modes for different-sized metal cations (Fig. 3): tetracoordination for small cations: penta- and hexacoordination for medium cations; and octacoordination for large cations. The geometrical optimization with AMBER and ab initio calculations suggested that amide-armed cyclen **7** typically accommodated the Na$^+$ ion in the center of the coordinate cavity.[22,23] Although the diameter of the Na$^+$ ion is larger than the size of the 12-membered cyclen ring,[24] the cooperative coordination from sidearms and cyclen ring operated effectively in this Na$^+$ complexation. Similar macroring–sidearm cooperativity was demonstrated in the Na$^+$ complexes with armed cyclens **6** and **8**. These armed cyclens, however, are expected to form hexacoordinate Li$^+$ complexes, because the Li$^+$ cation is too small to form a stable octacoordinate complex. As has been well-established in lariat ethers and double-armed crown ethers,[19] the effective cation-ligation from the sidearm increases the coordination number of the macrocyclic ligand and the stability of the complex.[5] Therefore, the present type of armed cyclens is expected to exhibit Na$^+$ ion preference over

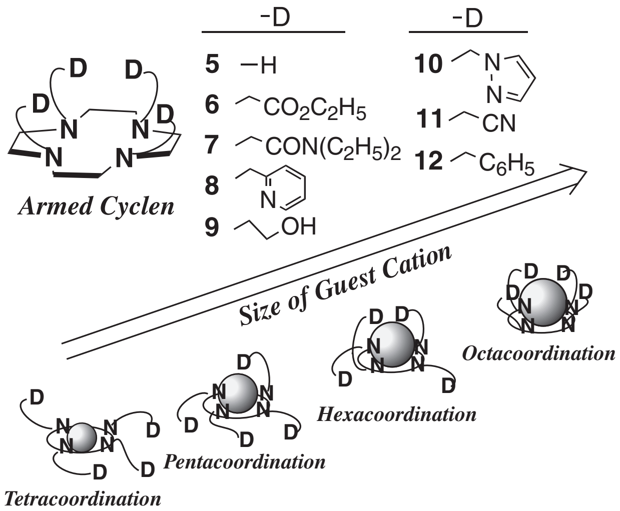

Fig. 3. Typical armed cyclens and their coordination modes.

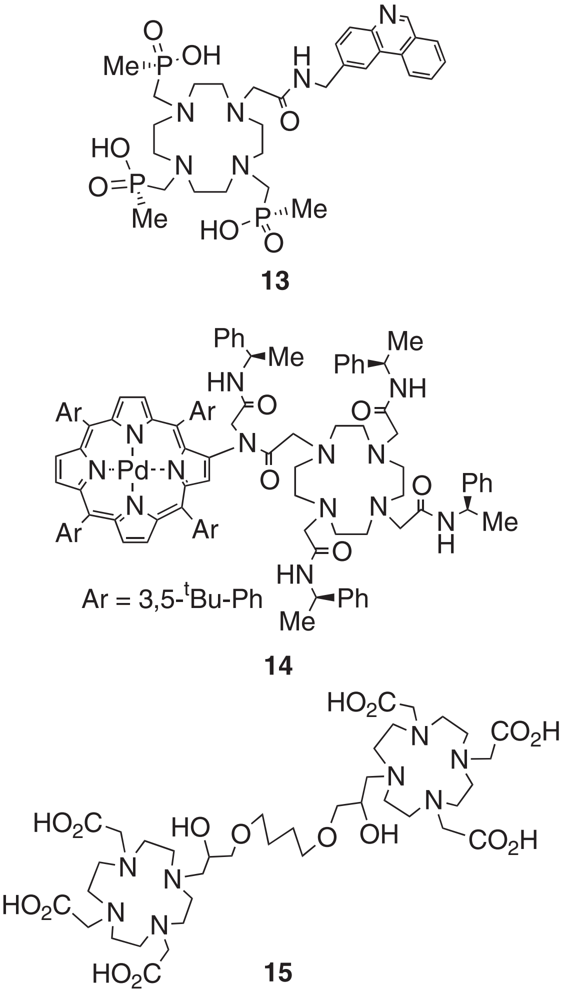

Fig. 4. Armed cyclens for lanthanide complexation.

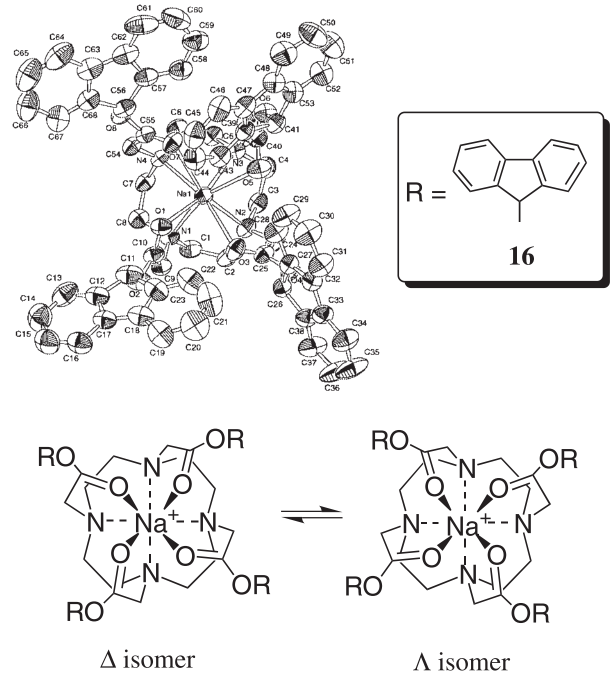

Fig. 5. Structure of ester-armed cyclen **16**–Na^+ complex. When viewed down the C_4 axis from the oxygen plane, the isomer in which that plane is twisted to the right with respect to the nitrogen plane is designated Δ. The twist is to the left for the Λ isomer.

Li^+ ion.

The "armed cyclen strategy" is applicable in developing a new series of three-dimensional ligands for other metal cations. Ca^{2+} ion and trivalent lanthanide cations are promising guests for armed cyclen ligands. Since their ion-sizes are closely similar to that of Na^+ ion,[24] the armed cyclens can act as octadentate ligands for these cations. Several armed cyclens for lanthanide complexation have been developed (Fig. 4).[25] The combinations of reactive lanthanide centers with the functionalized armed cyclens have practical applications: Gd^{3+} complexes as MRI reagents, and Eu^{3+} and Tb^{3+} complexes as luminescent materials.[26,27]

(2) Octadentate Cation Encapsulation. We prepared a variety of armed cyclen ligands specific for Na^+ ion.[28,29] The crystal structure of their Na^+ complexes demonstrated complete encapsulation of Na^+ cation, as predicted above. Figure 5 illustrates the crystal structure of ester-armed cyclen **16**–Na^+ complex. This has twisted square anti-prismatic coordination environment, in which four sidearms stand in the same direction and are bunched in a quadruple helicated fashion. In addition to ester-, amide-, and pyridine-armed cyclens **6–8**, 2-hydroxyethyl and 1-pyrazoylmethyl derivatives **9** and **10** were reported to similarly form three-dimensional metal complexes (Fig. 3).[30,31] Although the parent cyclen ring accommodates several transition metal cations in the 12-membered ring, the attachment of effective cation-ligating sidearms to the cyclen ring results in encapsulation of the Na^+ ion. When viewed from the sidearm side of the cyclen plane, four carbonyl-oxygen atoms of the sidearms are twisted by 20° or 25°. This armed cyclen, having no asymmetric carbon, gave both Δ- and Λ-type complexes (Fig. 5), but the introduction of chiral sidearms brought single stereoisomers in some armed cyclen systems.[32] Recently, several lanthanide complexes with armed cyclens were demonstrated to have similar helicated structures in the crystal states.[25] Calixarene derivatives having four cation-ligating arms were also reported to form octadentate metal complexes.[33,34] Since they do not have defined three dimensional structures upon octadentate complexation, the armed cyclens have unique helicated structures and interesting features for supramolecular architecture.

The armed cyclens have twisted helical structures upon octadentate complexation in solutions as well as in crystal states.[28,29] When achiral armed cyclen **16** complexed with NaCl, ^{13}C NMR signals for two cyclen ring carbons separately resonated at 53.7 and 49.1 ppm at 298 K in CD_3CN solution, and one signal was observed at 56.2 ppm for $–N–\underline{C}H_2–CO–$ carbons of four sidearms. Such inequivalence of the cyclen ring carbons has been attributed to a slow process involving either a rotation of the four sidearms or an inversion of the cyclen cycle (Fig. 5). Wainwright and Lincoln reported the detailed mechanism of interconversion between stereoisomers of alcohol-armed cyclen **9**–Na^+ complex.[35] Temperature-variant NMR experiments suggested that alcohol-armed cyclen has faster exchange kinetics than ester-armed cyclen. Thus, the stability of the quadruple helix is significantly influenced by the natures of sidearm, metal center, solvent, and temperature.

(3) Three Dimensional Cation Recognition. Figure 6 summarizes $\log K$ values of several armed cyclen–Na^+ complexes that largely depend on the sidearm structures.[29] The ester-armed cyclens **6**, **16–20** generally exhibited larger $\log K$ values (9.3–11.2) than alcohol- and amide-armed cyclens **21** and **22** ($\log K = 7.6$ and 6.4). Since the polarity of these sidearm functionalities increases in the order $–CH_2CO_2C_2H_5 < –CH_2CH(CH_3)OH < –CH_2CONHC_2H_5$,[36] the stability of the armed cyclen–Na^+ complex is significantly controlled by both the donor ability of each single sidearm and the sidearm/cyclen ring cooperativity. Some armed cyclens exhibited stability constants comparable to bicyclic cryptand [2.2.1] **24** ($\log K =$ 10.2),[37] indicating that the armed cyclens have flexible but organized donor arrangements suitable for octadentate complexation. These ester-armed cyclens still exhibited large stability constants for Na^+ complexation, even if bulky residues were attached (see **20**). Therefore, various substitutions on the sidearms are possible to functionalize the armed cyclens.

The guest selectivity of the armed cyclen can be tuned by a proper selection of sidearms. FAB-MS binding studies[28] revealed that ester-armed cyclen **6** typically exhibited high Na^+ ion selectivity over Li^+ and K^+ cations: The ratios of relative MS peak intensities of $[\text{cyclen} + \text{metal}]^+$ ions were calculated as 14 for $[\text{cyclen} + Na]^+/[\text{cyclen} + Li]^+$ and 25 for $[\text{cyclen} + Na]^+/[\text{cyclen} + K]^+$. Amide-armed cyclen **7** gave the $[\text{cyclen} + Na]^+$ ion with intensity similar to that of $[\text{cyclen} + Li]^+$ ion, indicating that it bound Li^+ and Na^+ cations similarly. Since the cyclen derivatives having no cation-ligating sidearm **11** and **12** predominantly gave protonated peaks $[\text{cyclen} + 1]^+$, the nature of the sidearm largely influenced alkali metal complexation. The armed cyclens also exhibited Na^+ ion selectivity in the liquid–liquid extraction experiments, in which the Na^+ ion was more effectively extracted than Li^+ and K^+ cations from an aqueous solution into an organic solution. When pyridine-armed cyclen **8** was employed, extraction percentages were recorded as 89% for Na^+ ion and less than 4% for Li^+ and K^+ ions.[28] Ester- and amide-armed cyclens **6** and **7** similarly offered Na^+ ion-selective extraction: 66% and 86% of the Na^+ ion added was extracted, while Li^+ and K^+ ions were rarely extracted ($<7\%$). Since cyclens **11** and **12** did not extract any alkali metal ion, the functionalized sidearm significantly enhanced the extraction performance. Although the polyamine ligands are easily protonated in the aqueous systems, the present type of armed cyclens still have high enough affinity to bind and extract Na^+ cations. Other macrocyclic receptors with es-

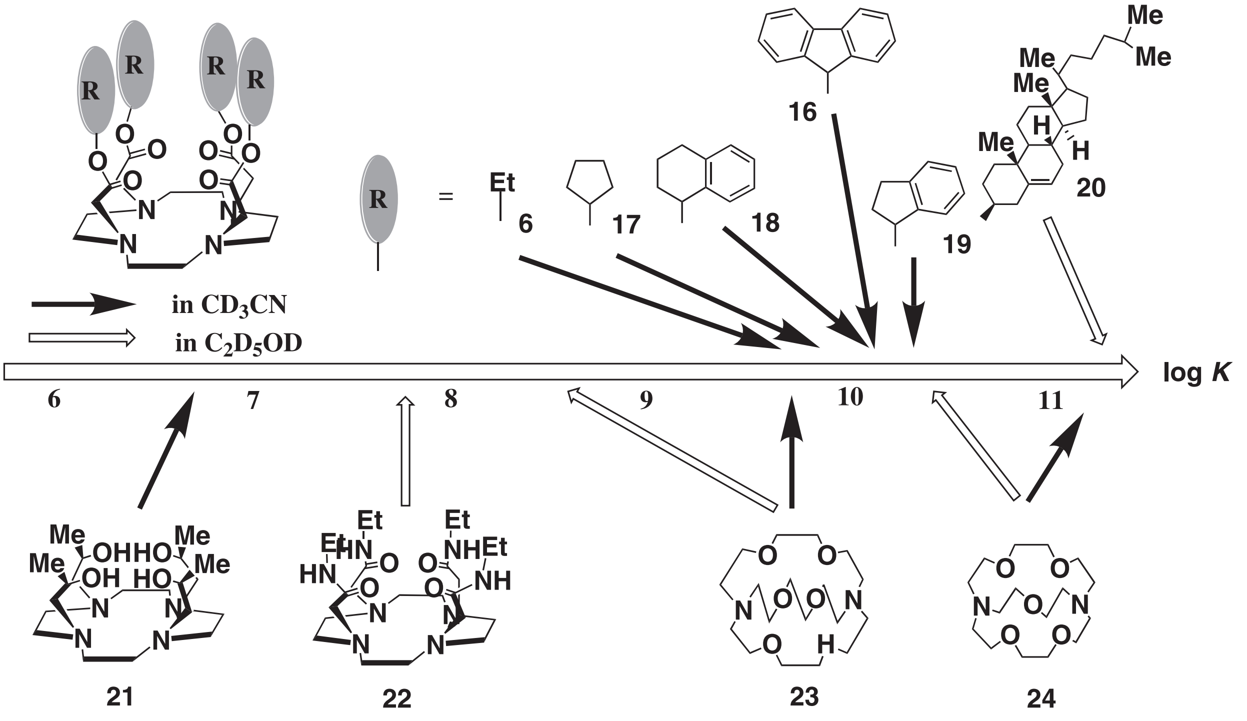

Fig. 6. Stability constants of armed cyclen–Na^+ complexes.

ter-functionalized sidearms such as diaza-12-crown-4 and 14-membered cyclam rarely extracted these metal ions,[38] indicating that the 12-membered cyclen ring worked as an effective scaffold for developing the Na^+ ion-selective receptors.

(4) Applications of Armed Cyclen Complexes. A series of armed cyclen metal complexes were designed to exhibit the sophisticated functions based on their coordination chemistry (Fig. 7). Wainwright et al. demonstrated that the alcohol-armed cyclen **25**–Cd^{2+} complex provided another binding cavity above the cyclen ring, in which organic guest anions cooperatively interacted with sidearm substituents and cationic Cd^{2+} center.[39] Since the ternary complex was effectively formed in the crystal state, the armed cyclen metal complexes can act as potential receptors for specific guests. Recently, Guo et al. reported the DNA-binding property of Bi^{3+} complex with pyridine-armed cyclen **8**.[40] This metal complex was highly cytotoxic against melanoma B16-BL6 and bound calf thymus DNA via non-covalent interaction. The hybridization of armed cyclen–metal complexes with other functional devices also provided an effective strategy for developing luminescent reagents of biological targets. Sherry et al. bound DOTA ligand to the N-terminus of a 12-mer peptide to characterize a specific peptide-protein recognition (see **26**).[41] Parker et al. and other groups presented interesting examples in which the armed cyclen ligands were combined with other functionalized moieties (see **13** and **14**).[25] These exhibited the sophisticated functions as well as high thermodynamic stability and long-term durability.

2. Armed Cyclens for Supramolecular Architecture

(1) Strategy for Supramolecular Architecture. The self-assembly and aggregation of the highly structured metal complexes provide a powerful methodology for supramolecular architecture. Although a large number of cyclen metal complexes have been characterized at the molecular level, only a few examples of cyclen derivatives were used as building blocks for this purpose. Tundo et al. and Moroi characterized micelle formation behaviors of 2-tetradecylcyclen **27**–metal complex.[42] Kimura et al. reported that Zn^{2+} complex with lipophilic cyclen ligand **28** formed a micelle-type aggregate in water and exhibited high catalytic activity in hydrolysis.[43] More recently, Gd^{3+} complexes with armed cyclen-based surfactants **29** and **30** were employed as MRI contrast agents.[44,45] Alcohol-armed cyclen **9** was demonstrated to form supramolecular crystal structure upon complexation with $NaBH_4$.[46] These observations strongly suggest that chiral armed cyclen complexes have potential in both supramolecular architecture and further chirality integration.

Cholesterol-armed cyclen **20**–metal complexes have interesting helical structures and further features as chiral building blocks for self-aggregation and chirality integration at the supramolecular level (Fig. 8): (1) a quadruple helical structure is built above the cyclen ring; (2) helicity of octadentate complex is regulated by chiral sidearms; (3) the metal center works as a charged group of amphiphile and a binding site for anionic guests; and (4) the cholesterol-functionalized sidearm provides a hydrophobic domain for self-aggregation and for guest accommodation. Although alkali metal complexes usually have

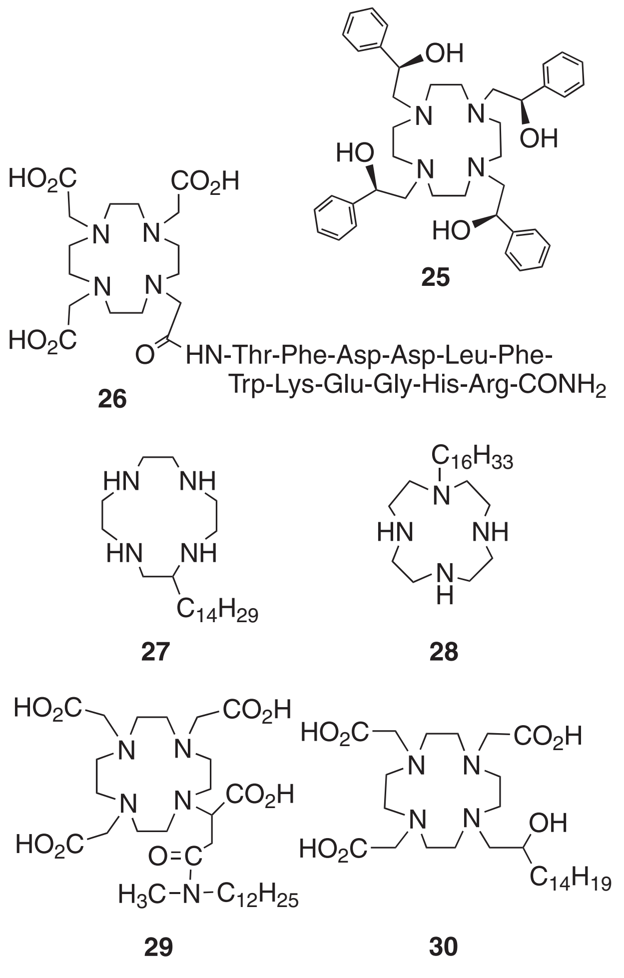

Fig. 7. Armed cyclens exhibiting the sophisticated functions upon metal complexation.

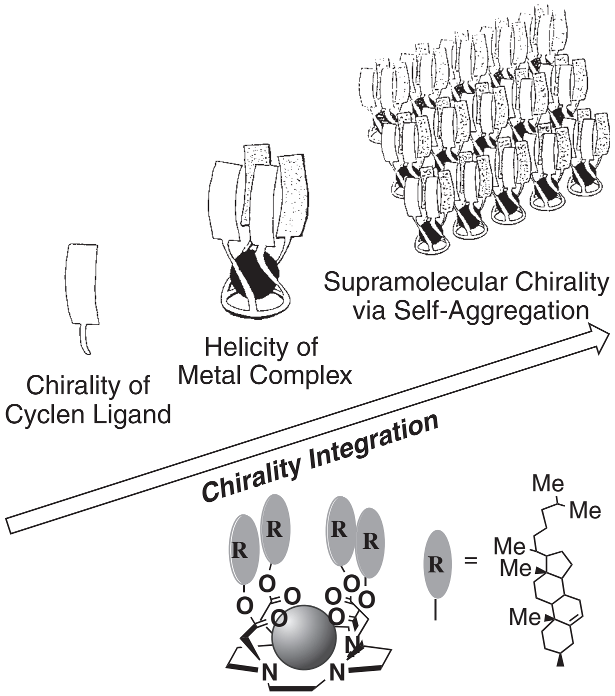

Fig. 8. Chirality integration based on self-aggregation of cholesterol-armed cyclen **20**–metal complex.

versatile coordination structures, low stability, and rapid kinetics, this cholesterol-armed cyclen formed stable and structured Na^+ complex which offered "chirality integration" at three different levels: chirality of cholesterol moieties; helicity on asymmetrically twisted octadentate Na^+ complex; and the integrated supramolecular chirality upon self-aggregation (Fig. 8).[47] As frequently observed in biological protein assemblies, the chirality can be transferred, amplified, and converted. For example, the chirality of amino acid residue, the helicity of protein segments, and supramolecular chirality based on protein aggregate are elegantly combined to create elegant supramolecular structures and functions. Similar chirality integration occured when the chiral armed cyclen metal complexes were arranged on the supramolecular scale.

(2) Self-Aggregation of Armed Cyclen Complex. Cholesterol derivatives have unique characteristics in molecular recognition chemistry.[48–53] Since such derivatives have convex hydrophobic surfaces, a series of chiral carbons, and reactive sites for chemical modifications, both cyclic and acyclic derivatives were used as amphiphiles, receptors, and scaffolds (Fig. 9). Sanders et al. prepared cyclic trimers and tetramers with a variety of polyether chains (see **31**). They acted as highly lipophilic ionophores which extracted alkali metal ions. Kikuchi et al. introduced steroidal units in the sidearms of azacyclophane. This armed cyclophane **32** formed monolayer structures at water/air interface and bound anionic dyes. Shinkai et al. reported that alkali metal complexes with cholesterol-armed crown ethers such as **33** formed gel materials. Since these cholesterol compounds are chiral, their aggregates are expected to offer chiral recognition at molecular and supramolecular levels.

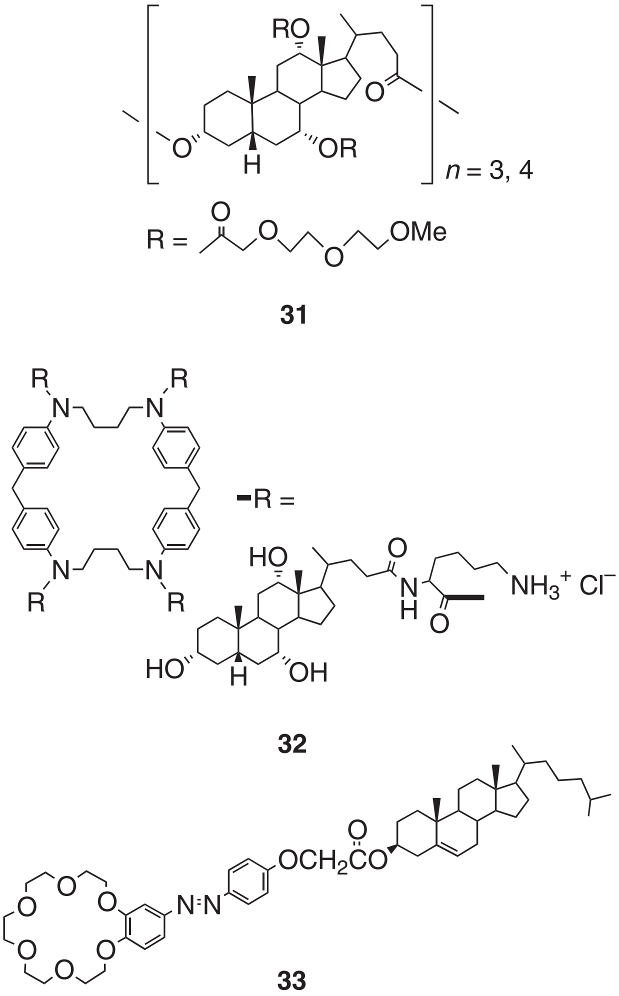

Fig. 9. Cholesterol derivatives for molecular recognition.

The cholesterol-armed cyclen **20**–Na^+ complex has an amphiphilic nature based on Na^+ cation and cholesterol sidearms. When this complex was dispersed in an aqueous ethanol solution ($H_2O/EtOH = 80/20$),[47] it spontaneously aggregated at neutral pH and gave no precipitate from its aqueous solution even after 10 days. The critical aggregation concentration was estimated as 4.0×10^{-6} mol dm^{-3} by fluorescence titration; this value is much smaller than those of common surfactants. Dynamic light scattering experiments showed that the aggregate had a mean hydrodynamic radius of 600 Å; a TEM picture taken after treatment of uranyl acetate showed a similar size (Fig. 10). Although the structure of this aggregate has not been fully characterized, many quadruple helicated complexes were assembled in the aqueous media. This series of armed cyclens are known to form lanthanide complexes that are stable even in aqueous solutions.[25] Since the lanthanide centers are incorporated in armed cyclen coordination environments, they can exhibit guest-dependent luminescence responses.[54]

(3) Chirality Induction via Self-Aggregation. The cholesterol-armed cyclen **20**–Na^+ complex itself exhibited no mesogenic property in the solid state, but provided an asymmetric, hydrophobic domain upon self-aggregation in aqueous solution.[47,55] When an excess of self-aggregate was added to an aqueous ethanol solution of dansyl-L-leucine anion (DNS-L-Leu$^-$), the fluorescence maximum of the guest anion shifted from 538 nm to 507 nm and the intensity was enhanced 6.5-fold.[47] These results clearly indicate that the guest anion was well accommodated in the hydrophobic domain of the self-aggregate. Since cationic DNS-ethylenediamine hydrochloride ($DNS\text{-}NHCH_2CH_2NH_3^+Cl^-$) induced no spectral change, the Na^+ cation bound with the cyclen worked as the binding site in this recognition process. More interestingly, the self-aggregate offered chirality induction of achiral DNS-glycine anion (DNS-Gly$^-$) in aqueous media. This achiral guest exhibited a negative CD signal around 280 nm upon incorporation, though it gave no CD signal in the absence of the aggregate (Fig. 11). Both sign and intensity of the observed CD spectrum were similar to those of DNS-D-Leu$^-$ recorded in the self-aggregate. Thus, the conformation of DNS-Gly$^-$ was asymmetrically fixed as true in the DNS-D-Leu$^-$ system. According to the studies reported by Polonski et al.,[56] these CD results suggested that the conformation of DNS-Gly$^-$ was fixed as "anti-clockwise" in the chiral self-aggregate. Although some self-aggregated amphiphiles offered interesting molecular recognition phenomena in aqueous solutions,[57–59] such chirality induction has rarely been reported.

This self-aggregate accommodated cationic armed cyclen complexes in a stereo-selective fashion, even if there were electrostatic repulsions with the polycationic surface of the self-aggregate. Since the Δ- and Λ-enantiomers of armed cyclen **16**–Na^+ complex slowly exchanged with each other in the solution (see Fig. 5), the guest complex exhibited UV absorption around

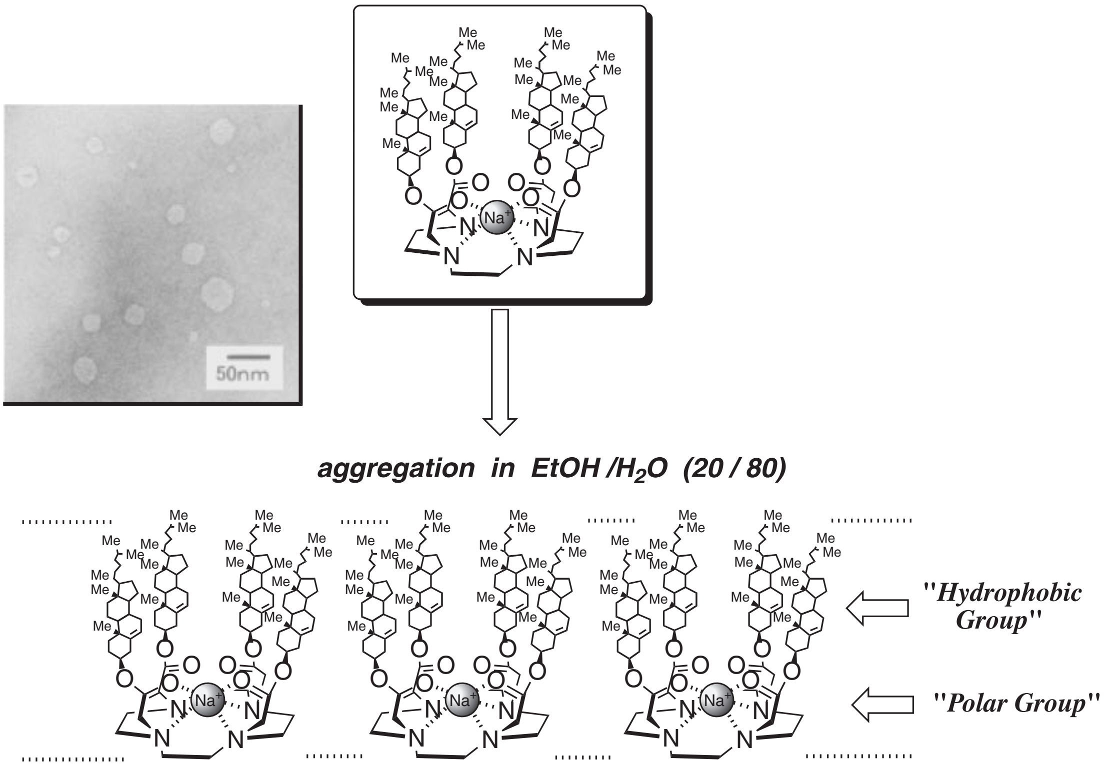

Fig. 10. Self-aggregate of cholesterol-armed cyclen **20**–Na^+ complexes in aqueous solution.

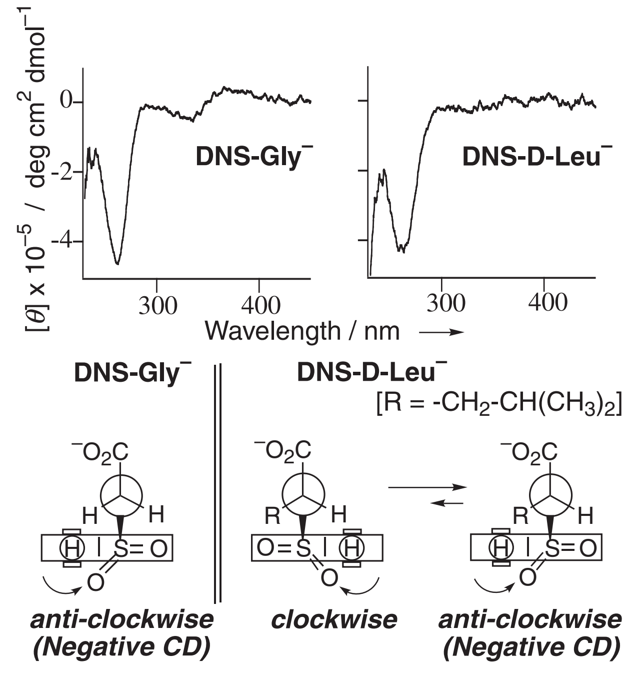

Fig. 11. CD spectra and preferred conformation of dansylglycine (DNS-Gly) and dansyl-D-leucine (DNS-D-Leu) anions incorporated in self-aggregate of cholesterol-armed cyclen **20**–Na^+ complexes.

280 nm and gave no CD signal in the aqueous solution. This showed the induced CD signal around 280 nm upon incorporation into the chiral self-aggregate of the armed cyclen **20**–Na^+ complex, indicating that one enantiomer of the guest complex was stabilized in the supramolecular environment more effectively than the other one.[55] Since Na^+ complex with chiral armed cyclen **19** gave a similar CD signal, the Na^+ complexes with armed cyclens **16** and **20** had similar quadruplicated helical geometry and recognized each other. With an increase of ethanol content in the aqueous solution, the intensity of the observed CD signal rapidly decreased and no CD signal appeared in 30% ethanol aqueous solution. Therefore, the formation of supramolecular aggregate played an essential role in the chirality induction process. The chirality induction of these guests was rarely observed in a cholesteryloxycarbonyl-4-methylmorpholine aggregate, albumin protein, or β-cyclodextrin cavity, demonstrating that the cholesterol-armed cyclen **20** formed a unique self-aggregate exhibiting chirality induction.

3. Concluding Remarks

Armed cyclens are particularly interesting receptors for Na^+ and lanthanide metal cations, offering three dimensional encapsulation of these guest cations at the molecular level. Since their cation receptor functions can be tuned by the proper selection of a cation ligating sidearm, the armed cyclen strategy has many applications in cation recognition chemistry. Since the armed cyclens have many electronic, structural, and geometrical variations, they offer a wide variety of molecular recognition based on their characteristic coordination chemistry. They also work as chiral building blocks for supramolecular architecture. Typically, cholesterol-armed cyclen **20**–Na^+ complex spontaneously formed an aggregate in the aqueous medium, which offered chirality induction at the supramolecular level. Extensive approaches towards self-assembly of potential receptors on gold and nano-particles were made and their results offered promising applications.[60] Although the number of examples exhibiting chirality integration at the supramolecular level is still limited, they allow us to evolve more intelligent and smart supramolecular architecture.

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References

1 P. D. Beer, P. A. Gale, and D. K. Smith, "Supramolecular Chemistry," Oxford Science Publication, Oxford (1999).

2 J. W. Steed and J. L. Atwood, "Supramolecular Chemistry," John Wiley & Son, Chichester (2000).

3 R. Hegeri, G. Pfeifer, G. Puhler, B. Dahlmann, and W. Baumeister, *FEBS Lett.*, **283**, 117 (1991).

4 G. W. Gokel, *Chem. Soc. Rev.*, **1992**, 39.

5 H. Tsukube, *Coord. Chem. Rev.*, **148**, 1 (1996).

6 K. Kimura, H. Sakamoto, and M. Nakamura, *Bull. Chem. Soc. Jpn.* (Account), **76**, 225 (2003).

7 D. I. Caulder and K. N. Raymond, *Acc. Chem. Res.*, **32**, 975 (1999).

8 L. R. MacGillivray and J. L. Atwood, *Angew. Chem., Int. Ed.*, **38**, 1018 (1999).

9 S. Leininger, B. Olenyuk, and P. J. Stang, *Chem. Rev.*, **100**, 853 (2000).

10 M. Shionoya and K. Tanaka, *Bull. Chem. Soc. Jpn.* (Accounts), **73**, 1945 (2000).

11 T. Tanase, *Bull. Chem. Soc. Jpn.* (Accounts), **75**, 1407 (2002).

12 Y. Kobuke and K. Ogawa, *Bull. Chem. Soc. Jpn.* (Accounts), **76**, 689 (2003).

13 R. Prabaharan and N. C. Fletcher, *Dalton Trans.*, **2003**, 2558.

14 M. E. Bluhm, B. P. Hay, S. S. Kim, E. A. Dertz, and K. N. Raymond, *Inorg. Chem.*, **41**, 5475 (2002).

15 L. J. Charbonniere, R. Ziessel, M. Guardigli, A. Roda, N. Sabbatini, and M. Cesario, *J. Am. Chem. Soc.*, **123**, 2436 (2001).

16 F. Renaud, C. Piguet, G. Bernardinelli, J.-C. G. Bunzli, and G. Hopfgartner, *J. Am. Chem. Soc.*, **121**, 9326 (1999).

17 S. Koeller, G. Bernardinelli, B. Bocquet, and C. Piquet, *Chem.—Eur. J.*, **9**, 1062 (2003).

18 S. J. A. Pope, A. M. Kenwright, S. L. Heath, and S. Faulkner, *Chem. Commun.*, **2003**, 1550.

19 G. W. Gokel and O. F. Schall, "Comprehensive Supramolecular Chemistry," Vol. 1, Pergamon Press, Oxford (1996).

20 A. E. Martell and R. D. Hancock, "Metal Complexes in Aqueous Solutions," Plenum Press, New York (1996).

21 S. Aoki, M. Zulkefeli, M. Shiro, and E. Kimura, *Proc. Natl. Acad. Sci. U.S.A.*, **99**, 4894 (2002).

22 K. Hori and H. Tsukube, *J. Inclusion Phenom.*, **32**, 311 (1998).

23 K. Hori, N. Dou, K. Okano, A. Ohgami, and H. Tsukube, *J. Comput. Chem.*, **23**, 1227 (2002).

24 R. D. Shannon, *Acta Crystallogr.*, **32**, 751 (1976).

25 D. Parker, R. S. Dickins, H. Puschmann, C. Crossland, and J. A. K. Howard, *Chem. Rev.*, **102**, 1977 (2002).

26 H. Miyake, S. Shinoda, and H. Tsukube, *Rare Earths*, **39**, 41 (2001).

27 D. Parker, *Coord. Chem. Rev.*, **205**, 109 (2000).

28 H. Tsukube, Y. Mizutani, S. Shinoda, T. Okazaki, M. Tadokoro, and K. Hori, *Inorg. Chem.*, **38**, 3506 (1999).

29 S. Shinoda, T. Nishimura, M. Tadokoro, and H. Tsukube, *J. Org. Chem.*, **66**, 6104 (2001).

30 S. Buoen, T. Dale, P. Groth, and J. Krana, *J. Chem. Soc., Chem. Commun.*, **1982**, 1172.

31 G. M. Norante, M. D. Vaira, F. Mami, S. Mazzi, and J. Stoppioni, *J. Chem. Soc., Chem. Commun.*, **1990**, 438.

32 H. C. Aspinall, *Chem Rev.*, **102**, 1807 (2002).

33 A. Arduini, E. Ghidini, A. Pochini, R. Ungaro, G. D. Andreetti, G. Calestani, and F. Ugozzoli, *J. Inclusion Phenom.*, **6**, 119 (1980).

34 S. G. Bott, A. W. Coleman, and J. L. Atwood, *J. Am. Chem. Soc.*, **108**, 1709 (1986).

35 R. Dhillon, S. F. Lincoln, S. Madbak, A. K. W. Stephens, K. P. Wainwright, and S. L. Whitbread, *Inorg. Chem.*, **39**, 1855 (2000).

36 a) J. A. Riddick and W. B. Bunger, "Organic Solvents," Wiley-Interscience (1970), p. 150 and p. 228. b) R.-Y. Lin and W. Dannhauser, *J. Phys. Chem.*, **67**, 1805 (1963).

37 R. M. Izatt, K. Paulak, and J. S. Bradshaw, *Chem. Rev.*, **91**, 1721 (1991).

38 H. Tsukube, S. Shinoda, Y. Mizutani, K. Takagi, and K. Hori, *Tetrahedron*, **53**, 3487 (1997).

39 C. B. Smith, A. K. W. Stephens, K. S. Wallwork, S. F. Lincoln, M. R. Taylor, and K. P. Wainwright, *Inorg. Chem.*, **41**, 1093 (2002).

40 X. Wang, X. Zhang, J. Lin, J. Chen, Q. Xu, and Z. Guo, *Chem. Commun.*, **2003**, 2379.

41 L. M. De Leon-Rodriguez, A. Ortiz, A. L. Weiner, S. Zhang, Z. Kovacs, T. Kodadek, and A. D. Sherry, *J. Am. Chem. Soc.*, **124**, 3514 (2002).

42 a) Y. Moroi, E. Pramauro, M. Gratzel, E. Pelizzetti, and P. Tundo, *J. Colloid Interface Sci.*, **69**, 341 (1979). b) Y. Moyoi, *Bull. Chem. Soc. Jpn.*, **54**, 3265 (1980).

43 E. Kimura, H. Hashimoto, and T. Koike, *J. Am. Chem. Soc.*, **118**, 10963 (1996).

44 J. P. Andre, E. Toth, H. Fischer, A. Seeling, H. R. Macke, and A. E. Merbach, *Chem.—Eur. J.*, **5**, 2977 (1999).

45 C. Glogard, R. Itovland, S. L. Fossheim, A. J. Aasen, and J. Klaveness, *J. Chem. Soc., Perkin Trans. 2*, **2000**, 1087.

46 R. Custelcean, M. Vlassa, and J. E. Jackson, *Chem.—Eur. J.*, **8**, 302 (2002).

47 S. Shinoda, T. Okazaki, T. Nishimura, K. Hori, and H. Tsukube, *Chem. Commun.*, **2001**, 976.

48 A. P. Davis, R. P. Bonar-Law, and J. K. M. Sanders, "Comprehensive Supramolecular Chemistry," Pergamon Press, Oxford (1996), Vol. 4, p. 257.

49 M. Miyata and K. Sada, "Comprehensive Supramolecular Chemistry," Pergamon Press, Oxford (1996), Vol. 6, p. 147.

50 V. Janout, C. D. Giorgio, and S. L. Regen, *J. Am. Chem. Soc.*, **122**, 2671 (2000).

51 G. W. Gokel and O. Murillo, *Acc. Chem. Res.*, **29**, 425 (1996).

52 S. Shinkai and K. Murata, *J. Mater. Chem.*, **8**, 485 (1998).

53 K. Ariga, Y. Terasaka, D. Sakai, H. Tsuji, and J. Kikuchi, *J.*

Am. Chem. Soc., **112**, 7835 (2000).
54 H. Tsukube, S. Shinoda, and H. Tamiaki, *Coord. Chem. Rev.*, **226**, 227 (2002).
55 T. Nishimura, S. Shinoda, and H. Tsukube, *Chirality*, **14**, 555 (2002).
56 T. Polonski, A. Chimiak, and M. Kochman, *Tetrahedron*, **30**, 641 (1974).
57 K. Ariga and T. Kunitake, *Acc. Chem. Res.*, **31**, 371 (1998).
58 P. Grandimi, F. Mancin, P. Tecilla, P. Scrimin, and U. Tonellato, *Angew. Chem., Int. Ed.*, **38**, 3061 (1999).
59 S. Kolusheva, T. Shahal, and R. Jelinek, *J. Am. Chem. Soc.*, **122**, 776 (2000).
60 D. M. Rudkevich, *Bull. Chem. Soc. Jpn.* (Accounts), **75**, 393 (2002).

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