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Cholesterol-armed cyclen–Na^+ complex as a chiral, helicated amphiphile for supramolecular architecture: self-aggregation and chirality induction in aqueous solution

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An octadentate Na^+ complex of chiral cholesterol-armed cyclen has a quadruple helicated structure and forms a stable self-aggregate in aqueous solution which offers chirality induction of achiral 5-dimethylaminonaphthalen-1-ylsulfonylglycine anion.

Several kinds of transition and lanthanide metal complexes are recognized as useful building blocks for supramolecular architecture,[1] because of their well-defined coordination topology, high thermodynamic stability and inert kinetics. In contrast, alkali metal complexes usually have versatile coordination structures, low stability and rapid kinetics, and hence their use for this purpose is limited. We demonstrate here that an octadentate Na^+ complex of chiral cholesterol-armed cyclen **1** forms a stable self-aggregate in aqueous solution which provides a unique microenvironment for chirality induction of achiral 5-dimethylaminonaphthalen-1-ylsulfonylglycine anion (DNS-Gly^-).[2] The employed cyclen **1**–Na^+ complex is a new type of chiral amphiphile furnished with three functional components (Fig. 1):[3] ester-armed cyclen as a twisted octadentate ligand;[4] four cholesterol groups as chiral and hydrophobic walls;[5] and the Na^+ ion as a charged group of amphiphile.[6] Since this Na^+ complex exhibits unexpectedly high stability and inert kinetics (log$K$ = 11.2 in C_2D_5OD), its self-aggregate is expected to offer three different levels of chirality in the aqueous solution: (1) chirality of cholesterol moieties; (2) helicity on asymmetrically twisted octadentate Na^+ complex; and (3) integrated chirality of highly structured Na^+ complexes on a supramolecular scale.

A series of metal complexes with tetra-armed cyclens are known to have C_4 symmetry in which four sidearms are arranged as a quadruple helicate *via* twisted square-antiprismatic coordination.[7] Actually, cyclen **2**–NaCl complex gave ^{13}C NMR signals for two carbons of the cyclen ring separately resonating at 51.50 and 49.51 ppm in $CDCl_3$ at 295 K, while a single signal was observed at 55.12 ppm for N-CH_2-CO-carbons of four sidearms. Although the enantiomerization can proceed either by a rotation of the four sidearms or an inversion of the cyclen cycle,[8] these observations indicated that cyclen **2**–Na^+ complex maintained unique quadruplicated helical structures in the solution (Fig. 1). Chiral cyclen **1**–NaCl complex similarly exhibited two separate ^{13}C NMR signals for cyclen ring carbons at 53.01 and 48.46 ppm, though each cholesterol moiety on the cyclen arm has several asymmetric carbons. As reported in some Na^+ complexes with chiral tetra-armed cyclens,[9] cyclen **1**–Na^+ complex is thought to have only a single C_4 orientation in which four chiral cholesterol moieties are arranged in an asymmetrically helicated fashion.

Cholesterol-armed cyclen **1**–NaCl complex spontaneously aggregated in an aqueous ethanol solution (H_2O–EtOH = 80/20, v/v; pH = 7.2, bis-tris-HCl)[10] and gave no precipitate from its aqueous solution after 10 days. The critical aggregation concentration was estimated as 4.0×10^{-6} mol dm^{-3} by fluorescence titrations, which was much smaller than those of common micelle-forming surfactants. Dynamic light scattering experiments showed that the aggregate had a mean hydrodynamic radius of 600 Å, and a TEM picture taken after treatment of uranyl acetate also indicated that it was of similar size (Fig. 2). Interestingly, this self-aggregate accommodated DNS-amino acid anions in the hydrophobic domains. When an excess of self-aggregate was added to an aqueous ethanol

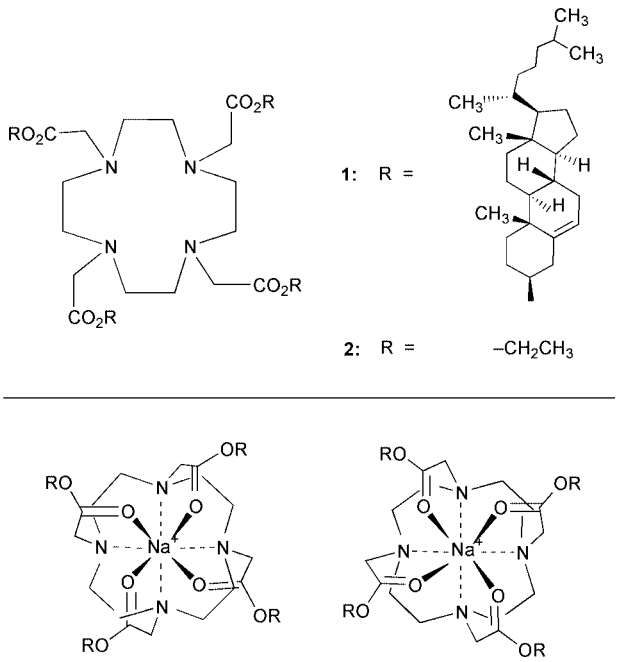

Fig. 1 Armed cyclens and quadruplicated helical structures of their Na^+ complexes.

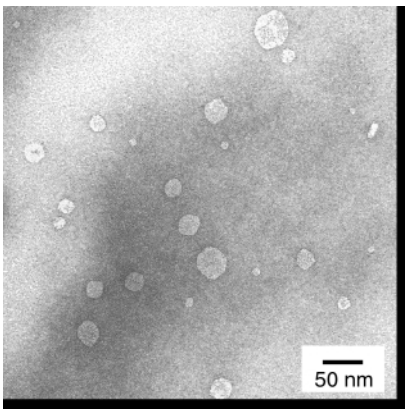

Fig. 2 TEM Picture of dispersed self-aggregates of cyclen **1**–NaCl complexes.

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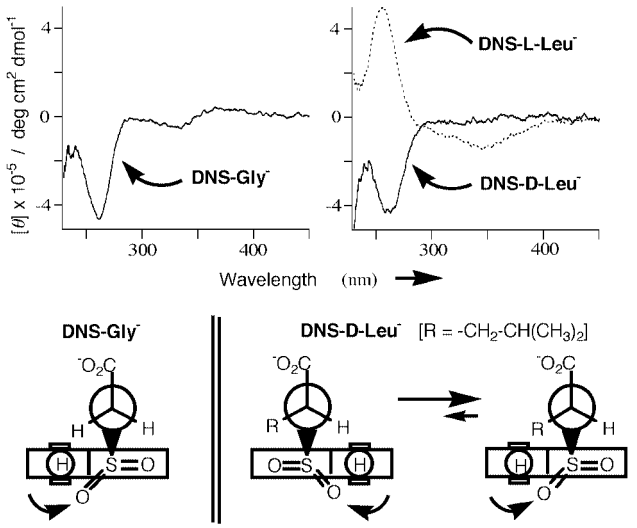

Fig. 3 CD Spectra and preferred conformations of dansyl-glycine (DNS-Gly) and dansyl-leucine (DNS-Leu) anions incorporated in self-aggregate of cyclen **1**–NaCl complexes. [**1**–NaCl] = 3.0×10^{-5} mol L^{-1}; [DNS-Gly$^-$] = 5.0×10^{-5} mol L^{-1}; [DNS-Leu$^-$] = 6.5×10^{-5} mol L^{-1}. The indicated CD spectra of DNS-D- and L-Leu anions were corrected by subtraction of those in the bulk aqueous phases.

solution of DNS-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. Cholesteryloxycarbonyl-4-methylmorpholine was examined for comparison. This also formed a water-soluble aggregate in the presence of Na^+ ion, but the resulting aggregate rarely accommodated DNS-amino acid anions. Therefore, the assembling of four cholesterol moieties on the octadentate Na^+ complex platform provided an effective microenvironment for inclusion of DNS-amino acid anions in the aqueous solution.

The self-aggregate of cyclen **1**–NaCl complexes further offered chirality induction of achiral anion substrates upon inclusion. Typically, DNS-Gly$^-$ was incorporated in the self-aggregate and exhibited a negative CD signal around 280 nm (Fig. 3). Both sign and intensity of the observed CD spectrum were similar to those of DNS-D-Leu$^-$ recorded in the self-aggregate, indicating that the conformation of DNS-Gly$^-$ was asymmetrically fixed as true in DNS-D-Leu$^-$ system. Such chirality induction phenomena were reported when the degree of freedom of achiral molecules was severely restricted in the solids, membranes, micelles and inclusion compounds.[11] Polonski *et al.* reported that the CD signal observed with chiral DNS-amino acid originated from unsymmetrical twisting of the sulfonamide group in relation to the naphthalene plane under the influence of hydrogen atom in the *peri*-position (Fig. 3).[12] Since the preferred conformation of DNS-D-Leu$^-$ was determined by the steric problem around the S=O bond rather than the *peri*-positioned hydrogen atom, the negative CD signal was indicative of 'anti-clockwise' conformation. The obtained CD results suggested that the 'anti-clockwise' conformation of DNS-Gly$^-$ was more stable than the 'clockwise' one, when this achiral anion was incorporated in the self-aggregate.

We demonstrated above that the self-aggregate of cyclen **1**–NaCl complexes having an asymmetrically helicated structure allowed chirality induction of the achiral guest anion upon inclusion. Since there are many structural variations in the armed cyclen–alkali metal complexes, their characteristic coordination chemistry provides further possibilities in the development of supramolecular architecture with fascinating functions.

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