Counteranion Driven Homochiral Assembly of a Cationic C3-Symmetric Gelator through Ion-Pair Assisted Hydrogen Bond

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Ⓢ *Supporting Information*

ABSTRACT: The helical handedness in achiral self-assemblies is mostly complex due to spontaneous symmetry breaking or kinetically controlled random assembly formation. Here an attempt has been made to address this issue through chiral anion exchange. A new class of cationic achiral C3-symmetric gelator devoid of any conventional gelation assisting functional units is found to form both right- and left-handed helical structures. A chiral counteranion exchange-assisted approach is successfully introduced to control the chirality sign and thereby to obtain preferred homochiral assemblies. Formation of anion-assisted chiral assembly was confirmed by circular dichroism (CD) spectroscopy, microscopic images, and crystal structure. The X-ray crystal structure reveals the construction of helical assemblies with opposite handedness for (+)- and (−)-chiral anion reformed gelators. The appropriate counteranion driven ion-pair-assisted hydrogen-bonding interactions are found responsible for the helical bias control in this C3-symmetric gelator.

Self-organization of an achiral or a dynamically racemic molecular system into well-defined helical nanostructures with controllable handedness is one of the exciting topics in supramolecular chirality.[1] This area of research is particularly attractive to understand and appreciate the asymmetric induction and homochirality in nature.[2] It was observed that, various noncovalent interactions are the major driving force to regulate the helical structures of achiral entities.[3,4] Among various noncovalent interactions, the hydrogen bond (H-bond) plays a significant role in helical self-assembly systems due to its directionality and specificity.[3a−g] But the main drawback of H-bonded systems is that it works mostly in nonpolar organic solvents and is not stable in aqueous media due to the random and competitive H-bonding nature of water molecules. To circumvent this drawback, introduction of ionic interaction into self-assembly has been considered as an alternate strategy to strengthen the H-bonds by virtue of its strong electrostatic interaction.[5] Moreover ionic assemblies will generate higher-order structures due to the electrostatic interaction along with different noncovalent interactions.[6] Ionic species are known to be stable in its hydrated state, which gives a unique opportunity to study ionic assemblies in physiological conditions. Finally, for ionic components, counterions play a critical role toward its

self-assembly.[7] For instance, an appropriate choice of ion-pair could eventually lead to an ion-pair assisted H-bond (IPA-H), which possesses both ionic interaction and H-bonds, hence satisfying the strength as well as directionality.[5]

Recently, there have been many attempts to elucidate the helical assembly formation in achiral and C3-symmetric molecules. For example, Meijer[8a] and Liu[8b,c] et al. have shown chiral symmetry breaking phenomena of benzene-1,3,5-tricarboxamide/tricarboxylate-based achiral molecules, where self-assembly was exclusively driven by directional H-bonds between amide groups, $\pi-\pi$ staking of the central benzene rings, and van der Waals interaction due to peripheral hydrophobic units. In addition, various strategies such as chiral additive,[7,8] light,[9a,b] clockwise/counterclockwise vortex,[9c] or spin coating direction,[9d] rotational and magnetic force,[9e] pH,[9f] etc. are known to induce chirality in supramolecular assemblies. But for any cationic component to control the helical handedness, one of the easiest approaches is to exchange its counteranion from an achiral one to chiral one. Herein we report for the first time the formation of chiral assembly from an ionic achiral C3-symmetric molecule, tris(4-pyridinecarbox-aldehyde) triaminoguanidinium chloride, **L·Cl⁻** (Figure 1a). Self-assembly of **L·Cl⁻** on surface leads to formation of right (P)- and left (M)-handed helical structures. The exchange of Cl⁻ counteranion of **L** with a chiral pyridinium salts of (+)- or (−)-menthylsulfate (**MS*⁻**) exhibited homochiral signature. The IPA-H bond between **MS*⁻** and positively charged nitrogen-rich guanidinium units, which elicits the molecule to arrange in a preferred way to give the helical homochiral twist, is evident in the crystal structure. Thus, a simple strategy has been effectively utilized to bias chirality of an ionic gelator.

The details of synthesis and characterization of **L·Cl⁻** is outlined in the Supporting Information. Although being deprived of any conventional gelation-assisting functional units, gelation experiment shows that **L·Cl⁻** forms a thermo reversible opaque gel in MeOH/H₂O (1:1, v/v) within 3−4 h, which was confirmed by inverted vial method (Figures 1a and S9). Conversely, the gel is formed within 4−5 min upon sonication, resulting in considerable decrease of critical gel concentration (CGC) from 6.2 to 3.4 wt %. In order to have a deeper understanding of the self-assembly process, the **L·Cl⁻**
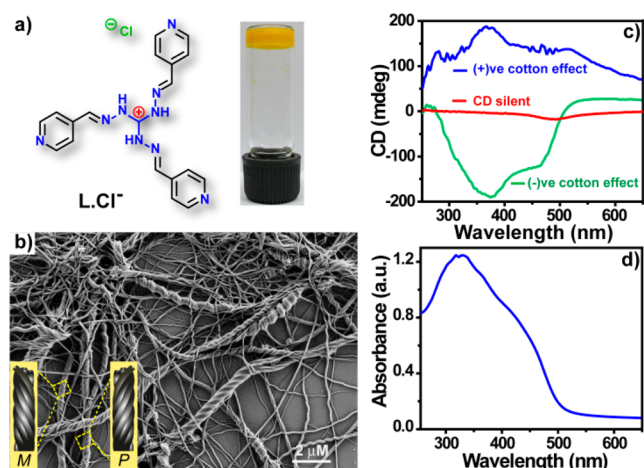
Figure 1. (a) Chemical structure of the gelator **L·Cl⁻** and photograph of the gel formed in MeOH/H₂O (1:1, v/v). (b) SEM image of the *P* and *M* helical ropes, inset shows the corresponding schematic. (c) CD spectra of three different thin films prepared from solutions of **L·Cl⁻** (15 mg/mL) in MeOH/H₂O (1:1, v/v). (d) UV−vis absorption spectrum of thin film of **L·Cl⁻**.

gel was imaged by scanning electron microscope (SEM). **L·Cl⁻** exhibits a network of helical fiber bundles or ropes composed of thin fibers of nanometer diameter and micrometer length (Figure 1b). A careful analysis of the SEM image illustrates that the single thin fibers are not helical in nature. However, in the course of assembly formation, fibers are bundled-up and intertwined with each other to form helical ropes with simultaneous chiral *M* and *P* twists (Figure 1b, inset).

Further to confirm the origin of chirality in bundled fibers, CD spectra of **L·Cl⁻** solutions with various concentrations in MeOH/H₂O (1:1, v/v) were measured. Surprisingly, in solution, no CD activity was observed. This might be due to existence of the disassembled monomeric species or optically inactive minor aggregates in dilute solution, which was further confirmed by variable-temperature UV and CD experiments (Figure S10).[8a] However, the drop-casted films from this solution on a circular quartz plate (20 mm diameter ×1 mm thick) exhibited CD signals (Figure 1c). The examination of different batches of drop-casted thin films prepared from same solution (15 mg/mL) showed CD signals with negative or positive Cotton effects having a dominant peak at 372 nm and a shoulder peak at 464 nm, which is consistent with the UV−vis absorption spectrum of the thin film (Figure 1d). It is also noticed that some samples are almost CD silent (Figure 1c, red line). This result indicates that there must be formation of chiral structures over the period of self-assembly process. However, the optical activity is stochastic with the appearance of negative CD signals (7 times), positive CD signals (6 times), and CD silent signals (4 times) (Figure S11). Based on both microscopic and spectroscopic experiments, we conclude that even though **L·Cl⁻** is achiral in nature, during self-assembly, it spontaneously forms kinetically controlled aggregates with *P* and *M* helicity. When the number of *M* twists exceeds the *P* twists or vice versa, the assembly shows CD activity, but, when the number of both *P* and *M* twists are comparable, and thus overall racemic, showing no macroscopic optical activity, and hence becomes CD silent.[8b]

Since *C₃*-symmetric **L·Cl⁻** gelator shows macroscopic helical properties, it is really essential to explore its precise molecular arrangements in aggregate state. So we crystallized **L·Cl⁻** as

molecular assembly of [**L·Cl⁻·9H₂O**] from MeOH/H₂O (1:1, v/v) mixture at a concentration below CGC. Figure 2a,b shows
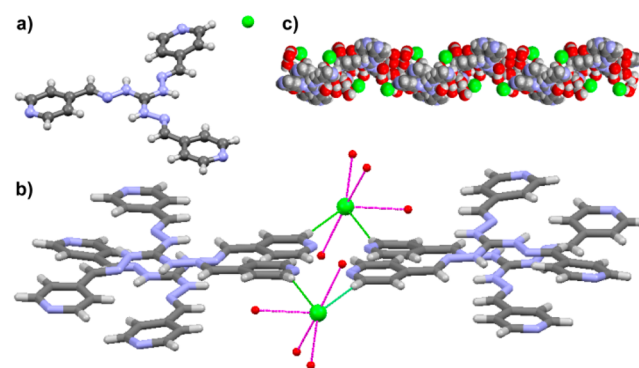
Figure 2. (a) Crystal structure of **L·Cl⁻** in ball and stick model, solvent molecules are omitted for clarity. (b) Packing model of **L·Cl⁻** showing the coordination of hydrated Cl⁻ anion with **L**, stabilized by multiple H-bonds. (c) 1D left-handed helical arrangements of **L·Cl⁻** in space fill model.

that Cl⁻ anion is located far away from the central cationic unit. Each Cl⁻ ion forms four H-bonds with four-water molecule (Figure 2b). The hydrated Cl⁻ ion connects the two cationic units by constructing two H-bonds with terminal pyridyl hydrogen atoms (Cl⁻···H−C; Figure 2b). Due to intrinsic positive charge of guanidinium units, two consecutive molecules stack in a slipped way and form a double propeller-type arrangement (Figure 2b). A careful analysis of the single crystal structure showed that this double propeller-shaped dimer and the corresponding hydrated Cl⁻ anion form a H-bonding network with the help of solvent (water) molecules. These results in a left-handed helix-like one-dimensional (1D) arrangement (Figures 2c and S12). More importantly the CD spectrum of **L·Cl⁻** in the crystalline phase displayed a negative Cotton effect (Figure S13), indicating that the overall framework in the resultant crystalline phase is chiral due to its unique mode of crystal packing (Figures 2c and S12). Based on this consequence, we establish a relationship between handedness of the helical ropes (from SEM image and CD signs of **L·Cl⁻**). When the *M* twists outnumbered the *P* twists, CD spectra showed a negative Cotton effect; conversely, it showed positive Cotton effect when the *P* twists outnumbered the *M* twists (Figure 1c).

Achieving a helical or twisted nanostructure from absolutely achiral molecule is a rousing issue, but without controllable handedness, it is incomplete. Since the central guanidinium unit of **L·Cl⁻** is cationic, exchange of its counteranion Cl⁻ with an optically active one could be a simple way to control its chirality.

In order to accomplish this, we searched for a suitable anion and perceived that guanidinium units are known to strongly bind with oxoanions (e.g., phosphate, carboxylate, and sulfate).[5] However, according to the Hofmeister series, the sulfate anion has maximum inclination to substitute Cl⁻ compared to phosphate and carboxylate. With this rationale, we opted for chiral pyridinium salts of (+)- and (−)-**MS*⁻** anion[7b] to exchange Cl⁻ counteranion of **L** (Scheme 1). The addition of **MS*⁻** anions led to salting out of **L** from aqueous solution and thus enabled us to isolate both **L·(+)-MS*⁻** and **L·(−)-MS*⁻** (Scheme 1 and SI).

Scheme 1. Random Formation of Optically Active Self-Assembled Structures from Achiral L·Cl⁻ and Control of Its Chirality by Counteranion Exchange Approach
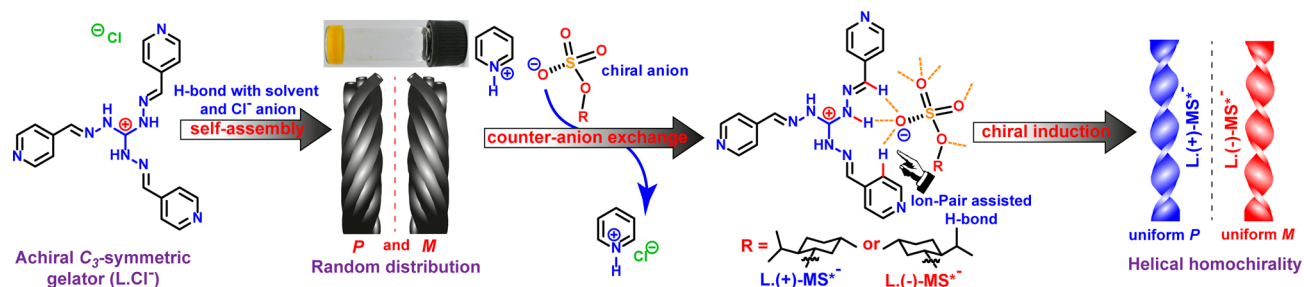
Both the counteranion exchanged compounds L·(+)-MS*⁻ and L·(−)-MS*⁻ also found to form thermo reversible gels (Figure S14). Compared to L·Cl⁻, CGC of these two compounds drastically decreased from 6.2 to 0.7 wt % under the same solvent composition (MeOH/H₂O; 1:1 v/v). This drastic change in CGC indicates that MS*⁻ counteranion plays an important role in self-assembly. Optical activity of L·(+)-MS*⁻ and L·(−)-MS*⁻ was verified by CD spectroscopy. Interestingly, L·(+)-MS*⁻ and L·(−)-MS*⁻ showed strong CD signals with positive and negative Cotton effects, respectively (Figure 3a). CD spectrum is a mirror image to each other
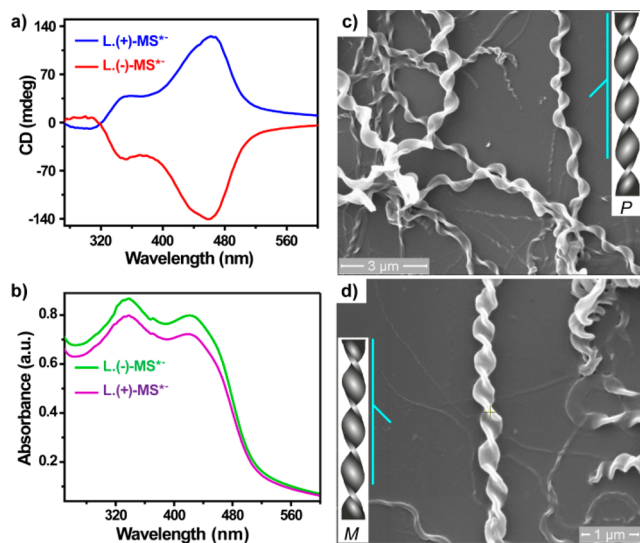

Figure 3. (a) CD and (b) UV−vis spectra of L·(+)-MS*⁻ and L·(−)-MS*⁻ thin films (concentration < CGC). SEM images of (c) right (P)- and (d) left (M)-handed twisted ribbons of L·(+)-MS*⁻ and L·(−)-MS*⁻ gel (0.7 wt % in MeOH/H₂O; 1:1, v/v), respectively.

having two major peaks at 353 and 464 nm and a crossover at 330 nm. However, corresponding UV−vis spectra did not show any considerable difference (Figure 3b). Interestingly, SEM image of L·(+)-MS*⁻ showed helical ribbons with P twists (Figures 3c and S15), whereas M twists was observed for L·(−)-MS*⁻ ribbons (Figures 3d and S15). Hence the exchange of the achiral counteranion with chiral anion could efficiently control the preferred homochiral states, homochiral P twists for (+)-MS*⁻ and M twists for (−)-MS*⁻ (Scheme 1).

The improved gelation feature of the anion-modified gelators made crystallization from an aqueous solution a tedious job. After several attempts, X-ray quality crystals were obtained by diffusion of diethyl ether into slightly acidic solution of L·(+)-MS*⁻ or L·(−)-MS*⁻ in methanol (Figure S16).

Compared to L·Cl⁻, crystal structure of L·(−)-MS*⁻ displayed that the counteranion MS*⁻ is intensely oriented toward central cationic unit, because of the electrostatic interaction between oppositely charged ions (Figures 4a and S16). This
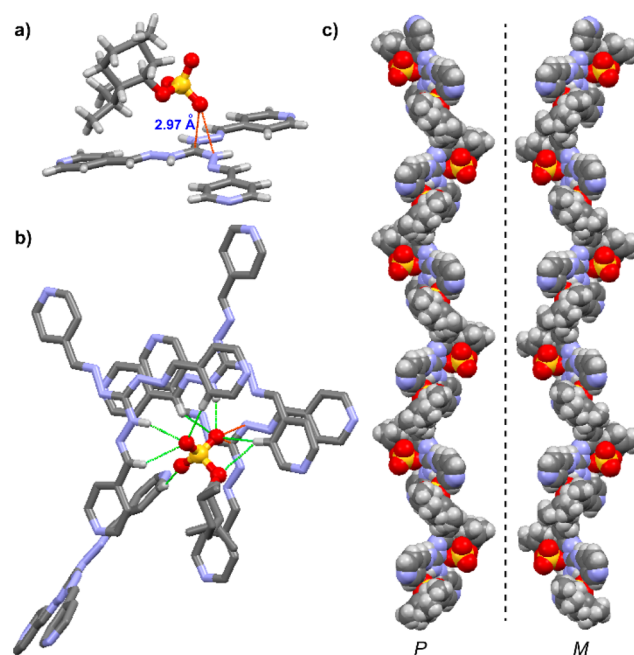
Figure 4. (a) Ion-pair contacts through electrostatic interaction and (b) crystal packing of L·(+)-MS*⁻, showing IPA-H bonds (solvent MeOH and noninteracting H atoms are omitted for clarity). (c) Right (P)- and Left (M)- handed helical molecular arrangement of L·(+)-MS*⁻ and L·(−)-MS*⁻ crystals, respectively in space fill model.

ion-pair contacts enable MS*⁻ to form eight H-bonds, two with guanidium N−H and six with different C−H of the L (Figure 4b). It was also noticed that two adjacent guanidinium units (L) are twisted with each other and H-bonded with MS*⁻ anions to result a left-handed (M) helical chain (Figures 4c and S17). However, in the case of L·(+)-MS*⁻, a right-handed (P) helical chain was observed (Figures 4c and S17). Most importantly, the crystallographic helical signs were exactly matched with SEM images (Figures 3, 4, S15, and S17). Solid-state structures of both L·(+)-MS*⁻ and L·(−)-MS*⁻ clearly indicate that the optically active arrangement was entirely driven by IPA-H bond(s). This IPA-H bond stretches the main interactions to stabilize the assembly even in aqueous solution (MeOH/H₂O; 1:1 v/v). The UV−vis absorption and CD spectra of L·Cl⁻ and L·(−)-MS*⁻/L·(+)-MS*⁻ showed significant difference in shape and position of the two peaks

present (Figures 1 and 3). This could be attributed to the difference in the available intermolecular interactions and packing of molecules as visualized by the crystal structure (Figures 2, 4, and S18−S20). The summary of the whole self-assembly process is given as a pictorial representation in Scheme 1.

In conclusion, it has been ascertained that exchange of an achiral counteranion with a chiral one can be an effective tool to bias the helical handedness of the assembly. Random formation of *P* and *M*-type helical twists in the self-assembly of cationic C_3-symmetric gelator is controlled to a preferred handedness. Our study demonstrates a radically new approach to successfully switch the handedness of random chirality to the desired homochiral assemblies. For the first time we have utilized this simple chiral counteranion exchange methodology to induce chirality to a cationic molecule. Moreover, the solid-state structure establishes that IPA-H bond plays key role to form chiral helical assembly. Currently we are exploring the possibility of other counteranions to bias the helical sense. In addition, further studies to memorize the generated chirality signs of this molecular system are underway.

■ ASSOCIATED CONTENT

ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b06312.

> Experimental details and data (PDF)
> Crystallographic data (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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