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Supramolecular polymerization of chiral molecules devoid of chiral centers

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Abstract

The iterative association of monomer units through noncovalent interactions often leads to chiral supramolecular polymers. Monomers comprising these materials can be further divided into those with chiral centers and those without. The latter class is often less studied but attractive since it features monomer designs with chirality at the core rather than the periphery of the molecules. In this mini-review, we summarize the existing strategies to construct supramolecular polymers from chiral molecules with no chiral centers and offer perspectives on fundamental trends and differences between them and their counterparts with chiral centers.

Keywords: supramolecular polymer; chirality; self-assembly; stereochemistry

INTRODUCTION

Supramolecular polymers (SPs) are defined as polymeric materials formed by directional, reversible noncovalent interactions that result in polymeric properties in the bulk and in solution.[1] This broad subset of materials has been the subject of excellent reviews and can be further refined into SPs formed by small molecules,[2–7] oligomers,[8] dendrimers,[9,10] foldamers[11,12] and polymers.[13,14] Among the myriad examples, there is no question that many have been inspired by biological macromolecular systems that are replete with structural and functional complexity. Along these lines, in both the biological and chemical worlds chirality represents information that can be translated across atomic, molecular, macromolecular and even macroscopic length scales.[15] How Nature uses homochiral amino acids and sugars highlights the role that chirality plays in the molecular recognition and biological processes central to life.[16] As a reminder, an object is considered chiral if it cannot be superimposed upon its mirror image by translation or rotation.[17] For the purposes of this mini-review, chirality can be considered *geometrical* for rigid molecular objects but *chemical* for a fluxional molecule in which any of its conformations cannot be brought into congruence with its mirror image under the observable conditions.[18]

The noncovalent association of small molecules often results in the formation of assemblies displaying supramolecular chirality.[19] This form of chemical chirality emerges upon the interaction of geometrically chiral molecules, or the dissymmetric association of achiral molecules. Supramolecular polymerization of achiral monomers gives racemic assemblies in the absence of any chiral information.[20] Geometrically chiral monomers can contain chiral information in the form of chiral centers in the solubilizing sidechain and therefore usually away from the molecular recognition site (referred to here as chiral-at-periphery)[21] or in the core of the molecule and nearer the molecular recognition event (chiral-at-core).[22] The relationship between monomer stereochemistry and assembly stereochemistry is fundamentally different for those monomers bearing chirality in the periphery and at the core. The focus of this mini-review will be on SPs formed by small molecule monomers that are geometrically chiral despite lacking chiral centers; also highlighted is how the nature and location of chirality relates to assembly stereochemistry and SP properties.[23]

The relationship between monomer structure and assembly stereochemistry is depicted in Fig. 1 for a set of structurally related simple monomers: a chiral-at-periphery benzene-1,3,5-tricarboxamide (BTA) monomer bearing chiral centers in the solubilizing sidechain (Fig. 1(a)), and a chiral-at-core [2.2]pCpTA monomer bearing planar chirality (Fig. 1(b)). The BTA monomer is achiral in the planar ground state but generates axial chirality when the amides tilt out of the arene plane to form intermolecular hydrogen bonds. The presence of the chiral center in the sidechain is a second element of chirality in addition to the axial chirality of the monomer. The result is two interconverting diastereomeric monomers that are capable of social and/or narcissistic self-assembly behavior, with the chirality of the assembly easily monitored by circular dichroism (CD) spectroscopy.[24] Readers are directed to a recent review on C_3-symmetric monomers for additional examples of this assembly mode.[25] For [2.2]pCpTA, the chiral plane is dictated by the irreversible covalent fixation of two substituted aromatic rings that cannot rotate with respect to each other. The formation of this covalent bond effectively fixes the supramolecular chirality forming the planar-chiral cyclophane. Upon assembly (e.g. of the R_p configuration), the planar chirality of the monomer is transferred to the helical-chirality of the SP (*P*-helix).[26]

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Several applications of helical SPs include asymmetric supramolecular catalysis,[27–31] amplification of chiroptical properties,[32–34] chiral recognition, shape memory[35] and sensing.[36] Of particular interest is the large influence supramolecular chirality can have on nonlinear optical properties such as circularly polarized luminescence (CPL).[37] Specific functions and applications of helical polymers and SPs have been discussed in a review by Maeda and coworkers.[19] Self-assembled structures such as SPs have been targeted for their ability to amplify the luminescence dissymmetry factor $|g_{\mathrm{lum}}|$ which is used to quantify the level of CPL as the difference between the intensity of the left- and right-handed light emission. Strategies to generate such CPL-active materials are outlined in a recent review by Liu and coworkers.[38]

The formation of helical SPs from small molecules represents many of the examples presented here and is an attractive option for fundamental study because of their tunability through synthetic control and characterization by simple, non-destructive methods such as NMR, IR and optical spectroscopies including CD and fluorescence spectroscopy. Molecules that are chiral despite having no chiral centers are often not biological in origin and therefore are not homochiral. In order to study the influence of optical purity on SP formation, monomers must be resolved or synthesized asymmetrically. Chiral HPLC is often employed for resolution, but limits the scale of the chemistry that can be studied.

In contrast to their covalent counterparts, SP noncovalent interactions are dynamic and their polymerizations often proceed to equilibrium, although recent examples of kinetically trapped assemblies have been reported.[39–43] The equilibrium association constant (K_a) defines the strength of the interaction between two molecular recognition units. The value of K_a is directly related to the degree of polymerization and is sensitive to temperature,

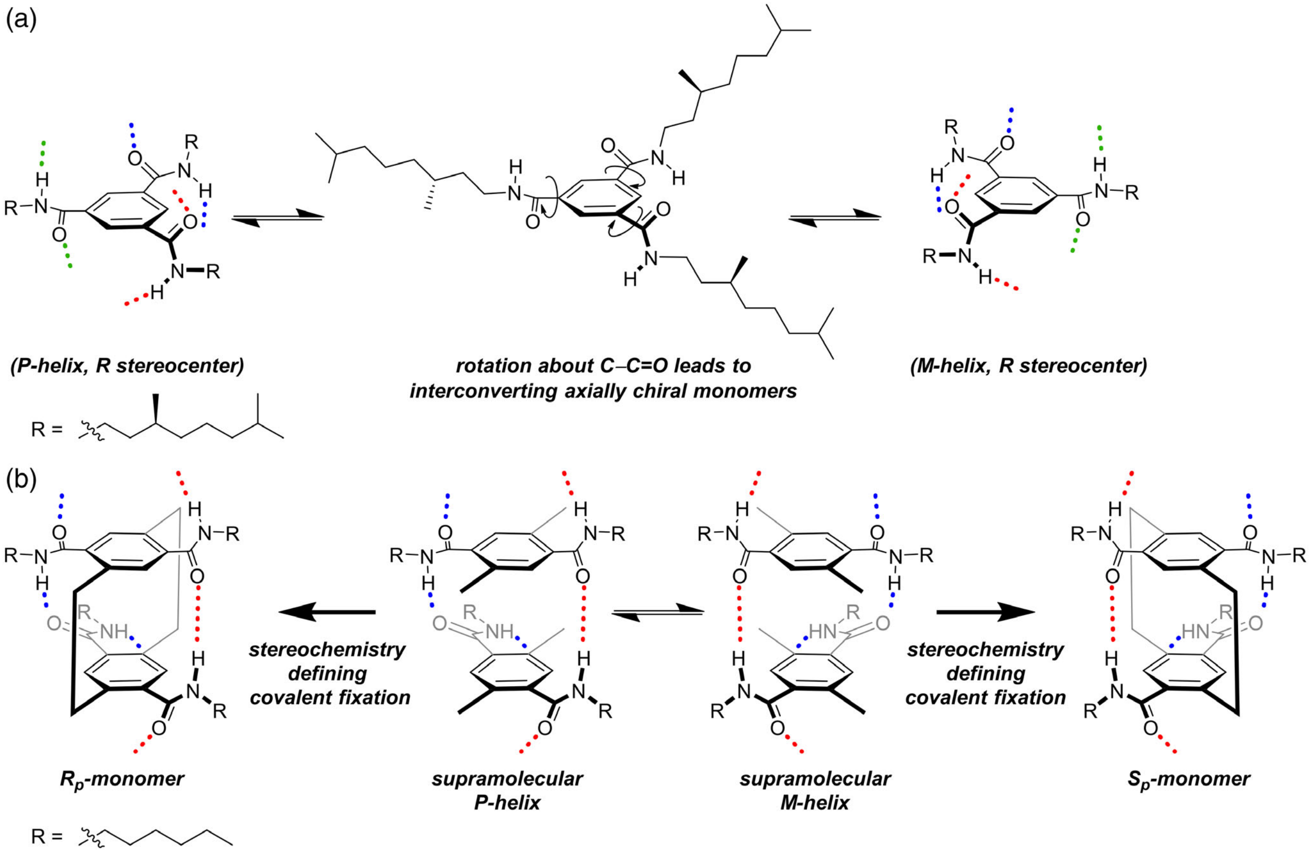


Figure 1. Two separate assembly paradigms for the formation of helical self-complementary SPs based on chiral amplification of planar monomers with chiral centers in the periphery (a) or chiral-at-core SPs without chiral centers (b).

solvent polarity and monomer concentration. A comprehensive essay on the history and future of SP chemistry was recently written by Professors Bert Meijer and Takuzo Aida, two pioneering researchers in the field.[44]

Early efforts in the field of SPs sought to provide new molecular recognition units[45–50] in order to improve the material properties of the resulting SPs by improving K_a, as well as to characterize the underlying mechanisms of SP formation. The two prevalent mechanisms for the assembly of SPs, isodesmic (equal-K)[51] and cooperative (nucleation–elongation),[52] differ in the dependence of K_a on growing oligomer size. The isodesmic mechanism is defined by a single K_a independent of oligomer size, while the cooperative mechanism is characterized by one association constant prior to the formation of a nucleus of critical size known as the nucleation constant (K_{nuc}), followed by a separate elongation constant (K_{elo}).[53,54] Positive cooperativity indicates that $K_{nuc} < K_{elo}$ favoring larger polymeric assemblies, while negative cooperativity indicates that $K_{nuc} > K_{elo}$ favoring smaller oligomeric assemblies. In certain cases where binding thermodynamics are sufficiently large, kinetically trapped and non-equilibrium assemblies with different assembly chirality can be formed.[55,56] Therefore, an understanding of thermodynamics, kinetics and mechanism are necessary to understand the relationship between monomer and assembly stereochemistry.

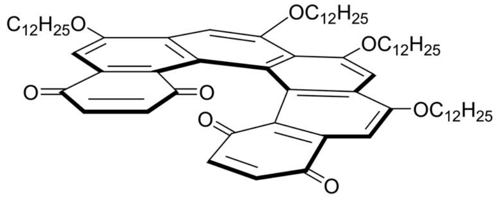
A common theme in the field of chiral SPs is chiral amplification[57] which occurs when a small enantiomeric excess (e.e.) in a reactant (i.e. a monomer) leads to a large e.e. in a product (i.e. a polymer). The phenomenon depends on homochiral *versus* heterochiral interaction energies (e.g. an *R* monomer with an *S* assembly or *R* assembly). The energetic preference of one assembly helix-sense over the other, coupled with the dynamic nature of SPs, allows assembly to proceed to thermodynamic equilibrium resulting in chiral amplification. The dependence of supramolecular helicity on monomer e.e. is therefore nonlinear (termed 'majority rules', assembly e.e. > monomer e.e.) with chiral amplification and linear (termed homochiral, assembly e.e. = monomer e.e.) without. The distinction between majority rules and homochiral assembly is dependent on monomer and assembly structure, location of chiral information and strength of noncovalent interactions. We additionally hope this review will clarify some trends observed and help practitioners design new homochiral or majority rules SPs.

Despite the overwhelming popularity of the chiral-at-periphery (analogous to BTAs) strategy for synthesizing and studying one-dimensional SPs, this mini-review will focus on SPs that do not feature chiral centers in the monomer. These SPs not only possess interesting structures but allow an expanded study of fundamentally important topics such as stereoselectivity, mechanism and pathway selection in supramolecular polymerization.

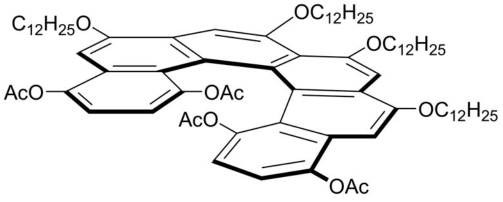
For purposes of organization, SP systems in this mini-review will be sorted by monomer geometrical chirality type, such as axial and planar chirality. Additionally, concave molecules with 'inherent chirality' have become attractive for the synthesis of SPs and, especially recently, so too have interlocked molecules exhibiting topological or 'mechanical chirality'.

Axial chirality: helicenes and biaryls

Axial chirality is a geometric chirality in which there are no chiral centers but an axis of chirality due to the arrangement of atoms in three-dimensional space.[58] The most prevalent molecules that possess axial chirality are allenes, helicenes and the biaryls, with the latter two being utilized for the construction of SPs. Interested readers can find summaries of the vast amount of work on allenes,[59] helicenes[60–62] and biaryls in other reviews.[63]



(+)-1, *large optical rotation, aggregation*



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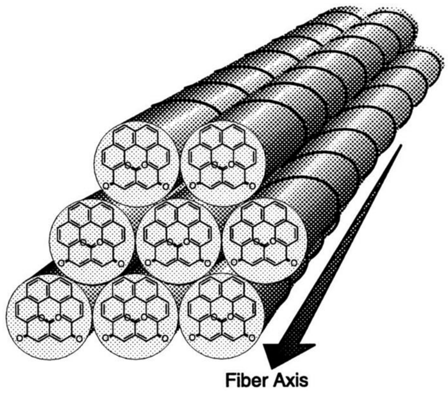


Figure 2. Monomeric structures of self-assembling [6]helicene bisquinone **(+)-1** and non-assembling [6]helicene bisacetate **(+)-2** studied by Katz and coworkers and the resulting SP fibers formed by **(+)-1**. Reproduced with permission from Verbiest *et al.*[65]

It was first reported in 1996 by Katz and coworkers that enantioenriched helicene-bisquinones (**(+)-1**) form supramolecular assemblies in *n*-dodecane.[64] When compared to the corresponding bis-acetates (**(+)-2**) which do not assemble, changes in the concentration dependence of chemical shift, optical rotation, UV–visible and CD indicated the formation of J-aggregates of **(+)-1** in solution (Fig. 2). The columnar aggregation of **(+)-1** was confirmed in the solid state[66] and it was discovered that films formed from these enantioenriched assemblies exhibited a strong enhancement in nonlinear optical properties.[65]

In 2011, Takeuchi and coworkers reported the hierarchical assembly of [7]helicenes with a fused phthalhydrazide unit (**3**). First, **3** forms lateral trimers by lactam–lactim tautomerization and intermolecular complementary hydrogen bonding, followed by vertical π-stacking of the trimeric helicene disks (Fig. 3).[67] The trimerization and assembly were present in solutions of toluene and chloroform, while polar solvents like dimethyl sulfoxide and methanol were found to disrupt the hydrogen bond trimerization and assembly. The enantiomeric purity of the monomer played a crucial role in determining whether elongated assemblies were

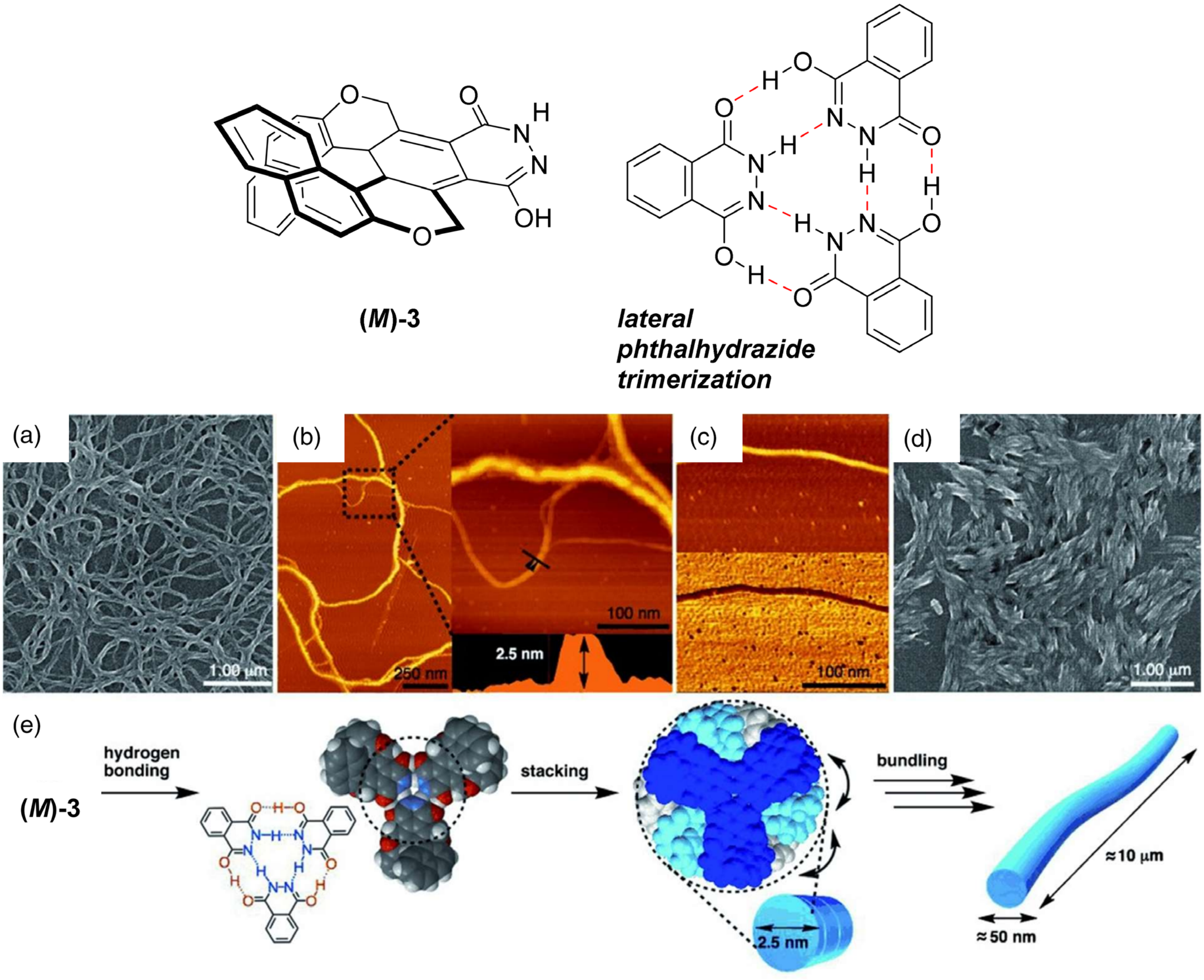


Figure 3. Takeuchi's [7]helicene with a fused phthalhydrazide unit capable of lateral phthalhydrazide trimerization followed by vertical supramolecular polymerization. (a) SEM image of ***M*-3** (0.5 mmol L^{-1}) prepared in toluene; (b), (c) AFM images of ***M*-3** prepared in toluene, (c) is the (lower) phase image; (d) SEM image of ***rac*-3** (0.5 mmol L^{-1}) prepared in toluene; (e) the plausible mechanism for the formation of fibrous aggregates from the trimeric disk of ***M*-3**. Reproduced with permission from Kaseyama *et al.*[67]

formed. This was attributed to the formation of mixed *P* and *M* trimers that then go on to form smaller assemblies. In another example of amplification of chiroptical properties through supramolecular chirality,[68] **3** in the assembled state exhibited CPL, with $|g_{\mathrm{lum}}|$ values that were the highest reported to date for chiral organic molecules.

The Würthner group, being interested in both twisted chirality of bay-substituted perylene bis(imide)s (PBIs)[69] and their supramolecular assemblies,[7] investigated the supramolecular polymerization of atropo-enantiomeric bay-substituted PBI derivatives and their self-sorting behavior.[70] Introduction of a biphenoxy bridge to the bay position of the PBIs (Fig. 4(a)) ensured configurational stability of the monomers **4**, allowing their resolution by chiral HPLC at room temperature. Supramolecular assemblies of the enantiopure monomer (***M*-4** or ***P*-4**) were formed through directional hydrogen bonding along the assembly axis between imide N–H and C=O along with complementary J-aggregates between the curved π-faces of **4**. These homochiral SPs were formed by the cooperative assembly mechanism and resulted in elongated nanowire assemblies with enhanced fluorescence (depicted in Fig. 4 (b)). Assembly of a racemic mixture of **4** (***rac*-4**) resulted in heterochiral self-sorting, with each monomer preferentially interacting with a monomer of opposite configuration and forming nanoparticle assemblies with greater thermodynamic preference than the homochiral assemblies. These results contrast with previous results of atropo-enantiomeric strapped PBI cyclophanes which preferentially formed π-facial homodimers over heterodimers.[71,72]

The attractive chiroptical properties associated with [*n*]helicenes, especially CPL, attracted interest from Matsuda and coworkers who in 2016 reported the synthesis of [5]helicenes **5a**–**5c**, along with their different assembly morphologies. Compound **5a** formed spherical aggregates in aqueous solutions while compounds **5b** and **5c** were found to form fibrous aggregates in heptane solution by TEM (Fig. 5). It was shown

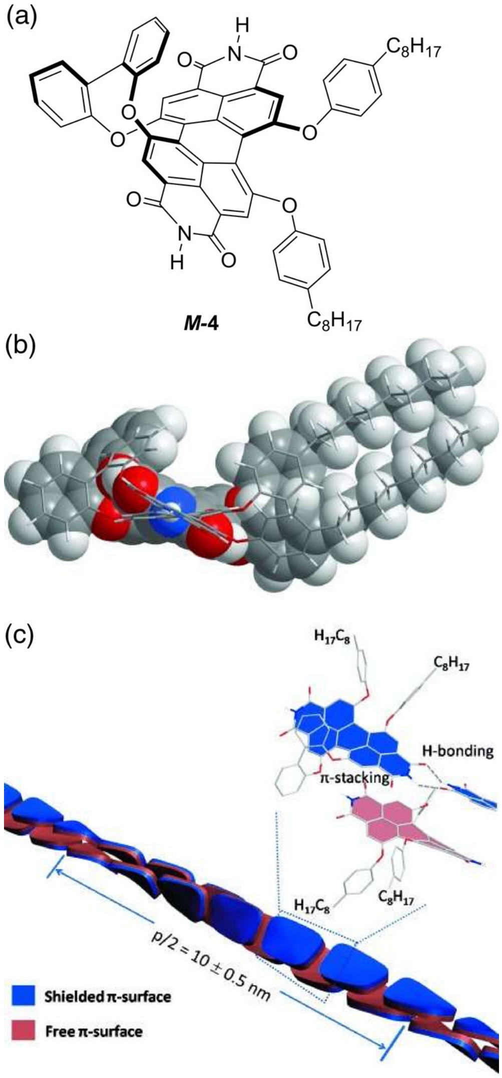


Figure 4. Chemical structure of ***M*-4** (a), the molecular mechanics optimized structure of ***M*-4** (b) and schematic representation of the supramolecular assembly of enantiopure ***M*-4** (c) composed of hydrogen bonding along the assembly axis and π-stacking interaction between the J-aggregated molecules of ***M*-4**. Reproduced with permission from Xie *et al.*[70]

that the aggregated states of the [5]helicenes exhibited a significant increase in fluorescence properties compared to the monomers due to suppression of some non-radiative decay pathways.[73]

In 2018 the group of Luis Sánchez reported the supramolecular polymerization of 5,7,8,10-tetrasubstituted [5]helicene derivatives with amide hydrogen bonding units on the 5- and 10-positions.[74] Two molecules were synthesized: one with a single amide hydrogen bonding unit at each position and a long alkyl solubilizing group (**6**) and one with two amide hydrogen bonding units at each position separated by a short alkyl linker (**7**). Compound **7** did not form SPs in solutions of methylcyclohexane (MCH), whereas compound **7** was shown to form SPs in solutions of MCH through amide hydrogen bonding (Fig. 6), which could be disrupted through the introduction of a small volume fraction of chloroform (*ca* 10%). Optical resolution of **6** and **7** could be achieved by chiral HPLC, and it was shown that both [5]helicene derivatives rapidly racemize in the molecularly dissolved state in chloroform. The assembly capable derivative **7**, however, is configurationally stable in its assembled state in MCH, indicating that supramolecular polymerization can raise the barrier to racemization. The non-assembly capable **6** on the other hand rapidly racemizes in MCH, ruling out solvent effects and confirming the contribution of SP formation to raising the racemization barrier. Interestingly, the supramolecular polymerization of racemic and optically pure **7** was described by different assembly mechanisms. As a racemic mixture, **7** assembled via an isodesmic mechanism as characterized by variable temperature UV–visible, while enantiopure ***M*-7** assembled via a cooperative mechanism characterized by variable temperature CD spectroscopy.

In 2007, Nakashima and coworkers presented a binaphthalene molecule (**8**) with two appended PBI units that exhibited good CPL properties.[75] It was later shown that, in the same molecules, CPL could be used to examine intermolecular aggregation of **8** even at high concentrations in opaque solutions.[76] A systematic study of their aggregation revealed that they form spherical aggregates in chloroform but more fibrous aggregates in higher MCH content.[77] Further examination of their assembly mode with respect to optical purity revealed that both racemic and optically pure mixtures assemble via an isodesmic mechanism,[78] consistent with other PBI derivatives.[79] Annealing of a racemic mixture assembled in $CHCl_3$/MCH (1:49) converted the homochiral extended fibril assemblies to heterochiral assemblies forming small nanoparticles observed by TEM. The thermodynamic favorability for heterochiral over homochiral interactions allowed the tuning of SP chain length through control of enantiomeric excess of the monomer feed, with higher monomer e.e. giving longer assembly fibers (Fig. 7).

Recently Liu and coworkers reported the supramolecular charge transfer (CT) polymers of axially chiral pyrene appended biaryl donors (***R*/*S*-Py**) and achiral electron acceptors such as tetracyanobenzene (TCNB), tetrafluoroquinone (TFQ), tetracyanoethylene (TCNE) and tetracyanoquinone (TCNQ) as a strategy to increase $|g_{\mathrm{lum}}|$ by accessing the stronger magnetic dipole allowed transitions of CT complexes (Fig. 8(a)).[80] Although CT bands were observed in the complexation of ***R*/*S*-Py** with all acceptors, TCNB proved to be the only acceptor with which emission was observed due to the larger energy gap between donor highest occupied molecule orbital (HOMO) and acceptor lowest unoccupied molecular orbital (LUMO) (Fig. 8(b)). The CT assemblies formed by ***R*/*S*-Py** and TCNB were shown in the solid state by X-ray crystallography, and emission was observed in single crystals, gels, powders and spin-coated films (Fig. 8(c)). The assemblies proved to be stimuli responsive as sonication resulted in gelation in organic solvents. The $|g_{\mathrm{lum}}|$ values reported (±0.017) were high for a pure organic sample, showing that this synthesis of CT SPs represents an attractive strategy for the enhancement of CPL in organic materials.

Planar chirality: [*n*.*n*]paracyclophanes

Planar chirality is a geometrical chirality that results from the arrangement of out-of-plane groups with respect to a chiral plane.[58] Common examples of planar-chiral molecules are the cyclophanes,[81,82] *E*-cycloalkenes,[83] metallocenes[84] and pillar[*n*] arenes.[85] Only two have thus far been applied to SPs, the pillar [*n*]arenes[86] and [*n*.*n*]paracyclophanes ([*n*.*n*]pCps, $n = 2$ or 3).[87]

The Ogoshi group first introduced pillar[5]arenes in 2008 (Fig. 9),[89] and proved their planar chirality by ^{1}H NMR observation of diastereotopic protons after introduction of chiral sidechains.[90] Racemization of pillar[5]arenes could occur by rotation of the aryl

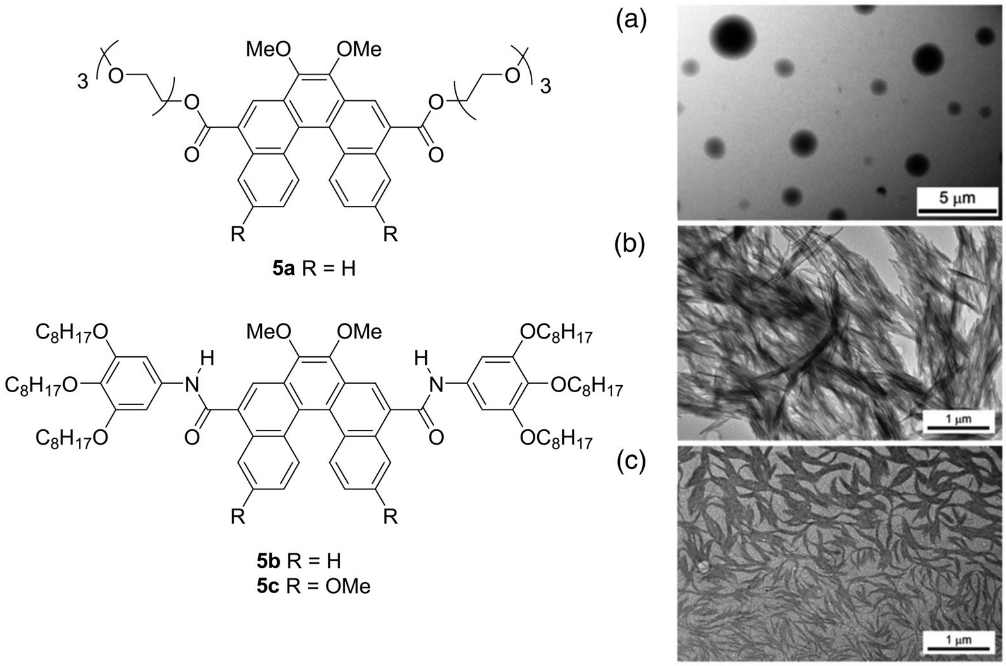


Figure 5. The [5]helicene monomers studied by Matsuda and coworkers. The morphology of the supramolecular assemblies of **5a** prepared from 99:1 water/MeCN solution (a), **5b** (b) and **5c** (c) prepared from heptane solution. Reproduced with permission from Hirose *et al.*[73]

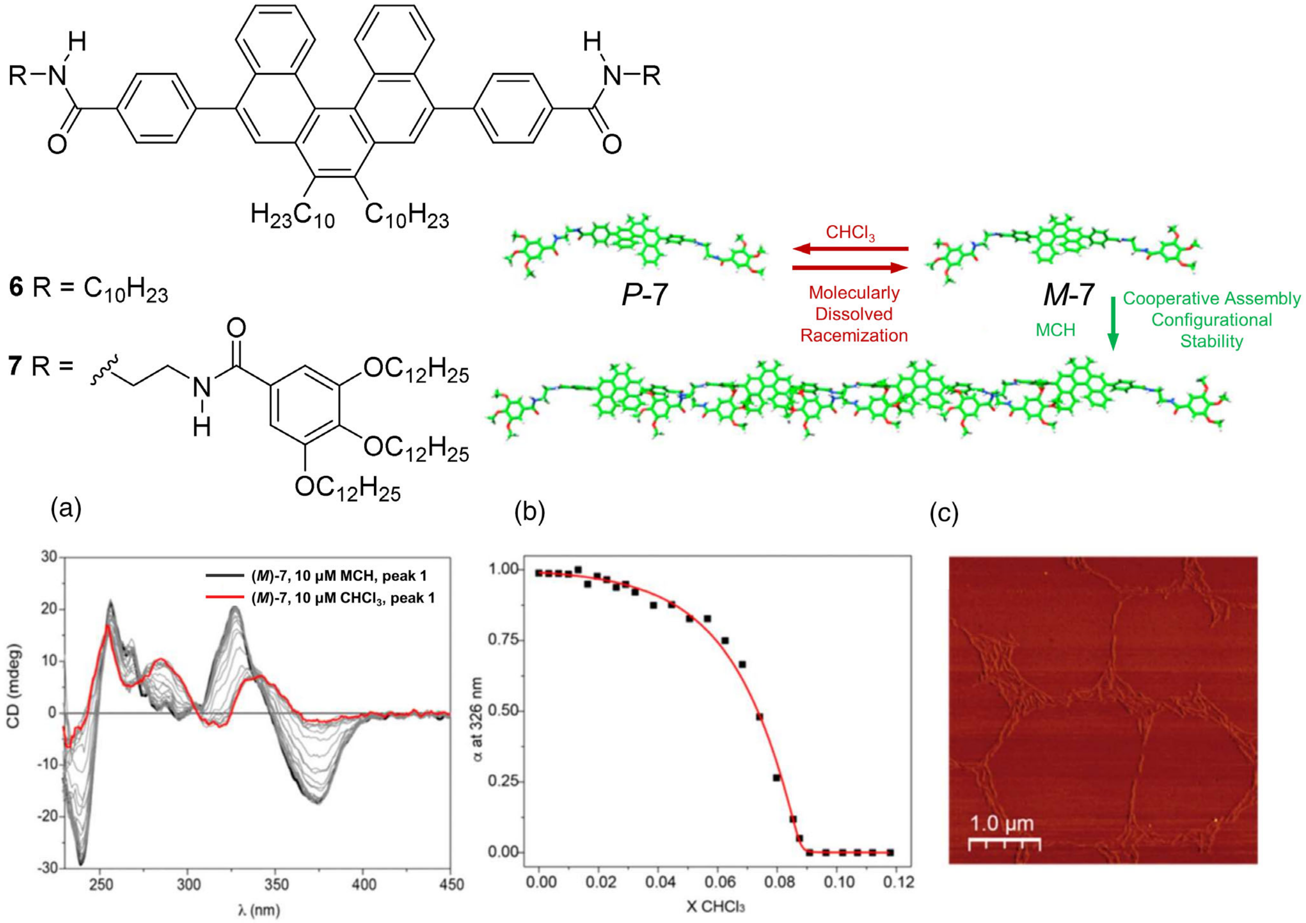


Figure 6. The [5]helicene monomers studied by Sánchez and coworkers. CD spectra of ***M*-7** in mixtures of MCH and $CHCl_3$ (a) and the corresponding denaturation curve (b). AFM phase image (c) of the columnar aggregates formed from ***M*-7** (10 μmol L^{-1}, 298 K, mica as surface). Reproduced with permission from Valera *et al.*[74]

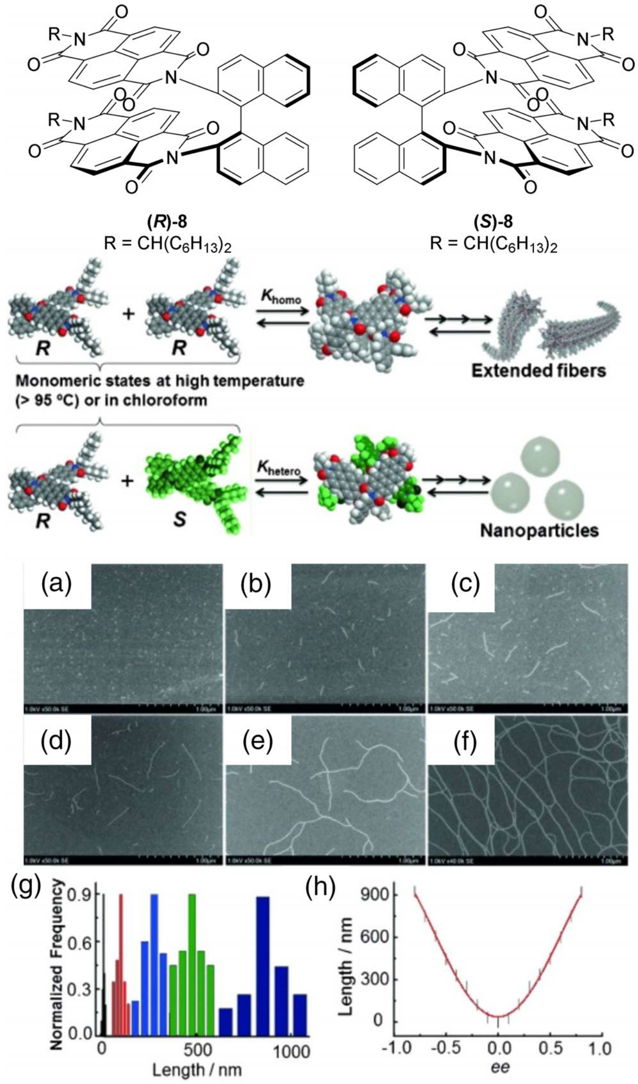


Figure 7. Axially chiral bichromophoric binaphthalene monomers **8** with appended PBIs studied by Nakashima and coworkers (top) and a schematic of their supramolecular assembly (middle). SEM images of the coassembly of (***R***)-**8** and (***S***)-**8** at e.e. values of 0.0 (a), 0.2 (b), 0.4 (c), 0.6 (d), 0.8 (e) and 1.0 (f). Histogram of the length distribution of nanofibers obtained by measuring 50 fibers (g) for e.e. values of 0.0 (black), 0.2 (red), 0.4 (blue), 0.6 (green) and 0.8 (navy blue). A plot of average length of nanofibers *versus* the e.e. value (h). Reproduced with permission from ref. 78.

rings through the central cavity, a process with a low barrier when substituted with linear alkyl sidechains, preventing isolation of planar-chiral enantiomers.[91] When bulkier substituents (cyclohexyl groups) were introduced, rotation of the aryl rings was slowed, and planar-chiral enantiomers were isolated.[92] Selective deprotection of one of the cyclohexyl ethers and functionalization with a complementary guest (cyanopentyl triazole)[93] through Cu(I) catalyzed click chemistry resulted in a complementary host–guest conjugate that acts as a monomer in the formation of planar-chiral SPs.[88] The planar-chiral enantiomers of monomer **9** could be separated by chiral HPLC, and their supramolecular polymerization analyzed at different e.e. values. Interestingly, the racemic mixture gave SPs of larger hydrodynamic radius than those formed by enantiomerically enriched monomers (Fig. 9).

Initially studied for their unique structural and optoelectronic properties endowed by the proximity of two covalently fixed aromatic rings, the class of molecules formed by [*n.n*]pCps where *n* is the length of the covalent bridge also possess planar chirality (Fig. 10). The lack of free rotation between the aryl decks leads to a chiral plane when appropriately substituted. When fixed with hydrogen bonding units, the [*n.n*]pCp skeleton can model a supramolecular dimer of 2,5-dimethylterephthalamides whose supramolecular chirality is fixed covalently, resulting in a planar-chiral-at-core monomer.

In 2016, our group reported the synthesis of a planar-chiral monomer based on [2.2]paracyclophane-4,7,12,15-tetracarboxamide ([2.2]pCpTA, **10**).[26] It was shown that in the solid state **10a**, although synthesized as a racemic mixture, forms homochiral assemblies through anti-parallel intramolecular (transannular)[95] and intermolecular amide hydrogen bonding (Fig. 10). In solutions of chloroform-*d*, the molecularly dissolved state of **10b** dominates at low concentrations, but assembly via an isodesmic mechanism can be observed by increasing the concentration ($K_a = 64$ L mol^{-1}). Nonpolar solvents like MCH promote elongated assembly formation ($K_a > 10^4$ L mol^{-1}). This study was followed by a computational study and confirmation of the isodesmic assembly mechanism for **10** based on the oligomer size independence of K_a due to the pathway selection of the *anti*-conformer and net cancellation of its assembly macrodipole.[96]

Following the successful proof of concept, we set out to synthesize the bridge expanded homolog of **10**, [3.3]paracyclophane-5,8,14,17-tetracarboxamide ([3.3]pCpTA, **11**). It was shown that **11a** also formed homochiral assemblies through anti-parallel hydrogen bonding similarly to **10** (Fig. 10(b)), although the solution phase assembly of **11b** in chloroform-*d* was 4-fold weaker. This was rationalized by an increase in monomer entropy and strain associated with the low energy staggered bridge conformers and the amides involved in hydrogen bonding. Notably, an increase in intramolecular π–π distance (3.3 Å *versus* 3.1 Å) due to the added bridge carbons led to a change in the supramolecular structure of the assembly after optimization of transannular and intermolecular hydrogen bonding. These structural changes include larger amide dihedrals, longer intermolecular π–π distances and an increase in helical pitch. It became apparent in the [*n.n*]pCpTA family of monomers that the location of the chirality at the core of the monomer/assembly structure provides a preference for homochiral assembly based on the geometric mismatching of monomers of opposite chirality engaged in intermolecular hydrogen bonding. This pattern of chiral-at-core structures assembling homochirally is present in the assembly of inherently chiral bowl-shaped molecules as well.

Inherent chirality: corannulenes, bowl peptides and subphthalocyanines

Inherently chiral concave molecules are geometrically chiral owing to their curvature when appropriately substituted, and were summarized recently in a review by Szumna.[97] Some bowl-shaped molecules possessing inherent chirality have been utilized for SPs including calix[*n*]arenes,[98] subphthalocyanines,[99] bowl peptides[100,101] and corannulenes.[102] The curvature of inherently chiral molecules leads to applications especially in molecular recognition, so it makes sense that they are well explored for SPs.

Amongst several other groups working on calix[4]arenes, the Rebek group developed monomers based on calix[4]arenes with urea hydrogen bonding units at the equator of the molecule and alkyl solubilizing groups at the pole (Fig. 11(a)).[105] The C_{4v}-symmetric calix[4]arenes form S_8 symmetric homodimeric capsules through 8-fold intermolecular hydrogen bonding in

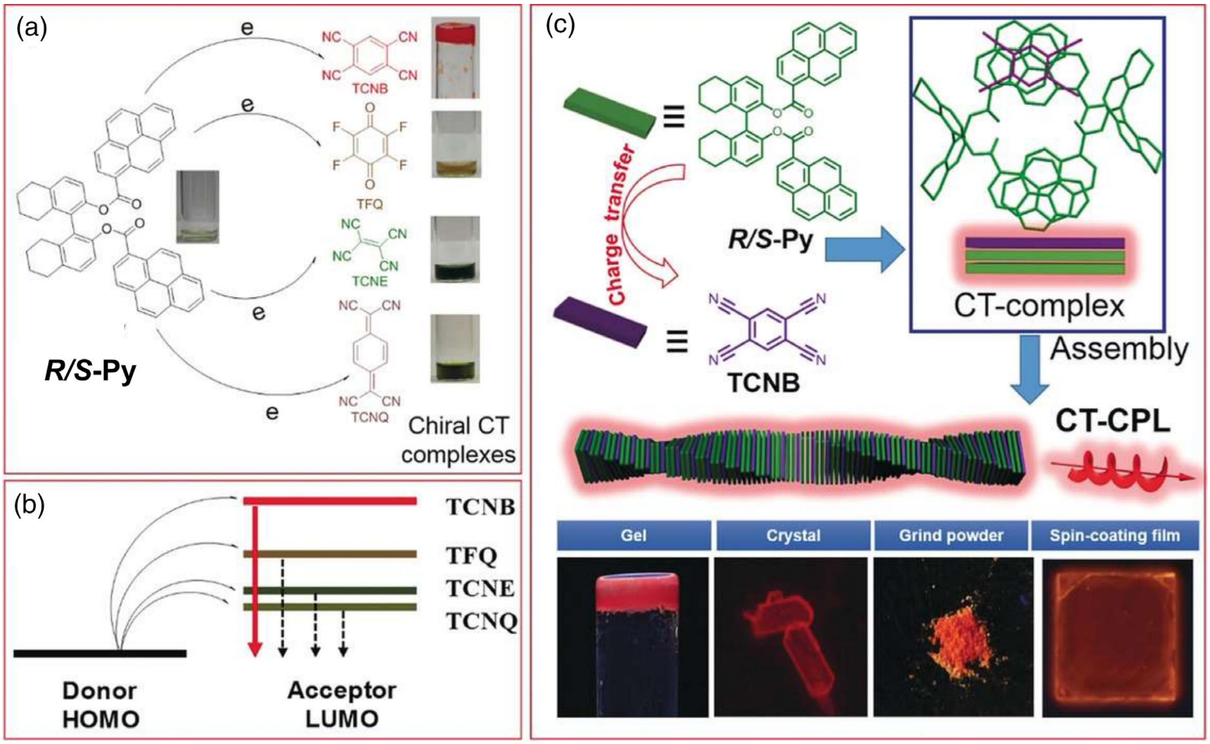
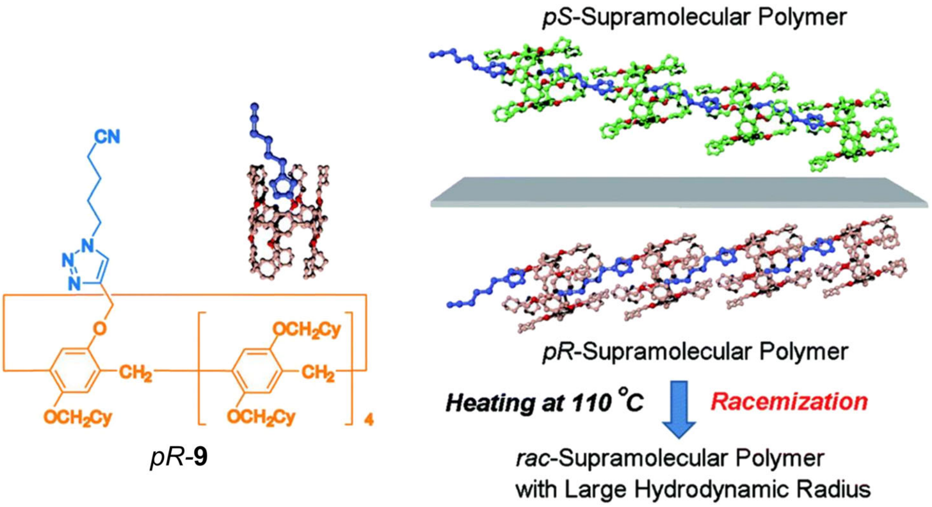


Figure 8. Chiral CT complexes formed between donor ***R/S*-Py** and various achiral acceptors and photos of their mixed solutions after treatment with ultrasound (a). Charge transfer diagram for donor HOMO and acceptor LUMO where solid lines indicate radiative transitions and dashed lines indicate non-radiative transitions (b). Schematic for the synthesis of CT SPs, their structural confirmation by single crystal X-ray diffraction, and their various emissive states (c). Reproduced with permission from Han *et al.*[80]

the presence of appropriate guest molecules (Figs 11(b) and 11(c)).[106,107] When sulfonylureas are introduced, strong heterodimer formation between sulfonylurea and urea derivatives leads not only to strong association, but also to chirality based on the direction of urea hydrogen bonding.[103,108] If a covalent linker is placed between the urea and sulfonylurea moieties, the result is a bifunctional complementary monomer that forms chiral AB SPs (Fig. 11(d)).[104,109,110] These polymeric capsules (polycaps, Fig. 11(e)) were found to form SPs with mechanical integrity that are dependent on guest identity and monomer sequence.

One of the largest efforts towards the synthesis and study of SPs formed from inherently chiral bowl-shaped molecules – both corannulenes and bowl peptides – came from the Aida group. In 2009, the Aida group introduced a chiral hydrogen bonding corannulene derivative capable of forming columnar liquid crystalline aggregates.[111] Tuning of the molecular structures in these corannulene derivatives led to a rational strategy for realizing



pR-**9**

Figure 9. Structure of pillar[5]arene monomer ***pR*-9** and structure of the homochiral SP and thermal response of SP racemization. Reproduced with permission from Ogoshi et. al.[88]

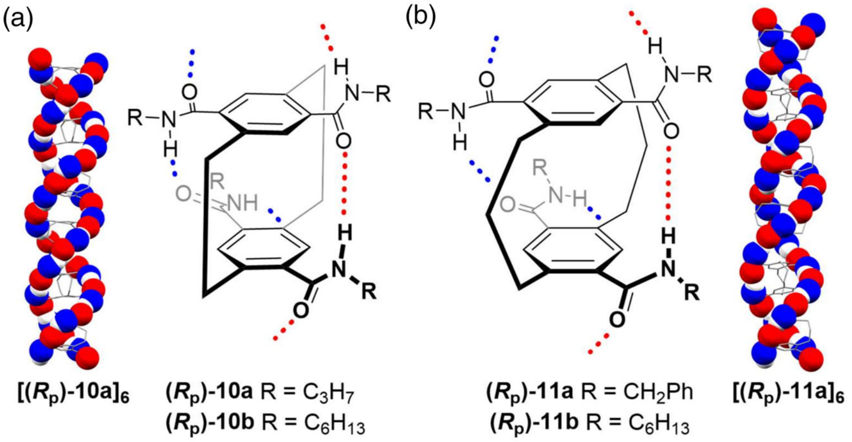


Figure 10. Monomer structures of **10** (a) and **11** (b) studied in our previous work, and the corresponding homochiral hexamers observed in the solid state by X-ray crystallography. Dashed lines indicate hydrogen bonding. Atoms involved in hydrogen bonding are shown as enlarged spheres. Reproduced with permission from Fagnani *et al*.[26] and Henderson *et al*.[94]

chain-growth SPs featuring (meta)stable monomers (**M**) and initiators (**I**) outlined in Figs 12(a) and 12(b). Crucial to this was research showing that hydrogen bond capable corannulene derivatives were metastable in their intramolecularly hydrogen bonded, monomeric state, leading to a raised bowl-to-bowl inversion barrier — a process that results in racemization of other substituted corannulenes (Fig. 12(c)).[113] This metastability allows a chiral sidechain or optically active solvent to funnel the reaction

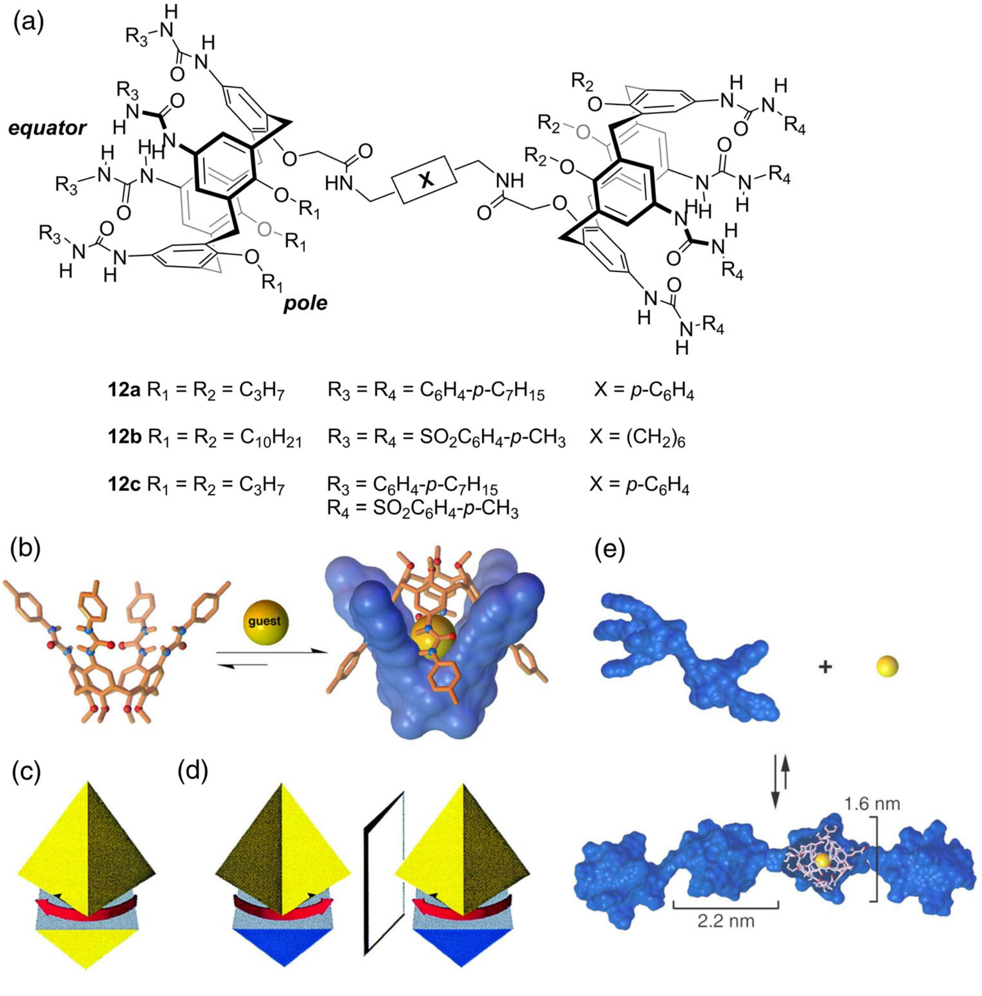


Figure 11. Molecular structure of polycaps (a), and the guest-induced dimerization of the calix[4]arene end groups (b). Symmetry of the homodimer (c) and the heterochiral resulting in two enantiomeric dimers based on directionality of equatorial H-bonding (d). Structure of the polycaps in the assembled form (e). Reproduced with permission from Castellano *et al*.[103,104]

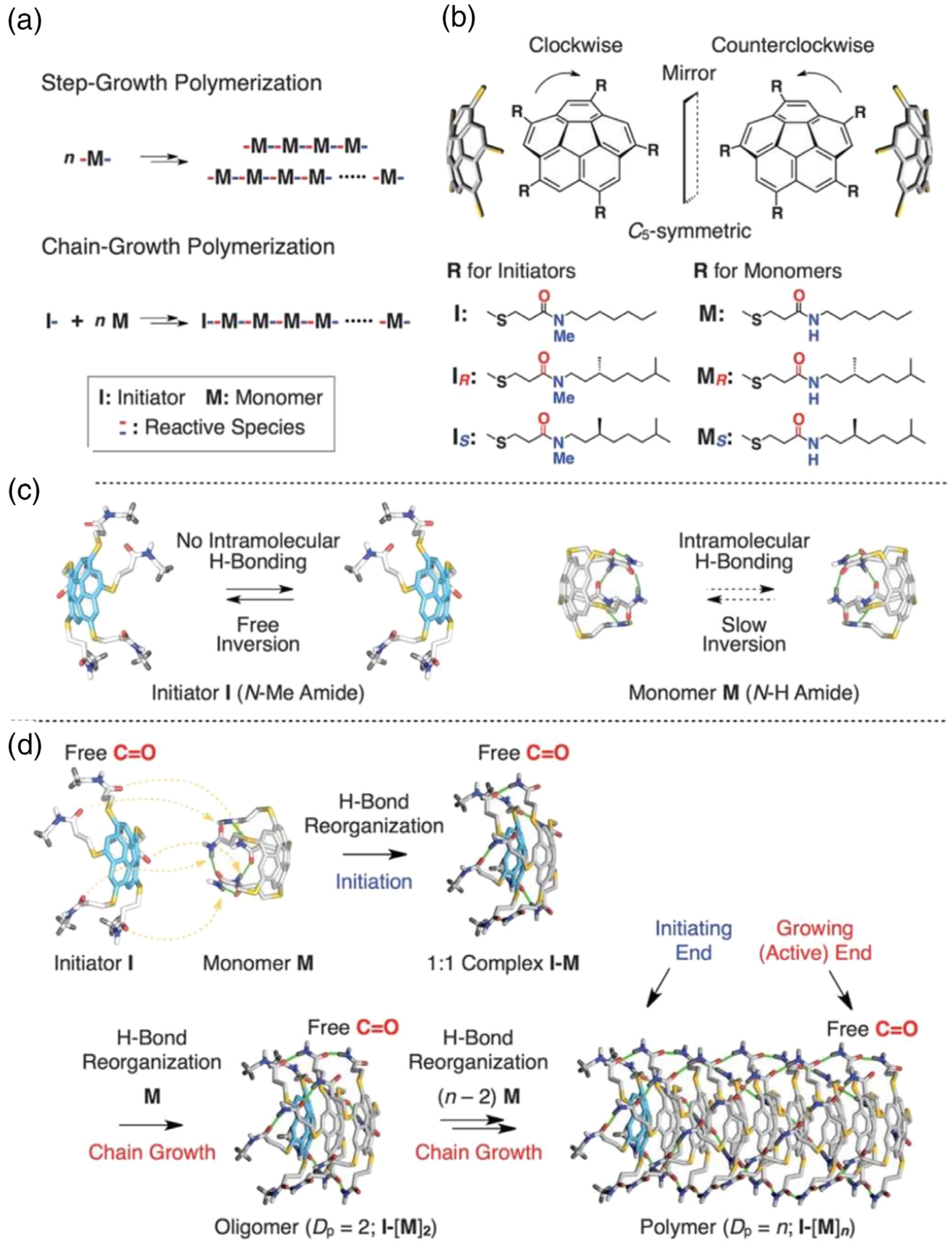


Figure 12. Differentiation between step-growth and chain-growth polymerization (a), and molecular structures of monomer (M) and initiator (b). Dynamic differences between monomer and initiator based on the presence or absence of intramolecular H-bonding and bowl inversion (c). Mechanism of initiation and propagation in chain-growth supramolecular polymerization (d). Reproduced with permission from Kang *et al.*[112]

mixture to the thermodynamically preferred bowl enantiomer. The metastability of M led to the realization of true chain-growth SPs, and the core-chirality of the monomer imparted by the chiral sidechain allowed their study by tandem size exclusion chromatography/CD spectroscopy.[112] The addition of an H-bond accepting tertiary amide initiator (**I**) led to disruption of intramolecular hydrogen bonding in **M**, and addition of another molecule of M in the chain propagation step (Fig. 12(d)). These reversible assemblies are also living SPs so that addition of more monomer results in clean chain extension.

Other work by the Aida group focused on the homochiral supramolecular polymerization of bowl-shaped peptides **14** and **15**.[114] Although the bowl-shaped macrocycles contain stereocenters, they also possess inherent chirality because of their concave structure (Fig. 13). These C_3- and C_4-symmetric monomers formed columnar liquid crystals and homochiral SPs in solution through intermolecular amide hydrogen bonding between the exocyclic amides.[115] The homochiral assemblies were shown to be a result of a large energetic penalty ($\Delta G_{\mathrm{rel}} = +2.3$ kcal mol^{-1}) based on steric interactions between heterochiral mismatched dimers.

In 2015, the group of David González-Rodríguez reported the homochiral supramolecular polymerization of inherently chiral bowl-shaped subphthalocyanine monomers (**16**, enantiomers denoted *α* and *β*). The subphthalocyanines feature a central boron atom with a rigid tetrahedral structure. Generally, these molecules disfavor chromophore aggregation in contrast with their more planar extended analog the phthalocyanines. In order to favor intermolecular assembly, the researchers employed a fluorine

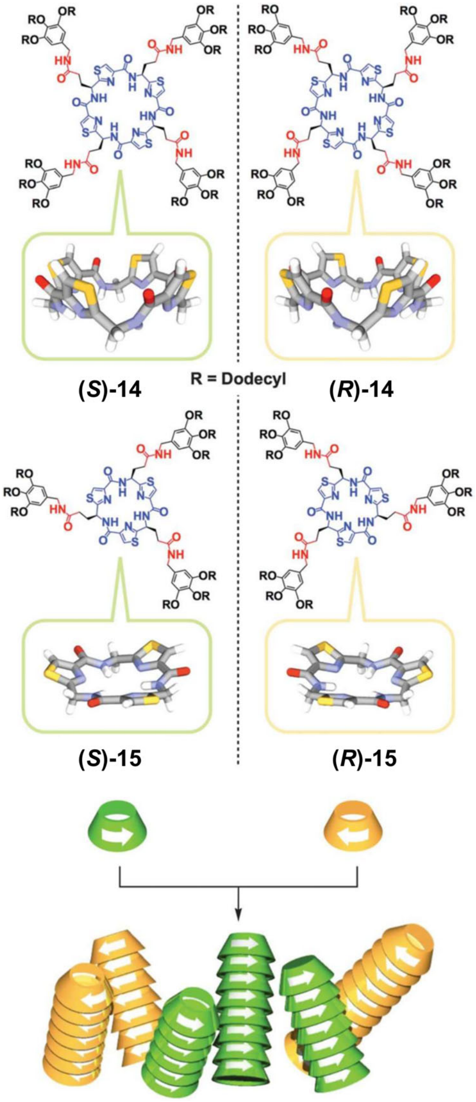


Figure 13. Molecular structure of bowl peptides **14** and **15** study by Aida and coworkers and their homochiral supramolecular polymerization. Reproduced with permission from Sato *et al.*[114]

atom at the central tetrahedral position that was small enough to reduce steric hindrance upon assembly, but also could produce a strong axial dipole moment. Three hydrogen bonding units were necessary to promote intermolecular association, and the lack of either fluorine atom or hydrogen bonding units resulted in no assembly (Fig. 14). The monomers are molecularly dissolved in 1,4-dioxane but assemble in MCH or high volume fractions of MCH/1,4-dioxane. This work further demonstrates that chirality introduced at the core of the molecule rather than the peripheral sidechains can result in homochiral assemblies.

Topological chirality: chiral catenanes

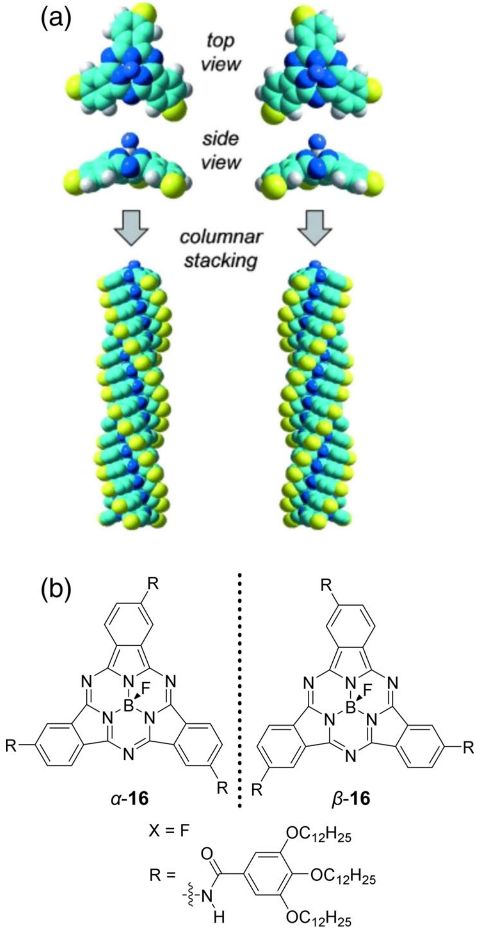


Figure 14. Structure of SPs formed by the assembly of subphthalocyanines **16**. Reproduced with permission from Guilleme *et al.*[116]

The interlocking of molecules resulting in the formation of catenanes and rotaxanes can lead to mechanically interlocked molecules with topological chirality.[117,118] Readers interested in polymeric materials composed of catenanes and rotaxanes are directed to a recent review.[119] By way of introduction, Fig. 15 depicts chirality in a [2]catenane based on work by Sauvage and coworkers[120] in which the C_2 symmetry of the phenanthroline ligand is broken by the addition of a phenyl substituent (Fig. 15 (b)), resulting in the formation of topologically chiral [2]catenanes (Fig. 15(c)).

Work from Meijer and coworkers introduced mechanical chirality through a Sauvage-type [2]catenane composed of two ureidopyrimidinone (UPy) hydrogen bonding units by templated ring closing metathesis (Fig. 16).[121] The resulting self-complementary ditopic monomer polymerizes through intermolecular quadruple hydrogen bonding to create an SP with alternating hydrogen bonding and mechanical bonding. Interestingly, polymeric structures were only observed by DLS when the Sauvage linkage was metalated. The absence of SPs when the Sauvage linkage was de-metalated is probably a result of intramolecular UPy contacts hindering intermolecular association. Although the topological chirality was not examined directly in this work, the formation of SPs from interlocked molecules represents an exciting opportunity in new SP chemistry.

CONCLUSIONS

SPs composed of chiral monomers with no chiral centers represent an opportunity to study not only stereoselective self-recognition but also factors affecting the configurational stability of chiral molecules with low barriers to racemization. SPs with helical chirality were first studied and their assemblies led to renewed interest in chiroptical properties emergent

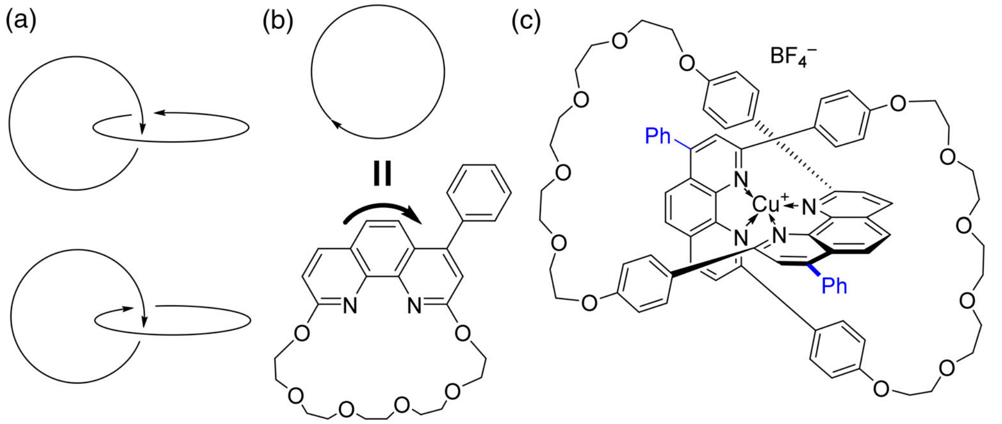


Figure 15. Schematic for a topologically chiral [2]catenane enantiomer (a) based on symmetry breaking of the macrocyclic phenanthroline ligand (b). A topologically chiral [2]catenane synthesized by Sauvage and coworkers (c). Reproduced with permission from ref. 120.

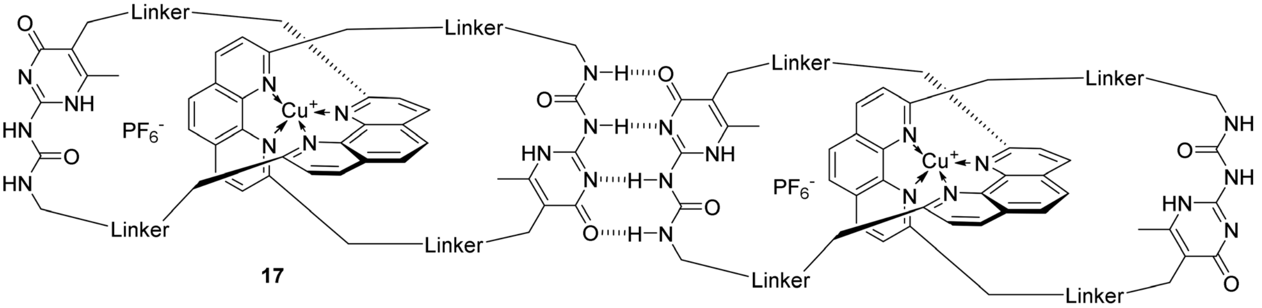


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Figure 16. Mechanically interlocked SPs formed by UPy functionalized [2]catenane **17**. Reproduced with permission from Teunissen *et al.*[121]

upon assembly. The synthesis of new monomers with planar chirality by our group and others has furthered understanding of factors dictating the supramolecular polymerization mechanism, thermodynamics and stereoselectivity. The development of chiral monomers with bowl chirality has also led to the first example of chain-growth SPs, as well as several examples of homochiral SPs due to the inherently curved nature of the monomer. New monomers with mechanical bonds provide fascinating topological chirality, with new derivatives yet to be explored.

Perspective

Although several examples of SPs formed by chiral molecules with no chiral centers have been reviewed here, new monomers are still needed to expand our understanding of the interplay between molecular chirality and SP chirality. Despite these limited examples, a trend becomes apparent that can excite the organic and supramolecular chemist. Those molecules in which chirality is positioned in the core of the molecule tend to have a higher propensity to form homochiral SPs. This can be rationalized by comparing the geometry of intermolecular interactions. In majority rules SPs, the energetic contributions to the stereoselectivity of assembly are the helix reverse penalty (HRP) and the mismatch penalty (MMP).[122] Especially important is the large HRP for introduction of a monomer unit whose supramolecular chirality does not match that of the growing polymer chain, resulting in extension of the polymer chain with opposite chirality. In chiral-at-core SPs, the MMP is inherently an HRP, meaning that there is a large energetic penalty to heterochiral association, favoring homochiral SPs. To continue to understand factors affecting stereoselective supramolecular polymerization, more monomers with chiral-at-core structures should be synthesized and their assemblies systematically studied.

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