DOI: 10.1002/anie.200801481

Supramolecular Chirality

Concomitant and Controllable Chiral/Racemic Polymorphs: From Achirality to Isotactic, Syndiotactic, and Heterotactic Chirality**

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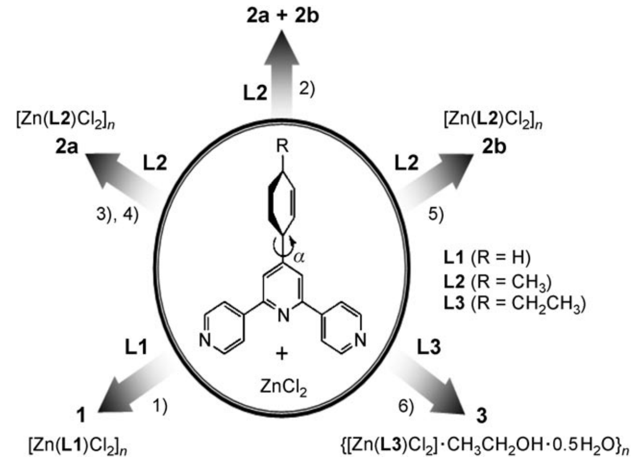
Supramolecular chirality, which is ubiquitous in natural substances, has now become one of the central issues of chemistry in both the academic and industrial sectors.[1,2] Spontaneous resolution, such that the enantiomers are segregated upon crystallization, stands out in the separation and control of chirality, and is widespread in the materials science of chiral crystalline solids, liquid crystals, and monolayers.[3] Notably, the phenomenon of achiral components resolving to yield chiral crystals is relatively rare compared to the analogous process with chiral components or auxiliaries.[3c] Therefore, a series of scientific questions arise: are there enantiophobic and enantiophilic molecules? Or are packing forces responsible for conglomerate formation?[3b,4]

Contrary to static chirality, which is sustained by covalent linking, supramolecular chirality mediated by noncovalent intermolecular interactions may enable the formation of thermodynamically stable assemblies based on certain dynamic equilibria.[1b] In state-of-the-art research on chiral coordination polymers,[5] Aoyama et al. provided a well-established example of controllable homochiral crystallization, in which adjacent helices constructed from achiral components adopt the same handedness through intermolecular water–nitrate hydrogen bonding.[6] Later, Yan et al. described an unusual example of partial spontaneous resolution, which showed the progression from achiral species to chiral dimers, to chiral 2D layers, and finally to concomitant chiral and racemic crystals.[7]

However, both of the above examples are not genuine polymorphs,[8] as they contain solvent molecules in their crystal structures that might preserve the homochiral discrimination but complicate the supramolecular interactions among chiral precursors. Herein, we report a unique example of concomitant and controllable chiral/racemic polymorphs for investigating how supramolecular chirality can be generated from achiral components.

The helix is one of the most attractive and evocative expressions of chirality,[9,10] especially one-dimensional (1D) metallohelical chains, which are proved to be more efficient chiral precursors than oligohelicates. We previously obtained a 1D helical chain **1** in the solvothermal reaction of zinc(II) chloride and 4′-phenyl-4,2′:6′,4″-terpyridine (**L1**; path 1 in Scheme 1).[11] In **1**, each zinc(II) ion is bonded with two chloride ions and further linked by two pyridyl nitrogen atoms, which leads to a helical chain along the 2_1 screw axis with a helical pitch of 19.3 Å (Figure S1 in the Supporting Information). The pyridyl rings offer weak intermolecular π–π interactions stabilized by CH···Cl hydrogen bonding to contact with adjacent helices, which generates a racemic compound with heterochiral packing fashion.



Scheme 1. Syntheses of complexes **1**–**3**. 1) EtOH, 100 °C; 2) EtOH/H_2O, 140 °C; 3) THF/H_2O, RT, layering; 4) *i*PrOH or *t*BuOH, 140 °C; 5) EtOH or MeOH, 140 °C; 6) EtOH/H_2O, 140 °C.

The ligand was suitably modified by introducing a *para*-methyl group to the phenyl ring (**L2**), in realization that the intermolecular interactions may be accordingly adjusted.[8b,c] Fortuitously, the solvothermal reaction in ethanol/water mixed solvent (path 2 in Scheme 1) yielded two concomitant crystals **2a** and **2b**. X-ray analyses[12] revealed homochiral packing for **2a** and heterochiral packing for **2b**, and hence a partial spontaneous resolution occurred.[7a] Unlike those in previously reported work,[6,7] **2a** and **2b** are genuine chiral/racemic polymorphs without solvent molecules in their crystal packing, and thus the supramolecular interactions among adjacent helices are predominantly responsible for the spontaneous resolution.

Compound **2a** crystallizes in chiral $P3_121$ space group and possesses a pseudo-3_1 screw axis in the helical structure (Figure 1). There are strong intermolecular π–π interactions (3.410–3.651 Å, dihedral angle between phenyl group and pyridyl ring $\alpha = 1.5$ and 24.5°) and CH···Cl hydrogen bonding

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[**] This work was financially supported by the National Natural Science Foundation of China (Grant nos. 20571050 and 20771072). We thank Xin-Hui Zhou and Prof. Dr. Jing-Lin Zuo at Nanjing University for the CD spectroscopy measurement and explanation.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.200801481.

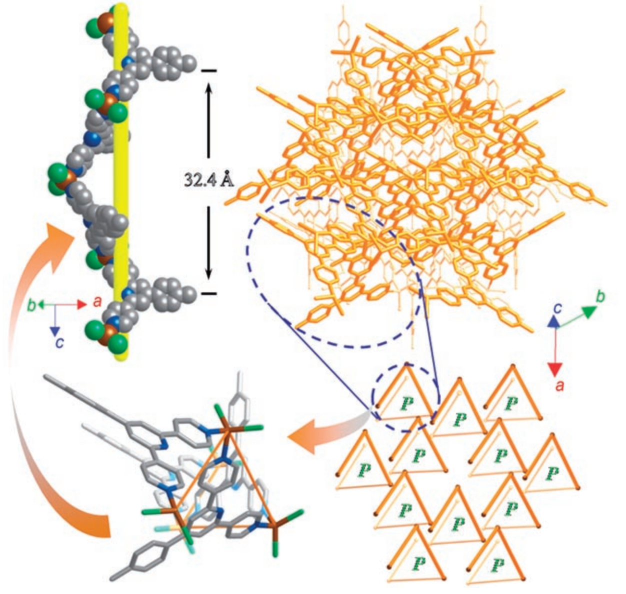

Figure 1. Left: side and top views of the 1D helix in **2a** (Zn gold; Cl green; N blue; C gray). Right: the dense homochiral packing (*P* helicity) and a schematic representation of **2a** (isotactic chirality).

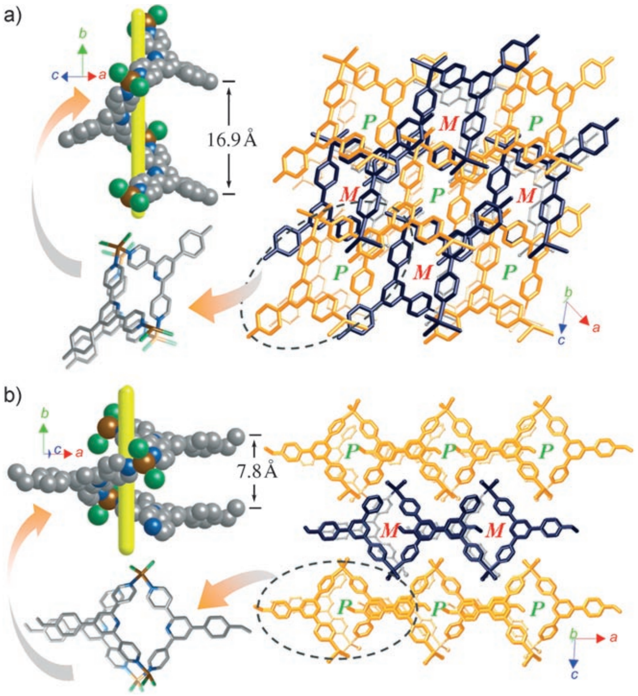

Figure 2. Left: side and top views of the 1D helices in a) **2b** and b) **3** (Zn gold; Cl green; N blue; C gray). Right: the heterochiral packing (*P* and *M* helicity) of **2b** (a, syndiotactic chirality) and **3** (b, heterotactic chirality). In **3**, the highly disordered solvent molecules are omitted.

(2.723–2.999 Å) in the crystal packing (Figure S2 in the Supporting Information). The zinc(II) centers are tetrahedrally coordinated in a slightly distorted fashion (103.6–122.9°, compared to the angle of an ideal tetrahedron of 109.5°), which is consistent with the long helical pitch of 32.4 Å, thus making feasible the dense crystal packing of **2a** (interstrand Zn⋯Zn distance 6.765–7.024 Å) for homochiral discrimination.

In contrast, **2b** has an isomeric helical structure with a 2_1 screw axis (Figure 2a) and crystallizes in the achiral $P2_1/n$ space group. The crystal packing of **2b** (interstrand Zn⋯Zn distance 7.512–8.793 Å) is not as dense as that of **2a**, reflected by the relatively weaker π–π interactions (3.601–3.756 Å, $\alpha = 30.2°$) and CH⋯Cl hydrogen bonding (2.815–2.981 Å, Figure S3 in the Supporting Information), the more distorted coordination environment of the zinc(II) centers (angle 99.5–123.4°) as well as a shorter helical pitch of 16.9 Å. Different from **2a**, the whole crystal of **2b** presents a heterochiral packing fashion, and therefore we assume that the intensively dense packing stabilized by strong intermolecular interactions would promote the spontaneous resolution process.

Thermogravimetric analyses (Figure S6 in the Supporting Information) reveal that the energetic difference between **2a** and **2b** is very small, but the two polymorphs are not interconvertible, probably because they lack solvent molecules in their crystal packing to enable solvent exchange,[6] which suggests that both products are thermodynamically stable. Although the intermolecular interactions play dominant roles in the spontaneous resolution, a solvent–solute effect should be considered in the supramolecular system,[13] and the effect of the methyl group in **L2** still needs to be explored. Based on the above consideration, we selected a series of polar protic solvents (methanol, ethanol, isopropyl alcohol, *tert*-butyl alcohol) in similar solvothermal reactions to examine the solvent–solute effect. Interestingly, in the cases of isopropyl alcohol and *tert*-butyl alcohol, the solvents crystallized the pure homochiral product **2a** (path 4 in Scheme 1), whereas in the cases of methanol and ethanol, the solvents crystallized the pure heterochiral products **2b** (path 5 in Scheme 1), as revealed by the perfectly matched X-ray power diffraction patterns (Figure 3).

Inspired by the general mechanism suggested by Borovkov et al.,[1c,13a] which clarified the solvent–solute effect on the induction of supramolecular chirality at the molecular level, we can offer a preliminary insight into the solvent-assisted spontaneous resolution presented herein. As concluded above, in the solid-state structures the dense packing would promote homochiral discrimination, and in the case of ethanol, solvent-crystallized heterochiral **2b**. When replacing ethanol (or methanol) with isopropyl alcohol or *tert*-butyl alcohol, the enhancement of hydrophobic interactions among the alkyl groups in **L2** and in the solvent molecules would assist the dense packing of adjacent helices to generate homochiral **2a**. Note that the dielectric constants of the polar protic solvents are in accordance with *t*BuOH < *i*PrOH < EtOH < MeOH, but one should be cautious about invoking solvent polarity at face value to exclusively explain the chirality sensing.[13a]

An apparent deviation existed in that the ethanol/water (4:1) mixed solvent with a higher dielectric constant than ethanol would lead to partial spontaneous resolution to yield **2a** and **2b**, thus impelling us to take into consideration the effect of the hydroxy groups in the ethanol molecules. In the light of Borovkov's approach, the spontaneous resolution

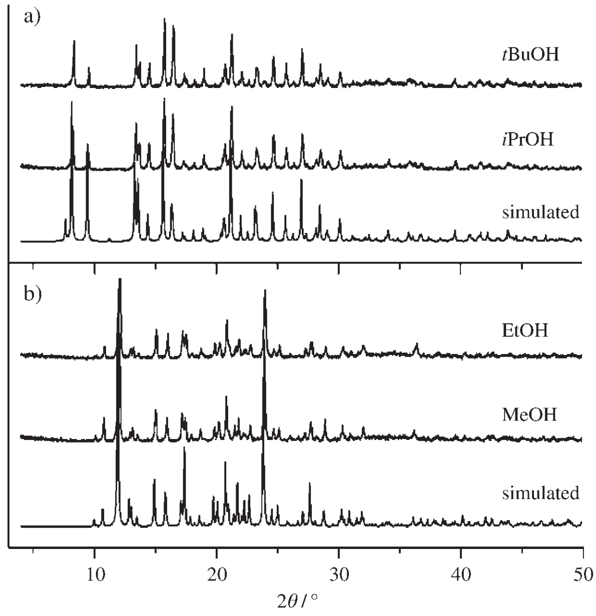

Figure 3. X-ray powder diffraction patterns for **2a** (a) and **2b** (b) obtained in different polar protic solvents.

observed by us could occur through the enhancement of either the hydrophobic aggregation effect induced by the bulky alkyl groups, or the steric repulsion effect between the polar hydroxy group in ethanol molecules and the nonpolar methyl group in **L2**. In the case of ethanol/water mixed solvent, the water molecules are able to electrostatically surround the hydroxy groups of the ethanol molecules, which increases the effective size of the polar substituents[13a] and thus enforces the steric repulsion effect toward dense packing. Besides, selected dipolar aprotic solvents (acetone, acetonitrile, or tetrahydrofuran) were proved to make homochiral discrimination feasible (Figure S7 in the Supporting Information), whereas nonpolar solvents (hexane or benzene) failed to yield analyzable products. The solvent–solute effect on the generation of supramolecular chirality described herein is roughly presented, and the mechanism for this phenomenon needs to be further investigated.

To further examine the influence of the alkyl chain length,[8b,c] the ligand was modified by substituting the methyl group (**L2**) with an ethyl group (**L3**). To our pleasant surprise, the solvothermal reaction (path 6 in Scheme 1) of $ZnCl_2$ and **L3** under the same conditions as those for generating concomitant **2a** and **2b** resulted in a single product **3**, with a packing fashion different from those of **2a** and **2b**. Although the helix of **3** (Figure 2b) possesses a 2_1 screw axis similar to that in **2b**, the intermolecular interactions are distinctive (π–π stacking 3.608–3.753 Å, $\alpha = 37.8°$, CH···Cl 2.904–2.996 Å; see Figure S4 in the Supporting Information). The highly distorted tetrahedral environment of the zinc(II) centers (93.5–121.0°) leads to the shortest helical pitch of 7.8 Å. Note that the π–π interactions in **3** are between two pairs of pyridyl–phenyl rings (unlike in **2a** and **2b**), and adjacent 1D helices with the same handedness are stabilized by dual up-and-down π–π interactions to form 2D homochiral layers. Adjacent layers cannot fulfill dense packing because of the short helical pitch and steric hindrance, and thus arrange in an alternate handedness manner and enclathrate highly disordered solvent molecules. This 2D homochiral packing is very rare,[7a,8c] and therefore we consider it distinguishable from the other two types of supramolecular chirality. By taking advantage of the proposed terminology for chiral coordination polymers,[14b] we represent the supramolecular chirality herein as isotactic (*P,P*/*M,M*; **2a**), syndiotactic (*P,M,P,M*; **1** and **2b**), and heterotactic (*P,P,M,M*; **3**) chirality.[15]

In conclusion, a unique example of concomitant and controllable chiral/racemic polymorphs is presented. Moreover, the generation of supramolecular chirality is preliminarily rationalized by varying the alkyl substituents in both ligand and solvent molecules, which reveals that intermolecular interactions are responsible for the supramolecular control of spontaneous resolution and in the assistance of solvent–solute effects. Accordingly, we implemented a progression from 1) achirality to supramolecular chirality, 2) partial to complete spontaneous resolution, and 3) isotactic and syndiotactic to heterotactic chirality. Further investigations will be focused on varying the solvents and ligands to clarify the intricate spontaneous resolution process.

Received: March 28, 2008
Revised: May 16, 2008

Keywords: chirality · helical structures · polymorphism · solvent effects · supramolecular chemistry

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[12] Crystal data for **2a**: $C_{22}H_{17}ZnN_3Cl_2$, $M_r = 459.66$, trigonal, space group $P3_121$ (no. 152), $a = 13.3238(10)$, $b = 13.3238(10)$, $c = 32.414(5)$ Å, $\gamma = 120.00°$, $V = 4983.3(9)$ Å^3, $Z = 9$, $\rho_{calcd} = 1.379$ g cm^{-3}, $\mu = 1.361$ mm^{-1}, $F(000) = 2106$, $T = 296(2)$ K, 12990 reflections collected, 5142 unique ($R_{int} = 0.0420$), $R_1 = 0.0516$, final $R_1 = 0.0731$, $wR_2 = 0.1314$, GOF = 1.023 for all data. Crystal data for **2b**: $C_{22}H_{17}ZnN_3Cl_2$, $M_r = 459.68$, monoclinic, space group $P2_1/n$ (no. 14), $a = 10.4621(11)$, $b = 16.9501(18)$, $c = 14.9931(17)$ Å, $\beta = 52.498(2)°$, $V = 2109.3(4)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.447$ g cm^{-3}, $\mu = 1.430$ mm^{-1}, $F(000) = 936$, $T = 296(2)$ K, 11589 reflections collected, 3703 unique ($R_{int} = 0.0317$), $R_1 = 0.0432$, final $R_1 = 0.0624$, $wR_2 = 0.1172$, GOF = 1.052 for all data. Crystal data for **3**: $C_{25}H_{26}ZnN_3Cl_2O_{1.5}$, $M_r = 528.76$, monoclinic, space group $P2_1/n$, $a = 13.700(3)$, $b = 7.7895(15)$, $c = 23.043(5)$ Å, $\beta = 93.914(2)°$, $V = 2453.5(8)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.431$ g cm^{-3}, $\mu = 1.244$ mm^{-1}, $F(000) = 1092$, $T = 296(2)$ K, 7609 reflections collected, 4038 unique ($R_{int} = 0.0163$), $R_1 = 0.0466$, final $R_1 = 0.0597$, $wR_2 = 0.1490$, GOF = 1.055 for all data. Data collections were performed on a Bruker Smart Apex CCD diffractometer ($Mo_{K\alpha}$ radiation, $\lambda = 0.71073$ Å) by using frames of 0.3 oscillations ($2\theta < 56°$) at $T = 296(2)$ K with SMART. The structures were solved by direct methods, and all non-hydrogen atoms were subjected to anisotropic refinement by full-matrix least-squares methods on F^2 by using the SHELXTL program (G. M. Sheldrick, SHELXTL 6.10, Bruker Analytical Instrumentation, Madison, WI, USA, **2000**). All hydrogen atoms of the ligands and EtOH were placed in calculated positions with fixed isotropic thermal parameters. The hydrogen atoms of the water molecules were located from the difference Fourier map and refined isotropically. The observed absolute structure (Flack) parameter (0.018) in **2a** apparently reveals that the coordinates correspond to the absolute structures of the molecules in the crystal. Although the structure of **2a** contains solvent-accessible voids of 208.00 Å^3, the largest peak is 0.65. Therefore, compound **2a** is considered to contain no solvent in the lattice. The asymmetric unit of **3** contains both solvent water molecules and EtOH molecules. The solvent EtOH molecules are disordered by translation over three sites, with site occupancy factors of 0.5, 0.25, and 0.25, respectively. CCDC 682963 (**2a**), 682964 (**2b**), and 682965 (**3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

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[15] The tacticity nomenclature (isotactic, syndiotactic, heterotactic) was originally used in organic polymer chemistry.[14a] Recently, Puddephatt and Wheaton[14b] invoked this set of concepts in the description of chiral coordination polymers, because in the usual nomenclature, the term heterochiral does not distinguish between the *R*,*S*,*R*,*S* and *R*,*R*,*S*,*S* sequences. Herein, we feel comfortable following this nomenclature in describing supramolecular chirality, because of the similar dilemma encountered and the novelty of the structure of **3**.