

Chiral Assemblies

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Supramolecular Chirality in Layered Crystals of Achiral Ammonium Salts and Fatty Acids: A Hierarchical Interpretation**

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The formation of chiral crystals from achiral compounds has attracted much attention because chemical reactions of achiral compounds under asymmetric conditions can lead to absolute asymmetric synthesis,^[1] which could be the key to the

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origin of homochirality of life.^[2] Some chiral systems are known in the solid state, in which robust supramolecular motifs, such as hydrogen-bonded networks and π - π stacking, are adopted to obtain chiral crystals with helical^[1e,3] and layered structures.^[4] However, even in these sophisticated supramolecular systems the nature of the relationship between the molecular structures and the appearance of supramolecular chirality^[5] in the crystals still remains ambiguous. Simpler achiral molecules, such as linear fatty acids, on the other hand, are expected to form chiral crystal structures in which the appearance of supramolecular chirality could be explicable on the basis of single molecules. These acids have readily analyzable structures, and thus a number of studies on their solid-state structure have been reported (e.g., layered crystal structures), including our recent results that show how certain amines and carboxylic acids form robust organic layer crystals involving a planar hydrogen-bonded network.^[6]

Very few chiral crystal structures of such simple fatty acids have been reported. However, to our surprise, the chirality in the crystal structures is not discussed at all.^[7] To understand the formation of chiral crystals composed of achiral compounds, a systematic way of thinking is also required. Herein, we propose a hierarchical approach to the generation of chiral layered crystals that start from achiral molecules (Figure 1).

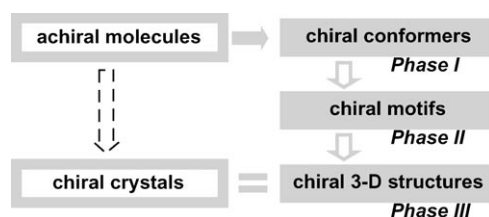
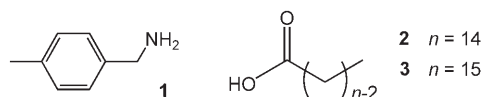


Figure 1. A hierarchical interpretation of supramolecular chirality in crystals generated from achiral molecules.

This approach includes the following three steps: 1) generation of chirality in an achiral single molecule as a result of fixing its conformation in an asymmetric way; 2) assembly into a chiral zero-, one-, or two-dimensional layer motif, in which the chirality in the single molecules spreads throughout the whole layer motif through regular noncovalent interactions, such as hydrogen bonds; and 3) formation of a chiral crystal, in which the chiral layers pile up directionally to form

a three-dimensional chiral structure. This approach would be adopted generally in crystals composed of various types of supramolecular assemblies.

Herein, we describe the preparation of two types of novel chiral layered crystals containing 4-methylbenzylamine (**1**) and the linear fatty acids myristic acid (**2**) and pentadecanoic acid (**3**), respectively, and the hierarchical interpretation of their chiral crystal structures.



The chiral crystals were obtained from 4-methylbenzylamine (**1**) and the linear fatty acid in THF. After evaporation of the solvent, the resulting powdery salts were recrystallized from several solvents to give single crystals suitable for X-ray diffraction studies. Figure 2 shows the crystal structures of ammonium myristate **1·2**^[8] and pentadecanoate **1·3**,^[9] both of which exhibit layered packing. In both crystals the carboxylate and ammonium ions assemble separately in planes with an identical inclination. A single layer is defined as a set of carboxylate and ammonium layers linked by a planar hydrogen-bonded network (see Figure 2a and 2c for **1·2**). The carboxylate and ammonium ions in a single layer in a crystal of **1·2** align in the same way as those in **1·3** (Figure 2b). However, the stacking manner is completely different between the two crystal systems: each single layer in the crystal of **1·2** stacks in a parallel way, whereas those of **1·3** stack in an opposite way with a 180° rotation. As a consequence, the crystal structure of **1·2** includes only translation as a chiral symmetry element, and thus belongs to the chiral space group $P1$, whereas the structure of **1·3** has a twofold helical axis perpendicular to each single layer and thus belongs to the chiral space group $P2_1$.

The X-ray single crystallographic analysis also revealed that the carboxylic group and the alkyl group of the alkyl carboxylate are staggered, as shown in the Newman projection in Figure 3 (top). The fixation of its conformation provides chirality to the twisted carboxylate in the crystal, thus forming *P* or *M* enantiomers.^[10] The 4-methylbenzylammonium ion in the crystal is also chiral for the same reasons as

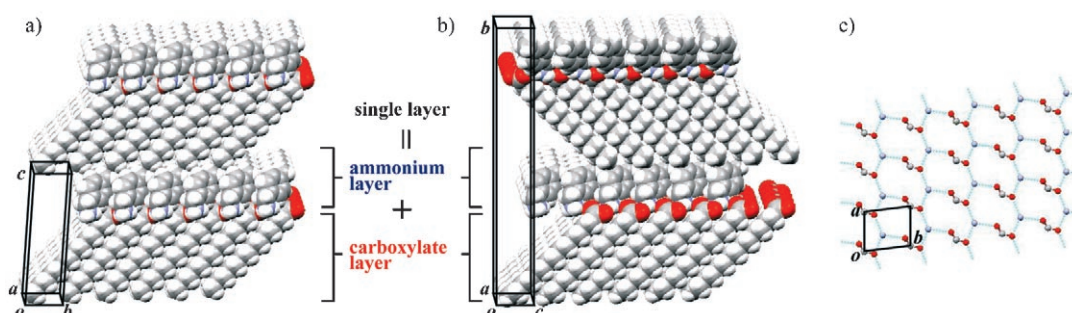


Figure 2. Chiral layered structures of the ammonium carboxylates **1·2** (a) and **1·3** (b). c) The planar hydrogen-bonded network in **1·2**. A set of carboxylate and ammonium layers is connected to construct a single layer. All figures are presented for the *P* crystal. C gray, N blue, O red, H white.

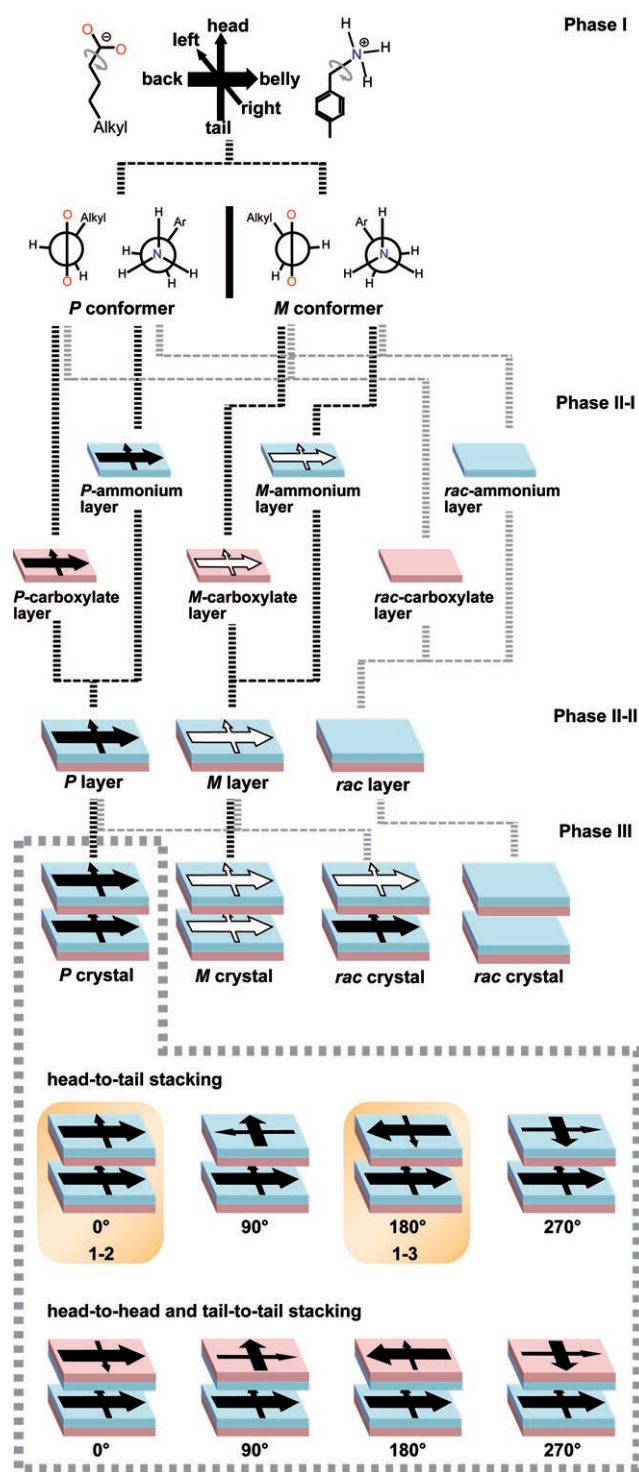


Figure 3. A hierarchical classification of layered crystals based on chirality and directionality. Three distinguishable axes are defined for conformationally chiral carboxylate and ammonium ions (phase I). These assemble to construct *P*-, *M*-, and *rac*-carboxylate and ammonium layers, respectively (phase II-I). The pink and blue plates denote the carboxylate and ammonium layers, black and white arrows denote *P* and *M* conformers, and thick and thin arrows denote back-to-belly and right-to-left axes, respectively. Single layers result from attaching the carboxylate and ammonium layers (phase II-II). Stacking of the single layers yields four types of layered crystals (phase III). The gray dotted box at the bottom shows the possible stacking manners of the single layers in terms of stacking faces and degrees of rotation. The difference of the degrees of stacking gives the two types of chiral layered crystals (**1-2** and **1-3**).

for the carboxylate. Thus, supramolecular chirality in the layered structures of **1-2** and **1-3** is attributed to the transmission of molecular chirality within the single twisted molecules of the single layer by regular assembly, and finally throughout the whole crystal by parallel stacking of these single layers.

We have previously reported that molecular-assembly mechanisms of complex chiral compounds, such as steroids, can be understood by considering the directionality within the molecules as defined by three distinguishable axes,^[11] in which the directionality of the helical aggregations is derived from the directionality of the chiral component itself and reflects on the directionality of the entire molecular assembly. In the same way, three axes can be defined for the conformationally chiral carboxylate and ammonium ions and then the 2D aggregation and layered stacking of these ions can be classified by their directionality (Figure 3).

The directionality within the chiral carboxylate and ammonium ions is initially defined by three axes (phase I in Figure 3). In the case of the carboxylate, the head and tail are defined as the carboxylic group and alkyl chain, respectively, and the belly and back as the sides with odd and even numbers of carbon atoms (thick arrow), respectively. Right and left are then spontaneously generated on the carboxylate (thin arrow). In the case of the ammonium ion, the head and tail are defined by the amino group and the methyl group on the aromatic ring near the amino group, respectively, and the back is the opposite side of the edge. Right and left are also generated spontaneously by this procedure.

The assembly manner of the carboxylate and ammonium ions in the single layer can now be clearly shown by defining the directionality of the chiral molecules (phase II-I in Figure 3). The *P* or *M* carboxylates assemble independently in planes with an identical inclination that connects the belly to the back along the crystallographic *a* axis and right to left along the *b* axis (see Figure 2a for the *P* carboxylate), respectively, which leads to two carboxylate layers that are mirror images of each other. The ammonium ions also form a layer. The ammonium ion has a planar body, and this plane lies parallel to a diagonal axis between the *a* and *b* axes, which means that the belly and back lie along the diagonal axis (see Figure 2a for the *P* ammonium). The *P* and *M* ammonium ions assemble independently in the plane to form two kinds of ammonium layers that are mirror images of each other. *P* and *M* conformers are also known to aggregate in *rac*-carboxylate and *rac*-ammonium layers in which supramolecular chirality is not generated, although this behavior is not observed in this system.^[6]

A single layer in the crystal contains carboxylate and ammonium layers. Although there are several possible combinations, only layers having certain combinations of chirality can be attached together to form *P*, *M*, and *rac* layers (phase II-II in Figure 3) as formation of a single layer requires the concordance of the period and shape of the unit cell, thus corresponding to chirality, between the carboxylate and ammonium layers.

As the chiral carboxylate and ammonium layers possess directionality, the single layers with supramolecular chirality also have directionality that can be defined by using the three

distinguishable axes—right and left sides, belly and back sides, and head and tail sides—and adapting them to that of the carboxylate for simplicity.

Finally, the stacking manner of these three kinds of layers determines whether or not supramolecular chirality is generated in the layered crystals (phase III in Figure 3). Stacking of only *P* layers leads to a *P* crystal and stacking of only *M* layers leads to an *M* crystal. A mixture of *P* and *M* layers, however, leads to a *rac* crystal, as does stacking of *rac* layers. Taking into account the directionality of the single layers, there are several ways of stacking them. Indeed, a difference in the stacking of the chiral single layers provides the two types of chiral layered structures observed in the crystals of **1·2** and **1·3**. The gray box in Figure 3 shows selected stacking patterns of the single layers with directionality in the chiral layered structure. It is expected that each single layer contacts in a head-to-tail or head-to-head and tail-to-tail manner. Moreover, each layer is assumed to stack with a rotation of 0, 90, 180, and 270°. In this way, there are at least eight ways to stack a single layer. 4-Methylbenzylammonium myristate (**1·2**) stacks in a head-to-tail manner with a 0° rotation, whereas 4-methylbenzylammonium pentadecanoate (**1·3**) stacks in a head-to-tail manner with a 180° rotation. The difference between the two types of chiral structures arises only from the degree of rotation of the layer stacking, and is presumably due to the even/odd effect of the alkyl chain in the carboxylate.

In summary, we have shown that supramolecular chirality in layered crystals of 4-methylbenzylammonium myristate and pentadecanoate can be understood at the molecular, single-layer, and whole-crystal levels on the basis of a hierarchical interpretation. In a future study, we expect that a correlation between the molecular structure and the stacking manner will reveal the fundamental cause of the generation of this chirality.

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- [9] Crystal data for **1·3**: C₂₃H₄₁NO₂, *M_r* = 363.58, monoclinic, space group *P*₂₁ (no. 4), *a* = 4.7364(6), *b* = 41.125(5), *c* = 5.6194(9) Å, β = 97.76(1)°, *V* = 1084.5(3) Å³, *T* = 93.2 K, *Z* = 2, μ (Cu_{K α}) = 5.31 cm^{−1}, ρ_{calcd} = 1.113 g cm^{−3}, 11804 reflections measured, 1973 of which were unique (*R_{int}* = 0.031) and were used in all calculations. The final *R*1 and *wR*2 values were 0.046 (observed data) and 0.111 (observed data), respectively. CCDC-286085 (**1·2**) and -286086 (**1·3**) 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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