

## Dipole-Induced Polymorphs of *trans*-2-Hydroxycycloheptanecarboxylic Acid with Virtually the Same Unit Cell

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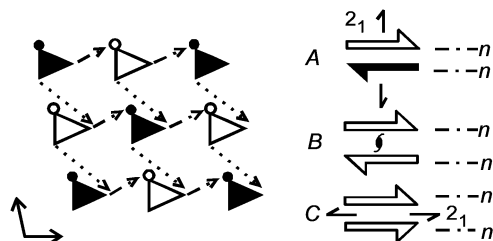
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The present work aims to elucidate how dipole effects govern polymorphism with hallmarks of isomorphism including partial isostructurality.<sup>1</sup> Polymorphism may be induced by conformational and close packing differences such as the monotropic dimorphism (disappearance and reappearance) of 1,2,3,5-tetraacetyl-*O*- $\beta$ -D-ribofuranose,<sup>2a</sup> or simply by different forms of rotation of water molecules.<sup>2b</sup> The polymorphism of *trans*-2-hydroxycycloheptanecarboxylic acid<sup>3</sup> can be attributed to the different ways of dipole cancellation. Dipoles are formed in the antidromic<sup>4</sup> rings of hydrogen-bonded molecules (Figure 1). These dipoles must cancel out over the whole crystal by antiparallel stacking of either molecular layers or crystal domains. In one of the dimorphs (**II**), the layer stacking is antiparallel, whereas in the unit cell of the second form (**I**), the layers are parallel. In the second crystal, the antiparallel alignment of the domains cancels out the dipole moment. However, the dimorphs **I** and **II** possess virtually the same unit cell, indicating a special form of isomorphism.

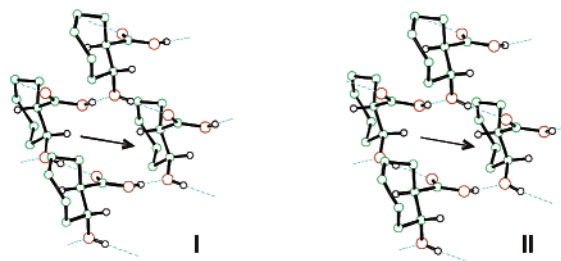
The pattern depicted in Figure 1 was first recognized<sup>6</sup> in the crystal structure of (1*R*\*,2*S*\*,4*S*\*)-4-*tert*-butyl-2-hydroxycyclopentanecarboxylic acid. The ring dipoles are canceled out by the sheets turning upon each other through 180° (Figure 1A) and generating screw axes perpendicular to the layer-building glide plane *n*. The antiparallel layer stacking defines a double layer (stacking mode A), which is then repeated along the monoclinic *b* axis with space group *P*2<sub>1</sub>/*n*.

The layers of the antidromic rings may also be rotated in two other ways. In both cases, screw axes turn the infinite layers upside down, but either perpendicular to (Figure 1B) or parallel with (Figure 1C) the direction of the glide-plane translation. In the perpendicular mode, the layer stacking becomes antiparallel, whereas in the parallel array, the new and old dipoles in the layers remain parallel. Both stacking modes, denoted B and C, define orthorhombic unit cells, as demonstrated by the crystals of the title compound.

When the title compound, crystallized from dibutyl ether and a few drops of *n*-hexane, was prepared for X-ray diffraction, first a poor-quality crystal (denoted **I**\*) revealed an orthorhombic unit cell with systematic absences, suggesting space group *Pnm*2<sub>1</sub>. However, the structure could not be solved. A second crystal from the same batch with the unit cell of **I**\* quite clearly exhibited space group *Pna*2<sub>1</sub>. The phase problem for this crystal (denoted **I**) could be solved, but the refinement converged only to *R* = 0.111 for 1712 reflections. Months later, after several attempts to obtain a better sample of **I**, a novel form (denoted **II**) was isolated from a new batch of crystals obtained from butan-2-one and a few drops of *n*-hexane. The new X-ray data indicated a unit cell with parameters identical to those of **I**. Within this unit cell, two symmetry operators are interchanged along the *b* and *c* axes. To maintain the same



**Figure 1.** Symbolic presentation of the close-packing pattern with heterochiral chains in parallel array. The alicyclic rings are omitted. The black and white triangles differentiate the enantiomers, while their points (two) are the OH groups, and the small circle denotes the CO moiety. Two white and two black triangles in diagonal array, generated by a glide plane *n*, produce the antidromic *R*<sub>4</sub><sup>4</sup>(18) rings.<sup>5</sup> The possible stacking modes of this layer, A, B, and C, are shown by antiparallel and parallel arrows rotated by screw axes around the orthogonal directions.



**Figure 2.** Perspective view of the antidromic *R*<sub>4</sub><sup>4</sup>(18) rings as found in **I** and **II**. The main direction (*c* axis) of the overall dipole is indicated.

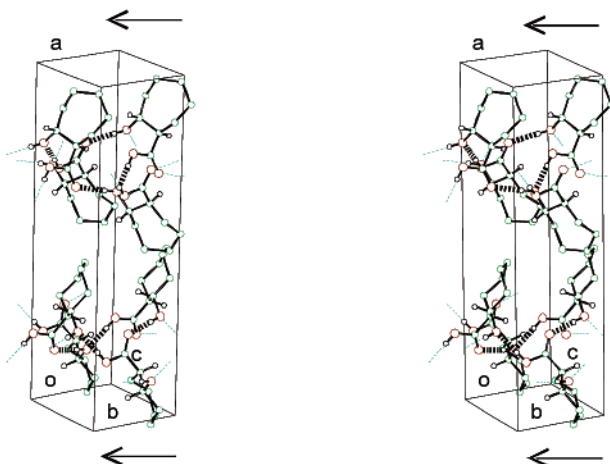
orientation of the unit cell axes from one polymorph to another, the nonstandard space group *Pn*2<sub>1</sub>*a* was ascribed to **II**, which permitted a good refinement, resulting in a final *R* = 0.037 for 1717 observations.

Although structures **I** and **II** differ, within experimental error they display the same geometry<sup>7</sup> of the cycloheptane ring and its functions. The puckering of the tetrameric *R*<sub>4</sub><sup>4</sup>(18) rings formed around the *a* axis by glide plane *n* is also similar (Figure 2). The overall dipole of the tetramer points in the direction of the *c* axis. Within this folded tetramer, the  $\Delta x$  components of the OH...O(H) hydrogen bonds point in opposite directions and therefore compensate each other. In accordance with the alternatives denoted as stacking modes B and C, the rotation of this tetramer along the *b* axis results in the unit cell of **II** (Figure 4), while along the *c* axis it leaves the directions of the ring dipoles parallel (**I**).

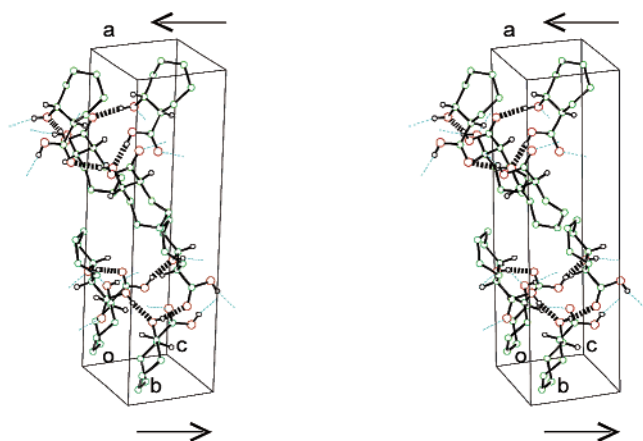
The intrinsic property of antiparallel alignment of domains formed by the unit cells of **I** (Figure 3) can be understood if the unit cells of **I** and **II** are compared. The upper halves of the unit cells are isostructural,<sup>1</sup> while in the lower halves the rotations are mutually perpendicular. As a result, the lower halves are related by a two-fold axis assigned along the *a* axis. It follows that a 180°

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**Figure 3.** Stereoview of the close packing of **I**, showing an upper and a lower  $R_4^4(18)$  ring with *parallel* orientation of the corresponding hydrogen bonds. The direction of the overall layer dipoles is shown by parallel arrows.



**Figure 4.** Stereoview of the close packing of **II**, showing an upper and a lower  $R_4^4(18)$  ring with *antiparallel* orientation of the hydrogen bonds. The direction of the overall layer dipoles is shown by antiparallel arrows. The different choices of origin in space groups  $Pna2_1$  and  $Pn2_1a$  account for the different locations of the tetramers in the unit cells of **I** and **II**.

turn of one of the unit cells around the  $a$  axis reveals the isostructural relationship between the lower layers and vice versa. Accordingly, independently from the upper halves, they are also isostructural.

This relationship between the unit cells explains the nature of domain stacking in **I**. In each domain of **I**, infinite layers of  $R_4^4(18)$  rings are stretched out in the  $bc$  plane. The adjacent layers are held together in a parallel array by weak van der Waals forces. Such domains of **I** with variable thickness are stacked upon each other in antiparallel order. Consequently, each frontier between the antiparallel domains is a double layer of **II** ( $B$  stacking). Thus, **I** unavoidably contains layers of **II** in random sequence. In other words, (a) a pure form of **I** cannot be isolated, (b) the amount of **II** in **I** may vary from crystal to crystal, (c) the presence of **II** terminates the structure refinement of **I**, and (d), finally, with an increasing percentage of **II** in **I**, the superposition of systematic absences shown by space groups  $Pna2_1$  and  $Pn2_1a$  increasingly resembles that of  $Pnm2_1$ . These conclusions were confirmed by (i)

treatment of **I** as a twin of two domains with opposite dipole orientations and (ii) a test of the atomic coordinates of **I** and **II** on the intensities collected from crystal **I**\* archived previously with the uncertain space group  $Pnm2_1$ . The twin refinement did not improve the fit of the model. The anisotropic LSQ treatment of the **I**\* data set with the atomic coordinates of **I** resulted in  $R = 0.155$  for 1718 unique reflections in the space group  $Pna2_1$ , while they did not respond to the atomic coordinates of **II**. This suggests that layers of  $B$  stacking are present among the domains of  $C$  stacking and their amount is higher in **I**\* than in **I**, whereas **II** is formed exclusively by layers of  $B$  stacking.

To summarize, dimorphs **II** (pure form) versus **I** and **I**\* (mixed forms), possessing virtually the same unit cell, involve an unprecedented form of polymorphism. Both forms are built up from the same layer, with different sequences of orientation; therefore, their description as polytypes<sup>8a</sup> (one-dimensional polymorphs<sup>8b</sup>) was also investigated. Because the polytypes, including a few reported cases of organic structures,<sup>8c,d</sup> differ in at least one of their lattice parameters, it is difficult to classify polymorphs **I** and **II** in terms of the IUCr nomenclature of polytypism,<sup>8c</sup> developed exclusively for inorganic crystals, even if the restrictive rules are relaxed.<sup>8f</sup> The question of the relationship between the stacking of **I** and **I**\* or any other sequence of antiparallel domains will form the subject of further investigations.

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**Supporting Information Available:** Crystallographic data on **I** and **II** (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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