BASIC CRYSTAL SYMMETRIES GENERATED BY MOLECULAR DIMERS

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Abstract: *In the last years numerous attempts have been made to recognize deterministic elements of crystallization among the stochastic factors. E.g. a series of crystals, formed by equal amount of mirror related cyclic molecules* $(CH_2)_n$ *n = 5→8, bearing two vicinal hydrogen-bond donor/acceptor functions (e.g. OH, COOH) were found to represent seven of eight patterns of close packing. In each structure there are H-bonded homochiral (⇒⇒⇒⇒) or heterochiral (⇒→⇒→) chains assembled either in antiparallel or in parallel mode. We also revealed that these patterns of basic crystal symmetries can be deduced from the linear or lateral association of molecular dimers with either* C_i, C_2 *or* C_s *symmetry.*

1. BASIC PATTERNS OF CRYSTAL ARCHITECTURE

The crystal structure determinations of numerous 1,2-disubstituted cycloaliphatic molecules such as cyclopentanes, cyclohexanes, cycloheptanes and cyclooctanes resulted in the recognition of basic (almost canonical) patterns of supramolecular close packing (Kálmán *et al.*, 2001; 2002a). In accordance with the files of the Cambridge Structural Database (*CSD*) the patterns represent the most popular space groups assumed by organic molecules in the solid state: $P2_1/c$ (35%), $P\bar{1}$ (19%), $C2/c$ (7%).

1.1 Early fact gathering

The simplicity of the compounds offered an opportunity to study intermolecular hydrogen bond interactions generated by two vicinal (*cis*- or *trans*) functions located on an alicyclic ring: $(CH_2)_n$ n = 5, 6, 7 or 8. Each 2-hydroxy-1-cycloaliphatic-carboxylic acid (functions: OH and COOH) forms two intermolecular hydrogen bonds, while each 2-hydroxy-1-cycloaliphatic-carboxamide (functions: OH and $CONH_2$) forms three. The hydrogen bonds *HB*1 (OH···OC) and *HB*2 (*X*H···OH, *X* = O or N) are independent of the stereoisomerism exhibited by these compounds. Every crystal is *racemic*, which means that each crystal has the same amount (1:1) of mirror related molecules in the unit cell. Overall, the crystal structures investigated (Kálmán *et al.*, 2001) reflected six of eight possible basic patterns of supramolecular self-assembly organised by the parallel or antiparallel arrangement of hydrogen bonded homo- (⇛⇛⇛⇛) or heterochiral (⇛→⇛→) chains of the molecules.

1.2 Deduction of the basic forms of close packing

The ninth pattern, observed first in *trans*-2-hydroxy-1-cyclooctanecarboxylic acid (hereinafter 8T), could not be inferred from the parallel/antiparallel arrays of the molecular chains. It was revealed only by the combination of the *HB*1 and *HB*2 bonds. They, depending on symmetry relationships between the molecules, may generate four motifs: *translation* forms homochiral tapes (*T*), *screw axis* generates helices (*H*), *glide plane* forms heterochiral meanders (*M*), while *inversion center* joins heterochiral rings (*R*). One of their independent combinations (*R*:*R*) corresponds to the linear association of heterochiral (C_1) dimers. Studying this pattern, it became apparent that the linear association of C_1–dimers, joined by twelve membered rings, generates automatically new dimers which are the links between them. These dimers differ in the acceptor group(s) of the hydrogen bonds. The "OC" dimers are formed by the OH···OC hydrogen bonds, whereas the "OH" dimers are formed by the *X*H···OH hydrogen bonds. Along the parallel ribbons of 8T molecules these OC and OH dimers alternate. In other words, the heterochiral connection between two dimers of either type generates the other dimer, and this linear array is therefore unique. It can be regarded as the corner stone of close packing patterns recognized in our works.

This recognition prompted us to generate all of the lateral and linear associations of the dimers maintained by twelve-membered rings with C_1, or C_2 symmetry and assembled either in antiparallel or in parallel mode. They can be classified into six basic patterns of close packing as depicted in Fig. 1 (**1-3**) and Fig. 2 (**4-6**).

1. Linear assoc. of C_1–dimers (OC and OH dimers together): *space group* $P\ \bar{1}$,
2. Lateral assoc. of C_1–dimers in parallel array: *space group* $P\ \bar{1}$,
3. Lateral assoc. of C_1–dimers in antiparallel array: *space group* $C2/c$,
4. Linear assoc. of C_2–dimers polymerized into parallel helices: *space group* $Pca2_1$,
5. Linear assoc. of C_2–dimers polymerized into antiparallel helices: *sp. group.* $P2_1/c$,

6. Lateral assoc. of C_2–dimers polymerized into antiparallel helices: *sp. group.* $P2_1/c$.

In addition, glide planes (C_g) may also form heterochiral dimers without ring closure:

7. Lateral assoc. of C_g–dimers in parallel array: basic *space group Pc,*
8. Lateral assoc. of C_g–dimers in antiparallel array: basic *space group Pn,*
the alternative crystal packings*: space group* either $P2_1/n$ or $Pna2_1$.

Both glide plane-generated patterns **7** and **8** are hallmarked by 18-membered antidromic rings (Jeffrey & Saenger, 1991) which generate significant total dipole moment. Since dipoles must cancel out over the whole crystal, antiparallel stacking of the layers is compulsory. This can be done by screw axes (2_1) either perpendicular to (*space group* $P2_1/n$), or parallel (*space group* $Pna2_1$) with the best planes of the rings.

The synthesis of novel compounds enabled us to demonstrate experimentally all dimer forms (except **7**) by X-ray diffraction.

1.3 Future: Crystal engineering

From these works it was recognised (Kálmán *et al.*, 2002a) that (a) Pattern **1** could easily be deduced from pattern **2** if all *HB*1 bonds turn simultaneously from the respective homochiral chains to their neighbouring enantiomers and *vice versa.* (b) The carboxamide analogue (CO*X*, *X* = NH_2) of 8T (CO*X*, *X* = OH) also crystallises with pattern **1**, therefore they are isostructural (Kálmán *et al.*, 2002b). This prompted us to extend our "symmetry *versus* structure" investigation, termed *combinatorial crystal chemistry*, to novel chemical structures. In accordance with expectation, a superposition of patterns **1** and **2** was obtained by the replacement of –OH function with $-NH_2$ moiety. The series of *cis*-2-amino-1-cyclopentane- to -cyclooctanecarboxylic acids is isostructural in space group $P\bar{1}$. This is a unique case in which the common form of crystallisation is controlled by the *deterministic* formation of the expected hydrogen bond pattern, rather than by the stochastic effects of anisotropic forces.

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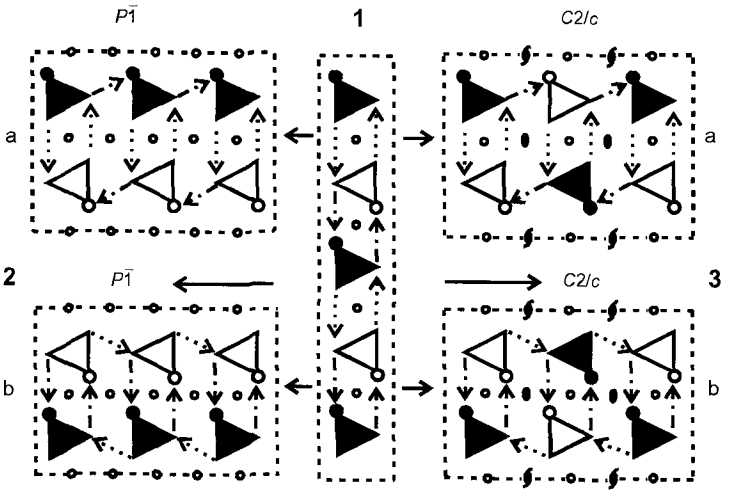

Fig. 1. Linear (**1**) and lateral (**2** and **3**) associations of OH and OC dimers of C_1 symmetry.

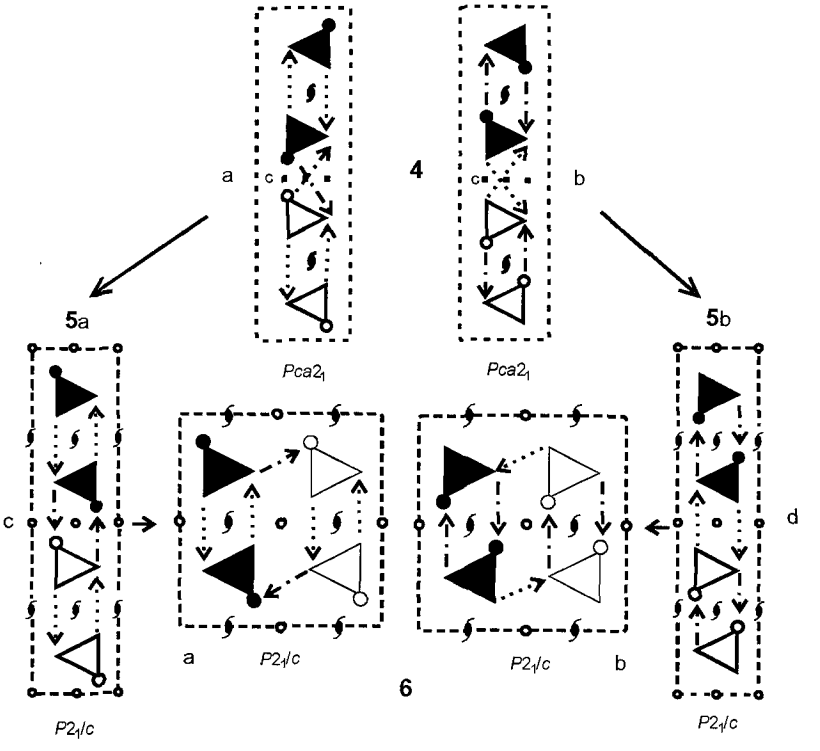

Fig. 2. Linear and lateral associations of homochiral dimers polymerized into parallel (**4**) and antiparallel (**5**, **6**) helices.