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Supramolecular similarities between a diastereomer pair and their truncated derivative: common tetrameric synthon and isostructurality

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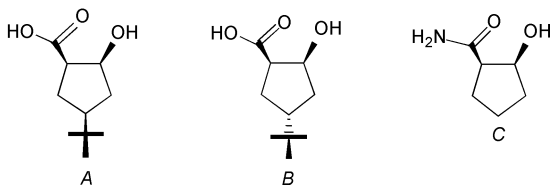
A common tetrameric supramolecular synthon and an unexpected isostructurality reveal similarities between the crystal structures of three related cyclopentane derivatives fused together by OH···O and NH···O hydrogen bonds.

Since the fundamental statements of Lehn[1] the concept that crystals are solid state supermolecules built by connecting molecules with intermolecular interactions has been widely accepted by both organic and structural chemists. In particular, Desiraju[2,3] has made relevant contributions to this concept by classifying the governing principles of supramolecular chemistry. He distinguishes anisotropic long range forces (hydrogen bonds) from the similarly important isotropic van der Waals forces. The magnitude of the latter is proportional to the size of the molecule.[4] From this it follows that packing similarities between crystals of small molecules can primarily be attributed to directional interactions. A basic description of these similarities can be given by means of supramolecular synthons.[2,3] When similarities, expressed by synthons and/or the corresponding graph set notations,[5] extend to the three dimensional arrangement of the molecules, crystals may be homo- or even isostructural.[6,7] Present work demonstrates an inherent relationship between graph set notations, synthons and isostructurality.



Crystal structures of three chemically-related small molecules *A*, *B* and *C* exemplify:

(1) a common tetrameric supramolecular synthon which establishes a genetical connection between the structures of diastereomers *A* and *B*. They crystallize with the two most frequently occurring space groups in CSD,[8] *i.e.* $P2_1/c$ (20%) and $P\bar{1}$ (35.5%).
(2) an unprecedented form of isostructurality discovered between the monoclinic ($P2_1/c$) structures of *B* and its *tert*-butyl-free derivative *C*. The isostructurality[6] of two small molecules differing substantially both in volume (by 33.5%) and shape forced us to reconsider the early view of Kitaigorodskii[9] on the conditions and limits of isomorphism.

The three crystal structures† **A**, **B** and **C** have a common OH···O=C (No. 1), and an alternative (O=C)–XH···OH (X = O for *A* and *B*, or NH for *C*) hydrogen bond (No. 2), respectively. In structure **C** there is an additional –NH···O=C(–$\underline{\text{N}}\text{H}_2$) hydrogen bond (No. 3). Structure **A**, with space group $P\bar{1}$, is composed from pairs of parallel and infinite rows of the 'all-*cis*' diastereomers *A* bound by the hydrogen bonds No. 1 [Fig. 1(A)]. Each row is homochiral and an enantiomer of the other. Each enantiomer pair is fused together by the No. 2 hydrogen bonds around an inversion center located at 0, ½, ½, closing a 12-membered ring described by graph set notation $R_2^2(12)$. This very closed pattern of the No. 1 and 2 hydrogen bonds topologically hinders the formation of the most common synthon **1**[2] between the well separated carboxyl groups. Instead of synthon **1** (Fig. 2), there is a second ring described by the $R_4^4(12)$ graph set notation which is enlarged by two additional –OH moieties from a third and fourth molecule,[10] respectively. This tetrameric synthon (Fig. 2) is located around the inversion center at ½, ½, ½ and repeated by unit translation.

The triclinic $P\bar{1}$ structure of diastereomer *A* is a *par excellence* case of the simplest molecular self-complementarity. Similarly, diastereomer *B* builds up a canonical structure with the most common space group $P2_1/c$. In structure **B** [Fig. 1(B)] hydrogen bonds No. 1 link the glide plane-related molecules parallel with the *c* axis. Pairs of parallel but folded and heterochiral rows are held together by the same tetrameric synthons recognized in the triclinic structure **A**. The $R_4^4(12)$ rings are closed around inversion centers at 0,0,0, 0,0, ½, *etc.* The 'homochiral parts' of this network are constructed by the No. 2 hydrogen bonds around the screw axes at 0,0,¼, 0,0,¾, *etc.*, forming infinite helices around the *b* axis. Thus, the infinite ribbons in structure **A** maintained by centres of inversion and

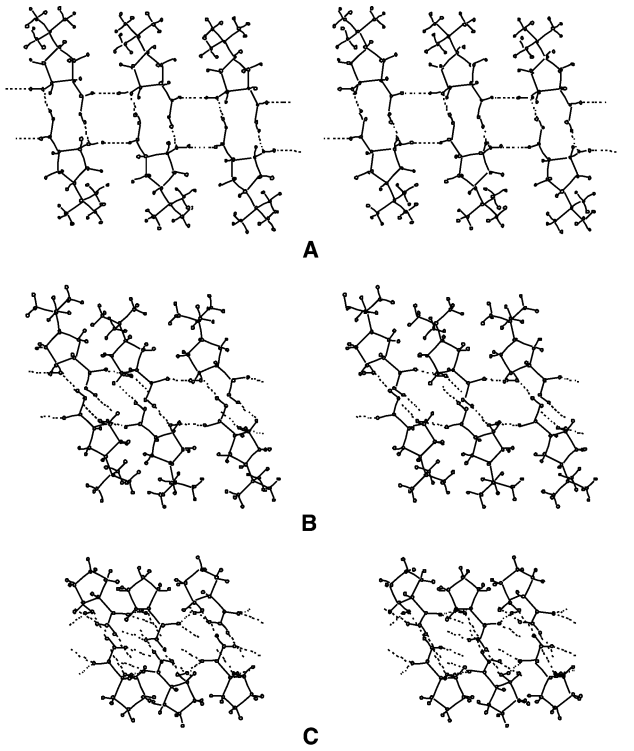


Fig. 1 Stereoview of the structures **A**, **B** and **C**. In **A**, projected in the (−1, −1,0) plane for clarity, hydrogen bonds form C(6) chains and $R_2^2(12)$ dimers. The generated $R_4^4(12)$ rings – identified as a tetrameric synthon – can also be recognized in structures **B** and **C** related by visible degree of isostructurality.

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translation are self-organized into 2D-stacks in structure **B** by the homochiral screw axes and heterochiral glide planes. They jointly generate centres of inversion surrounded by the supramolecular synthons **1***. From structure **A** it follows that the formation of this synthon is sterically preferred. *Mutatis mutandis* [*i.e.* $R_2^2(12)$ dimers of **A** are replaced by C(6) helices] this conclusion is also valid for structure **B**. This underscores the genetic relationship between these structures which can be regarded as *configurational* polymorphs.[11] The close relationship between their space groups $P\bar{1}$ and $P2_1/c$ is also shown[12] by migration and multiplication of pseudo-symmetries 2_1* and *c** in oblique unit cells with space group $P\bar{1}$ and $Z = 8$.

Interestingly, the higher ($P2_1/c$) and the lower ($P\bar{1}$) degree of self-complementarity exhibited by the *B* and *A* molecules equally result in the same packing coefficient[13] (0.68) for structures **B** and **A**. Nevertheless, the predominance of the monoclinic molecular array over a triclinic close packing is shown by the structure of molecule *C* [Fig. 1(C)]. It is a truncated (*i.e. tert*-butyl moiety-free) form of both diastereomers *A* and *B* and instead of a CO_2H group it possesses a $CONH_2$ moiety. However, **B** and **C** are homostructural[6,7] (Fig. 1) which implies that the tetrameric synthon is also retained. Naturally, owing to the OH $\rightarrow$ NH_2 replacement, now it is the enlarged form of the dimeric supramolecular synthon **3** (Fig. 2). From these it follows that the directional[4] hydrogen bond network in structure **B** is so stable that it survives the elimination of the bulky *tert*-butyl moiety. In other words, in special circumstances a small molecule such as *B* can maintain nearly isostructural close packing with an even smaller molecule *C*. Even the presence of an additional supramolecular synthon **4** (Fig. 2) built by hydrogen bond No. 3 cannot alter this pattern either.

The supramolecular synthon **1*** or **3*** is a common hallmark of the structural similarity shown by these related structures. It can be attributed to their special feature, *i.e.* two pairs of donor/acceptor functions maintaining the most common supramolecular cements, the OH···O and NH···O hydrogen bonds, which are located in the vicinal position on a small but flexible (pseudo-rotation) spacer. The *synclinal* position of the 1,2-*cis*-substituents on the flexible cyclopentane ring provides genuine steric conditions to the observed supramolecular arrangement.

This raises the question, how does the *cis*$\rightarrow$*trans* isomerization of the vicinal functions modify the close packing found in these structures? Moreover, how does the migration of the bulky *tert*-butyl moiety influence the pattern so stable in structure **B**? Modeling of structure **B** with molecules *A* revealed that such a packing is hindered by very short H···H contacts (*ca.* 1.15 Å). These and further questions will be answered in a full paper[14] to be published elsewhere.

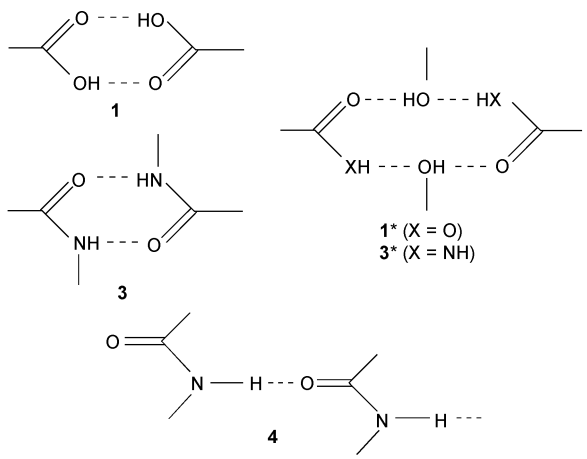

Fig. 2 The tetrameric synthon found in structures **A** and **B**. In **C**, $-CO_2H$ groups are replaced by –CONH moieties. **1**, **3** and **4** are the most common supramolecular synthons as labelled by Desiraju.[2]

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Notes and references

† *Crystal data*: Enraf-Nonius CAD-4, Mo-Kα radiation for **A**, Cu-Kα radiation for **B** and **C**.

For **A**: $C_{10}H_{18}O_3$, M = 186.24, colorless block, triclinic, space group $P\bar{1}$, a = 5.931(1), b = 6.200(1), c = 15.591(3) Å, α = 84.30(4), β = 89.97(4), γ = 62.28(4)°, V = 516.0(2) Å^3, Z = 2, D_c = 1.199 Mg m^{-3}, μ = 0.087 mm^{-1}, T = 293 K, $R(F^2)$ = 0.0477, $R(wF^2)$ = 0.1249, R_{tot} = 0.091, N_o = 2998, N_o/N_v = 24.2.

For **B**: $C_{10}H_{18}O_3$, M = 186.24, colorless block, monoclinic, space group $P2_1/c$, a = 16.862(2), b = 6.104(1), c = 10.519(3) Å, β = 107.03(4)°, V = 1035.2(4) Å^3, Z = 4, D_c = 1.195 Mg m^{-3}, μ = 0.704 mm^{-1}, T = 293 K, $R(F^2)$ = 0.0541, $R(wF^2)$ = 0.1415, R_{tot} = 0.0732, N_o = 2084, N_o/N_v = 16.6.

For **C**: $C_6H_{11}NO_2$, M = 129.16, colorless block, monoclinic, space group $P2_1/c$, a = 11.693(2), b = 7.225(1), c = 7.902(2) Å, β = 103.70(3)°, V = 648.6(2) Å^3, Z = 4, D_c = 1.323 Mg m^{-3}, μ = 0.819 mm^{-1}, T = 293 K, $R(F^2)$ = 0.0406, $R(wF^2)$ = 0.1238, R_{tot} = 0.0437, N_o = 1274, N_o/N_v = 15.2.

CCDC 182/1800. See http://www.rsc.org/suppdata/cc/b0/b005422o/ for crystallographic files in .cif format.

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