

Novel, predicted patterns of supramolecular self-assembly, afforded by tetrameric $R_4^4(12)$ rings of C_2 symmetry in the crystal structures of 2-hydroxy-1-cyclopentanecarboxylic acid, 2-hydroxy-1-cyclohexanecarboxylic acid and 2-hydroxy-1-cycloheptanecarboxylic acid

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Determination of the crystal structures of the homologous ($1R^*,2R^*$)-*trans*-2-hydroxy-1-cyclopentanecarboxylic acid (5T), ($1R^*,2S^*$)-*cis*-2-hydroxy-1-cyclohexanecarboxylic acid (6C) and ($1R^*,2S^*$)-*cis*-2-hydroxy-1-cycloheptanecarboxylic acid (7C) proved a predicted pattern of supramolecular close packing. The prediction was based on the common features observed in the crystal structures of six related 2-hydroxy-1-cyclopentanecarboxylic acids and analogous carboxamides [Kálmán *et al.* (2001). *Acta Cryst.* **B57**, 539–550]. This pattern is characterized by tetrameric $R_4^4(12)$ rings of C_2 symmetry formed from dimeric $R_2^2(12)$ rings. The C_2 symmetry of such tetramers is not common in the literature, usually they have C_i symmetry. Both types of tetramers are formed from dimers with similar or opposite orientation. The $R_2^2(12)$ dimers differ in their hydrogen bonds. In 5T the monomers are joined by a pair of O1–H···O2=C bonds, whereas in 7C they are joined by a pair of O3–H···O1–H bonds. In 6C 60% of the disordered $R_2^2(12)$ dimers are similar to those in 7C, while 40% resemble those in 5T. Apart from these hydrogen-bonding differences and the ring-size differences, the three crystals exhibit isostructurality.

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Dedicated to Professor A. Messmer on the occasion of his 80th birthday.

1. Introduction

In a previous paper (Kálmán *et al.*, 2001) we reported on the crystal structures of six related cyclopentane derivatives,¹ which exhibit five forms of close packing governed by two vicinal functions (either OH *versus* COOH or OH *versus* CONH₂). In each of the six racemic crystal structures there is a common hydrogen bond of the type O–H···O=C (hereinafter *HB1*), which leads to the formation of either hetero- or homochiral chains. These chains are crosslinked by a second hydrogen bond of the type X–H···O–H (X = O or N; hereinafter *HB2*), which can give rise to the formation of homochiral helices, heterochiral meanders or heterochiral dimers. As a result, the chains of *HB1* bonds are arranged either in parallel or in antiparallel mode.

¹ (I): ($1R^*,2S^*$)-2-hydroxy-1-cyclopentanecarboxamide, (II): ($1R^*,2R^*$)-2-hydroxy-1-cyclopentanecarboxamide, (III): ($1R^*,2R^*,4S^*$)-4-*tert*-butyl-2-hydroxy-1-cyclopentanecarboxamide, (IV): ($1R^*,2S^*,4R^*$)-4-*tert*-butyl-2-hydroxy-1-cyclopentanecarboxylic acid, (V): ($1R^*,2S^*,4S^*$)-4-*tert*-butyl-2-hydroxy-1-cyclopentanecarboxylic acid, (VI): ($1R^*,2S^*,5R^*$)-5-*tert*-butyl-2-hydroxy-1-cyclopentanecarboxylic acid.

The five patterns of supramolecular self-assembly (Kálmán *et al.*, 2001) are as follows. In the crystals of (IV) the *HB1* bonds form homochiral (ho) tapes assembled in antiparallel

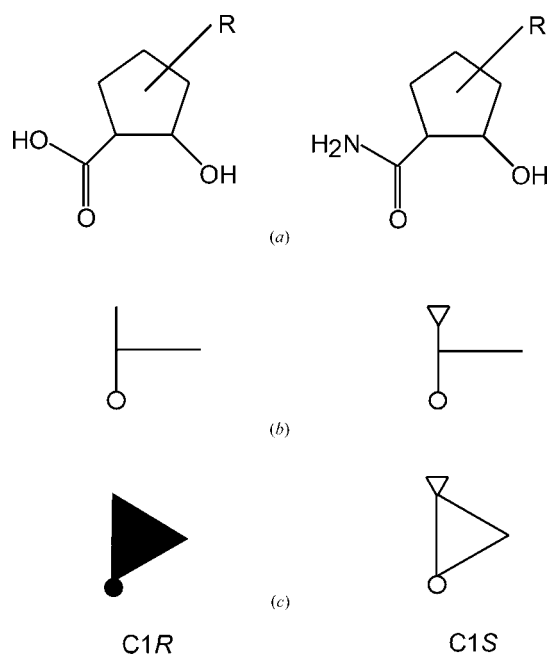


Figure 1
Diagrams symbolizing the functional groups (OH, COOH and CONH₂) on the cyclopentane rings (a). An OH group is denoted by a straight line, the NH₂ group by a triangle and the OC group by a circle (b). To distinguish between the enantiomers, the symbols are presented (c) as white or black (*R* enantiomer) triangles.

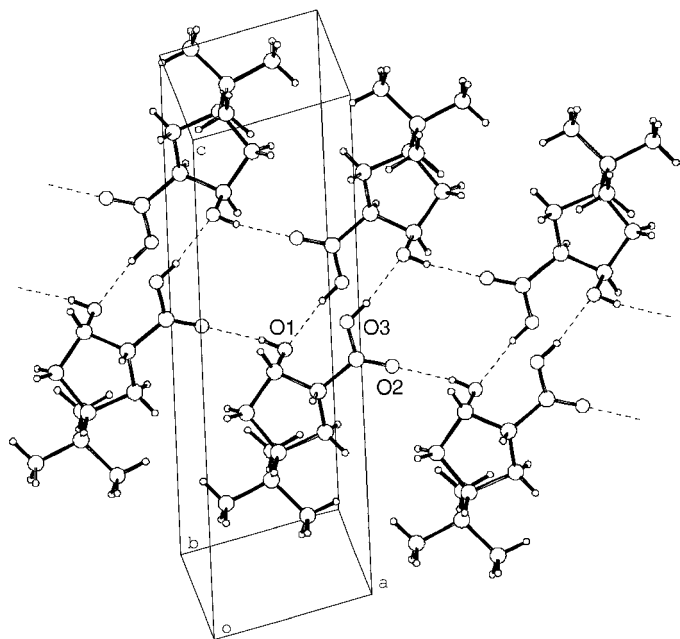


Figure 2
Perspective view of the crystal structure of (IV) showing a translation-generated row of homochiral molecules opposed by a row of $\bar{1}(1\frac{1}{2}, \frac{1}{2})$ center of inversion-related enantiomers. $R_2^2(12)$ and $R_4^4(12)$ rings formed by both dimers and tetramers can be observed.

(a) mode, this pattern therefore being denoted *hoa1*. In (III) the homochiral chains comprise helices, again assembled in antiparallel mode, this pattern being denoted *hoa2*. The isostructural crystals of (I) and (V) are characterized by heterochiral (*he*) meanders in antiparallel mode; this pattern being denoted *hea1*. In contrast, in the crystals of (VI) the heterochiral meanders are parallel (*p*), this pattern therefore being denoted *hep1*. Finally, the structure of (II) is comprised of parallel helices, this pattern being denoted *hop2*.

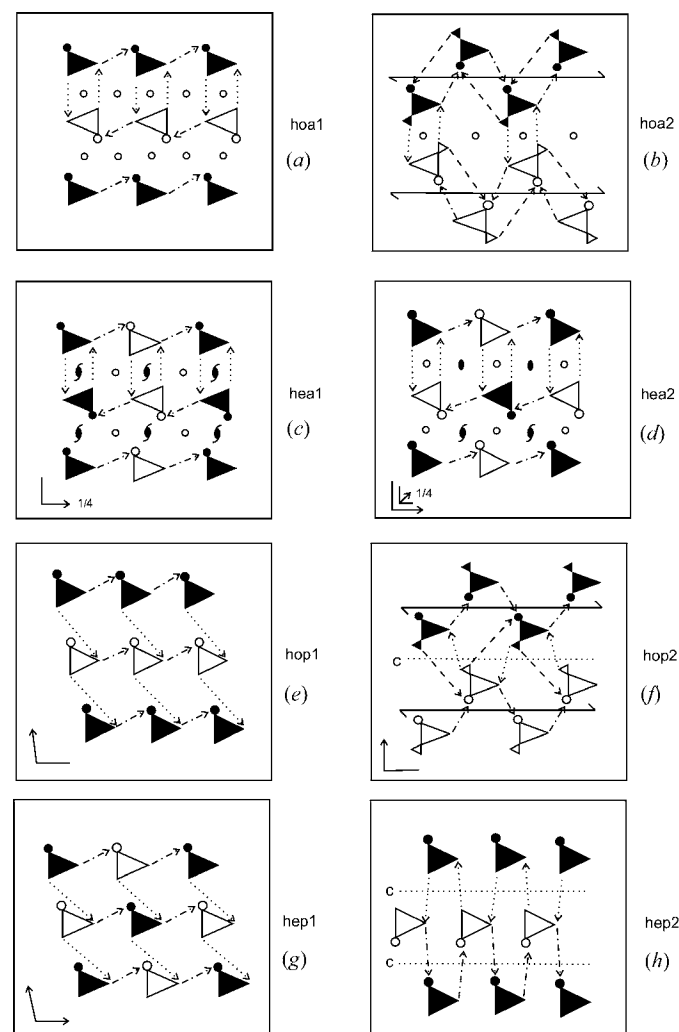


Figure 3
Eight patterns of the supramolecular self-organization of small molecules held together by their common hydrogen bonds O—H...O=C. Homochiral chains in a parallel array give rise to a pattern with space group $Pca2_1$ (*hop2*; Fig. 3e). Here, in (II), the third hydrogen bond is indicated by $-\cdot-\cdot-$. In an antiparallel array, they can be organized either by translation (*hoa1*; Fig. 3a) or *via* a screw axis (*hoa2*; Fig. 3b). In (III) the third hydrogen bond is also indicated by $-\cdot-\cdot-$. The heterochiral chains are organized into antiparallel arrays with space groups $P2_1/c$ (*hea1*; Fig. 3c) and $C2/c$ (*hea2*; Fig. 3d). The self-assembly of heterochiral chains into parallel arrays gives rise to $R_4^4(18)$ rings (Fig. 3g), which are antidromic (Jeffrey & Saenger, 1991). To cancel out the dipoles generated by such layers (pattern *hep1*), in (VI) they are stacked in an antiparallel mode (space group $P2_1/n$). The other two patterns (*hop1* and *hep2*; Fig. 3e and Fig. 3h) were deduced from patterns *hep1* and *hop2*, respectively (see the text).

The characteristic features of these close packings can be symbolized by omitting the five-membered ring from Fig. 1(a) and depicting the functional groups by graphical symbols as in Fig. 1(b). A straight line represents an OH group, a circle a CO group and a triangle an NH₂ group. To distinguish between the C1-*R* and C1-*S* enantiomers, the symbols are converted into black or white triangles (Fig. 1c), respectively. As an example, Fig. 2 shows the crystal structure of (IV) taken from Kálmán *et al.* (2001), while the symbolic presentation of pattern *hea1* is depicted in Fig. 3(a).

The patterns of the other five crystal structures, (I)–(III), (V) and (VI), are also depicted with similar symbols (Figs. 3b, c, f and g). A topological analysis of the motifs (helix, meander, ring and tape) found in the five patterns gave rise to three further patterns: *hea2*, *hop1* and *hep2* (Figs. 3d, e and h). They were deduced as follows.

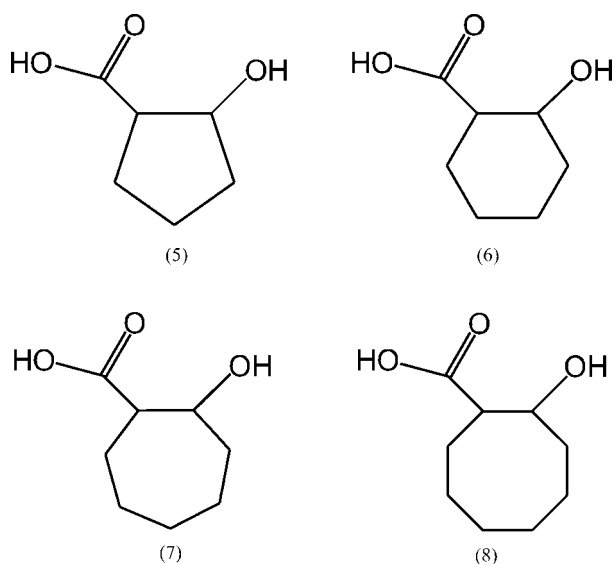


Figure 4

Chemical structures of 2-hydroxy-1-cyclopentanecarboxylic acid (5), 2-hydroxy-1-cyclohexancarboxylic acid (6), 2-hydroxy-1-cycloheptancarboxylic acid (7) and 2-hydroxy-1-cyclooctancarboxylic acid (8). Each structure comprises *cis* and *trans* stereoisomers.

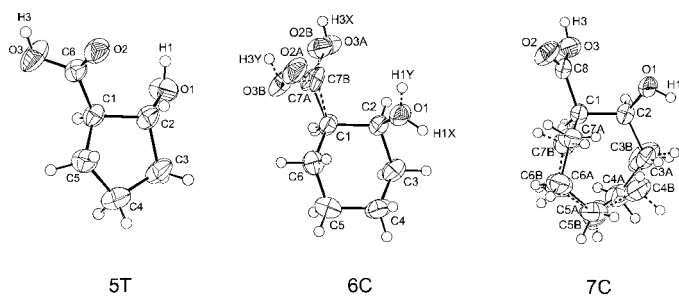


Figure 5

Molecular structures of 5T, 6C and 7C, showing their common atomic numbering. The conformational disorder displayed by 6C (COOH and OH groups) and 7C (cycloheptane ring) is shown by dotted lines.

(i) If the screw axes are omitted from the pattern *hop2* (Fig. 3f), an independent pattern is obtained. The heterochiral meanders of this pattern, denoted *hep2* (Fig. 3h), are equally formed by *HB1* and *HB2* bonds.

(ii) A shift of the central column in pattern *hep1* (Fig. 3g) by half of the corresponding unit-cell vector (π), either upwards or downwards, gives rise to a new pattern, denoted *hop1* (Fig. 3e).

(iii) Finally, if the central row of pattern *hea1* (Fig. 3c) is shifted horizontally by π , the enantiomeric molecules are joined around inversion centers (depicted in Fig. 3d), whereas the $R_4^4(12)$ rings (Etter, 1990; Bernstein *et al.*, 1995) of *hea1* would be coiled into infinite helices. The helical elevation of the adjoining dimers makes such a pattern sterically hindered. To avoid such steric hindrance, twofold axes (2) are necessary. They are provided in space group *P2/c* (No. 13) or in *C2/c* (No. 15). According to Zorky's (1993) close-packing rules, space group *C2/c* is more advantageous than *P2/c*. Indeed, a search of the Cambridge Crystallographic Database (CSD, October 2001 release, 245 932 entries; Allen & Kennard, 1993) shows the space group *C2/c* (7.4%) to be 14 times more frequent than space group *P2/c* (0.5%). The crystal structure determinations of the title compounds substantiated this conclusion: the pattern *hea2* (Fig. 3d) with space group *C2/c* was confirmed.

Our studies on the close-packing behaviour displayed by the six disubstituted and trisubstituted cyclopentane derivatives (Kálmán *et al.*, 2001) have now been extended to the homologous 2-hydroxy-1-cyclohexancarboxylic acids, 2-hydroxy-1-cycloheptancarboxylic acids and 2-hydroxy-1-cyclooctancarboxylic acids. Besides (1*R**,2*R**)-*trans*-2-hydroxy-1-cyclopentanecarboxylic acid (5T), both the *cis* and *trans* stereoisomers of these carboxylic acids (Fig. 4) could be crystallized and subjected to X-ray crystallography. Three of them, 5T, (1*R**,2*S**)-2-hydroxy-1-cyclohexancarboxylic acid (hereinafter 6C) and (1*R**,2*S**)-2-hydroxy-1-cycloheptancarboxylic acid (hereinafter 7C) crystallized in the space group *C2/c*.

2. Experimental

2.1. Synthesis

The syntheses, characterization and chemical reactions of 5T, 6C and 7C were reported earlier (Bernáth *et al.*, 1970, 1972).

2.2. Data collection, structure solution and refinement

Details of the cell data, data collection and refinement are provided in Table 1.² Each data set was collected at room temperature on CAD-4 diffractometers equipped with graphite monochromators. Standard reflections (three for each data collection, measured every 60 min) indicated some crystal decay for the 5T and 6C samples, which were then

² Supplementary data for this paper are available from the IUCr electronic archives (Reference: DE0014). Services for accessing these data are described at the back of the journal.

Table 1
Experimental details.

	5T	6C	7C
Crystal data			
Chemical formula	C ₆ H ₁₀ O ₃	C ₇ H ₁₂ O ₃	C ₈ H ₁₄ O ₃
Chemical formula weight	130.14	144.17	158.19
Cell setting, space group	Monoclinic, C ₂ /c	Monoclinic, C ₂ /c	Monoclinic, I ₂ /c
<i>a</i> , <i>b</i> , <i>c</i> (Å)	17.383 (2), 6.188 (1), 12.361 (1)	21.436 (8), 5.974 (1), 12.095 (3)	22.876 (5), 6.224 (1), 11.793 (2)
β (°)	101.16 (1)	97.70 (3)	95.56 (3)
<i>V</i> (Å ³)	1304.5 (3)	1534.9 (7)	1671.2 (5)
<i>Z</i>	8	8	8
<i>D_x</i> (Mg m ⁻³)	1.325	1.248	1.257
Radiation type	Mo <i>K</i> α	Cu <i>K</i> α	Cu <i>K</i> α
No. of reflections for cell parameters	25	25	25
θ range (°)	13.13–14.26	30.08–34.52	37.13–39.89
μ (mm ⁻¹)	0.106	0.807	0.785
Temperature (K)	293 (2)	293 (2)	293 (2)
Crystal form, color	Block, colorless	Block, colorless	Block, colorless
Crystal size (mm)	0.40 × 0.25 × 0.15	0.40 × 0.25 × 0.03	0.35 × 0.25 × 0.20
Data collection			
Diffractometer	Enraf–Nonius CAD-4	Enraf–Nonius CAD-4	Enraf–Nonius CAD-4
Data collection method	ω -2 θ scans	ω -2 θ scans	ω -2 θ scans
Absorption correction	Psi scan	Psi scan	Psi scan
<i>T</i> _{min}	0.9589	0.7383	0.7707
<i>T</i> _{max}	0.9843	0.9762	0.8588
No. of measured, independent and observed parameters	3396, 1575, 838	1794, 1597, 1287	6926, 1720, 1574
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$	$I > 2\sigma(I)$
<i>R</i> _{int}	0.0217	0.0104	0.0186
θ _{max} (°)	27.97	75.63	75.98
Range of <i>h</i> , <i>k</i> , <i>l</i>	-22 → <i>h</i> → 22 -8 → <i>k</i> → 8 -16 → <i>l</i> → 16	-26 → <i>h</i> → 26 0 → <i>k</i> → 7 0 → <i>l</i> → 15	-28 → <i>h</i> → 28 -7 → <i>k</i> → 7 -14 → <i>l</i> → 14
No. and frequency of standard reflections	3 every 60 min	3 every 60 min	3 every 60 min
Intensity decay (%)	1	16	0
Refinement			
Refinement on	<i>F</i> ²	<i>F</i> ²	<i>F</i> ²
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, <i>S</i>	0.0428, 0.1419, 0.819	0.0356, 0.1355, 1.128	0.0384, 0.1482, 1.377
No. of reflections and parameters used in refinement	1575, 84	1597, 122	1720, 148
H-atom treatment	Mixed	Mixed	Mixed
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.1000P)^2 + 0.0000P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.1000P)^2 + 0.0000P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.1000P)^2 + 0.0000P]$, where $P = (F_o^2 + 2F_c^2)/3$
(Δ/σ) _{max}	0.000	0.001	0.000
$\Delta\rho$ _{max} , $\Delta\rho$ _{min} (e Å ⁻³)	0.18, -0.155	0.189, -0.157	0.151, -0.153

Computer programs used: CAD-4 EXPRESS (Enraf–Nonius, 1992), XCAD4 (Harms, 1996), SHELXS97 (Sheldrick, 1997a), SHELXL97 (Sheldrick, 1997b), PLATON (Spek, 1998).

corrected by means of the program XCAD4 (Harms, 1996). All reflections were corrected for Lorentz and polarization effects. The space groups (uniquely, C₂/c) were determined from unit-cell volume, symmetry and systematic absences. In order to have similar unit-cell projections, the unit cell of 7C was then transformed into a body-centred form with space group I₂/c. The crystallographic phase problems were solved by direct methods, using the program SHELXS97 (Sheldrick, 1997a). The atomic positions for each structure were refined with anisotropic displacement parameters in *F*² mode, with the program SHELXL97 (Sheldrick, 1997b). The positions of the H atoms bound to O atoms were located in difference-Fourier maps, while the others were generated from assumed geometry and were refined isotropically in riding mode. In the final stage of the anisotropic refinement of 7C, conformational

disorder of the cycloheptane ring was recognized. Around the substituted C1 and C2, two ring conformations could be distinguished, with occupancy factors of 0.841 (5) and 0.159 (5), respectively. The greatest positional disorder is displayed by C4. The dominant form is *twist chair*, whereas the other conformation is close to the ideal *chair* shape (Hendrickson, 1967). For 6C, the first stage of refinement was finished at *R*₁ = 0.0410 and *wR*₂ = 0.1318 for 1239 [$I > 2\sigma(I)$] reflections. However, the Hirshfeld (1976) test for the O3–C bond (diff = 11.43 e.s.d.s) strongly suggested the need for revision of the oxygen positions. A rotational (*ca* 180°) disorder of the 1-COOH moiety, accompanied by a similar turn of the 2-OH group, was then revealed. Additional refinement of the revised oxygen positions substantially improved the structure model of 6C (Table 1).

3. Results and discussion

3.1. Survey of the structures at a molecular level

The molecular structures of the title compounds are depicted in Fig. 5. The small but flexible cyclopentane ring of 5T, with puckering parameters of $Q = 0.418$ (3) Å, $\varphi = 169.1$ (33)° (Cremer & Pople, 1975), assumes a conformation intermediate between $C_3(1)$ and $C_2(3)$ (Altona *et al.*, 1968). Similar to the *trans* isomers (II) and (III) (Kálmán *et al.*, 2001), the C6–C1–C2–O1 torsion angle is high: 79.5 (2)°. The homologous cyclohexane ring of 6C exhibits a chair conformation with puckering parameters of $Q = 0.561$ (2) Å, $\varphi = 93.0$ (31)° and $\theta = 176.7$ (2)°. The OH group is axial and the COOH moiety is in the equatorial position. The corresponding C7–C1–C2–O1 torsion angle is 60.1 (1)°, which is substantially larger than the mean value of 48.0 (3.4)° for the four *cis*-1,2-disubstituted cyclopentane derivatives (Kálmán *et al.*, 2001). The conformational disorder of the cycloheptane ring in 7C (85% is close to a *twist chair*, while 15% assumes a *chair* conformation; Hendrickson, 1967) has no influence on the torsion angle of the axial hydroxy and equatorial carboxyl groups; it is again low: 52.9 (1)°.

3.2. Hydrogen-bond networks

3.2.1. Close-packing pattern hea2 and isostructurality. The three crystal structures are depicted in Figs. 6–8. In accordance with the pattern hea2 (Fig. 3*d*), an infinite ladder of $R_2^2(12)$ dimers joined laterally (*i.e.* *ca* perpendicularly to the principal dimer axis) is developed along the *c* axis by hydrogen bonds (Table 2). From patterns hoa1 and hea2 it follows that a lateral junction between $R_2^2(12)$ dimers (and analogous helices, *e.g.* hea1) automatically generates $R_4^4(12)$ rings. In 7C the meanders are formed by HB1 bonds, while in 5T the meanders are formed by HB2 bonds. Consequently, the hydrogen bonds also differ in the $R_2^2(12)$ dimers. As shown by the schematic view in Fig. 9, the monomers are joined by a pair of O1–H...O2=C (HB1) bonds in model (a), whereas in model (b) they are joined by a pair of O3–H...O1–H (HB2) bonds. Models (a) and (b) further differ in the directions of the hydrogen bonds in the tetramers of C_2 symmetry. In model (a) the C=O moieties are embedded in the dimers, whereas in model (b) they form the links between the dimers. These models,

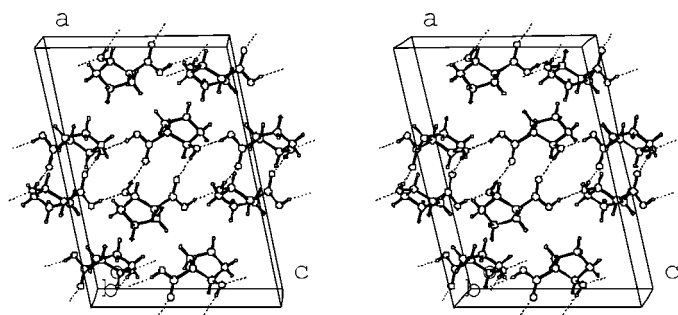


Figure 6
Stereoview of the crystal structure 5T, showing the hydrogen-bonded $R_2^2(12)$ OC dimers and $R_4^4(12)$ tetramers.

however, can be interconverted by a simultaneous rotation of both OH and COOH groups by *ca* 180°. The dimers are distinguished here in terms of the acceptor group, which is either OC (5T) or OH (7C), these patterns being denoted hea2_C and hea2_H, respectively. In 6C disorder of the two dimers was found, with a ratio of 6:4 in favour of the pattern hea2_H.

In each case, the structure-cementing $R_4^4(12)$ tetramers of C_2 symmetry, resembling a hammock stretched between two trees, are similarly folded around the twofold axes. The shape of the tetramers is elongated because of the substantial

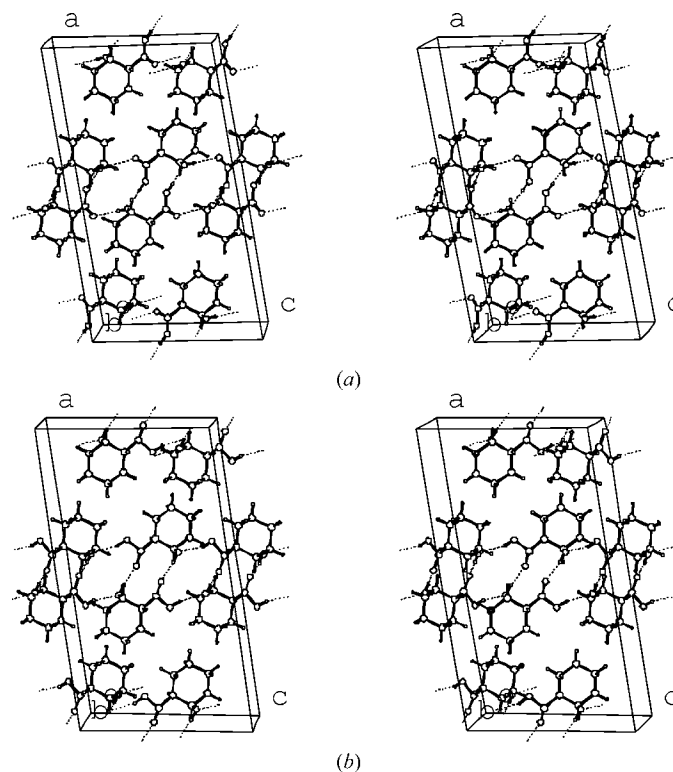


Figure 7
Stereoview of the crystal structure 6C, showing the hydrogen-bonded $R_2^2(12)$ dimers and $R_4^4(12)$ tetramers. 60% of the disordered structure is formed by (a) OH dimers and 40% by (b) OC dimers.

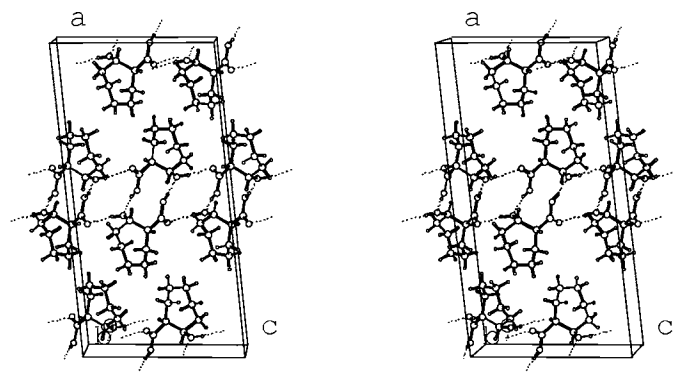


Figure 8
Stereoview of the crystal structure 7C, showing the hydrogen-bonded $R_2^2(12)$ OH dimers and $R_4^4(12)$ tetramers. To provide the same view of the close packing as in Figs. 6 and 7, the unit cell is transformed into its body-centred form with space group $I2/c$.

Table 2
Hydrogen bonds and their descriptors.

	5T	6C (40%)	6C (60%)	7C
O1—H1(xy z)···O2	$-x, -y + 1, -z$	$-x, -y, -z$	$x, -y, z + \frac{1}{2}$	$x, -y, z + \frac{1}{2}$
$D \cdots A$ (Å)	2.770 (2)	2.69 (1)	2.724 (2)	2.792 (1)
$H \cdots A$ (Å)	1.95	1.89	1.92	2.00
$\angle D-H \cdots A$ (°)	177.5	165.5	167.4	162.1
Symmetry operator	Inversion center	Inversion center	Glide plane	Glide plane
O3—H(xy z)···O1	$x, -y + 1, z - \frac{1}{2}$	$x, -y, z - \frac{1}{2}$	$-x, -y, -z$	$-x, -y, -z$
$D \cdots A$ (Å)	2.619 (2)	2.717 (6)	2.67 (1)	2.642 (1)
$H \cdots A$ (Å)	1.81	1.92	1.87	1.83
$\angle D-H \cdots A$ (°)	166.5	163.4	164.7	169.8
Symmetry operator	Glide plane	Glide plane	Inversion center	Inversion center

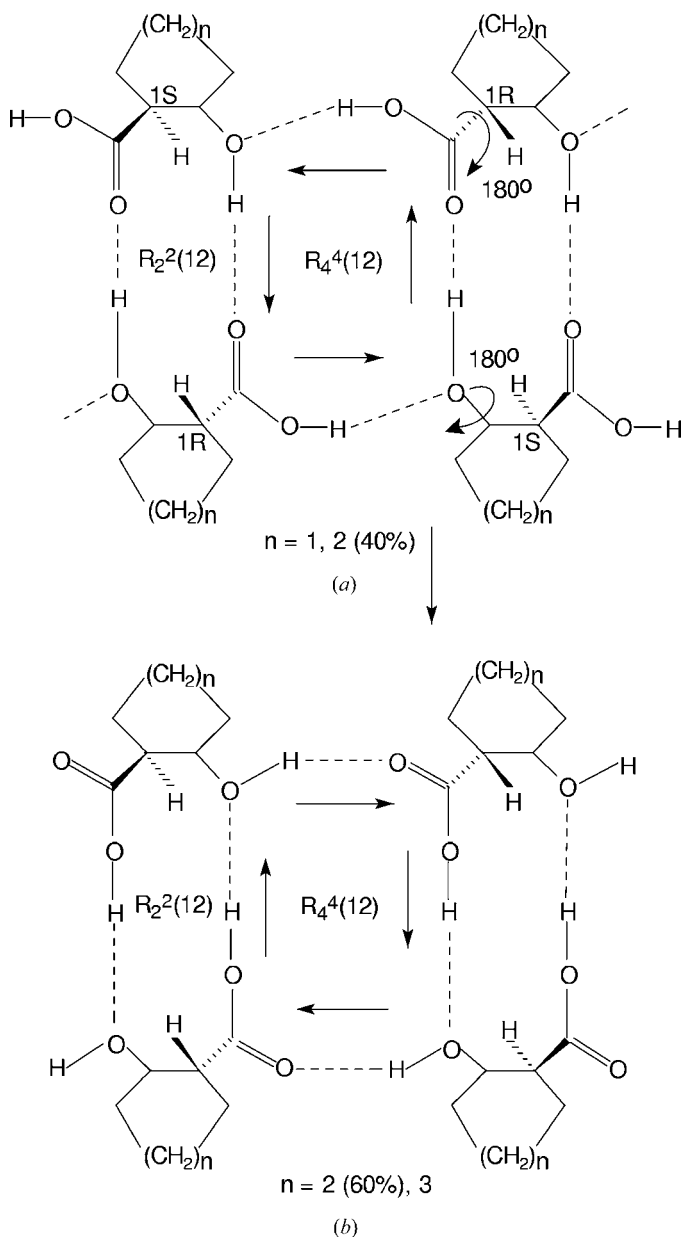


Figure 9
Schematic view of (a) the OC and (b) OH dimers held together in the form of $R_4^4(12)$ tetramers of C_2 symmetry. The ring size is given by $n = 1, 2$ and 3 for cyclopentane, cyclohexane and cycloheptane. The OC and OH dimers can be interconverted by simultaneous rotation (*ca* 180°) of the COOH and OH moieties. The homodromic (Jeffrey & Saenger, 1991) character of the rings formed by the tetramers is shown by the direction (anticlockwise *versus* clockwise) of the arrows.

separation of the carboxyl groups (Figs. 6–8). Both hydrogen-bonded tetrameric rings are homodromic (Jeffrey & Saenger, 1991), but the directions of the hydrogen bonds are opposite (Fig. 9). If the chirality of C1 in the upper right corner of both models is *R*, then in $hea2_C$ it is anticlockwise, while in $hea2_H$ it is clockwise. In accordance with the empirical close-packing rules (Zorky, 1993), the apolar regions of the molecules are related by screw axes. This results in space group $C2/c$, with similar close packing for 5T, 6C and 7C. In a first approach, their similarity is demonstrated by the low unit-cell similarity indices $\Pi_{6C-7C} = 0.04$ and $\Pi_{5T-6C} = 0.09$ (Kálmán *et al.*, 1993). At a deeper level this similarity is indicated by the volumetric indices of isostructurality (I_v ; Fábián & Kálmán, 1999). With regard to the fact that the volumes of the cyclopentane, cyclohexane and cycloheptane rings differ by 16–40%, an I_v value of 68% indicates significant close-packing similarity between 6C (*chair*) and 7C (*twist-chair/chair*). The significant differences in ring puckering (see above) and stereoisomerism of 5T and 6C give rise to a lower index of isostructurality ($I_v = 45\%$; Fábián & Kálmán, 1999). Nevertheless, Figs. 6–8 clearly reveal the homostructurality (Kálmán & Párkányi, 1997) between 5T, 6C and 7C.

3.2.2. Lateral association of heterochiral $R_2^2(12)$ dimers to form $R_4^4(12)$ tetramers. In contrast with the first structure determinations (Kálmán *et al.*, 2001), the roles of the HB1 and

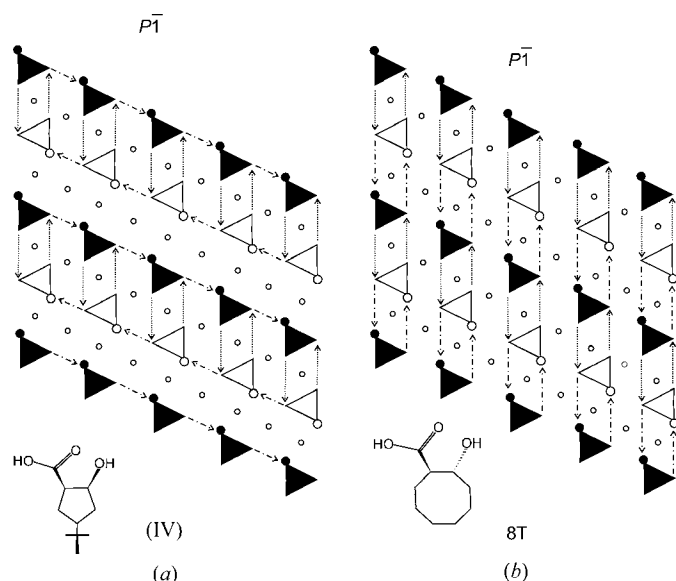


Figure 10
Projections of the molecular symbols applied for the structures of (IV) and (1*R**,2*R**)-*trans*-2-hydroxy-1-cyclooctanecarboxylic acid (8T). The structure of (IV) with the pattern $hoal_H$ can be converted with the same space group $P\bar{1}$ into that of 8T if all HB1 bonds (----->) are turned simultaneously by *ca* 120° to the enantiomeric molecules in the same columns. The OH and OC dimers thus form infinite rows.

HB2 bonds in *5T* versus *7C* proved interchangeable. In *6C* the exchange is partial, only 40% of the heterochiral $R_2^2(12)$ dimers being joined by *HB1* bonds. *5T*, *7C* and in particular the mixed structure demonstrate the equal importance of *HB1* and *HB2* bonds. It follows that each of the patterns depicted in Fig. 3 (except for *hep1* and *hep2*) has a counterpart in which the roles of the two hydrogen bonds are exchanged.

The equivalence of the OC and OH dimers shown in Fig. 9 suggested analysis of their topological combination. The lateral association of these dimers may take place with identical (homochiral, *i.e.* black-to-black-to-black...) or alternating (heterochiral, white-to-black-to-white...) orientation of the enantiomers. With identical orientation, OH dimers form tetramers arranged in rings, compatible with the simplest racemic space group $P\bar{1}$ (Fig. 2). Similar $R_4^4(12)$ tetramers, likewise with C_i symmetry, may be assembled from the OC dimers. In contrast, when the OH or OC dimers are connected with alternating (heterochiral) orientation, the tetramers assume C_2 symmetry. The OC dimers afford the tetramers observed in *5T* (Fig. 6), whereas the OH dimers yield the tetramers that occur in *7C* (Fig. 8). Besides these four lateral associations (patterns *hoa1_H*, *hoa1_C*, *hea2_H* and *hea2_C*), there exists only one linear association of the heterochiral OH and OC dimers. This pattern (Fig. 10*b*) can be obtained from that of *hoa1_H* (Fig. 10*a*) if all *HB1* bonds turn simultaneously from the respective homochiral chains to their neighboring enantiomers. The result is a linear association of $R_2^2(12)$ dimers joined alternately by *HB1* and *HB2* bond pairs. In other words, the linear association of two dimers (either OH or OC) with C_i symmetry automatically generates the other type of dimer. Recently, this pattern was experimentally demonstrated. Molecules of (1*R**,2*R**)-*trans*-2-hydroxy-1-cyclooctanecarboxylic acid (hereinafter *8T*) crystallize with this pattern (Kálmán *et al.*, 2002). This crystal structure confirms

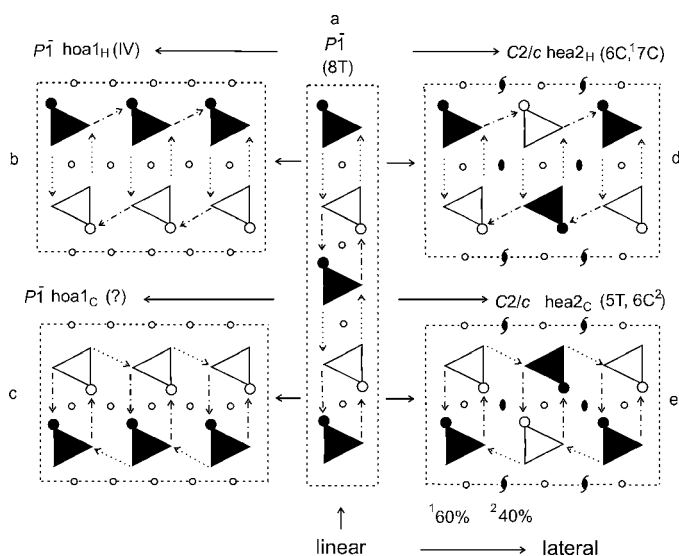


Figure 11

The four possible forms of lateral association of OC and/or OH dimers and their relationship to the only permitted linear sequence of the heterochiral dimers. The corresponding crystal structures and their space groups are also listed.

the equal importance of the *HB1* and *HB2* bonds, revealed by the crystal structures of the title compounds. This pattern, depicted in Fig. 10(*b*), is shown by a single row in the center of Fig. 11. Its connection to the four patterns based on heterochiral $R_2^2(12)$ dimers underscores the close relationship between the patterns, irrespective of their C_i and/or C_2 symmetry.

Finally, it is worth noting that $R_4^4(12)$ tetramers with C_2 symmetry are not common in the literature. A search among the files archived in the CSD (Allen & Kennard, 1993) revealed *ca* 70 entries involving $R_4^4(12)$ tetramers. They are formed almost exclusively around inversion centers, mostly in the space group $P2_1/c$. In only one of the five structures (FUCKOD, HXMACA10, PYZDCX, SURYUZ and YAWHUZ) solved in centred space group No. 15 ($C2/c$, $I2/a$ or $I2/c$) does the $R_4^4(12)$ tetramer have twofold symmetry. In ethylene-diammonium-*N,N,N',N'*-tetraacetic acid sulfate monohydrate (YAWHUZ), two carboxylic groups with two water molecules join an $R_4^4(12)$ tetramer around a twofold axis (Shkolnikova *et al.*, 1993).

4. Conclusions

After early fact-gathering on the supramolecular similarities (Kálmán *et al.*, 2000) exhibited by six cyclopentane derivatives, three further basic patterns of molecular close packing were deduced (Kálmán *et al.*, 2001). One of them, pattern *hea2*, was revealed in structures *5T*, *6C* and *7C*, which exhibit isostructurality. Each structure possesses a tetramer arranged in an $R_4^4(12)$ ring with C_2 symmetry. Irrespective of their symmetry (either C_i or C_2), such tetramers are formed whenever the two $R_2^2(12)$ dimers are joined laterally. In accordance with Zorky's (1993) close-packing principles, these tetramers, as templates, result in crystals that with high probability assume the space group $C2/c$ and their isostructurality is deterministic. The linear association of heterochiral dimers (*8T*) and patterns in which heterochiral dimers are fused to homochiral helices (*i.e.* dimers with C_2 symmetry are polymerized into helices; Zorky, 1993) will be discussed in a future paper (Kálmán *et al.*, 2002).

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