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# Two polymorphs of a β-lactam (*trans*-13-azabicyclo[10.2.0]tetradecan-14-one). Concomitant crystal polymorphism and isostructurality

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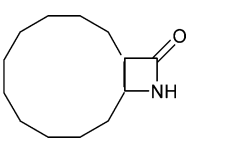
**Two polymorphs of *trans*-13-azabicyclo[10.2.0]tetradecan-14-one display a unique example of isostructurality, differing only in the orientation of a given hydrogen bond with respect to the β-lactam bond. This slight difference can be attributed to the twofold rotation of the carbocyclic macroring of $C_2$ symmetry, which in the crystal structure is hardly noticeable.**

Polymorphs[1] can in general be recognized by virtue of their different unit cell parameters and often from the different crystal symmetries. In contrast, the present paper reports on an uncommon form of polymorphism, involving topographically different orientations of a given NH···O hydrogen bond. Polymorph **I** crystallized from methanol, whereas the twinned crystals of **II** grew from acetone. Both polymorphs are monoclinic and their orthogonal (*b*) axes accommodate the homochiral helices of azetidin-2-one moieties linked by hydrogen bonds. The fact that the *b* axis is considerably longer in **I** (7.629 Å) than in **II** (7.267 Å) can be attributed to the different orientations of the O lone-pair electrons that accept the hydrogen bond. The hydrogen bond arrangement may be either antiperiplanar (**I**) or synperiplanar (**II**) with respect to the endocyclic amide bond of the planar β-lactam ring.

We recently investigated the basic forms[2] of supramolecular self-assembly of small chiral molecules (*e.g.* 2-hydroxy-cyclopentanecarboxylic acids and carboxamides and their cyclohexane, cycloheptane and cyclooctane homologues) linked by two or three hydrogen bonds of OH···O and NH···O types in racemic crystals. To study the close packing of similarly small molecules linked by only one hydrogen bond, we have focused our interest on β-lactams. Compounds in which the azetidin-2-one moiety is *cis*-fused to a cyclopentane[3] or a cyclohexane[4a] ring form monoclinic crystals which display isostructurality, whereas the cycloheptane[4b] derivative is orthorhombic. The length of their common, helix-bearing axis increases monotonously in the interval 6.147–6.683 Å. In contrast, the structure of 4-methyl-10-aza-*trans*-bicyclo[7.2.0]-undeca-2,5,7-trien-11-one[5] involves a shorter orthogonal axis (5.706 Å). In spite of this and the *trans* junction, it demonstrates a relaxed form of isostructurality[6a] with the cyclopentane- and cyclohexane-fused derivatives. To shed light on these phenomena, the title compound (Scheme 1) was selected for further investigation. The first X-ray-quality crystals (**I**) were obtained from methanol. The orthogonal *b* axis of the monoclinic structure is substantially longer (7.629 Å) than that in the *cis*-fused cycloheptane derivative (6.683 Å), which indicates an elongation of the azetidin-2-one helices.† The crystals of **II** are twinned; the twin domains are related by a rotation of 180° around the *a* axis. The *b* axis of this monoclinic crystal, which invariably bears the homochiral chains of hydrogen-bonded β-lactam rings, is shorter by 0.362 Å than that in **I**. Accordingly, the *a* and *c* axes are somewhat longer than those in **I**; $\Delta a = 0.104$ and $\Delta c = 0.452$ Å. The low unit cell similarity index[6a] ($\Pi = 0.008$) and the high volumetric index[6b] ($I_v = 75\%$) indicate that **I** and **II** are isostructural; their common space group is $P2_1/c$.




**Scheme 1**

Polymorphs **I** and **II** can be distinguished only *via* the different orientations of a given hydrogen bond with respect to the β-lactam bond. The azetidin-2-one rings in the flattened helices may assume one or other of two orientations: (a) the C=O bonds are nearly perpendicular to, or (b) nearly parallel to the screw axis. In the former case (Fig. 1A), only the O lone pairs distal to the β-lactam bonds can form hydrogen bonds with the neighbouring molecules. These molecules are linked by hydrogen bonds that are antiperiplanar to the β-lactam bond. In the latter case (Fig. 1B), the proximal O lone pairs form the hydrogen bonds, which are synperiplanar to the β-lactam bond. The result is a shorter *b* axis. The formation of **I** and **II** from different solvents is facilitated by the almost perfect $C_2$ symmetry of the 12-membered rings

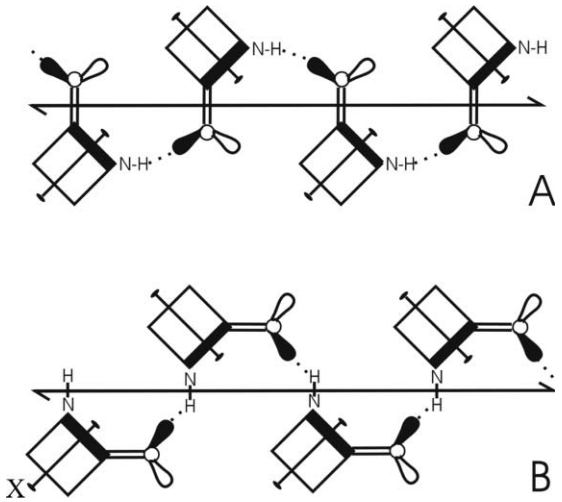



**Fig. 1** Symbolic presentation of the flat azetidin-2-one helices. For clarity, the alicyclic rings are omitted; only the directions of their twofold axes ($C_2$) with respect to the screw axis are indicated. (A) The C=O groups of the β-lactam rings intersect the screw axis, while the N–H bonds are nearly parallel to the screw axis. In this array the O lone-pair electrons (black) distal to the C–N β-lactam bond (bold) form the N–H…O=C hydrogen bond, which makes an antiparallel torsion angle with the β-lactam bond. (B) A turn of 180° around the $C_2$ axes of the ″omitted″ cyclododecane rings replaces the C=O moieties by the N–H bonds. Consequently, the O lone-pair electrons (black) pointing toward the screw axis are involved in the hydrogen bond synperiplanar with the β-lactam bond, while the direction of the hydrogen bonds is altered.

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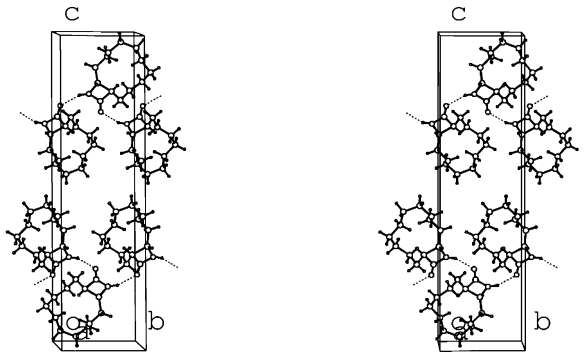


**Fig. 2** Stereoview of the close packing of **I**, formed by two antiparallel helices; space group $P2_1/c$.

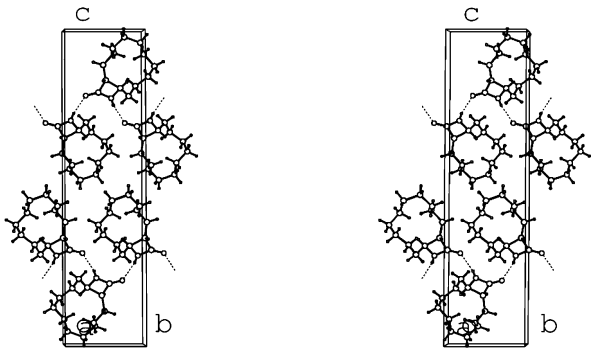


**Fig. 3** Stereoview of the close packing of **II**. It can be seen that in **I** and **II** the positions of the cyclododecane rings are the same; only the positions of the C=O and N–H groups are interchanged.

(Fig. 2 and 3). A turn of the molecules through 180° around the molecular $C_2$ axis tilted at *ca.* 45° to the screw axis alters only the orientation of the O=C–N–H moiety, while rotation of the alicyclic ring leads to no noticeable effect. The visible result is either the anti- or the synperiplanar N–C=O···N′ torsion angle.

To check the solvent dependence of the observed polymorphism, novel crystals were obtained from diisopropyl ether. The diffraction pattern exhibited by these crystals (**III**) could be indexed with an orthorhombic unit cell, two axes of which are the same as those in **I**, while the third axis is tripled. The one-dimensional polymorphism (*i.e.* polytypism)[7a,b] with a tripled unit cell is the first example of a previously unrecognized phenomenon among organic crystals: the polytypes of D,L-homocysteine thiolactone hydrochloride[7c] and 2,2-aziridinedicarboxamide,[7d] for instance, are related by doubled cells. The structure of **III** was solved in space group $P1$, but the refinement, based on data collected by a serial diffractometer, could not be completed beyond $R(F^2) = 0.29$. Twelve molecules are stacked upon each other along the *c* axis. In **I** and **II** the hydrogen bonded chains are homochiral with $2_1$ symmetry, whereas in **III** they are heterochiral with some sort of disorder. The chirality of the chains is determined by the cyclododecane rings of $C_2$ symmetry. The disorder of the chains in **III** may be attributed to the space-filling similarities of the enantiomeric molecules. They may replace each other at random in the hydrogen-bonded chains. The imperfect replacement of the $2_1$ axes by glide planes *n* leads to the new ribbon being folded, but the length of the unit cell does not change in the direction of the propagation.

To summarize, the polymorphs **I** and **II** are isostructural. Only the dimorphs of *trans*-2-hydroxycycloheptanecarboxylic acid,[8] with virtually the same unit cell, are known to display a similar phenomenon. However, both cases of polymorphism with isostructurality are clearly distinct from the polytypism[7e,f] represented by **I** and **III**. The elucidation of the polytypic stacking in **III** is in progress.

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## Notes and references

† Crystal data: Enraf Nonius CAD-4, Cu-K$\alpha$ radiation, $\lambda = 1.54184$ Å. For **I**. $C_{13}H_{23}NO$, $M = 209.32$, colourless block, monoclinic, space group $P2_1/c$, $a = 5.858(1)$, $b = 7.629(1)$, $c = 28.237(3)$ Å, $\beta = 97.97(1)°$, $V = 1249.7(3)$ Å$^3$, $Z = 4$, $D_c = 1.113$ Mg m$^{-3}$, $\mu = 0.532$ mm$^{-1}$, $T = 293$ K, $R(F^2) = 0.0389$, $R(wF^2) = 0.1121$, $R_{tot} = 0.0710$, $N_o = 2599$, $N_o/N_v = 16.3$.
For **II**. $C_{13}H_{23}NO$, $M = 209.32$, twinned, colourless plate, monoclinic, space group $P2_1/c$, $a = 5.962(1)$, $b = 7.267(1)$, $c = 28.689(1)$ Å, $\beta = 94.90(1)°$, $V = 1238.4(3)$ Å$^3$, $Z = 4$, $D_c = 1.123$ Mg m$^{-3}$, $\mu = 0.536$ mm$^{-1}$, $T = 293$ K, $R(F^2) = 0.0830$, $R(wF^2) = 0.2765$, $R_{tot} = 0.1221$, $N_o = 6416$, $N_o/N_v = 46.8$.† For **III**. $C_{13}H_{23}NO$, $M = 209.32$, colourless plate, orthorhombic, $a = 5.862(1)$, $b = 7.631(1)$, $c = 83.900(5)$ Å, $V = 3753.1(8)$ Å$^3$, $Z = 12$, $D_c = 1.111$ Mg m$^{-3}$, $\mu = 0.531$ mm$^{-1}$, $T = 293$ K. The structure in the ″tripled unit cell″ of **I** was solved in space group $P1$ with $R(F^2) = 0.2991$, $N_o = 30296$. CCDC 241104–241105. See http://www.rsc.org/suppdata/cc/b4/b408505a/ for crystallographic data in .cif or other electronic format.

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