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A case of concomitant polymorphism and spontaneous resolution: the tetragonal phase of 5-hydroxymethyl-7,7,*N*-trimethyl-6-oxabicyclo[3.2.1]-octane-1-carboxamide

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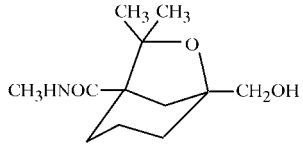
The title compound, $C_{12}H_{21}NO_3$, crystallizes in two polymorphic forms, *viz*. the tetragonal form described here and the monoclinic form described previously [Foces-Foces, López-Rodríguez, Pérez, Martín & Pérez-Hernández (2007). *Cryst. Growth Des.* **7**, 905–911]. The differences in the conformations of the hydroxymethyl and methylaminocarbonyl substituents have important consequences in the hydrogen-bond interaction motifs and, therefore, in the packing arrangements. These forms are concomitant polymorphs with melting points differing by 3 K.

Comment

The structures of ten 7,7-dialkyl-5-hydroxymethyl-6-oxabicyclo[3.2.1]octane-1-carboxamide derivatives, including the monoclinic polymorph, (I), of the title compound, have been determined recently (Foces-Foces *et al.*, 2007). All the reported compounds crystallized as racemates, and the conformations of the hydroxymethyl and *N*-alkylamide groups were found to be closely related to the type of hydrogen-bond interactions in which they were involved. As part of our structural studies on the inclusion of water molecules into the hydrogen-bond pattern of condensed organic materials, new crystallization attempts of *N*-alkylamide derivatives in saturated aqueous solutions of tetrachloromethane/*n*-hexane were undertaken. In the case of 5-hydroxymethyl-7,7,*N*-trimethyl-6-oxabicyclo[3.2.1]octane-1-carboxamide, crystals with different habits (plates, and needles in a small quantity) were observed in the same batch, suggesting the presence of concomitant polymorphs (Bernstein, 2002).

The plates of (I) belong to the centrosymmetric monoclinic $P2_1/c$ group, while the needles, (II), crystallize in the noncentrosymmetric tetragonal $P4_1$ or the enantiomeric $P4_3$ space group. However, these crystals, which were separated manually, did not show optical activity, suggesting spontaneous resolution (50:50 mixture of pure enantiomers) of the racemic sample. Several new crystallization attempts were performed under similar conditions and only the monoclinic phase was obtained. This behaviour seems to be not uncommon and has been previously (Dunitz & Bernstein, 1995) and recently reported (Lennartsson *et al.*, 2007). In the alkylaminocarbonyl derivatives with ethyl as the alkyl group and with propyl instead of methyl substituents, crystals slightly different in shape appear in the same batch, but all were confirmed to belong to the form described previously.



(II)

Of the two possible enantiomeric space groups $P4_1$ or $P4_3$ for the tetragonal form (II), the former, consistent with the 1*R*,5*R* enantiomer (negative value for the C1—C2—C3—C4 torsion angle), was selected (Fig. 1), since the absolute structure cannot be determined reliably. In both polymorphic forms, the bicyclic core is rather rigid and the features distinguishing the forms concern the conformations of the hydroxymethyl and methylaminocarbonyl substituents, which result in different hydrogen-bond patterns. In the monoclinic form, having $Z' = 2$, the hydroxy group is disordered over two positions (*A* and *B*, with occupancies of 2:1) adopting, for the same enantiomer (1*R*,5*R*), the −*gauche*/*gauche* conformations with respect to the ether bridge [O1—C1—C2—O2*A*/*B* = −61.4 (3)/49.0 (4) and 63.3 (3)/−48.4 (4)° for the two independent molecules]. In the tetragonal form (Table 1 and Fig. 1), the +*gauche*/−*gauche* conformation is observed (1*R*,5*R* enantiomer), although with significant differences in the amide disposition [C4—C5—C7—O3 = −53.2 (2) and 53.2 (2)° *versus* −68.6 (4)° in (I) and in (II), respectively].

The presence of the two concomitant polymorphs, with a donor/acceptor ratio of less than 1 for OH, –O– and –CONHCH$_3$ groups, can be attributed to the different hydrogen-bonding possibilities. In the reported *N*-alkylamide derivatives (Foces-Foces *et al.*, 2007), the following three types

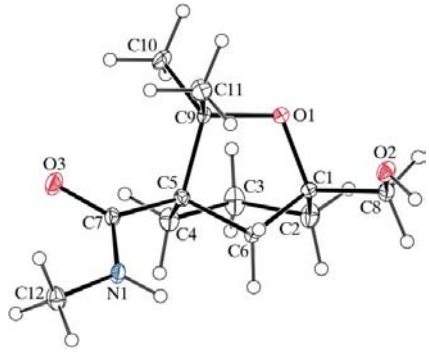


Figure 1
The molecular structure of (II), shown with 30% probability displacement ellipsoids.

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of paired hydrogen-bond interactions were related to the conformations of the hydroxy and methylaminocarbonyl substituents: (1) OH···O=C and NH···O_{ether}; (2) OH···O_{ether} and NH···O=C; and (3) OH···O=C and NH···OH. In tetragonal form (II), the N—H···OH bond connects molecules along the fourfold screw axis into one-dimensional frameworks [*C*(8) graph-set notation (Bernstein *et al.*, 1995); Fig. 2*a* and Table 2]. The hydroxy group acts as both donor to the carbonyl group and as acceptor of a hydrogen bond from the amide as in type 3, while the ether atom O1 is only involved in a C—H···O interaction (Table 2). These homochiral chains are then assembled along the *a* and *b* axes through OH···O=C and C—H···O_{ether} bonds into a three-dimensional network (Fig. 2*b*). However, in monoclinic form (I), type 1 is observed and the amide group is hydrogen bonded to the ether bridge O1, forming heterochiral chains with a *C*(6) graph-set motif. Despite the disorder of the hydroxy group, the hydrogen-bonding pattern is not affected, since in each conformation the hydroxy group is hydrogen bonded to the same carbonyl group. The combination of these interactions results in a two-dimensional network (Fig. 3). The differences in the crystal structures of the two polymorphs are reflected in the simulated powder diffraction spectra (Spek, 2003) shown in Fig. 4.

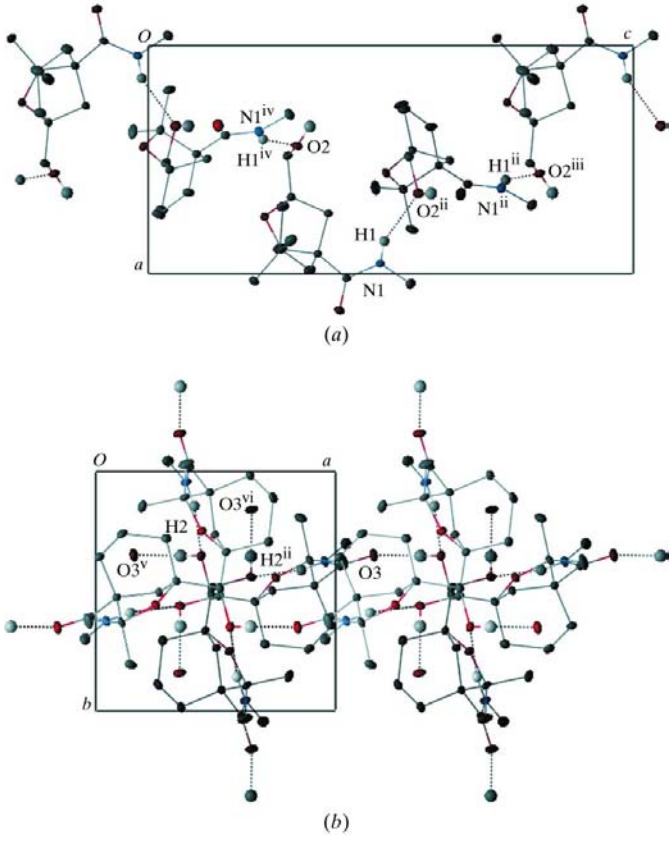

Figure 2
(*a*) The homochiral *C*(8) chain, along the *c* axis, resulting from the linkage of the molecules *via* N—H···OH hydrogen bonds (dotted lines). (*b*) The three-dimensional hydrogen-bonded framework viewed down *c* and showing the OH···O=C hydrogen bonds responsible for connecting the chains. H atoms not involved in the N—H···OH or O—H···O=C hydrogen-bond interactions have been omitted for clarity. [Symmetry codes: (ii) $-y+1, x, z+\frac{1}{4}$; (iii) $-x+1, -y+1, z+\frac{1}{2}$; (iv) $y, -x+1, z-\frac{1}{4}$; (v) (v) $x-1, y, z$; (vi) $-y+1, x-1, z+\frac{1}{4}$.]

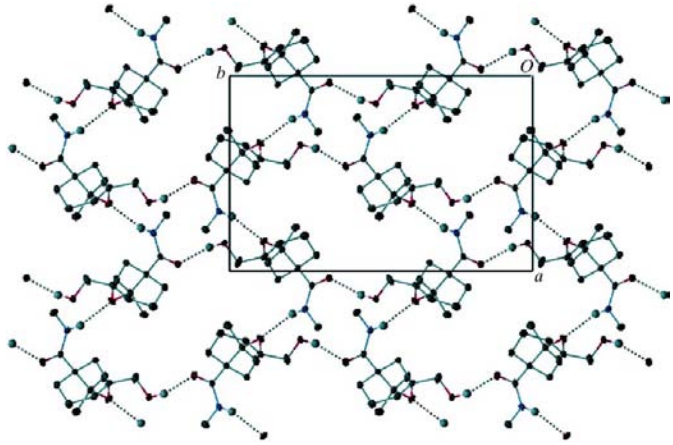

Figure 3
The two-dimensional structure in monoclinic polymorph (I), formed by heterochiral *C*(6) chains along the *a* axis (NH···O_{ether} contacts) connected by OH···O=C bonds. Only the major component of the disorder of the hydroxy group has been maintained. H atoms not involved in the hydrogen-bond interactions have been omitted for clarity.

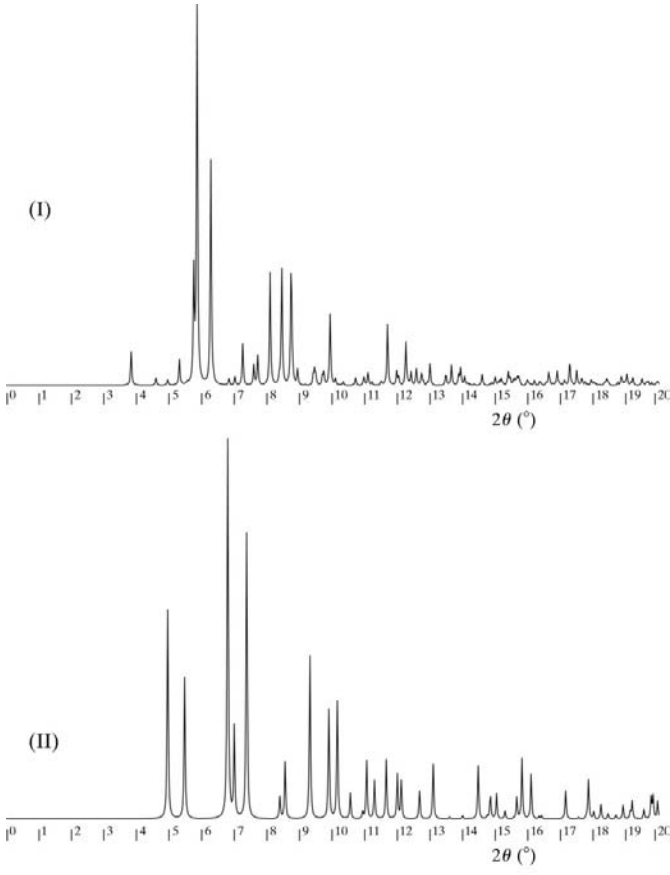

Figure 4
Simulated powder diffraction spectra: (I) the monoclinic phase and (II) the present tetragonal phase.

The proposed rule correlating the molecular conformation of the substituents and the pattern of strong hydrogen-bond interactions in the racemic derivatives (Foces-Foces *et al.*, 2007) is fulfilled by this polymorph. However, the presence of only one enantiomer in the structure drastically affects the crystal packing, since the dimer or synthon formed by centrosymmetrically related molecules, common to the most populated type 3, is absent.

Experimental

The synthesis of the title compound has been reported recently (Foces-Foces *et al.*, 2007) and crystals were obtained upon crystallization from a saturated aqueous tetrachloromethane/*n*-hexane (50%) solution. Crystals of the two morphologies were obtained in the same batch, *viz*. plates (monoclinic form with m.p. 451 K, previously reported) and needles in a small quantity (m.p. 454 K) corresponding to the present tetragonal form (II). The needles were separated manually and did not show optical activity in a chloroform solution (Perkin–Elmer 241). No structural phase transition was detected on cooling the sample from room temperature to 170 K.

Crystal data

$C_{12}H_{21}NO_3$
M_r = 227.30
Tetragonal, $P4_1$
a = 8.2616 (18) Å
c = 17.517 (4) Å
V = 1195.6 (4) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 170 (2) K
0.60 × 0.12 × 0.12 mm

Data collection

Nonius KappaCCD area-detector diffractometer
2593 measured reflections
1412 independent reflections
1282 reflections with $I > 2\sigma(I)$
R_{int} = 0.032

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.050
$wR(F^2)$ = 0.142
S = 1.00
1412 reflections
145 parameters
1 restraint
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.38 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}

Table 1
Selected torsion angles (°).

C1—C2—C3—C4	−41.3 (4)	C4—C5—C7—N1	109.3 (3)
O1—C1—C8—O2	64.3 (3)	C12—N1—C7—C5	−179.5 (3)
C4—C5—C7—O3	−68.6 (4)	C9—C5—C7—O3	56.1 (4)

Friedel pairs were merged during the final cycles of refinement due to the absence of significant anomalous dispersion effects. All H atoms were located in difference Fourier maps and subsequently allowed to refine as riding on their respective C, N and O atoms [C—H = 0.98 (CH_3) or 0.99 Å (CH_2), N—H = 0.88 Å and O—H = 0.84 Å, with U_{iso}(H) = 1.2U_{eq}(C,N) and 1.5U_{eq}(O)].

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O2—H2···O3^{v}	0.84	1.94	2.779 (3)	179
N1—H1···O2^{ii}	0.88	2.13	2.936 (4)	152
C6—H6B···O1^{ii}	0.99	2.39	3.292 (4)	152

Symmetry codes: (ii) $-y+1, x, z+\frac{1}{4}$; (v) $x-1, y, z$.

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *WinGX* (Farrugia, 1999), *PLATON* (Spek, 2003) and *Mercury* (Macrae *et al.*, 2006).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: TR3030). Services for accessing these data are described at the back of the journal.

References

Altomare, A., Burla, M. C., Camalli, M., Cascarano, G. L., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *J. Appl. Cryst.* **32**, 115–119.
Bernstein, J. (2002). *Polymorphism in Molecular Crystals*. IUCr Monographs on Crystallography No. 14. New York: Oxford University Press.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Dunitz, J. D. & Bernstein, J. (1995). *Acc. Chem. Res.* **28**, 193–200.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Foces-Foces, C., López-Rodríguez, M., Pérez, C., Martín, J. D. & Pérez-Hernández, N. (2007). *Cryst. Growth Des.* **7**, 905–911.
Lennartsson, A., Wiklund, T. & Håkansson, M. (2007). *CrystEngComm*, **9**, 856–859.
Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl. Cryst.* **39**, 453–457.
Nonius (2000). *KappaCCD Server Software*. Nonius BV, Delft, The Netherlands.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.