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Cocrystallization and configurations of *myo*-inositol-1,2-L-camphor acetals in two crystal structures

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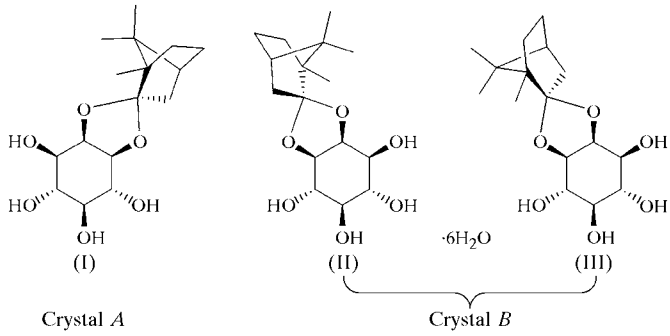
The inositol rings in (1*S*,2*R*,3*R*,4*S*,5*S*,6*R*,7*S*,8*S*,11*S*)-*myo*-inositol-1,2-camphor acetal {systematic name: (1*R*,2*S*,3*S*,4*R*,-5*S*,6*R*)-5,6-[(1*S*,2*S*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptane-2,2-diyldioxy]cyclohexane-1,2,3,4-tetrol}, $C_{16}H_{26}O_6$, and (1*R*,-2*S*,3*S*,4*R*,5*R*,6*S*,7*R*/*S*,8*S*,11*S*)-*myo*-inositol-1,2-camphor acetal trihydrate {systematic name: (1*S*,2*R*,3*R*,4*S*,5*R*,6*S*)-5,6-[(1*S*,-4*S*,6*R*/*S*)-1,7,7-trimethylbicyclo[2.2.1]heptane-2,2-diyldioxy]-cyclohexane-1,2,3,4-tetrol trihydrate}, $C_{16}H_{26}O_6\cdot 3H_2O$, adopt flattened chair conformations with the latter crystal containing two stereoisomers in a 0.684 (2):0.316 (2) ratio, similar to that found both in solution and by calculation. Both molecules pack in the crystals in similar two-dimensional layers, utilizing strong O—H···O hydrogen bonds, with the trihydrate cell expanded to incorporate the additional hydrogen-bonded water molecules.

Comment

The title compounds were studied as part of a programme to prepare chiral inositol derivatives (Baars & Hoberg, 2006; Cousins *et al.*, 2004). The structure of (I) was noted (Pietrusiewicz *et al.*, 1992) but no structural parameters have been reported. Previous studies of *myo*-inositol derivatives as listed in the Cambridge Structural Database [Allen, 2002; CSD Version 5.27 (updated August 2006); refcodes are given in capitals] indicate that these molecules frequently show novel conformational/packing effects, *e.g.* molecular dynamics simulation confirmed two stable conformations (XADWII; Dillen *et al.*, 2000) and 'thermosalient behaviour' (HADKIG; Steiner *et al.*, 1993). The camphor unit (bicyclo[2.2.1]heptane) has been found to be invariant (Clegg *et al.*, 1995). Along with the structure of (I) (crystal *A*), we report a novel structure containing cocrystallized (II) and (III) (crystal *B*) in a ratio corresponding approximately to their relative concentrations in solution as determined by NMR. In both cases, the L-camphor used in the synthesis determined the absolute configuration assigned here, since anomalous dispersion affects, as expected, were insufficient [*e.g.* the Flack parameter for crystal *B* was −0.2 (7)]. Friedel pairs in the data have been retained for future reference purposes.



The asymmetric unit in each crystal contains one independent *myo*-inositol-1,2-camphor acetal unit (Figs. 1–3); in crystal *B*, there are also three water molecules. For crystal *A*, the inositol fragment absolute configuration of C1(*S*), C2(*R*), C3(*R*), C4(*S*), C5(*S*), C6(*R*), and for crystal *B* the opposite [C1(*R*), C2(*S*), C3(*S*), C4(*R*), C5(*R*), C6(*S*)], was determined from the chemical synthesis based on L-camphor. In both crystals, the acetal linkages to the *myo*-inositol unit are similar to those observed previously [TEKPUU (Spiers *et al.*, 1996), NOZCIO (Spiers *et al.*, 1997), and PINMEE and PINMII (Chung *et al.*, 1994)]. For (I), the five-membered link stereochemistry (O1/C1/C2/O2/C7; Table 1) to the L-camphor unit is similar to that reported for the dihydroxybutanedioic acid dimethyl ester (NAFWEW; Mikolajczyk *et al.*, 1996).

The L-camphor unit is present in crystal *B* in two sites corresponding to the two alternative configurations of attachment at the C7 atoms [(II) and (III) in the scheme]; the two are distinguished by primed and unprimed labels (Figs. 2 and 3). An initial refinement of the primed and unprimed atoms with one common isotropic *U* factor and freely refined occupancies indicated unambiguously that only these two related stereoisomers were present; the two sets were then

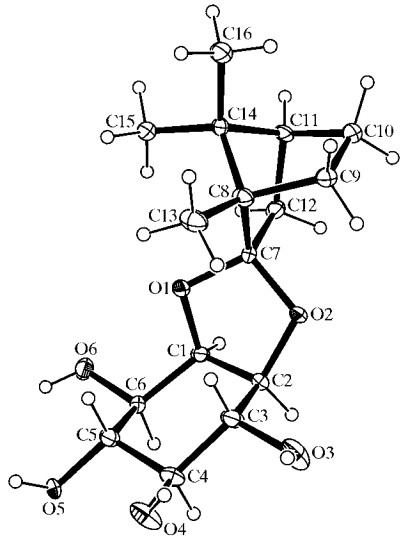


Figure 1
The molecular structure of (I) (Farrugia, 1997); displacement ellipsoids are shown at the 30% probability level.

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grouped and refined to a final stereoisomer ratio of 0.685 (2):0.315 (2). The four C7,C7′—O1,O2 distances were refined to a common dimension, giving the results in Table 3 (see *Experimental*). The observed ratio in solution from NMR was 75:25 in DMSO-d_6. We determined the relative electronic energies (gas phase) using the *Amsterdam Density Functional* program system (SCM, 2006) [with VWN local density approximation (Vosko *et al.*, 1980)], optimizing the structures and starting from the X-ray coordinate positions. The difference between the stereoisomers (II) and (III) was 0.45 kcal mol^{-1}, in good agreement with both solid state and solution observations. Compound (I) was estimated to be less stable than (II) by 11 kcal mol^{-1}, somewhat larger than expected.

In all structures, the inositol ring adopts a slightly flattened chair conformation, as shown by the Cremer & Pople (1975) parameters (Table 5). In (I), the best 'arms' of the chair are atoms C1, C6, C3 and C4 [the mean out-of-plane distance is 0.014 (2) Å], with atoms C2 and C5 lying 0.528 (4) and −0.727 (5) Å, respectively, from the plane; for crystal *B*, the corresponding best parameters are C2, C3, C5 and C6 [0.0193 (8) Å], with C1 and C4 at 0.513 (2) and −0.696 (2) Å, respectively. The five-membered rings O1/C1/C2/O2/C7(C7′) (rings 2*A* and 2*B*; Table 5) adopt twist conformations (Evans

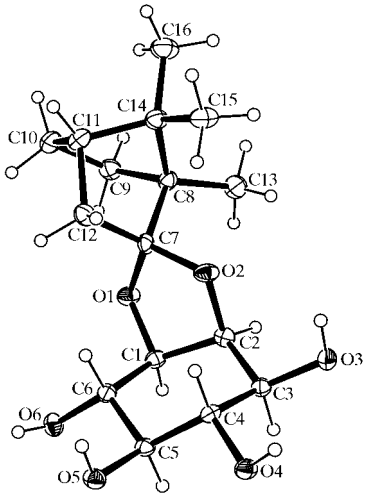

Figure 2
The molecular structure of (II) (Farrugia, 1997); displacement ellipsoids are shown at the 30% probability level.

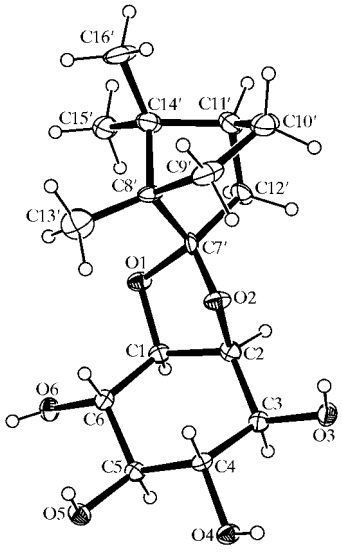

Figure 3
The molecular structure of (III) (Farrugia, 1997); displacement ellipsoids are shown at the 30% probability level.

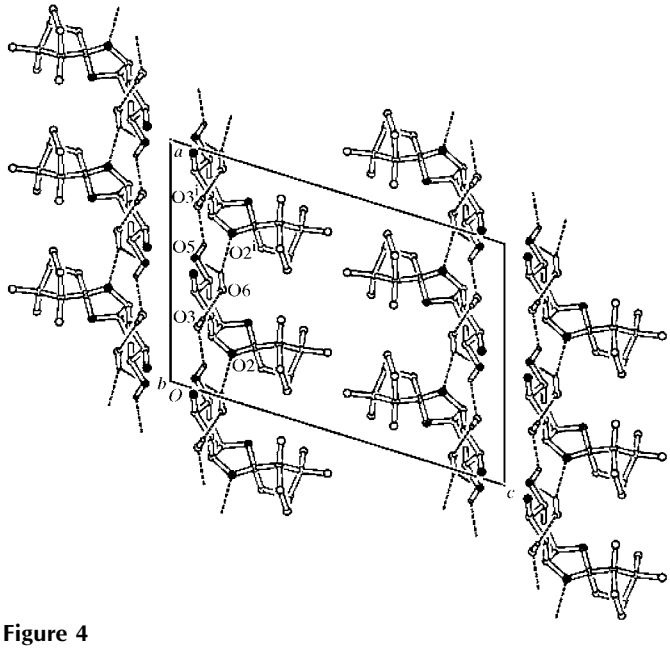

Figure 4
The packing of crystal *A*, viewed down the *b* axis. Only H atoms involved in selected hydrogen bonds (dashed lines) are shown. For symmetry designations, see Table 2.

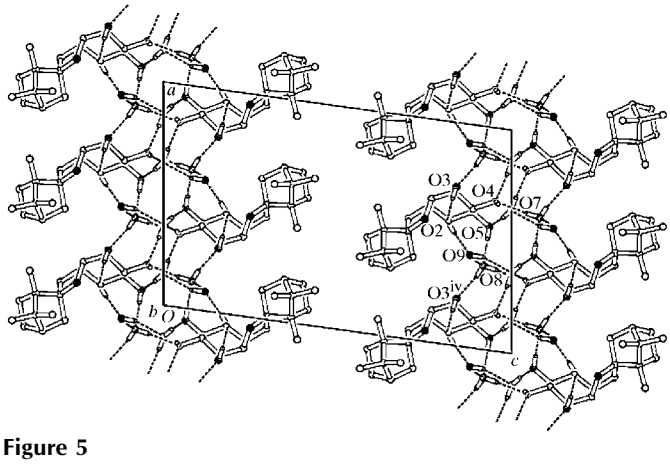

Figure 5
The packing of crystal *B*, viewed down the *b* axis. Only the major stereoisomer (II) and H atoms involved in selected hydrogen bonds (dashed lines) are shown for clarity. For symmetry designations, see Table 4.

& Boeyens, 1989). The L-camphor fused rings adopt envelope or boat configurations for the five- and six-membered rings, respectively, as expected (Clegg *et al.*, 1995).

The crystal packing (Tables 2 and 4) can be described as similar two-dimensional layers normal to the *c* axis (Figs. 4 and 5). These layers are formed from strong O—H···O hydrogen-bond interactions involving all inositol O atoms in *A*, and both inositol and water O atoms in crystal *B* as acceptors. The L-camphor rings pack 'head-to-head' separating the layers. The close C—H···O interactions in crystal *B* (not listed in Table 4) are regarded as fortuitous [even though they fulfil the normal criteria (Desiraju & Steiner, 1999)], because of their location and the availability of the acceptor O atoms (Fig. 5). There is also a fortuitous short contact (O—H4···H6O = 1.99 Å) in (I) between two H atoms involved in strong hydrogen bonds (Table 2).

Experimental

The mixed acetals were prepared according to the method of Lindberg *et al.* (2002).

Crystal *A*

Crystal data

$C_{16}H_{26}O_6$
M_r = 314.37
Monoclinic, *C*2
a = 12.700 (3) Å
b = 6.9721 (17) Å
c = 18.422 (5) Å
β = 107.275 (3)°
V = 1557.7 (7) Å^3
Z = 4
D_x = 1.341 Mg m^{-3}
Mo *K*α radiation
μ = 0.10 mm^{-1}
T = 169 (2) K
Hexagonal, colourless
0.47 × 0.33 × 0.03 mm

Data collection

Bruker–Nonius APEX2 CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (Blessing, 1995)
T_{min} = 0.796, T_{max} = 0.997
8809 measured reflections
2953 independent reflections
2026 reflections with $I > 2\sigma(I)$
R_{int} = 0.055
θ_{max} = 26.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.113
S = 1.08
2953 reflections
206 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0452P)^2 + 0.8396P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.009
$\Delta\rho_{max}$ = 0.27 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}

Table 1
Selected geometric parameters (Å, °) for crystal *A*.

O1—C7	1.441 (4)	O2—C7	1.466 (4)
O1—C1	1.451 (4)	C1—C2	1.531 (5)
O2—C2	1.458 (4)	C7—C8	1.562 (5)
C7—O1—C1	104.5 (2)	O1—C1—C6	112.0 (2)
C2—O2—C7	108.2 (2)	O2—C7—C8	112.8 (3)
O1—C1—C2	100.2 (2)	O1—C7—C12	113.0 (3)
C7—O2—C2—C1	19.2 (3)	C2—O2—C7—C12	−114.2 (3)

Table 2
Hydrogen-bond geometry (Å, °) for crystal *A*.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O6—H6O···O2^{i}	0.84	2.23	3.034 (3)	159
O5—H5O···O3^{i}	0.84	2.12	2.752 (4)	132
O4—H4O···O6^{ii}	0.84	2.11	2.951 (4)	175
O3—H3O···O6^{ii}	0.84	2.18	2.964 (4)	156

Symmetry codes: (i) $x+\frac{1}{2}, y-\frac{1}{2}, z$; (ii) $x, y+1, z$.

Crystal *B*

Crystal data

$C_{16}H_{26}O_6{\cdot}3H_2O$
M_r = 368.42
Monoclinic, *C*2
a = 13.1708 (17) Å
b = 6.9513 (9) Å
c = 20.737 (3) Å
β = 97.899 (2)°
V = 1880.5 (4) Å^3
Z = 4
D_x = 1.301 Mg m^{-3}
Mo *K*α radiation
μ = 0.11 mm^{-1}
T = 163 (2) K
Plate, colourless
0.73 × 0.40 × 0.12 mm

Data collection

Bruker *P*4 CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (Blessing, 1995)
T_{min} = 0.795, T_{max} = 0.987
11666 measured reflections
3205 independent reflections
2697 reflections with $I > 2\sigma(I)$
R_{int} = 0.021
θ_{max} = 26.4°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.027
$wR(F^2)$ = 0.059
S = 0.96
3205 reflections
345 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0383P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.14 e Å^{-3}

Table 3
Selected geometric parameters (Å, °) for crystal *B*.

O1—C7	1.430 (3)	O2—C2	1.4380 (18)
O1—C1	1.4352 (16)	O2—C7	1.477 (3)
O1—C7′	1.487 (6)	O4—C4	1.4370 (16)
O2—C7′	1.431 (6)	O6—C6	1.420 (2)
C7—O1—C1	108.18 (15)	C1—O1—C7′	106.9 (3)
C7—O1—C1—C2	−37.82 (18)	C8—C9—C10—C11	0.1 (3)
C7′—O1—C1—C2	−12.9 (3)	C7—O1—C7′—C12′	−153.3 (13)
C1—O1—C7—C12	−105.7 (4)	C8′—C9′—C10′—C11′	1.2 (9)

All the L-camphor atoms in (II) and (III) (C7–C16 and their H atoms) were freely refined in two sets, each with one common occupancy factor restrained so that the sum of the two was unity. The final occupancies were 0.685 (2) and 0.315 (2). The final difference maps showed no significant discrepancies, justifying this choice of disorder modelling. The four C7,C7′—O1,O2 distances were restrained to a common dimension [with an s.u. of 0.01, using the *SHELXL97* SADI option (Sheldrick, 1997)]. All H atoms bound to carbon were constrained to their expected geometries (C—H = 0.98–1.00 Å). H atoms on inositol O atoms were restrained to tetrahedral

Table 4
Hydrogen-bond geometry (Å, °) for crystal *B*.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H3O···O6^{i}	0.84	1.91	2.7294 (16)	167
O4—H4O···O7	0.84	1.87	2.6908 (16)	165
O5—H5O···O8	0.84	1.91	2.7394 (16)	172
O6—H6O···O9^{ii}	0.84	1.95	2.7762 (17)	166
O7—H7*A*···O4^{iii}	0.853 (15)	1.903 (14)	2.7490 (16)	172 (2)
O7—H7*B*···O5^{i}	0.852 (15)	1.836 (15)	2.6746 (16)	168 (2)
O8—H8*A*···O3^{iv}	0.829 (16)	1.900 (16)	2.7199 (16)	170 (2)
O8—H8*B*···O4^{v}	0.829 (11)	2.127 (14)	2.9236 (15)	161 (2)
O9—H9O*A*···O7^{v}	0.837 (12)	1.967 (14)	2.7754 (17)	162 (2)
O9—H9O*B*···O8	0.849 (11)	2.153 (13)	2.9436 (18)	155 (2)

Symmetry codes: (i) $x, y+1, z$; (ii) $x, y-1, z$; (iii) $-x+\frac{3}{2}, y+\frac{1}{2}, -z+2$; (iv) $x-\frac{1}{2}, y-\frac{1}{2}, z$; (v) $-x+1, y, -z+2$.

Table 5
Cremer & Pople (1975) parameters for rings (Å, °) (*PLATON*; Spek, 2003).

Structure	Ring[a]	*Q*	θ	φ	Conformation
(I)	1	0.550 (4)	13.8 (4)	190.2 (17)	Distorted chair $^{2}C_{5}$
(II), (III)	1	0.5276 (14)	165.87 (15)	17.8 (6)	Distorted chair[b] $^{1}C_{4}$
(I)	2*A*	0.429 (3)	–	206.1 (5)	Twist $^{2}T_{1}$
(II)	2*A*	0.392 (2)	–	46.2 (3)	Twist $^{2}T_{3}$
(III)	2*B*	0.492 (3)	–	92.8 (4)	Twist $^{3}T_{4}$
(I)	3*A*	0.999 (4)	89.5 (2)	59.9 (2)	Boat $B_{2,5}$
(II)	3*A*	0.990 (4)	89.2 (3)	59.9 (2)	Boat $B_{2,5}$
(III)	3*B*	0.981 (8)	89.1 (6)	57.0 (5)	Boat $B_{2,5}$
(I)	4*A*	0.590 (4)	–	253.1 (4)	Envelope ^{3}E
(II)	4*A*	0.593 (5)	–	252.0 (5)	Envelope ^{3}E
(III)	4*B*	0.588 (8)	–	250.2 (8)	Envelope ^{3}E
(I)	5*A*	0.594 (4)	–	323.7 (3)	Envelope ^{5}E
(II)	5*A*	0.592 (3)	–	324.3 (3)	Envelope ^{5}E
(III)	5*B*	0.601 (9)	–	324.6 (8)	Envelope ^{5}E

Notes: (*a*) (1) C1–C6; (2*A*) O1/C1/C2/O2/C7; (2*B*) O1/C1/C2/O2/C7′; (3*A*) C7–C12; (3*B*) C7′–C12′; (4*A*) C7/C8/C14/C11/C12; (4*B*) C7′/C8′/C14′/C11′/C12′; (5*A*) C8–C11/C14; (5*B*) C8′–C11′/C14′. (*b*) Opposite absolute configuration: $180-\theta$, $180+\varphi$.

positions, with O—H distances of 0.84 Å (AFIX 87). The positions of water H atoms were restrained to O—H distances of 0.84 (1) Å (DFIX). All methyl, tertiary and O-bound H atoms were refined with U_{iso}(H) values of, respectively, 1.5, 1.2 and 1.5 times U_{eq} of the parent atom. In the absence of significant anomalous scattering, the values of the Flack (1983) parameter were indeterminate (Flack & Bernardinelli, 2000).

For both compounds, data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT* and *SADABS* (Sheldrick, 2003); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *PLUTON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PLATON* (Spek, 2003).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GZ3065). Services for accessing these data are described at the back of the journal.

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