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Hydrogen-bonding patterns of two dihydroxylactone derivatives

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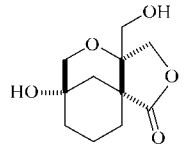
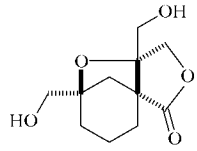
In the hydrogen-bonding networks of 8-hydroxy-5-hydroxymethyl-3,6-dioxatricyclo[6.3.1.0^{1,5}]dodecan-2-one and 5,7-bis(hydroxymethyl)-3,6-dioxatricyclo[5.3.1.0^{1,5}]undecan-2-one, both $C_{11}H_{16}O_5$, layers and double strands, respectively, lead to the formation of chains connected by hydroxy-to-hydroxy contacts, where the hydroxymethyl group, present in both structures, acts as a donor. The secondary structures differ in the hydrogen bonding of these chains *via* the second hydroxy group, which is involved in hydroxy-to-carbonyl and hydroxy-to-hydroxy bonds, respectively.

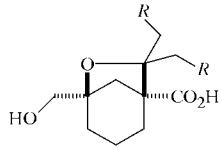
Comment

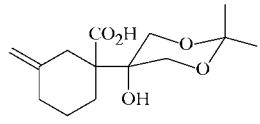
In the construction of hydrogen-bonded arrays by using molecular descriptors with unbalanced hydrogen-bond donor/acceptor ratios, the donor/acceptor imbalance might be redressed by inclusion of molecules of water (Desiraju, 1990). Bridged oxacycles in molecules possessing axially oriented hydroxy/carboxylic acid groups were considered promising candidates for studying the incorporation of water molecules into their hydrogen-bond patterns (Carrasco *et al.*, 2001). Our continuous interest in the study of the hydrated/anhydrous crystalline packing of such molecules has led us to consider the synthesis of the hydroxy acid 5,7,7-tris(hydroxymethyl)-6-oxabicyclo[3.2.1]octane-1-carboxylic acid, (III) (R = OH), a dihydroxylated homologue of the diethyl derivative (IV) (R = Me), which adopts a hydrated tubular-shaped structure in the solid state (Pérez *et al.*, 2000). In the present paper, we report the crystal structures of the related lactones (I) and (II).

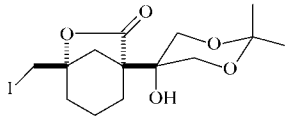
The molecular structures (Figs. 1 and 2) are quite rigid and contain three structural moieties that will be discussed separately. In both compounds and according to the notation of Giacovazzo *et al.* (1992), the γ-butyrolactone ring adopts conformations intermediate between $^1T_5$ half chair and E_5 envelope. The ring puckering parameters (Cremer & Pople, 1975) for the atom sequence C1–C5 [q_2 = 0.355 (2) and 0.312 (2) Å, and φ_2 = −23.3 (3) and −29.8 (4)°] indicate that the conformation in (I) is essentially $^1T_5$ with a contribution

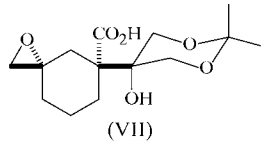

(I)


(II)


(III) R=OH
(IV) R=CH_3


(V)


(VI)


(VII)

from E_5, while in (II), the conformation is E_5 with a contribution from $^1T_5$. The cyclohexane ring adopts a $^1C_4$ chair conformation, slightly distorted towards a $^1H_6$ half chair in (I) and towards an E_6 envelope in (II) for the sequences C1/C11–C8/C12 and C1/C11/C7–C10 [Q = 0.602 (2) and 0.655 (2) Å, θ = 15.4 (2) and 27.1 (2)°, and φ = −29.1 (5) and −59.1 (4)°]. The differences in the puckering amplitude could be ascribed to the different size of the oxacycle bridge; the larger size of the oxane ring in (I) compared with the oxolane ring in (II) is associated with the lowest torsion angles in the bonds shared with this ring (Tables 1 and 3). The oxane ring exhibits a $^1C_4$ chair conformation distorted toward a $^3H_2$ half chair for the atom sequence C1/C12/C8/C7/O6/C5 [Q = 0.561 (2) Å, θ = 20.1 (1)° and φ = 81.4 (5)°], whereas the oxolane ring adopts a conformation intermediate between $^1T_2$ and E_2 for the C1/C11/C7/O6/C5 sequence [q_2 = 0.474 (2) Å and φ_2 = 26.9 (2)°]. Another difference between the two structures is that the hydroxymethyl group attached to atom C5 is *gauche*- [in (I)] and *trans*-oriented [in (II)] with respect to atom C1 (Tables 1 and 3, and Figs. 1 and 2). As far as conventional O—H···O bonds are concerned, two hydrogen-bonding networks are observed, *viz.* layers and staircase-ladders, which are closely related to the relative disposition of the dialcohols in each

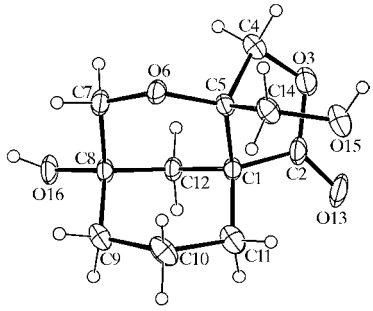


Figure 1
The molecular structure of (I), shown with 30% probability displacement ellipsoids.

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molecule, as previously observed in 1,3-diols (Nguyen *et al.*, 2001; Schmittel *et al.*, 2004). In both crystal structures, molecules connected by hydroxy-to-hydroxy bonds form chains, although the structures differ in the chirality of the components within each chain and the linkage between them, as described below.

The molecules of (I) are linked into a sheet *via* a combination of hydroxy-to-hydroxy and hydroxy-to-carbonyl hydrogen bonds (Table 2). The formation of these sheets can be described in terms of chains with glide-related molecules running in the (102) direction (Fig. 3). Hydroxy-to-carbonyl contacts between chains, related by translation, are responsible for the extension in the *a* direction, so producing the two-dimensional network. C—H···O contacts exist (Table 2) within the sheet and between centrosymmetric sheets (dashed lines in Fig. 4), forming a three-dimensional framework.

In (II), each strand is formed by molecules related only by translation along *a*, where the hydroxy group of the hydroxymethyl group at atom C5 acts as a donor. The second hydroxy group connects screw-related strands (Fig. 5), giving rise to the staircase-ladder structure (Fig. 6*a*), as also observed in some recently reported 1,3-dialcohol derivatives (Nguyen *et al.*, 2001). Another type of double-stranded ladder formed by dialcohols is the step-ladder structure represented schematically in Fig. 6(*b*), which has also been observed in the hydroxy acid analogues of (I) and (II) (Carrasco *et al.*, 2001). In (II), as pointed out by Nguyen *et al.* (2001), each hydroxy group (*gauche*-oriented) acts as a donor and an acceptor of hydrogen bonds, showing (i) the preference of this type of ladder structure to be composed of only one enantiomer and (ii) the

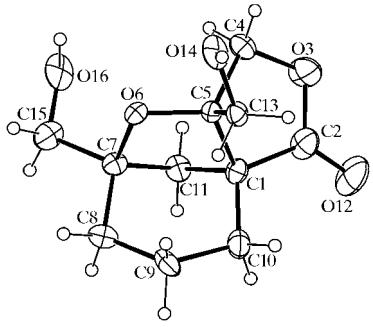

Figure 2
The molecular structure of (II), shown with 30% probability displacement ellipsoids.

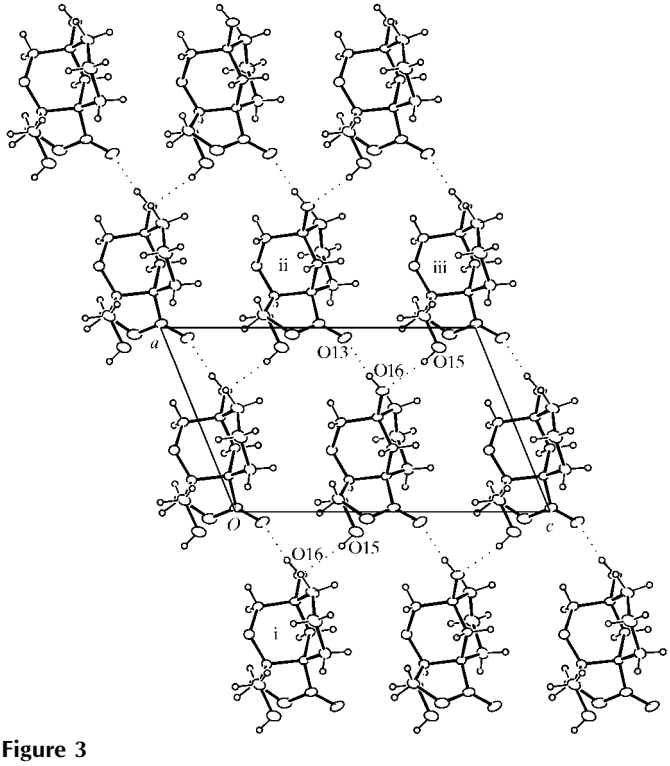

Figure 3
A two-dimensional hydrogen-bonded layer in (I), formed *via* a combination of hydroxy-to-hydroxy and hydroxy-to-carbonyl contacts. [Symmetry codes: (i) $x-1, \frac{1}{2}-y, z-\frac{1}{2}$; (ii) $1+x, y, z$; (iii) $x+1, \frac{1}{2}-y, z+\frac{1}{2}$.]

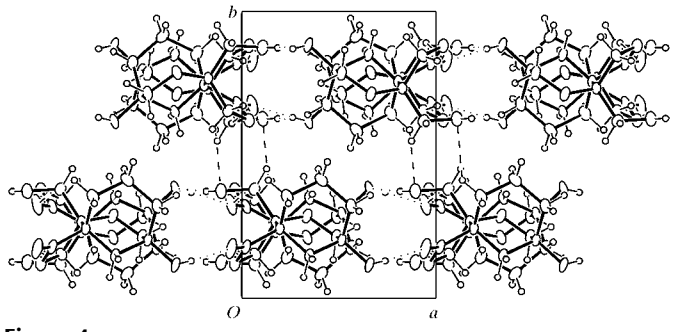

Figure 4
A packing diagram of (I), illustrating the disposition of the sheets. Dotted and dashed lines represent O—H···O and C—H···O hydrogen bonds, respectively.

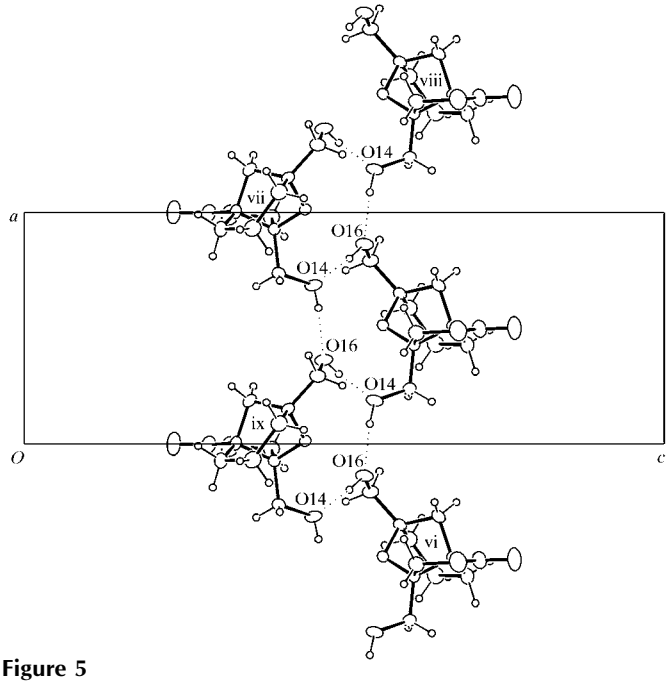

Figure 5
One-dimensional hydrogen-bonded staircase ladders in (II), formed by hydroxy-to-hydroxy bonds. [Symmetry codes: (vi) $x-1, y, z$; (vii) $\frac{1}{2}+x, \frac{1}{2}-y, 1-z$; (viii) $x+1, y, z$; (ix) $-\frac{1}{2}+x, \frac{1}{2}-y, 1-z$.]

twofold screw axis as the most probable symmetry for this type of ladder.

The O···O intramolecular (*A* = O14···O16), interstrand (*B* = O16···O14^{ii}) and intrastrand (*C* = O14···O16^{i}) distances (Figs. 5 and 6*a*) of 5.396 (2), 2.700 (2) and 2.682 (2) Å characterizing this ladder are in the upper and lower end of the range reported by Nguyen *et al.* (2001). In (I), the intramolecular (O15···O16), interstrand (O16···O13^{ii}) and intrastrand (O15···O16^{i}) (Fig. 3) distances of 6.466 (3), 2.881 (2) and 2.715 (2) Å are all larger than the *A*, *B* and *C* distances in (II). The structures of the two compounds highlight the competition between the O—H···OH and O—H···O=C hydrogen bonds. We also note that (II) is less dense than (I) (the total packing coefficients are 0.685 and 0.712) and has a lower melting point (452–453 *versus* 464–465 K).

Only weak C—H···O interactions (Table 4) connect pairs of double strands, related by glide planes, along *c* into a three-dimensional network of corrugated centrosymmetric sheets (dashed lines in Fig. 7). The larger displacement parameters for atoms O3 and O12 in (II) can be associated with the lack of O—H···O contacts for these atoms.

Dihydroxy like hydroxy/carboxylic acid functions are hydrogen bonded in linear anhydrous strands with two parallel strands crosslinked through additional hydrogen bonds. It would also be expected that incorporation of water molecules into dihydroxy hydogen-bonded networks might disrupt the dimeric motif, creating single-strand arrays in a favourable conformation for ring packing. Further extension of the hydrogen bonding in the perpendicular direction can lead to the formation of a hydrated tubular-shaped structure in the solid state (Carrasco *et al.*, 2001). Work toward this end is in progress.

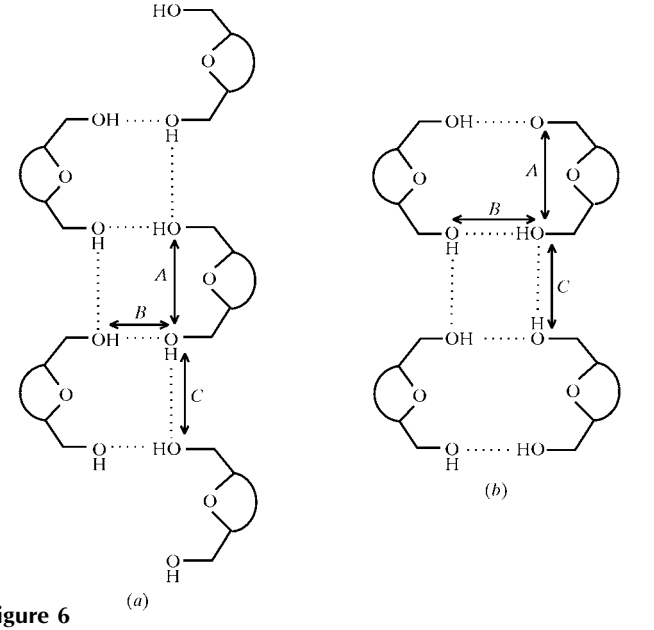

Figure 6
A schematic representation of the two categories of double-stranded ladders, *viz.* (*a*) staircase and (*b*) step-ladder. *A*, *B* and *C* denote intramolecular, interstrand and intrastrand distances, respectively. The dialcohol molecules are represented as curved rods linking the two $-CH_2OH$ groups and the oxacycle bridge.

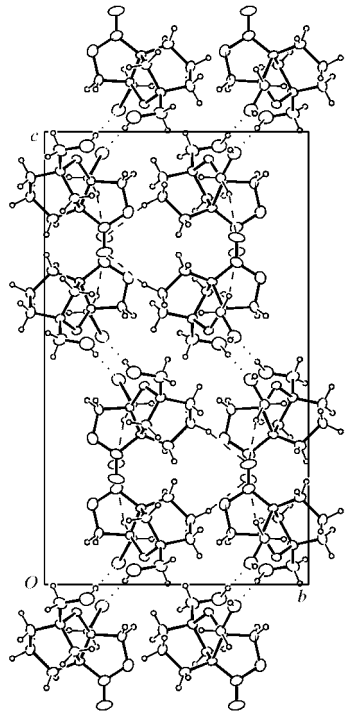

Figure 7
A packing diagram of (II), illustrating the disposition of the staircase ladders. Dotted and dashed lines represent O—H···O and C—H···O hydrogen bonds, respectively.

Experimental

A solution of lithium diisopropylamide was prepared by dissolving diisopropylamine (8.3 g, 80 mmol) in anhydrous tetrahydrofuran (THF, 100 ml), cooling the solution to 233 K in a dry ice–acetone bath and adding *n*-butyllithium (80 mmol, 72.8 ml, 1.1 *M* in hexane) under an atmosphere of argon. A solution of 3-methylenecyclohexanecarboxylic acid (5.68 g, 40 mmol) in cold THF (233 K, 30 ml) was injected *via* cannula and reacted for 40 min at 233 K. The reaction mixture was heated to 323 K for an additional 2 h. The resulting bright-yellow solution was cooled (233 K) and 2,2-dimethyl-1,3-dioxan-5-one (5.20 g, 40 mmol) was added dropwise (*via* syringe pump) over a period of 2 h. After completion of the addition, the mixture was stirred for 2.5 h at 233 K. The quenched reaction mixture was treated with aqueous HCl solution (5%, 200 ml) and the aqueous phase was extracted with ether (150 ml). The organic phase was washed with water, dried over $MgSO_4$, concentrated and purified on silica gel to give (V) (yield 9.61 g, 35.6 mmol, 89%). To a solution of (V) (8.10 g, 30 mmol) in acetone (130 ml), diisopropylamine (4.6 ml, 30 mmol) was added dropwise. The resulting salt was concentrated *in vacuo* and dissolved in anhydrous dichloromethane (150 ml). Iodine (7.8 g, 30 mmol) in dichloromethane (150 ml) was injected under argon and reacted for 48 h at room temperature. The quenched reaction mixture was shaken with aqueous sodium thiosulfate (10%, 30 ml), dried and evaporated *in vacuo*. The residue was purified by chromatography on silica gel to afford an unstable solid identified as iodolactone (VI) (yield 10.8 g, 27.3 mmol, 91%). Iodolactone (VI) (10 g, 25.3 mmol) was dissolved in THF (80 ml). To the cold solution was added potassium hydroxide (2.13 g, 38 mmol) dissolved in water (130 ml). After completion of the addition, the mixture was stirred for 30 min at 298 K. The quenched reaction mixture was treated with aqueous HCl solution (5%, 100 ml) and water (100 ml). The organic phase was dried and concentrated to give

the unstable epoxide (VII) (yield 6.95 g, 24.3 mmol, 96%). The white solid so obtained was dried by passing argon through and transferred under an anhydrous atmosphere. A solution of this solid in dichloromethane (100 ml) was cooled (195 K) under argon and treated with *p*-toluenesulfonic acid (3 mg) in dichloromethane (60 ml). The reaction was stirred for 30 min at room temperature. The quenched reaction was washed with water (60 ml), dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (5–15% ethyl acetate in *n*-hexane) to give dihydroxylactones (I) (2.72 g, 11.93 mmol) and (II) (2.80 g, 12.28 mmol). Single crystals of (I) and (II) suitable for X-ray analysis were grown at room temperature from damp carbon tetrachloride/*n*-hexane.

Compound (I)

Crystal data

$C_{11}H_{16}O_5$
M_r = 228.24
Monoclinic, $P2_1/c$
a = 8.067 (3) Å
b = 11.029 (3) Å
c = 12.769 (4) Å
β = 112.12 (2)°
V = 1052.4 (6) Å^3
Z = 4
D_x = 1.440 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2404 reflections
θ = 6.4–27.6°
μ = 0.11 mm^{-1}
T = 295 (2) K
Prism, colourless
0.50 × 0.20 × 0.15 mm

Data collection

Nonius KappaCCD diffractometer
φ and ω scans
8698 measured reflections
2404 independent reflections
1989 reflections with $I > 2\sigma(I)$
R_{int} = 0.043
θ_{max} = 27.6°
$h = -8 \rightarrow 10$
$k = -14 \rightarrow 13$
$l = -16 \rightarrow 14$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.045
$wR(F^2)$ = 0.121
S = 1.08
2404 reflections
147 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0513P)^2 + 0.3909P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.29 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}

Table 1
Selected torsion angles (°) for (I).

C5—C1—C2—O3	−28.3 (2)	C1—C5—O6—C7	−39.6 (2)
C1—C2—O3—C4	9.1 (2)	C12—C8—C9—C10	50.8 (2)
C2—O3—C4—C5	14.4 (2)	C9—C8—C12—C1	−61.5 (2)
O3—C4—C5—C1	−30.7 (1)	C11—C1—C12—C8	68.4 (2)
C2—C1—C5—C4	34.3 (1)	C12—C1—C11—C10	−62.4 (2)
C12—C1—C5—O6	46.1 (2)	C9—C10—C11—C1	50.1 (2)
C5—C1—C12—C8	−59.0 (2)	C8—C9—C10—C11	−44.6 (2)
C7—C8—C12—C1	64.3 (2)	C1—C5—C14—O15	57.0 (2)
O6—C7—C8—C12	−58.1 (2)	O16—C8—C14—O15	−98.9 (3)
C5—O6—C7—C8	45.7 (2)	O16—C8—C5—C14	162.3 (2)

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

D—H···A	D—H	H···A	D···A	D—H···A
O15—H15···O16^{i}	0.82	2.07	2.881 (2)	170
O16—H16···O13^{ii}	0.82	1.90	2.715 (2)	171
C14—H14A···O13^{iv}	0.97	2.48	3.384 (2)	154
C11—H11A···O15^{v}	0.97	2.55	3.254 (2)	129

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

Table 3
Selected torsion angles (°) for (II).

C5—C1—C2—O3	−22.1 (2)	C11—C7—C8—C9	57.2 (2)
C1—C2—O3—C4	3.6 (2)	C8—C7—C11—C1	−73.9 (2)
C2—O3—C4—C5	16.5 (2)	C10—C1—C11—C7	75.5 (2)
O3—C4—C5—C1	−28.6 (2)	C11—C1—C10—C9	−57.6 (2)
C2—C1—C5—C4	30.0 (2)	C8—C9—C10—C1	36.6 (2)
C11—C1—C5—O6	33.7 (2)	C7—C8—C9—C10	−36.5 (2)
C5—C1—C11—C7	−46.1 (2)	C1—C5—C13—O14	174.4 (1)
O6—C7—C11—C1	43.3 (2)	O6—C7—C15—O16	64.9 (2)
C5—O6—C7—C11	−22.9 (2)	O16—C15—C13—O14	62.2 (2)
C1—C5—O6—C7	−7.4 (2)		

Table 4
Hydrogen-bond geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
O14—H14···O16^{vi}	0.82	1.87	2.682 (2)	173
O16—H16···O14^{vii}	0.82	1.88	2.700 (2)	173
C9—H9A···O12^{viii}	0.97	2.55	3.470 (2)	159
C13—H13B···O12^{ix}	0.97	2.57	3.512 (2)	163

Symmetry codes: (vi) $x-1, y, z$; (vii) $x+\frac{1}{2}, -y+\frac{1}{2}, -z+1$; (viii) $-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$; (ix) $x-\frac{1}{2}, y, -z+\frac{3}{2}$.

Compound (II)

Crystal data

$C_{11}H_{16}O_5$
M_r = 228.24
Orthorhombic, *Pbca*
a = 7.8896 (6) Å
b = 12.7281 (10) Å
c = 21.8425 (18) Å
V = 2193.4 (3) Å^3
Z = 8
D_x = 1.382 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2511 reflections
θ = 5.2–27.5°
μ = 0.11 mm^{-1}
T = 295 (2) K
Plate, colourless
0.50 × 0.43 × 0.15 mm

Data collection

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R_{int} = 0.065
θ_{max} = 27.5°
$h = -10 \rightarrow 5$
$k = -16 \rightarrow 15$
$l = -23 \rightarrow 28$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.053
$wR(F^2)$ = 0.132
S = 1.03
2511 reflections
147 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0653P)^2 + 0.1829P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

All H atoms were located in difference Fourier maps and subsequently allowed to refine as riding on their respective C and O atoms [C—H = 0.97 Å, O—H = 0.82 Å and U_{iso}(H) = 1.2U_{eq}(C,O)]. The O atoms, except O6 in (II), have elongated displacement ellipsoids; however, split peaks for these atoms were not observed and consequently a disorder model was not used in the refinement.

For both compounds, data collection: *COLLECT* (Nonius, 2000); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; structure solution: *SIR97* (Altomare *et al.*, 1999); structure refinement: *SHELXL97* (Sheldrick, 1997); molecular graphics: *Xtal3.6* (Hall *et al.*, 1999); publication software: *SHELXL97*, *WinGX* (Farrugia, 1999) and *PLATON* (Spek, 2003).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SQ1188). Services for accessing these data are described at the back of the journal.

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