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(±)-1-Hydroxy-6,6-dimethyl-1*H*,6*H*-naphtho[1,2-*c*]furan-3,9-trione

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Key indicators

Single-crystal X-ray study
T = 295 K
Mean σ(C–C) = 0.004 Å
Disorder in main residue
R factor = 0.060
wR factor = 0.179
Data-to-parameter ratio = 12.9

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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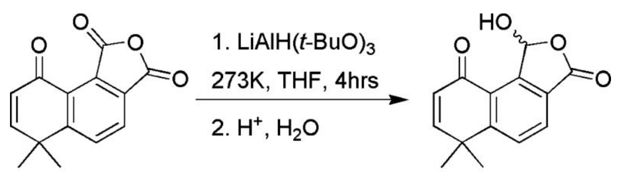
The title compound, $C_{14}H_{12}O_4$, crystallizes as discrete molecular species which form hydroxy-to-ketone hydrogen-bonded dimers disposed about crystallographic centres of symmetry.

Comment

The 1-hydroxyphthalide unit in the title compound, (II), is present in several natural products which display biological activity. For example, madurahydroxylactone (Jutten *et al.*, 2002) and its derivatives exhibit activity as esterone sulfatase inhibitors. 1-Hydroxyphthalides also have been used as precursors for the synthesis of inhibitors of platelet aggegation (Sugimoto *et al.*, 1984) and $GABA_B$ receptor antagonists (Donati *et al.*, 1989). 1-Hydroxyphthalides with a γ-ketone, as in compound (II), occur in natural product metabolites of *aspergillus duricaulis* (Achenbach *et al.*, 1985) and the basidiomycete *Hyphoderma radula* (Henkel *et al.*, 1997). We report here the structural elucidation of (II), prepared by regioselective reduction of anhydride (I) previously obtained from 4,4-dimethylcyclohexane-1,3-dione (Henderson *et al.*, 2006).



(I) (II)

Compound (II) crystallizes in the space group $P2_1/c$ as discrete molecular species and is isomorphous with 1-hydroxy-6,6-dimethyl-7,8-dihydronaphtho[1,2-*c*]furan-3,9(1*H*,6*H*)-dione (hyphodermin B) (Henderson *et al.*, 2006). All three rings and carbonyl atom O3 are coplanar. In the structure of hyphodermin B, the cyclohexyl ring is disordered with C7 modelled as two C atoms with 50% occupancy above and below the plane. The methyl groups on C6 lie above and below this plane with the Fourier synthesis showing an eclipsed conformation for the H atoms on these two groups. Carbonyl atom O4 is twisted slightly out of the plane of the molecule, the pseudo-torsion angle O4—C9···C9b—C1 being 8.7 (3)°. The geometry of the 1-hydroxyphthalimide ring is in good accord with that observed for other 1-hydroxyphthalide compounds (Valente *et al.*, 1998; Khoo & Hazell, 1999; Paulus *et al.*, 1994). In these two structures and in (II), the molecules form $R_2^2(14)$ (Bernstein *et al.*, 1995) O—H···O hydroxy-to-ketone hydrogen-bonded dimers about a crystallographic centre of symmetry (Table 2 and Fig. 1). This hydroxy-to-

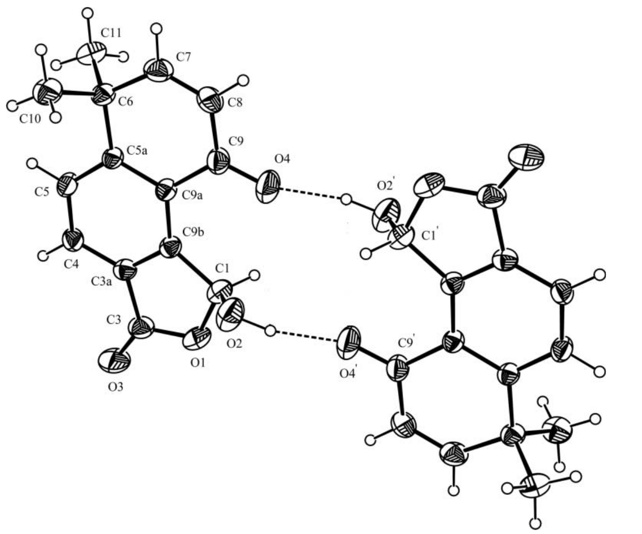


Figure 1
View of the major component of the molecule of (II), shown in its hydrogen-bonded dimer. The symmetry code of the primed atoms (′) is $2 - x, 2 - y, 1 - z$). Displacement ellipsoids for non-H atoms are drawn at the 30% probability level and H atoms are shown as circles of arbitrary radii.

ketone dimerization mode is rare, with only six examples previously reported (Rath *et al.*, 2005, and references therein).

Experimental

Lithium tri-*tert*-butoxyaluminohydride (165 mg, 0.64 mmol) was added to tetrahydrofuran (THF, 10 ml) at room temperature and stirred vigorously. The solution was then cooled to 273 K, anhydride (I) (Henderson *et al.*, 2006) (155 mg, 0.64 mmol) was added and the solution stirred for 4 h at 273 K. Ammonium chloride (5 ml) and HCl (1 *M*, 15 ml) were added and the aqueous phase extracted with dichloromethane (DCM, 3 × 25 ml). The combined organic phases were washed with brine (2 × 30 ml), dried ($MgSO_4$) and the solvent removed *in vacuo* to give a brown solid (143 mg). Purification by silica-gel chromatography (ethyl acetate–hexane, 1:1) gave compound (II) (38 mg, 24%). Slow evaporation of a chloroform solution gave pale-orange crystals (m.p. 452–453 K); λ_{max} (KBr/cm^{-1}) 3421 (*m*, *br*), 2970 (*w*, *br*), 1767 (*s*), 1655 (*s*), 1607 (*m*); δ_H (200 MHz, $CDCl_3$) 1.57 (6H, *s*, 2 × CH_3), 6.48 (1H, *d*, *J* 10.2, H7), 7.04 (1H, *s*, H1), 7.08 (1H, *d*, *J* 10.2, H8), 7.84 (1H, *d*, *J* 8, H5), 8.08 (1H, *d*, *J* 8.4, H4); δ_C (100 MHz, $CDCl_3$) 185.7 (C9), 167.9 (C3), 159.2 (C7), 157.0 (C5a), 148.3 (C9b), 132.0 (C9a), 130.0 (C4), 129.1 (C5), 126.7 (C3a), 126.5 (C8), 97.5 (C1), 39.0 (C6), 29.9, 29.4 (2 × CH_3); (ESMS, −ve) 243, (M^-, 100%), (ESMS, +ve) 245 (MH$^+$, 30%), 267 (MNa$^+$, 100%), 251 (MLi$^+$, 100%); HRMS calculated $C_{14}H_{11}O_4$ 243.0657, found 243.06564.

Crystal data

$C_{14}H_{12}O_4$
$M_r = 244.24$
Monoclinic, $P2_1/c$
$a = 10.4825$ (13) Å
$b = 7.0735$ (17) Å
$c = 16.081$ (3) Å
$\beta = 90.556$ (12)°
$V = 1192.3$ (4) Å^3
$Z = 4$
$D_x = 1.361$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 12.7$–17.4°
$\mu = 0.10$ mm^{-1}
$T = 295$ K
Plate, pale orange
0.45 × 0.40 × 0.15 mm

Data collection

Rigaku AFC-7R diffractometer
ω–2θ scans
Absorption correction: ψ scan (North *et al.*, 1968)
$T_{min} = 0.956$, $T_{max} = 0.985$
2395 measured reflections
2100 independent reflections
1441 reflections with $I > 2\sigma(I)$
$R_{int} = 0.018$
$\theta_{max} = 25.0°$
$h = -12 \rightarrow 12$
$k = -8 \rightarrow 0$
$l = -9 \rightarrow 19$
3 standard reflections every 150 reflections intensity decay: 0.3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.060$
$wR(F^2) = 0.179$
$S = 1.05$
2100 reflections
163 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0794P)^2 + 0.8739P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.60$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C1	1.468 (4)	O4—C9	1.231 (4)
O1—C3	1.359 (4)	C1—C9*B*	1.508 (4)
O2*A*—C1	1.343 (4)	C3—C3*A*	1.474 (4)
O2*B*—C1	1.3404	C3*A*—C9*B*	1.362 (4)
O3—C3	1.190 (4)	C7—C8	1.311 (5)
C1—O1—C3	111.1 (2)	O1—C3—O3	122.1 (3)
O1—C1—C9*B*	103.3 (3)	O3—C3—C3*A*	130.5 (3)
O2*A*—C1—C9*B*	112.3 (3)	C3—C3*A*—C9*B*	109.5 (3)
O2*B*—C1—C9*B*	110.98	C6—C7—C8	125.9 (3)
O1—C1—O2*B*	111.20	C7—C8—C9	121.8 (3)
O1—C1—O2*A*	107.8 (3)	O4—C9—C8	122.0 (3)
O1—C3—C3*A*	107.4 (3)	O4—C9—C9*A*	120.4 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2*A*—H2*A*···O4^i	0.95	1.81	2.709 (4)	156

Symmetry code: (i) $-x + 2, -y + 1, -z + 1$.

Significant residual electron density in the vicinity of the H atom bonded to C1 suggested the presence of minor enantiomeric disorder of the hydroxy group in the crystal structure. This was modelled with occupancy factors of 0.9 for the major component and 0.1 for the minor component. The carbon-bound H atoms were constrained as riding atoms, with C—H = 0.95 Å. U_{iso}(H) values were set at $1.2U_{eq}$ of the parent atom. The hydroxy H atom of the major component was located in a difference Fourier synthesis and constrained with O—H = 0.95 Å. The O and H atoms of the minor group were constrained with C—O = 1.34 Å and O—H = 0.95 Å.

Data collection: *MSC/AFC7 Diffractometer Control Software* (Molecular Structure Corporation, 1999); cell refinement: *MSC/AFC7 Diffractometer Control Software*; data reduction: *TEXSAN* for Windows (Molecular Structure Corporation, 2001); program(s) used to solve structure: *TEXSAN* for Windows; program(s) used to refine structure: *TEXSAN* for Windows and *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *TEXSAN* for Windows and *PLATON* (Spek, 2003).

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