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(5*R*,5a*R*,8a*R*,9*S*)-5-(3,4-dihydroxy-5-methoxyphenyl)-9-fluoro-5,8,8a,9-tetrahydrofuro[3′,4′:6,7]naphtho[2,3-*d*]-1,3-dioxol-6(5a*H*)-one acetone solvate

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Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.005 Å
R factor = 0.047
wR factor = 0.132
Data-to-parameter ratio = 8.0

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

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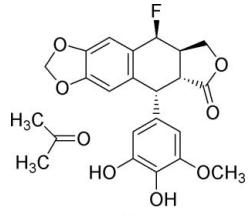
The title compound, $C_{20}H_{17}FO_7\cdot C_3H_6O$, is a potential anti-tumour agent. Its absolute configuration was assigned based on that of the synthetic precursor. Intermolecular O—H···O hydrogen bonds link the molecules in the crystal structure into layers parallel to (010). These layers are stabilized by weak interlayer C—H···O hydrogen bonds.

Comment

Semi-synthetic analogues of the naturally occurring podophyllotoxin have attracted much interest in the past two decades as a result of the development of etoposide (VP-16) and teniposide (VM-26) as anticancer drugs (Damayanthi & Lown, 1998; Silverberg *et al.*, 2000; Van Vliet *et al.*, 2001). It has been well established, in these years, that the introduction of an F atom into some biomolecules can result in important modifications of their biological properties (Welch & Eswarakrishnan, 1991; Filler *et al.*, 1993). In order to find new compounds with high anticancer reactivity, our group has synthesized several fluorinated podophyllotoxins (He *et al.*, 2004). We report here the crystal structure of one of them, (I), as its acetone solvate.



(I)

The molecular structure of (I) is shown in Fig. 1. Selected molecular parameters and hydrogen-bond geometric characteristics are listed in Tables 1 and 2, respectively. The asymmetric unit contains one molecule of (I) and one molecule of acetone. The absolute configuration was assigned according to the known configuration of the starting material, as the chiral centres were not affected by the reaction. Intermolecular O—H···O hydrogen bonds play an important role, resulting in the formation of polymeric layers parallel to (010). These layers are stabilized by weak interlayer C—H···O hydrogen bonds.

Experimental

To a solution of 4β-3′,4′-dimethylpodophyllotoxin-3′4′-quinone (120 mg, 0.31 mmol) in CH_2Cl_2 (10 ml) was added dropwise (diethylamino)sulfur trifluoride (DAST, 0.04 ml) at 233 K under nitrogen. The reaction solution was stirred for 30 min at 233 K and then allowed to warm to room temperature. Water (0.1 ml) was added

dropwise to quench the unreacted DAST. The reaction solution was diluted with CH_2Cl_2 (50 ml), and washed with saturated aqueous $NaHCO_3$ and water. The organic phase was dried over $MgSO_4$. After removal of the solvent *in vacuo*, the solid was purified by silica gel column chromatography (CH_2Cl_2–AcOEt, 5:1, *v*/*v*) and crystallized from acetone to afford the pure title compound as crystals (yield 75%). M.p. 533–535 K. ^{1}H NMR (500 MHz, DMSO-d_6, p.p.m.): δ 7.12 (*s*, 1H), 6.61 (*s*, 1H), 6.28 (1*s*, 1H), 6.05 (*d*, 2H, J = 10 Hz), 5.80 (*s*, 1H), 5.70 (*dd*, J = 2.54 Hz, 1H), 4.52 (*s*, 1H), 4.46 (*m*, 1H), 4.13 (*m*, 1H), 3.64 (*s*, 3H), 3.21 (*m*, 1H), 3.87 (*m*, 1H); MS (ESI): *m*/*z* 389 ([*M*−H]$^-$); IR (KBr, cm^{-1}): 3170, 1774, 1618, 1504, 1484, 933.

Crystal data

$C_{20}H_{17}FO_7\cdot C_3H_6O$
M_r = 446.43
Monoclinic, *C*2
a = 19.1786 (9) Å
b = 7.7058 (3) Å
c = 14.0757 (7) Å
β = 92.373 (2)°
V = 2078.4 (2) Å^3
Z = 4
D_x = 1.427 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 7291 reflections
θ = 2.9–27.5°
μ = 0.11 mm^{-1}
T = 296.1 K
Platelet, colourless
0.41 × 0.28 × 0.08 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
ω scans
Absorption correction: multi-scan (Higashi, 1995)
T_{min} = 0.923, T_{max} = 0.991
9048 measured reflections
2486 independent reflections
2086 reflections with $F^2 > 2\sigma(F^2)$
R_{int} = 0.023
θ_{max} = 27.5°
$h = -24 \rightarrow 24$
$k = -10 \rightarrow 8$
$l = -18 \rightarrow 18$

Refinement

Refinement on F^2
$R(F)$ = 0.047
$wR(F^2)$ = 0.132
S = 1.01
2484 reflections
312 parameters
H-atom parameters constrained
$w = 1/[0.0025F_o^2 + 1\sigma(F_o^2)]/(4F_o^2)$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.28 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

F1—C6	1.413 (4)	O4—C10	1.432 (5)
O1—C3	1.201 (4)	O5—C16	1.362 (3)
O2—C3	1.342 (5)	O5—C17	1.414 (3)
O2—C4	1.458 (5)	O6—C18	1.371 (3)
O3—C9	1.381 (4)	O7—C19	1.355 (3)
F1—C6—C5	108.7 (2)	O3—C9—C8	127.8 (3)
O1—C3—C2	129.2 (3)	O4—C11—C9	110.5 (3)
O1—C3—O2	121.4 (3)	O4—C11—C12	127.8 (3)
O2—C3—C2	109.3 (3)	O6—C18—C16	122.1 (2)
C4—O2—C3	110.6 (3)	O7—C19—C18	121.8 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O6—H601···O5	0.92	2.26	2.691 (3)	108
O7—H701···O6	0.94	2.41	2.753 (3)	102
C4—H41···F1	0.97	2.47	2.865 (4)	104
O6—H601···O1^{i}	0.92	1.96	2.835 (2)	158
O7—H701···O6^{ii}	0.94	1.98	2.857 (3)	154
C20—H20···O3^{iii}	0.98	2.53	3.340 (3)	140

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

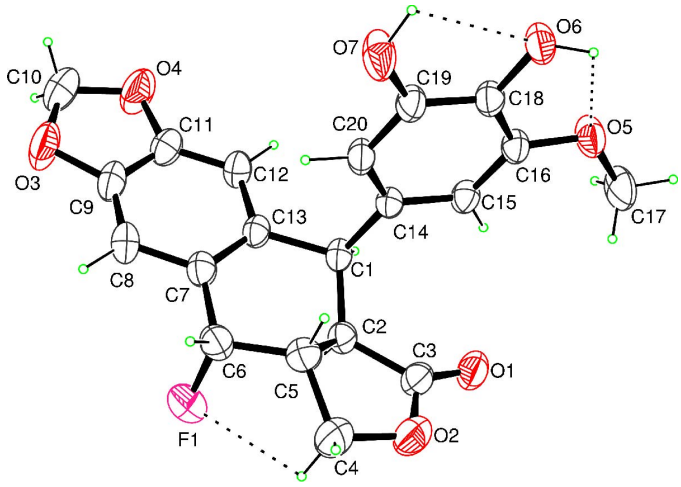


Figure 1
The molecule of (I) in the crystal structure. Displacement ellipsoids are drawn at the 50% probability level. Dashed lines indicate hydrogen bonds. The acetone solvent molecule has been omitted

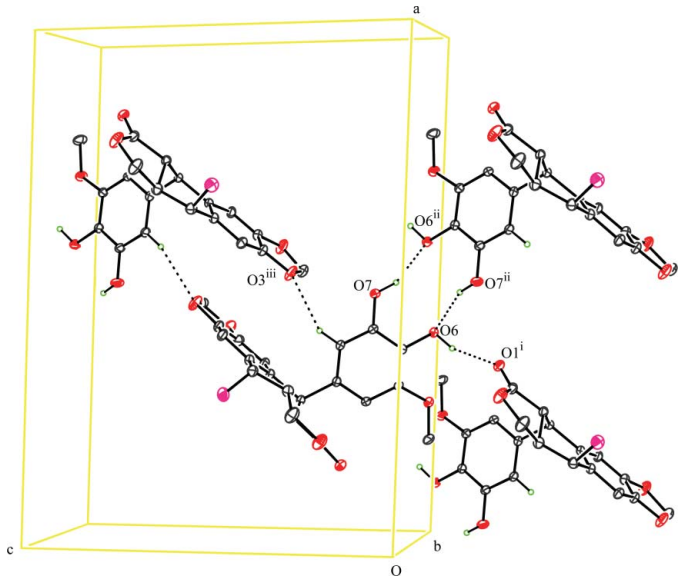


Figure 2
The molecular packing of (I), viewed approximately along the *b* axis. Dashed lines indicate hydrogen-bonding interactions (solvent molecules have been omitted for clarity). H atoms not involved in hydrogen bonding have been omitted (see Table 2 for symmetry codes).

Atoms H601 and H701 were found in a difference Fourier map and fixed in position. The other H atoms were placed in calculated positions with C—H = 0.96–0.98 Å and included in the final cycles of refinement in a riding model, with U_{iso}(H) = 1.2U_{eq}(carrier atoms).

Data collection: *PROCESS-AUTO* (Rigaku, 1998); cell refinement: *PROCESS-AUTO*; data reduction: *CrystalStructure* (Rigaku/MSC, 2004); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *CRYSTALS* (Watkin *et al.*, 1996); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *CrystalStructure* and *PLATON* (Spek, 2003).

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