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Eplerenone tetrahydrofuran solvate

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Key indicators

Single-crystal X-ray study
T = 295 K
Mean σ(C–C) = 0.007 Å
H-atom completeness 79%
Disorder in solvent or counterion
R factor = 0.070
wR factor = 0.229
Data-to-parameter ratio = 10.7

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

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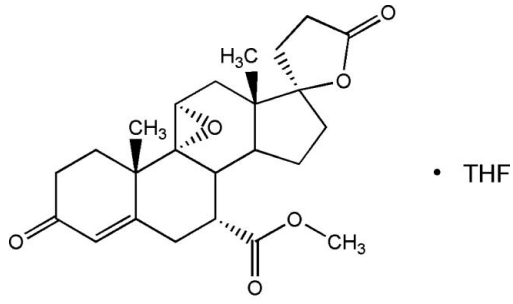
The eplerenone molecule of the title compound, $C_{24}H_{30}O_6 \cdot C_4H_8O$, contains three six-membered rings, two five-membered rings and one three-membered ring. In the crystal structure, the eplerenone molecules are linked *via* C—H···O hydrogen bonds, forming a 303 Å^3 cavity, which is occupied by two disordered solvent THF molecules.

Comment

Eplerenone is known as an aldosterone receptor antagonist (Grob *et al.*, 1985). Recently, we prepared single crystals of eplerenone from a tetrahydrofuran (THF) solution and determined the crystal structure of the title compound, (I).



(I)

The eplerenone molecule contains three six-membered rings, two five-membered rings and one three-membered ring (Fig. 1). Both five-membered rings display a similar envelope configuration. In the O3-containing ring, atom C18 lies at the flap position and is displaced by 0.386 (8) Å from the mean plane formed by the other four atoms; in the C15-containing ring, C13 lies at the flap position and is displaced by 0.683 (6) Å from the mean plane formed by the other four atoms. The C2═C3 bond distance (Table 1) shows typical C═C double-bond character.

Atom O5 of the C23-containing ester group forms an intramolecular C—H···O hydrogen bond with the C14-methine group (Fig. 1 and Table 2); the C9—C8—C23—O5 torsion angle is 72.7 (5)°. The C7—C8—C23—O6 torsion angle is 16.2 (5)°, leading to a shorter O6···C7 contact of 2.706 (6) Å. These structural features are identical with those found in the crystal structure of eplerenone dichloromethane solvate (Grob *et al.*, 1997).

In the crystal structure, adjacent eplerenone molecules are linked to each another *via* C—H···O hydrogen bonds involving the carbonyl groups (Table 2), forming a 303 Å^3 cavity (Spek, 2003) which is occupied by two disordered THF solvent molecules (Fig. 2).

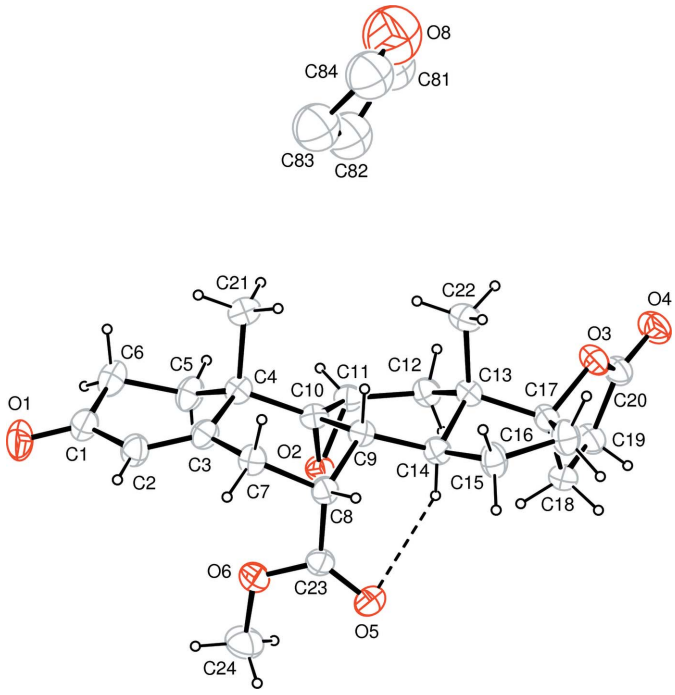


Figure 1
The molecular structure of (I) with 30% probability displacement ellipsoids (arbitrary spheres for H atoms). The minor disorder component of the THF solvent molecule has been omitted for clarity. The dashed line indicates the intramolecular hydrogen bond.

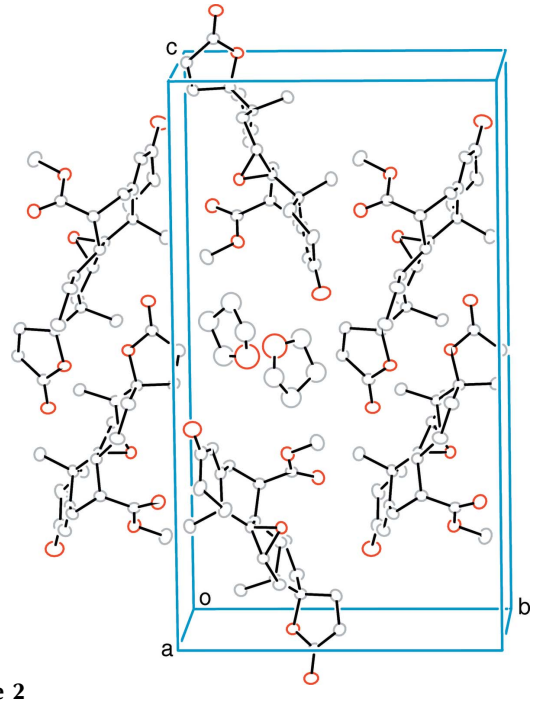


Figure 2
The packing of (I). H atoms and the minor disorder component of THF have been omitted for clarity.

Experimental

A microcrystalline powder sample of eplerenone was prepared in the manner reported by Grob *et al.* (1997). Single crystals of (I) were obtained from a THF solution of eplerenone.

Crystal data

$C_{24}H_{30}O_6\cdot C_4H_8O$
M_r = 486.58
Orthorhombic, $P2_12_12_1$
a = 8.2974 (7) Å
b = 13.1968 (11) Å
c = 23.3855 (15) Å
V = 2560.7 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 295 (2) K
0.32 × 0.19 × 0.13 mm

Data collection

Rigaku RAXIS-RAPID IP diffractometer
Absorption correction: none
24665 measured reflections
3304 independent reflections
2006 reflections with $I > 2\sigma(I)$
R_{int} = 0.053

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.070
$wR(F^2)$ = 0.229
S = 1.07
3304 reflections
308 parameters
10 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.31 e Å^{-3}
$\Delta\rho_{min}$ = −0.35 e Å^{-3}

Table 1
Selected bond lengths (Å).

O1—C1	1.241 (7)	O5—C23	1.198 (6)
O3—C20	1.346 (5)	O6—C23	1.316 (6)
O3—C17	1.487 (5)	C2—C3	1.335 (7)
O4—C20	1.209 (6)		

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

D—H···A	D—H	H···A	D···A	D—H···A
C11—H11···O4^{i}	0.98	2.60	3.410 (6)	140
C12—H12B···O1^{ii}	0.97	2.55	3.499 (7)	168
C14—H14···O5	0.98	2.48	3.096 (6)	120
C19—H19B···O1^{ii}	0.97	2.58	3.240 (7)	125
C21—H21A···O5^{iii}	0.96	2.55	3.344 (7)	141

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

An initial difference Fourier map indicated that the solvent THF molecule is disordered, and a two-site disorder model was adopted in the refinement. Isotropic refinement for the two disordered components gave occupancies of 0.521 (9) and 0.479 (9), respectively. Geometrical restraints were used, and the displacement parameters of some pairs of atoms were kept equal to each other. The H atoms of the disordered THF molecules were not located. Methyl H atoms were placed in calculated positions, C—H = 0.96 Å, and torsion angles were refined to fit the electron density; U_{iso}(H) = 1.5U_{eq}(C). Other H atoms were placed in calculated positions, C—H = 0.93–0.98 Å, and refined in riding mode with U_{iso}(H) = 1.2U_{eq}(C). In the absence of significant anomalous scattering effects, Friedel pairs were merged; the absolute configuration of (I) was not determined.

Data collection: *PROCESS-AUTO* (Rigaku, 1998); cell refinement: *PROCESS-AUTO*; data reduction: *CrystalStructure* (Rigaku/MSC, 2002); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1993); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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