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10β-Hydroxy-6α-(3,4,5-trimethoxyphenyl)-2,3,6,6aα,7,9,9aβ,10-octahydroisobenzofuro[5,6-*g*][1,4]benzodioxin-7-one

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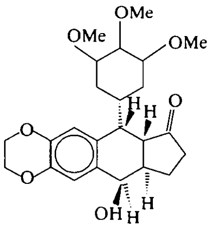
Abstract

The title compound, $C_{23}H_{24}O_8$, is the first crystal structure to be reported with an isobenzofuro[5,6-*g*][1,4]-benzodioxin tetracyclo skeleton. The furan ring has an envelope form, while the two non-aromatic six-membered rings have a twisted planar form. Two molecules are linked by hydrogen bonding, giving dimeric units.

Comment

As a continuation of our research into 2,3-dihydro-1,4-benzodioxin chemistry, we are interested in the preparation of the corresponding podophyllotoxin analogues (Capilla & Pujol, 1996; Forsey *et al.*, 1989). The preparation of the title compound, (I), with four stereogenic centres is difficult in view of its possible epimerization. The present X-ray crystal structure analysis has been carried out in order to determine the relative configurations at these stereogenic centres, and the title compound is the first reported crystal structure with an isobenzofuro[5,6-*g*][1,4]benzodioxin tetracyclo skeleton.



(I)

For the isomer where C4 has an *R* form, atoms C3, C13 and C14 have *S* forms. The five-membered ring has an envelope form, with the C3 atom 0.348 (2) Å out of the plane defined by the remaining four atoms. This form is the most common in the Cambridge Structural Database (Allen & Kennard, 1993) for podophyllotoxin-analogue compounds, with the exception of 2-methylisodeoxypicrophyllotoxin diethyl ether solvate and 2-trifluoromethylisodeoxypicrophyllotoxin (Beard *et al.*, 1987). The non-aromatic six-membered rings have a twisted planar form, with C8 −0.370 (3) and C9 0.349 (3) Å out of the plane defined by O3, O4 and the C atoms of the aromatic ring, and C3 0.348 (2) and C14 −0.450 (2) Å out of the plane defined by C4, C13 and the C atoms of the aromatic ring. This is due to the planarity of the aromatic moiety and to the difference between the aromatic and the Csp^3—Csp^3 bond lengths. This fact also produces an increase in the O3—C7—C10, O4—C10—C7, C4—C5—C12 and C13—C12—C5 bond angles [mean angle 122.0 (5)° for the benzodioxin ring and 123.28 (10)° for the second ring].

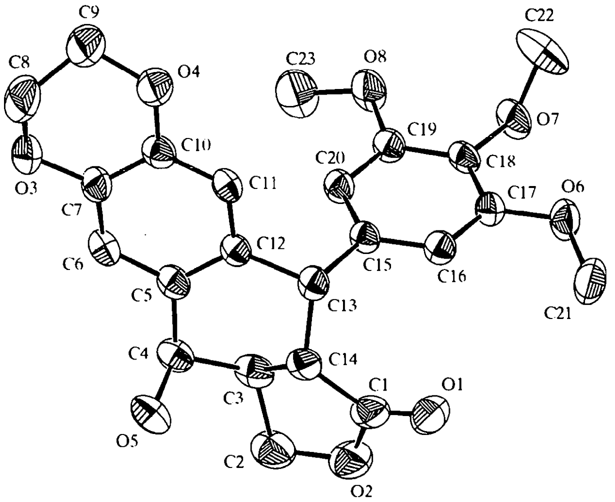


Fig. 1. The molecular structure of (I), showing 50% probability displacement ellipsoids. H atoms are omitted for clarity.

The 3,4,5-trimethoxyphenyl substituent is rotated by −19.3 (3)° with respect to the aromatic moiety plane. The steric hindrance between the methoxy substituents results in a deviation of the O—C_{ar}—C_{ar} bond angles from the theoretical 120° value. The average values for the three types of angles are 116.0 (14) (O6—C17—C18 and O8—C19—C18), 123.7 (2) (O6—C17—C16 and O8—C19—C20) and 120.18 (3)° (O7—C18—C17 and O7—C18—C19), while these values are 115.5 (12), 124.2 (13) and 120.2 (11)° from 96 observations of 83 crystal structures in the Cambridge Structural Database.

Experimental

Crystals of the title compound were obtained by diffusion of hexane into an ethyl acetate solution of (I) at room temperature.

Crystal data

$C_{23}H_{24}O_8$
$M_r = 428.42$

Mo *K*α radiation
$\lambda = 0.71069$ Å

Triclinic
$P\bar{1}$
$a = 8.608\ (3)$ Å
$b = 10.393\ (4)$ Å
$c = 12.455\ (5)$ Å
$\alpha = 109.36\ (4)^\circ$
$\beta = 102.24\ (3)^\circ$
$\gamma = 92.10\ (3)^\circ$
$V = 1020.4\ (7)$ Å^3
$Z = 2$
$D_x = 1.394$ Mg m^{-3}
D_m not measured

Cell parameters from 25 reflections
$\theta = 12\text{–}21^\circ$
$\mu = 0.106$ mm^{-1}
$T = 293\ (2)$ K
Prism
0.3 × 0.2 × 0.2 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
4261 measured reflections
4219 independent reflections
3636 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.008$
$\theta_{\rm max} = 29.96^\circ$
$h = -12 \rightarrow 11$
$k = -14 \rightarrow 13$
$l = 0 \rightarrow 17$
3 standard reflections
frequency: 120 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.057$
$wR(F^2) = 0.141$
$S = 1.044$
4219 reflections
376 parameters
H atoms: see text
$w = 1/[\sigma^2(F_o^2) + (0.0737P)^2 + 0.2731P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max} = 0.482$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.210$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

O3—C8	1.433 (3)	O5—C4	1.436 (3)
O4—C9	1.446 (3)	C8—C9	1.476 (4)
C17—O6—C21	116.27 (18)	C5—C12—C13	123.38 (18)
C18—O7—C22	113.57 (19)	O6—C17—C18	116.40 (17)
C19—O8—C23	118.33 (18)	O6—C17—C16	123.46 (18)
O1—C1—C14	130.3 (2)	O7—C18—C17	120.15 (18)
C12—C5—C4	123.17 (18)	O7—C18—C19	120.20 (18)
O3—C7—C10	121.45 (19)	O8—C19—C18	115.67 (17)
O4—C10—C7	122.45 (18)	O8—C19—C20	123.95 (18)
C2—O2—C1—C14	−1.8 (3)	O3—C7—C10—O4	−0.4 (3)
C1—O2—C2—C3	21.1 (3)	C4—C5—C12—C13	3.4 (3)
C2—C3—C4—O5	48.1 (3)	C5—C12—C13—C14	−17.8 (2)
C3—C4—C5—C12	−19.7 (3)	C11—C12—C13—C15	−72.3 (2)
C8—O3—C7—C10	−14.3 (3)	O2—C1—C14—C3	−18.5 (2)
C9—O4—C10—C7	−16.8 (3)	C15—C13—C14—C1	48.4 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O5—H5O···O3$^{\rm i}$	0.87 (4)	1.92 (3)	2.770 (3)	166 (3)

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

The positions of all H atoms were located from a difference map and their atomic coordinates and isotropic displacement parameters were refined.

Data collection: *CAD-4/PC* (Kretschmar, 1996). Cell refinement: *CAD-4/PC*. Data reduction: *CFEO* (Solans, 1978). Program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997*a*). Program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997*b*). Molecular graphics: *ORTEP* (Brueggemann & Schmid, 1990). Software used to prepare material for publication: *PLATON* (Spek, 1990).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: OS1046). Services for accessing these data are described at the back of the journal.

References

Allen, F. H. & Kennard, O. (1993). *Chem. Des. Autom. News*, **8**, 31–37.
Beard, A. R., Drew, M. G. B., Mann, J. & Wong, L. T. F. (1987). *Tetrahedron*, **43**, 4207–4209.
Brueggemann, R. & Schmid, G. (1990). PC version of *ORTEP*3.2. University of Ulm, Germany.
Capilla, A. S. & Pujol, M. D. (1996). *Synth. Commun.* **26**, 1729–1738.
Forsey, S. P., Rajapaksa, D., Taylor, N. J. & Rodrigo, R. (1989). *J. Org. Chem.* **54**, 4280–4290.
Kretschmar, M. (1996). *CAD-4/PC*. Version 2.0. PC version of *CAD-4 Software*. Version 5.0. University of Tübingen, Germany.
Spek, A. L. (1990). *Acta Cryst.* A**46**, C34.
Sheldrick, G. M. (1997*a*). *SHELXS97. Program for the Solution of Crystal Structures*. University of Göttingen, Germany.
Sheldrick, G. M. (1997*b*). *SHELXL97. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
Solans, X. (1978). *CFEO*. University of Barcelona, Spain.

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Androst-4-ene-3,6,17-trione

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Abstract

The title steroid, $C_{19}H_{24}O_3$, has flattened *A* and *B* rings and a 14α *D*-ring conformation. The crystal structure is stabilized by numerous C—H···O hydrogen bonds.

Comment

Steroids with a Δ^4-3,6-dione functional group occur naturally (Tischler *et al.*, 1988) and are known to be potent inhibitors of aromatase, an enzyme that is the target for curing oestrogen-dependent carcinoma and in the modulation of reproductive processes. Androst-4-ene-3,6,17-trione (AT) is a synthetic androgen and a suicide substrate for aromatase (Covey & Hood,