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24(*R*)-Acetyloxy-1 α ,2 α -epoxycholesta-4,6-dien-3-one hydrate

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Received 24 March 2000

Accepted 30 May 2000

Data validation number: IUC0000159

In the title compound, C₂₉H₄₂O₄·H₂O, cyclohexane rings *A* and *B* are in the sofa conformation, ring *C* is in a chair conformation and the five-membered ring *D* is in an envelope conformation. The structure is stabilized by inter- and intramolecular C—H···O and O—H···O hydrogen bonds.

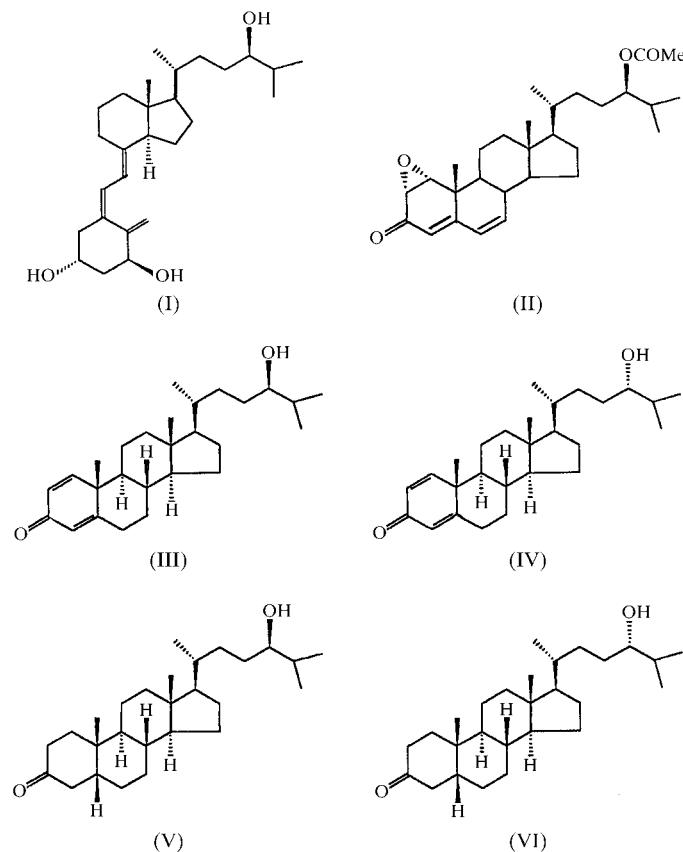
Comment

1 α ,24(*R*)-Dihydroxy vitamin D₃ [tacalcitol, (I); Takeshita *et al.*, 1977; Ochi *et al.*, 1979; Okamoto *et al.*, 1995; Fall *et al.*, 1997] displays antipsoriatic activity. The title compound, (II), which contains an 1 α ,2 α -epoxide ring and a 24-acetate group is the major intermediate in the synthesis of vitamin D₃. The absolute configuration at C-24 in these molecules was assigned by physical methods involving optical rotation (Klyne & Stokes, 1954) and NMR spectra (Ikekawa *et al.*, 1975; Koizumi *et al.*, 1975; Seki *et al.*, 1975; Koch *et al.*, 1983; Meenakshi *et al.*, 1997).

We have synthesized intermediates (III) [24(*R*)-hydroxycholesta-1,4-dien-3-one] and (IV) [24(*S*)-hydroxycholesta-1,4-dien-3-one], which are epimeric at C-24, from the corresponding ketones (V) [24(*R*)-hydroxycholestan-3-one] and (VI) [24(*S*)-hydroxycholestan-3-one]. The title compound, (II), was synthesized from (III) by acylation, bromination, dehydrobromination and epoxidation. The melting point (393–395 K; Ochi *et al.*, 1979) of epimer (III) agrees with the reported values, while the melting point of the title compound is 373–375 K. There is a solvent water molecule present in the structure. The packing of the molecule is established by inter and intramolecular C—H···O and O—H···O hydrogen bonds. Water H atoms were fixed using the program *HYDROGEN* (Nardelli, 1999).

Rings *A* (C1–C10), *B* (C5–C10), *C* (C8–C14) and *D* (C13–C17) adopt sofa, sofa, chair and envelope conformations, respectively. Substituents at C8 and C9, and C13 and C14 are at diaxial positions in the cyclohexane rings leading to a *trans*

conformation [torsion angles H8—C8—C9—H9 = 179° and C18—C13—C14—H14 = 177°]. The priority sequence attached to the chiral carbon C24 has an '*R*' designation as per the listed coordinates. The absolute conformation could not be determined unequivocally as the structure contains only light atoms. The side chain attached to the *D* ring is in an all-*trans* conformation.



The best plane passing through ring *A* makes a dihedral angle of 14.2 (1)° with the best plane passing through cyclohexane ring *B*. The dihedral angles between rings *B* and *C*, and between rings *C* and *D* are 8.7 (2) and 9.6 (2)°, respectively.

Experimental

24(*R*)-Hydroxycoprastan-3-one, obtained from lithocholic acid by acetylation with acetic anhydride and pyridine, afforded 24(*R*)-acetoxycoprastan-3-one. This, on bromination with bromine and acetic acid and subsequent dehydrobromination (Wilds & Djerassi, 1946), afforded 24(*R*)-acetoxycholesta-1,4-dien-3-one. Further bromination with *N*-bromosuccinimide and dehydrobromination (Kaufmann *et al.*, 1950) of the resulting bromide gave 24(*R*)-acetoxycholesta-1,4,6-trien-3-one. Epoxidation of the trienone with 30% aqueous hydrogen peroxide under alkaline conditions yielded the title compound. Single crystals were obtained by slow evaporation from a solution in methanol.

Crystal data

C₂₉H₄₂O₄·H₂O
M_r = 472.64
 Monoclinic, *P*2₁
a = 10.642 (3) Å
b = 11.719 (2) Å
c = 10.977 (3) Å
 β = 108.04 (2)°
V = 1301.7 (6) Å³
Z = 2

D_x = 1.206 Mg m⁻³
 Cu *K*α radiation
 Cell parameters from 25 reflections
 θ = 10–27°
 μ = 0.638 mm⁻¹
T = 293 (2) K
 Rectangular, colourless
 0.20 × 0.15 × 0.10 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
 $\omega/2\theta$ scans
 2848 measured reflections
 2712 independent reflections
 2262 reflections with *I* > 2σ(*I*)
*R*_{int} = 0.016

θ_{\max} = 74.86°
h = 0 → 13
k = 0 → 13
l = -13 → 13
 3 standard reflections
 frequency: 120 min
 intensity decay: <3%

Refinement

Refinement on *F*²
R[*F*² > 2σ(*F*²)] = 0.056
wR(*F*²) = 0.162
S = 1.123
 2712 reflections
 322 parameters
 H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0950P)^2 + 0.2101P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} = 0.010$
 $\Delta\rho_{\max} = 0.27 \text{ e \AA}^{-3}$
 $\Delta\rho_{\min} = -0.55 \text{ e \AA}^{-3}$
 Extinction correction: *SHELXL97*
 Extinction coefficient: 0.0091 (15)

Table 1

Selected geometric parameters (Å, °).

O1–C3	1.223 (5)	O3–C24	1.462 (4)
O2–C1	1.431 (5)	O4–C28	1.194 (5)
O2–C2	1.451 (5)	O1W–H1W	0.94 (5)
O3–C28	1.339 (4)	O1W–H2W	1.03 (5)
C1–O2–C2	60.7 (3)	O2–C1–C10	117.9 (3)
C28–O3–C24	119.0 (3)	O2–C2–C1	59.0 (3)
O2–C1–C2	60.3 (3)	H1W–O1W–H2W	111 (6)
C2–O2–C1–C10	112.9 (4)	C20–C22–C23–C24	-175.9 (4)
C1–O2–C2–C3	-110.8 (4)	C22–C23–C24–C25	177.9 (4)
O2–C1–C2–C3	101.3 (4)	C23–C24–C25–C26	-175.3 (4)
C13–C17–C20–C22	-178.3 (3)	C24–O3–C28–C29	175.4 (3)
C17–C20–C22–C23	-155.3 (4)		

Table 2

Hydrogen-bonding geometry (Å, °).

<i>D</i> –H··· <i>A</i>	<i>D</i> –H	H··· <i>A</i>	<i>D</i> ··· <i>A</i>	<i>D</i> –H··· <i>A</i>
O1W–H1W···O4	0.95 (6)	2.15 (6)	3.085 (18)	174 (5)
O1W–H2W···O1 ⁱ	1.03 (6)	1.78 (6)	2.799 (18)	170 (5)
C1–H1···O1 ⁱⁱ	0.98	2.46	3.430 (6)	169

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

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *XCAD4* (Harms, 1996); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); software used to prepare material for publication: *SHELXL* and *PARST* (Nardelli, 1983, 1995).

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24(*R*)-Acetyloxy-1 α ,2 α -epoxycholesta- 4,6-dien-3-one hydrate. Erratum

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Nadamuni^b and A. Srikrishna^c**

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In the paper by Rajalakshmi *et al.* [*Acta Cryst.* (2000), **C56**, e307–308], it is incorrectly stated that ‘the priority sequence attached to the chiral carbon C24 has an ‘*R*’ designation as per the listed coordinates’. This is corrected as ‘the priority sequence attached to the chiral carbon C24 has an ‘*S*’ designation as per the listed coordinates’.