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Solving the problem of the configuration of the double bond at C22 in (25*S*)-23-acetyl-5β-furost-22-ene-3β,26-diyl diacetate

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Key indicators

Single-crystal X-ray study
T = 300 K
Mean σ(C–C) = 0.004 Å
Disorder in main residue
R factor = 0.045
wR factor = 0.133
Data-to-parameter ratio = 11.4

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

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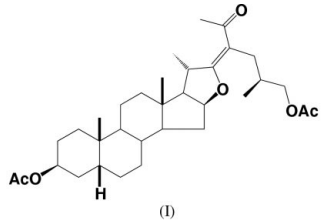
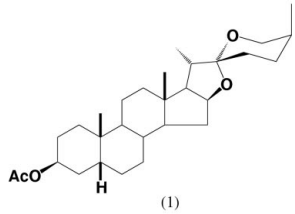
The crystal structure of the title compound, $C_{33}H_{50}O_6$, confirms that the double bond at C22, with a length of 1.355 (3) Å, has an *E* configuration, in agreement with NMR data.

Comment

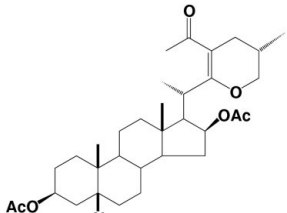
Sarsasapogenin, (1), is a potentially useful starting material for the partial synthesis of biologically important steroids (Marker, 1940). However, few studies have been carried out using this molecule, mainly because of its poor functionality. On the other hand, confusing data have been published regarding the transformation of its side chain.



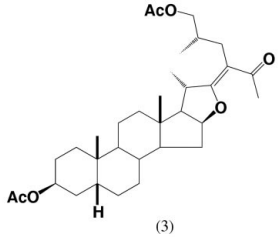
(I)



(1)



(2)



(3)

Earlier reports (Cameron *et al.*, 1955; Zderic *et al.*, 1962; Uhle, 1965; Tian *et al.*, 1994) mention that the reaction of steroidal sapogenins of the 25*R* series with Ac_2O in the presence of Lewis acids, such as BF_3 or $AlCl_3$, affords 23-acetylfurost-22-enes, analogous to (I). However, the reported data agree better with 23-acetyl-22,26-epoxycholest-22-ene, similar to (2), a new steroidal skeleton recently described (Sandoval-Ramírez *et al.*, 1999).

Our current work deals with further modifications of the side chain of (1), using Ac_2O/BF_3 (Sandoval-Ramírez *et al.*, 2003). Using this system (see Experimental), we were able to prepare (*E*)- and (*Z*)-(25*S*)-23-acetyl-5β-furost-22-ene-3β,26-diyl diacetate, *viz*. (I) and (3), respectively. The configuration of the double bond at C22 was initially established by NMR—NOESY (nuclear Overhauser effect spectroscopy) experiments. We report here the crystal structure of (I).

The title compound (Fig. 1 and Table 1) displays the expected *A*–*E* steroidal nucleus, including a *cis* *A*/*B* junction. Atoms C22 and C23 display sp^2 hybridization, with a

C22═C23 bond length of 1.355 (3) Å. The configuration of this double bond is unambiguously determined as *E*, with the C24/C25/C26 side chain oriented toward the α face of the *A*–*E* ring system. The absolute configuration for the 11 chiral centres in (I) was assigned assuming unchanged chiral centres for the *A*–*D* nucleus, relative to the starting material, giving the following configurations: 3*S*, 5*R*, 8*R*, 9*S*, 10*S*, 13*S*, 14*S*, 16*S*, 17*R*, 20*S* and 25*S*. Therefore, the acetolysis of sarsasapogenin, using the experimental conditions here described, does not modify the stereochemistry of the stereogenic centres at C20 and C25.

The crystal structure of (I) confirms the configuration of the double bond at C22, previously determined in solution, and is in agreement with the NOESY spectrum, in which a proximity between the proton at C20 and protons of the methyl group C23″ is observed.

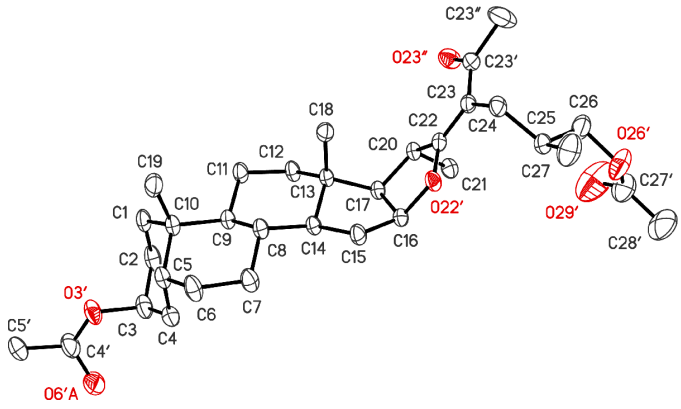


Figure 1
The structure of (I), with displacement ellipsoids drawn at the 25% probability level. For clarity, H atoms and the minor disorder component O6′ have been omitted.

Experimental

Compound (I) was prepared by acetolysis of sarsasapogenin: 100 mg of (1) was dissolved in 1 ml of acetic anhydride in a 10 ml round-bottomed flask and 0.2 ml of BF_3–Et_2O was added with magnetic stirring at room temperature. After 15 min the reaction was complete (monitored by thin-layer chromatography). The reaction mixture was poured over ground ice and vigorously agitated. The suspension was extracted with CH_2Cl_2; the organic phase was neutralized with a saturated solution of $NaHCO_3$ and then washed with brine and water. It was dried over anhydrous $MgSO_4$ and evaporated to dryness under reduced pressure. The resulting white solid was purified by chromatography on silica gel using hexane–ethyl acetate as eluant (4:1), giving four products: compound (2), yield 49%; (I) as white crystals, m.p. 407–409 K, yield 16%; (3), yield 7%; and one more, yield 25%, which is described elsewhere (Sandoval-Ramírez *et al.*, 2003). Single crystals of (I) were obtained by slow evaporation of a heptane/AcOEt solution (9:1) at room temperature.

Crystal data

$C_{33}H_{50}O_6$
M_r = 542.73
Monoclinic, $P2_1$
a = 12.9463 (14) Å
b = 7.3819 (10) Å
c = 16.8664 (17) Å
β = 98.562 (6)°
V = 1593.9 (3) Å^3
Z = 2
D_x = 1.131 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 68 reflections
θ = 4.6–12.5°
μ = 0.08 mm^{-1}
T = 300 (1) K
Prism, colourless
0.65 × 0.50 × 0.38 mm

Data collection

Bruker *P*4 diffractometer
$2\theta/\omega$ scans
Absorption correction: none
7849 measured reflections
4144 independent reflections
3498 reflections with $I > 2\sigma(I)$
R_{int} = 0.028
θ_{max} = 28.0°
$h = -17 \rightarrow 8$
$k = -1 \rightarrow 9$
$l = -22 \rightarrow 22$
3 standard reflections
every 97 reflections
intensity decay: <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.045
$wR(F^2)$ = 0.133
S = 1.05
4144 reflections
363 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0712P)^2 + 0.1538P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}
Extinction correction: *SHELXTL-Plus*
Extinction coefficient: 0.016 (3)

Table 1
Selected geometric parameters (Å, °).

C20—C22	1.513 (3)	C24—C25	1.530 (4)
C20—C21	1.529 (3)	C25—C26	1.517 (4)
C22—O22′	1.355 (3)	C25—C27	1.522 (4)
C22—C23	1.355 (3)	C26—O26′	1.444 (4)
C23—C23′	1.459 (4)	O26′—C27′	1.297 (5)
C23—C24	1.526 (3)	C27′—O29′	1.185 (6)
C23′—O23″	1.227 (3)	C27′—C28′	1.461 (7)
C23′—C23″	1.503 (4)		
C22—C20—C17	102.84 (17)	O23″—C23′—C23″	115.6 (3)
C22—C20—C21	108.32 (15)	C23—C23′—C23″	119.8 (3)
C17—C20—C21	111.4 (2)	C23—C24—C25	114.32 (19)
O22′—C22—C23	119.43 (18)	C26—C25—C27	110.7 (2)
O22′—C22—C20	110.42 (18)	C26—C25—C24	111.7 (3)
C23—C22—C20	130.0 (2)	C27—C25—C24	109.8 (2)
C22—O22′—C16	110.99 (15)	O26′—C26—C25	109.3 (3)
C22—C23—C23′	120.0 (2)	C27′—O26′—C26	120.7 (3)
C22—C23—C24	117.8 (2)	O29′—C27′—O26′	120.2 (4)
C23′—C23—C24	122.1 (2)	O29′—C27′—C28′	124.7 (5)
O23″—C23′—C23	124.5 (2)	O26′—C27′—C28′	114.7 (4)

Disorder was observed for the carbonyl O atom of the OAc group on C3. This site was split into two components, O6′ and O6′*A*. Site-occupancy factors refined to 0.47 (1) and 0.53 (1) for O6′ and O6′*A*, respectively. H atoms were placed at idealized positions and were treated as riding atoms, with C—H distances constrained to 0.96 (methyl groups), 0.97 (methylene CH_2) or 0.98 Å (methine CH), and with U_{iso}(H) = xU_{eq}(parent C) (x = 1.5 for methyl groups and x = 1.2 for methylene CH_2 and methine CH groups).

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXTL-Plus* (Sheldrick, 1998); program(s) used to refine structure: *SHELXTL-Plus*; molecular graphics: *SHELXTL-Plus*; software used to prepare material for publication: *SHELXTL-Plus*.

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