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(20*S*)-Methyl-3-oxochola-1,4,22-trien-24-oate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.052
wR factor = 0.123
Data-to-parameter ratio = 11.1

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

Methyl-3-oxochola-1,4,22-trien-24-oate, $C_{25}H_{34}O_3$, is a naturally occurring steroid, the configuration at C20 of which has not yet been determined. Here we report the synthesis and the crystal structure analysis *via* X-ray diffraction of the 20*S*-epimer. The analytical data are in good agreement with those reported for the natural product.

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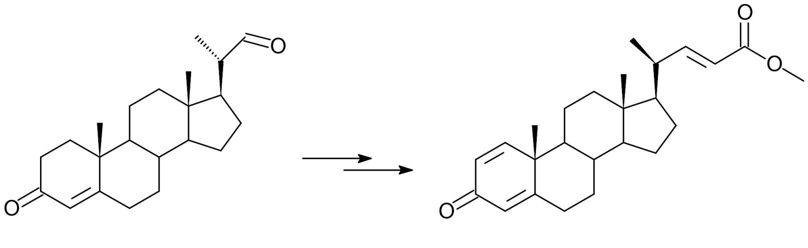
Comment

We have described (Linker *et al.* (2001) the crystal structure of (20*R*)-methyl-3-oxochola-1,4,22-trien-24-oate. Comparison of its NMR data with the naturally occurring steroid [isolated by Tomono *et al.* (1999)] shows differences mainly in the side chain ^{1}H NMR chemical shifts. Our assumption of a different configuration at C20 in the natural product might be supported by comparison with the 20*S*-epimer. Starting from (20*S*)-3-keto-bisnor-4-cholen-22-al, an epimeric mixture (at C20) of the two methyl esters has been synthesized in a four-step procedure. Repeated crystallizations allow for an easy separation and the analytical data of the title compound are in good agreement with the published data, so that an X-ray analysis should prove its relative configuration.


(II) (I)

All bond lengths and angles of the steroidal skeleton are within normal range (Duax & Norton, 1975) and in accordance with the epimeric product. The *D* ring adopts a conformation between 13β-envelope and 13β,14α-half-chair [Δ = 12.84°, ψ_m = 47.1°; calculated according to Altona *et al.* (1968)]. Significant differences between the two epimers are observed in the side-chain torsion angles which are presented in Table 1. The configuration at C20 can be determined to be *S*, since the stereochemistry inside the cholan-type ring system is known. The substituents at C20 are staggered with respect to those at C17, but in this case C22 is *anti* to C16. The side chain is orientated towards the ring system. Our results allow an unambiguous structural determination of the isolated natural compound as (20*S*)-methyl-3-oxochola-1,4,22-trien-24-oate.

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Experimental

The mixture of epimeric methyl esters was obtained from 3-keto-bisnor-4-cholen-22-al by epimerization with H_2SO_4/EtOH, Horner—Wittig reaction, re-esterification and DDQ-dehydration. Purification by column chromatography (cyclohexane–ethyl acetate = 2:1, R_F = 0.30) and crystallization from cyclohexane led to the pure (20*R*)-methyl ester. The mother liquor was evaporated and after four crystallizations from cyclohexane (once with the addition of active charcoal), the pure methy ester (I) was obtained as fine needles (m.p. = 411–412 K) after standing overnight at room temperature.

Crystal data

$C_{25}H_{34}O_3$
$M_r = 382.52$
Orthorhombic, $P2_12_12_1$
$a = 10.0940\ (2)$ Å
$b = 13.5844\ (3)$ Å
$c = 16.1679\ (3)$ Å
$V = 2216.96\ (8)$ Å^3
$Z = 4$
$D_x = 1.146$ Mg m^{-3}

Mo $K\alpha$ radiation
Cell parameters from 27079 reflections
$\theta = 2.9$–$27.5°$
$\mu = 0.07$ mm^{-1}
$T = 293\ (1)$ K
Plate, colourless
$0.30 \times 0.30 \times 0.05$ mm

Data collection

Nonius KappaCCD diffractometer
399 frames *via* ω-rotation ($\Delta\omega = 1°$) with four sets at different κ-angles and two times 75 s per frame
27 079 measured reflections
2863 independent reflections

1585 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.053$
$\theta_{\rm max} = 27.5°$
$h = -13 \rightarrow 13$
$k = -17 \rightarrow 17$
$l = -20 \rightarrow 20$
Intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.053$
$wR(F^2) = 0.123$
$S = 1.00$
2863 reflections
257 parameters

H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0657P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} = 0.001$
$\Delta\rho_{\rm max} = 0.11$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.13$ e Å^{-3}

Table 1
Selected torsion angles (°).

C17—C13—C14—C15	46.8 (2)	C13—C17—C20—C21	174.6 (2)
C13—C14—C15—C16	−34.7 (3)	C16—C17—C20—C21	54.3 (3)
C14—C15—C16—C17	9.0 (3)	C17—C20—C22—C23	143.4 (3)
C14—C13—C17—C16	−40.3 (2)	C21—C20—C22—C23	−92.8 (4)
C15—C16—C17—C13	19.6 (3)		

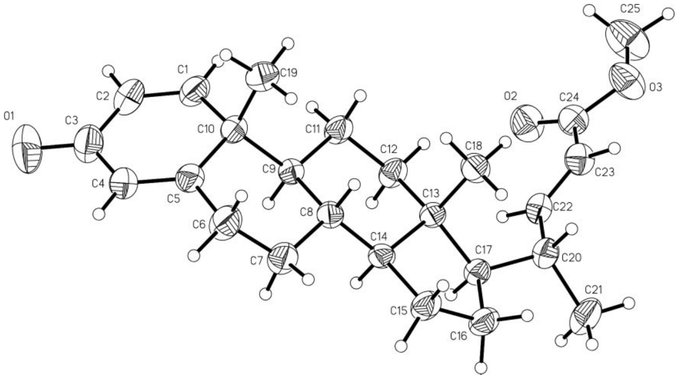

Figure 1
View (*SHELXTL-Plus*; Sheldrick, 1991) of the title compound showing the labelling of all non-H atoms. Displacement ellipsoids are shown at 30% probability levels. H atoms are drawn as circles of arbitrary radii.

H atoms were placed in calculated positions with $U_{\rm iso}$ constrained to be 1.5 times $U_{\rm eq}$ of the carrier atom for the methyl-H and 1.2 times $U_{\rm eq}$ for the remaining H atoms.

Data collection: *COLLECT* (Nonius, 1998); cell refinement: *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* and *SCALEPACK*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus* (Sheldrick, 1991); software used to prepare material for publication: *SHELXL*97 and *PARST*95 (Nardelli, 1995).

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