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(+)-(1*S*,2*S*,4*S*,4a*R*,5*R*,6*S*,9*S*,10*S*)-4-Benzyloxy-9,10-(carbonyldioxy)-1-methoxymethoxy-4a,6,-8,8-tetramethyl-7-methylenedodecahydro-6,9-ethanobenzocyclooctene-5-ol

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Key indicators

Single-crystal X-ray study
T = 297 K
Mean σ(C–C) = 0.004 Å
R factor = 0.042
wR factor = 0.126
Data-to-parameter ratio = 10.5

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

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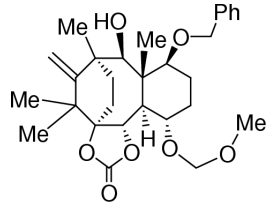
The title tetracyclic compound, $C_{29}H_{40}O_7$, has been obtained unexpectedly in a synthetic study of the natural diterpenoid, paclitaxel. There is an intramolecular O—H···O hydrogen bond between the hydroxy and benzyloxy groups.

Comment

The title compound, (I), was prepared in a synthetic study on paclitaxel (registered as Taxol), which is a well documented natural diterpenoid with potent antitumor activity (Georg *et al.*, 1995). This compound, (I), was unexpectedly generated, in 95% yield, by the C—C bond formation (between C11 and C12 in Fig. 1) in an SmI_2-mediated cyclization reaction of a tricyclic precursor possessing the aldehyde-allyl chloride system (Chinen *et al.*, 2003). Although compound (I) was found to be a different isomer from that used in the synthesis of paclitaxel, this reaction is worthy of investigation because a strained tetracyclic skeleton containing an eight-membered ring was produced in good yield. Since the geometry of the compound could not be fully determined based on NMR experiments, the X-ray analysis has been carried out.



(I)

The molecular structure is shown in Fig. 1. An eight-membered ring is formed by C9/C10/C21/C26/C11/C12 with the C13/C14 or C15/C16 links. The bridge C12/C13/C14/C9 is nearly planar. However, other bridges between atoms C9 and C12 are skewed, the torsion angles of C10—C9···C12—C11 and C16—C9···C12—C15 being 14.5 (2)° and 19.3 (2)°, respectively. The C11—C12 and C11—C26 bond distances are elongated [1.571(4) and 1.582 (4) Å], suggesting strain in the fused ring system (Table 1). The cyclohexane moiety, C21—C26, is present in a chair form, with the benzyloxy and methoxymethoxy groups in equatorial positions. The hydroxy group O4—H4 forms an intramolecular hydrogen bond with the benzyloxy atom O5 (Table 2).

Experimental

The cyclohexane unit (C9, C14, C13, C12, C15, C16 in Fig. 1) was prepared according to the reported procedure (Nicolaou *et al.*, 1995),

whereas the substituted cyclohexane unit (C21–C26) was synthesized from D-glucal (Momose *et al.*, 2000). Coupling of these two units by a Shapiro reaction (Nicolaou *et al.*, 1995), followed by further manipulation of the functional groups and a subsequent SmI_2-mediated cyclization reaction, afforded the title compound, (I). Crystals were grown from a toluene solution by slow evaporation (m.p. 427–430 K). The specific rotation, $[\alpha]_D$, at 295 K is +24° (c = 0.46, $CHCl_3$ where c is a concentration of units g per 100 cm^{-3}).

Crystal data

$C_{29}H_{40}O_7$
M_r = 500.63
Orthorhombic, $P2_12_12_1$
a = 13.754 (2) Å
b = 21.026 (7) Å
c = 9.1287 (10) Å
V = 2639.9 (10) Å^3
Z = 4
D_x = 1.260 Mg m^{-3}
Mo Kα radiation
Cell parameters from 25 reflections
θ = 10.0–11.2°
μ = 0.09 mm^{-1}
T = 297 K
Prism, colourless
0.50 × 0.40 × 0.40 mm

Data collection

Rigaku AFC-7*R* diffractometer
ω scans
Absorption correction: none
4059 measured reflections
3419 independent reflections
2443 reflections with $I > 2\sigma(I)$
R_{int} = 0.016
θ_{max} = 27.5°
$h = -7 \rightarrow 17$
$k = 0 \rightarrow 27$
$l = -11 \rightarrow 4$
3 standard reflections
every 150 reflections
intensity decay: 0.8%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.042
$wR(F^2)$ = 0.126
S = 1.02
3419 reflections
326 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0632P)^2 + 0.271P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

C9—C10	1.556 (4)	C13—C14	1.535 (5)
C9—C14	1.495 (4)	C15—C16	1.531 (5)
C9—C16	1.542 (4)	C21—C22	1.545 (4)
C10—C21	1.545 (4)	C21—C26	1.567 (3)
C11—C12	1.571 (4)	C22—C23	1.515 (4)
C11—C26	1.582 (4)	C23—C24	1.514 (4)
C12—C13	1.566 (4)	C24—C25	1.507 (4)
C12—C15	1.538 (4)	C25—C26	1.552 (4)
C9—C14—C13—C12	2.8 (4)	C9—C16—C15—C12	35.4 (4)

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

D—H···A	D—H	H···A	D···A	D—H···A
O4—H4···O5	0.82	2.04	2.711 (2)	139

The hydroxyl H atom was located in a difference synthesis and allowed to ride on the O atom with $U_{iso}(H) = U_{eq}(O)$. The other H atoms were positioned geometrically, with C—H set equal to 0.95 Å, and fixed with $U_{iso}(H) = 1.2U_{eq}$(parent atom). The positions of the H atoms were recalculated after each cycle of refinement, except for the last. The absolute configuration of the molecule was assigned, based on the known stereochemistry at atom C25, derived from C-4 of D-glucal (Momose *et al.*, 2000). 150 Friedel-pair reflections were merged before the final refinement, since the Flack (1983) parameter was 3.0 (8).

Data collection: *WinAFC Diffractometer Control Software* (Rigaku, 1999); cell refinement: *WinAFC Diffractometer Control Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 2001); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *TEXSAN*.

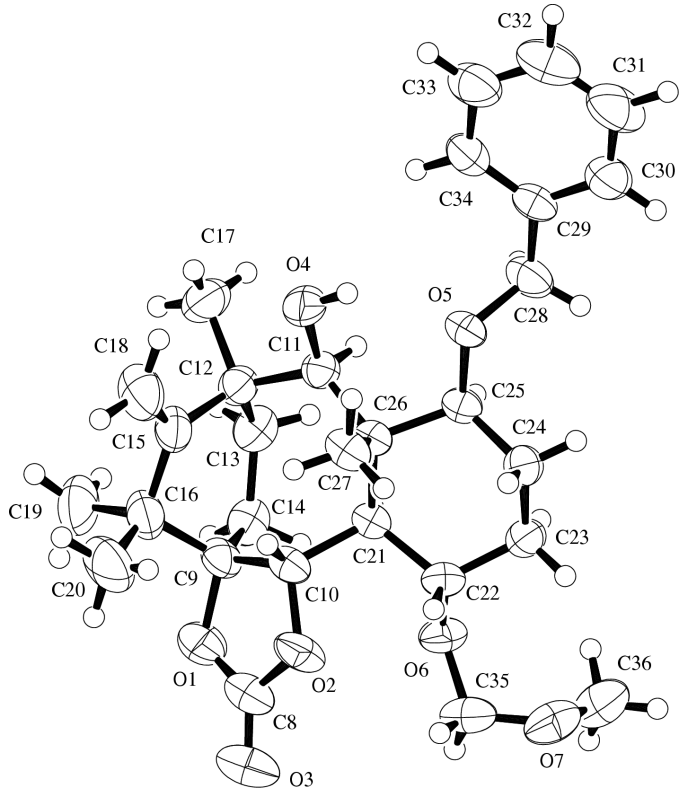


Figure 1
The molecular structure of (I), with displacement ellipsoids drawn at the 50% probability level.

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