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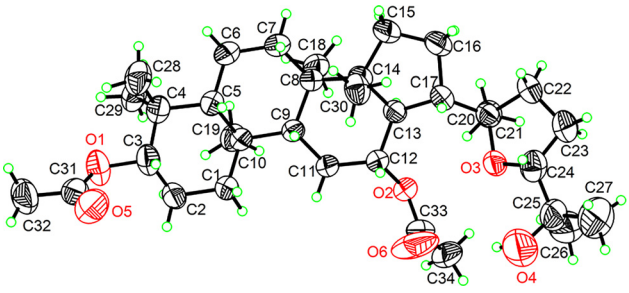
The crystal structure of (3*S*,12*R*,20*R*,24*R*)-3,12-diacetyl-20,24-epoxy-dammarane-3,12,25–triol–ethyl acetate (4/1), $C_{34}H_{56}O_6 \cdot 0.25(C_4H_8O_2)$



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Abstract

$C_{34}H_{56}O_6 \cdot 0.25(C_4H_8O_2)$, orthorhombic, $P2_12_12_1$ (no. 19), a = 8.17152(14) Å, b = 17.6728(3) Å, c = 23.1916(5) Å, V = 3349.18(11) Å^3, Z = 4, $R_{gt}(F)$ = 0.0416, $wR_{ref}(F^2)$ = 0.1143, T = 293 K.

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The molecular structure is shown in the Figure. Table 1 contains crystallographic data, and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.26 × 0.22 × 0.17 mm
Wavelength:	Cu *K*α radiation (1.54184 Å)
μ:	0.59 mm^{-1}
Diffractometer, scan mode:	Xcalibur, ω
θ_{max}, completeness:	66.4°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	29,847, 5859, 0.032
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 5252
$N(param)_{refined}$:	373
Programs:	Bruker [1], OLEX2/superflip [2–4], SHELX [5]

Source of material

20(*R*)-Protopanaxdiol (PPD), systematic name: (3*S*,8*R*,9*R*,10*R*,12*R*,13*S*,14*S*,17*S*)-17-((*R*)-2-hydroxy-6-methylhept-5-en-2-yl)-4,4,8,10,14-pentamethylhexadecahydro-1*H*-cyclopenta[*α*]phenanthrene-3,12-diol was prepared successively from *Panax quinquefolium* L. with 50% citric acid and sodium hydrate in glycerol and purified by silica-gel column chromatography to afford white powder. After that, the needle-like pure product was obtained by recrystallization in ethyl acetate. The mixture of PPD in pyridine was treated with acetic anhydride at 70 °C for 30 h to obtain 3,12-diacetyl PPD. *m*-CPBA was added to the solution of 3,12-diacetyl PPD in dichloromethane at 0 °C, and the mixture was stirred at room temperature to get the objective compound. After evaporation under vacuum, the residue was dissolved with ethyl acetate, and the organic solution was washed with water and brine, dried over anhydrous sodium sulfate. After filtration, the filtrate was evaporated to dryness under vacuum and purified by silica-gel column chromatography (petroleum ether:ethyl acetate = 10:1, *v/v*). Suitable crystals were obtained by recrystallization in absolute methanol. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.03 (d, J = 6.3 Hz, 1H), 4.50 (dd, J = 11.2, 4.8 Hz, 1H), 3.69 (dd, J = 9.9, 4.8 Hz, 1H), 2.08 (dd,

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Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
O1	0.2965 (3)	1.04858 (12)	0.61510 (10)	0.0793 (7)
O2	0.6228 (2)	0.56559 (9)	0.56498 (7)	0.0537 (4)
O3	0.7469 (2)	0.43671 (10)	0.63374 (9)	0.0613 (5)
O4	0.4529 (4)	0.3530 (2)	0.6549 (3)	0.1536 (18)
H4	0.450376	0.390360	0.634015	0.230*
O5	0.0892 (3)	1.03529 (17)	0.67588 (15)	0.1065 (10)
O6	0.3954 (4)	0.5196 (2)	0.60265 (16)	0.1379 (14)
C1	0.3917 (3)	0.84060 (15)	0.59558 (13)	0.0598 (6)
H1A	0.357904	0.806218	0.565229	0.072*
H1B	0.351647	0.820649	0.631905	0.072*
C2	0.3143 (4)	0.91851 (16)	0.58489 (15)	0.0668 (8)
H2A	0.347252	0.936935	0.547239	0.080*
H2B	0.196049	0.913782	0.585071	0.080*
C3	0.3659 (4)	0.97456 (16)	0.63042 (13)	0.0648 (7)
H3	0.320372	0.958660	0.667588	0.078*
C4	0.5510 (3)	0.98530 (15)	0.63713 (12)	0.0576 (6)
C5	0.6288 (3)	0.90481 (13)	0.64292 (11)	0.0513 (6)
H5	0.586492	0.885209	0.679536	0.062*
C6	0.8144 (3)	0.90717 (16)	0.65105 (14)	0.0617 (7)
H6A	0.866572	0.918220	0.614430	0.074*
H6B	0.842483	0.947267	0.677843	0.074*
C7	0.8775 (4)	0.83208 (15)	0.67400 (13)	0.0620 (7)
H7A	0.834054	0.824317	0.712470	0.074*
H7B	0.995726	0.834725	0.677092	0.074*
C8	0.8318 (3)	0.76345 (14)	0.63634 (11)	0.0488 (5)
C9	0.6456 (3)	0.76645 (13)	0.62133 (10)	0.0454 (5)
H9	0.589326	0.759477	0.658274	0.054*
C10	0.5796 (3)	0.84396 (13)	0.59735 (10)	0.0476 (5)
C11	0.5964 (3)	0.69713 (13)	0.58483 (11)	0.0520 (6)
H11A	0.478841	0.698022	0.579176	0.062*
H11B	0.647350	0.701492	0.547193	0.062*
C12	0.6440 (3)	0.62073 (13)	0.61110 (10)	0.0467 (5)
H12	0.571541	0.608600	0.643490	0.056*
C13	0.8212 (3)	0.61840 (14)	0.63038 (10)	0.0465 (5)
H13	0.888871	0.623227	0.595702	0.056*
C14	0.8614 (3)	0.68699 (15)	0.66973 (10)	0.0519 (6)
C15	1.0396 (4)	0.66928 (18)	0.68670 (15)	0.0714 (8)
H15A	1.114988	0.690461	0.658722	0.086*
H15B	1.064561	0.690253	0.724340	0.086*
C16	1.0527 (4)	0.58349 (18)	0.68779 (14)	0.0670 (8)
H16A	1.072960	0.566058	0.726803	0.080*
H16B	1.142427	0.566938	0.663506	0.080*
C17	0.8885 (3)	0.55065 (14)	0.66516 (11)	0.0521 (6)
H17	0.816770	0.544054	0.698654	0.063*
C18	0.9406 (3)	0.76656 (16)	0.58186 (13)	0.0620 (7)
H18A	1.047698	0.747638	0.590907	0.093*
H18B	0.949040	0.817948	0.568767	0.093*
H18C	0.892687	0.736034	0.552074	0.093*
C19	0.6409 (4)	0.86066 (15)	0.53550 (11)	0.0597 (7)
H19A	0.748045	0.882832	0.537275	0.090*
H19B	0.567048	0.895153	0.516927	0.090*
H19C	0.645695	0.814339	0.513939	0.090*
C20	0.9082 (3)	0.47245 (15)	0.63696 (12)	0.0539 (6)
C21	0.9763 (3)	0.47503 (17)	0.57605 (13)	0.0617 (7)
H21A	0.998000	0.424479	0.562975	0.093*
H21B	1.076060	0.503751	0.575766	0.093*
H21C	0.898002	0.498510	0.550922	0.093*
C22	1.0087 (4)	0.41941 (18)	0.67609 (15)	0.0711 (8)
H22A	1.119466	0.413726	0.661708	0.085*
H22B	1.012909	0.438611	0.715245	0.085*
C23	0.9177 (4)	0.34538 (19)	0.67359 (17)	0.0809 (9)
H23A	0.938965	0.314549	0.707372	0.097*
H23B	0.945039	0.316918	0.639152	0.097*
C24	0.7412 (4)	0.37337 (18)	0.67221 (14)	0.0705 (8)
H24	0.711208	0.391365	0.710752	0.085*
C25	0.6112 (5)	0.31835 (19)	0.65139 (19)	0.0875 (10)
C26	0.6448 (6)	0.2957 (3)	0.5919 (2)	0.1137 (14)
H26A	0.666310	0.339918	0.568995	0.171*
H26B	0.551672	0.269476	0.576497	0.171*
H26C	0.738509	0.262987	0.591025	0.171*
C27	0.6086 (8)	0.2493 (3)	0.6909 (3)	0.163 (3)
H27A	0.705822	0.219844	0.684782	0.245*
H27B	0.514101	0.219036	0.682425	0.245*
H27C	0.604421	0.265572	0.730373	0.245*
C28	0.5795 (5)	1.02915 (19)	0.69387 (15)	0.0834 (10)
H28A	0.554398	0.997018	0.726057	0.125*
H28B	0.509981	1.072920	0.694769	0.125*
H28C	0.691860	1.044750	0.696050	0.125*
C29	0.6229 (4)	1.03253 (16)	0.58781 (14)	0.0710 (8)
H29A	0.739799	1.034503	0.591587	0.107*
H29B	0.579142	1.082901	0.589412	0.107*
H29C	0.594755	1.009761	0.551562	0.107*
C30	0.7586 (4)	0.68266 (18)	0.72570 (11)	0.0667 (7)
H30A	0.773193	0.728309	0.747539	0.100*
H30B	0.793754	0.640119	0.748262	0.100*
H30C	0.645063	0.676864	0.716006	0.100*
C31	0.1592 (4)	1.07094 (19)	0.63960 (16)	0.0749 (9)
C32	0.1074 (6)	1.1474 (2)	0.6177 (2)	0.1060 (14)
H32A	0.168749	1.185997	0.637237	0.159*
H32B	−0.007188	1.154495	0.624984	0.159*
H32C	0.127734	1.150406	0.577030	0.159*
C33	0.4942 (4)	0.52106 (19)	0.56493 (16)	0.0712 (8)
C34	0.4909 (5)	0.4702 (2)	0.51405 (17)	0.0887 (11)
H34A	0.463668	0.498971	0.480257	0.133*
H34B	0.410393	0.431434	0.519857	0.133*
H34C	0.596611	0.447416	0.509095	0.133*

J = 19.2, 7.1 Hz, 6H), 1.28 (d, *J* = 12.6 Hz, 3H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.12 (s, 3H), 1.00 (d, *J* = 7.5 Hz, 3H), 0.95 (d, *J* = 11.6 Hz, 3H), 0.89 (s, 3H), 0.87 (d, *J* = 2.3 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 171.10, 170.92, 86.10, 85.14, 80.56, 73.77, 70.46, 55.65, 51.02, 50.88, 49.15, 45.32, 39.47, 38.49, 38.39, 37.82, 36.93, 34.16, 29.84, 28.11, 27.96, 27.36, 26.80, 26.15, 23.53, 23.43, 22.39, 22.16, 21.28, 18.04, 17.32, 16.50, 15.76, 15.66. **HRMS** calcd. for $C_{34}H_{57}O_6[M+H]^+$ 561.41497; found: 561.41297.

Experimental details

All H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, U_{iso} (H) = $1.5U_{eq}$(C) for methyl H atoms, and for methine and methylene H atoms with U_{iso} (H) = $1.2U_{eq}$ (C).

The solvent molecule was presumed to be an ethyl acetate molecule on the basis of the 106 $Å^3$ void, and the fact that ethyl acetate is commonly used as solvent for growing the crystals. The absolute configuration was derived from the synthesis and the configuration of the educts.

Comment

The ocotillol-type saponins belong to a rare class of ginsenosides characterized by a tetrahydrofuran ring on the side chain [6]. It has been reported to have multiple therapeutic properties like anti-inflammatory [7], anti-myocardial ischemia [8–10], antibacterial [11] and neuroprotective [12], among which, 20(*R*)-epimer is responsible for more biological and pharmacological activities [13]. Our understanding of 20(*R*)-ocotillol-type ginseng saponins has advanced tremendously in the last few years. Investigations related to pharmacological and stereo-selective activities of 20(*R*)-ginseng saponins have been helpful in verifying the functions and values of the corresponding 20(*S*)-isomers.

The asymmetric unit of the title compound consists of one independent dammarane and ethyl acetate with a lower occupancy. The C-3 carbon atom in the molecule is in *S*-form (see the Figure). Notably, the C-20 and C-24 configurations of the title compounds are *R*, *R*, respectively. The bond lengths and angles are all in the expected ranges. Two carbon-oxygen double bonds exist in the compound, the C–O bond distance (C31–O5) is 1.197(5) Å, the C–O bond distance (C33–O6) is 1.191(4) Å. The angles of C24–O3–C20, O5–C31–O1 and C6–C33–O2 are 109.5(2), 123.5(3), 123.7(3)°, respectively.

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