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Crystal structure of (20*R*)-20,25-epoxy-dammaran-3,12-dione, C₃₀H₄₈O₃

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Abstract

C₃₀H₄₈O₃, orthorhombic, $P2_12_12_1$ (no. 19), $a = 7.8710(16)$ Å, $b = 13.800(28)$ Å, $c = 24.561(49)$ Å, $V = 2667.9(9)$ Å³, $Z = 4$. $R_{\text{gt}}(F) = 0.0488$, $wR_{\text{ref}}(F^2) = 0.1264$, $T = 293(2)$ K.

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The crystal structure is shown in the figure. Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

Source of material

(20*R*)-20,25-Epoxy-dammaran-3,12-dione {systematic name: (8*R*,9*R*,10*R*,13*R*,14*R*,17*S*)-4,4,8,10,14-pentamethyl-17-((*R*)-2,6,6-trimethyltetrahydro-2*H*-pyran-2-yl)tetradecahydro-3*H*-cyclopenta[*a*]phenanthrene-3,12(2*H*)-dione)} is synthesized by two-step oxidation reaction in turn.

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Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.24 × 0.20 × 0.18 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.07 mm ⁻¹
Diffractometer, scan mode:	Bruker P4, ω -scans
θ_{max} , completeness:	25.5°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	36598, 3755, 0.058
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 3755
$N(\text{param})_{\text{refined}}$:	306
Programs:	Bruker programs [1], SHELX [2, 3]

3-oxo-20(*R*)-panaxadiol was synthesized by Wu's method [4]. A solution of (20*R*)-panaxadiol in CH₂Cl₂ and pyridinium chlorochromate was stirred for 6 h at room temperature. The solvent was removed under reduced pressure to give a white solid. The white solid was dissolved in ethyl ether and washed with NaHCO₃, dried (MgSO₄) and concentrated under reduced pressure to give the crude product. The crude products were chromatographed using silica gel and eluted with [petroleum ether-EtOAc (8:1)] to give the pure product. (20*R*)-20,25-Epoxy-dammaran-3,12-dione is synthesized by reacting 3-oxo-20(*R*)-panaxadiol with DDQ in 1,4-dioxane at 110 °C temperature heating under reflux for 3 h. The mixture was concentrated in vacuo. The residue was dissolved in water and extracted with ethyl acetate. The organic phase was washed with water, dried over Na₂SO₄. The residue was separated by silica column chromatography [petroleum ether-EtOAc (8:1)] to give a white solid. (m.p.: 255–257 °C). Analysis calcd. for C₃₀H₄₈O₃: 456.36035; found: MS (ES⁺): m/z 457.36740 ($M + 1$).

Experimental details

All H atoms were included in calculated positions and refined as riding atoms, with C–H = 0.96–0.97 Å, with $U_{\text{iso}}(\text{H}) = 1.5 U_{\text{eq}}(\text{C})$ for methyl H atoms and 1.2 $U_{\text{eq}}(\text{C})$ for all other H atoms. The absolute configuration was derived from the synthesis and the configuration of the educts.

Discussion

Panaxadiol (PD), one of the protopanaxadiol-type of ginsenoside with a dammarane skeleton can be obtained by acid hydrolysate. It has been reported to exhibits pharmacological

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
O1	0.5403(4)	0.0979(3)	0.93692(15)	0.1245(16)
O2	−0.2557(2)	0.51504(19)	0.91667(10)	0.0612(7)
O3	−0.0353(3)	0.81548(16)	0.87134(9)	0.0503(6)
C1	0.1790(4)	0.2605(2)	0.93094(14)	0.0466(8)
H1A	0.1200	0.2839	0.9630	0.056 [*]
H1B	0.0938	0.2385	0.9052	0.056 [*]
C2	0.2866(5)	0.1760(3)	0.9469(2)	0.0754(12)
H2A	0.3114	0.1822	0.9854	0.091 [*]
H2B	0.2184	0.1180	0.9425	0.091 [*]
C3	0.4476(4)	0.1598(3)	0.91873(14)	0.0548(9)
C4	0.5020(4)	0.2195(2)	0.86911(13)	0.0452(8)
C5	0.3736(3)	0.3029(2)	0.85588(12)	0.0399(7)
H5	0.2856	0.2721	0.8336	0.048 [*]
C6	0.4493(4)	0.3811(3)	0.81930(13)	0.0506(8)
H6A	0.5318	0.4185	0.8398	0.061 [*]
H6B	0.5077	0.3509	0.7890	0.061 [*]
C7	0.3111(4)	0.4487(3)	0.79765(12)	0.0493(8)
H7A	0.2330	0.4115	0.7754	0.059 [*]
H7B	0.3633	0.4973	0.7745	0.059 [*]
C8	0.2108(3)	0.4996(2)	0.84292(11)	0.0367(7)
C9	0.1455(3)	0.4205(2)	0.88304(11)	0.0334(6)
H9	0.0664	0.3817	0.8613	0.040 [*]
C10	0.2768(3)	0.3450(2)	0.90543(11)	0.0356(7)
C11	0.0326(4)	0.4662(2)	0.92820(12)	0.0430(7)
H11A	−0.0176	0.4148	0.9498	0.052 [*]
H11B	0.1032	0.5051	0.9521	0.052 [*]
C12	−0.1071(3)	0.5289(2)	0.90503(12)	0.0391(7)
C13	−0.0461(3)	0.6048(2)	0.86643(11)	0.0353(6)
H13	0.0383	0.6437	0.8860	0.042 [*]
C14	0.0494(3)	0.5526(2)	0.81925(11)	0.0364(7)
C15	0.0773(4)	0.6385(2)	0.78049(12)	0.0467(8)
H15A	0.1712	0.6784	0.7928	0.056 [*]
H15B	0.1011	0.6160	0.7439	0.056 [*]
C16	−0.0903(4)	0.6955(3)	0.78222(12)	0.0502(8)
H16A	−0.1662	0.6735	0.7536	0.060 [*]
H16B	−0.0691	0.7641	0.7772	0.060 [*]
C17	−0.1706(3)	0.6763(2)	0.83944(12)	0.0408(7)
H17	−0.2802	0.6438	0.8344	0.049 [*]
C18	0.3301(3)	0.5741(2)	0.87046(14)	0.0474(8)
H18A	0.4415	0.5466	0.8742	0.071 [*]
H18B	0.2864	0.5905	0.9058	0.071 [*]
H18C	0.3364	0.6315	0.8485	0.071 [*]
C19	0.3944(4)	0.3878(2)	0.94956(12)	0.0450(8)
H19A	0.3268	0.4167	0.9778	0.068 [*]
H19B	0.4665	0.4361	0.9336	0.068 [*]
H19C	0.4631	0.3371	0.9648	0.068 [*]
C20	−0.1998(4)	0.7701(2)	0.87181(12)	0.0430(7)
C21	−0.3336(4)	0.8320(3)	0.84224(16)	0.0644(10)
H21A	−0.3686	0.8843	0.8655	0.097 [*]
H21B	−0.4303	0.7925	0.8335	0.097 [*]
H21C	−0.2856	0.8578	0.8094	0.097 [*]
C22	−0.2601(5)	0.7509(3)	0.92976(13)	0.0587(9)
H22A	−0.3780	0.7306	0.9289	0.070 [*]

Table 2 (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
H22B	−0.1938	0.6986	0.9453	0.070 [*]
C23	−0.2436(6)	0.8396(3)	0.96542(15)	0.0798(13)
H23A	−0.3138	0.8916	0.9513	0.096 [*]
H23B	−0.2808	0.8248	1.0021	0.096 [*]
C24	−0.0601(7)	0.8700(3)	0.96583(17)	0.0900(15)
H24A	0.0078	0.8184	0.9815	0.108 [*]
H24B	−0.0475	0.9268	0.9887	0.108 [*]
C25	0.0072(5)	0.8932(3)	0.90871(18)	0.0675(11)
C26	0.2010(5)	0.8927(4)	0.9069(3)	0.110(2)
H26A	0.2420	0.8290	0.9155	0.166 [*]
H26B	0.2444	0.9382	0.9330	0.166 [*]
H26C	0.2385	0.9106	0.8711	0.166 [*]
C27	−0.0591(6)	0.9906(3)	0.8879(2)	0.0827(13)
H27A	−0.0269	0.9988	0.8504	0.124 [*]
H27B	−0.0113	1.0421	0.9092	0.124 [*]
H27C	−0.1807	0.9921	0.8908	0.124 [*]
C28	0.5037(5)	0.1462(3)	0.82144(15)	0.0714(12)
H28A	0.5336	0.1791	0.7884	0.107 [*]
H28B	0.3931	0.1177	0.8176	0.107 [*]
H28C	0.5856	0.0963	0.8287	0.107 [*]
C29	0.6855(4)	0.2542(3)	0.8783(2)	0.0782(13)
H29A	0.6861	0.3055	0.9047	0.117 [*]
H29B	0.7317	0.2775	0.8446	0.117 [*]
H29C	0.7533	0.2012	0.8913	0.117 [*]
C30	−0.0752(4)	0.4815(3)	0.79038(13)	0.0520(9)
H30A	−0.1704	0.5170	0.7763	0.078 [*]
H30B	−0.1144	0.4340	0.8160	0.078 [*]
H30C	−0.0175	0.4496	0.7610	0.078 [*]

activities, such as anti-tumor, anti-HIV and regulating cell cycle and apoptosis [5–8]. Because of its wide biological properties and its potential medicinal value, the extraction, synthesis and biological activity of panaxadiol and its derivatives have attracted much attention. In this paper, we report the crystal structure of the title compound, whose partial synthesis methods have been reported in other journals [4].

In the molecule of the title compound, bond lengths and angles within the five-membered rings are very similar to those given in the literature for panaxadiol [9–13].

The structure of the title compound and panaxadiol are equivalent except for the substituents at C(3) and C(6). Two carbon-oxygen double bond exist in the compound which was synthesized by two-step oxidation reaction. Both the first ring and the third ring contain a carbon-oxygen double bond. The C–O bond distance (C3–O1) is 1.208(6) Å, The C–O bond distance (C12–O2) is 1.218(4) Å. The distance of C–O Bond (C20–O3) in Tetrahydropyran Ring is 1.438(4) Å and the distance of C–O Bond (C25–O3) is 1.452(5) Å. The C25–O3–C20–C22, O1–C3–C2–C1, O1–C3–C4–C28 and O2–C12–C11–C9 torsion angles are 43.1(4)°, 170.9(4)°, 68.3(4)° and

125.0(3)°, respectively. The C25—O3—C20—C22 torsion angle indicates that the C20 position is *R*-form.

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References

1. Bruker: APEX3, SAINT-Plus, XPREP. Bruker AXS Inc., Madison, WI, USA (2016).
2. Sheldrick, G. M.: SHELXT – Integrated space-group and crystal-structure determination. *Acta Crystallogr.* **A71** (2015) 3–8.
3. Sheldrick, G. M.: Crystal structure refinement with SHELXL. *Acta Crystallogr.* **C71** (2015) 3–8.
4. Kim, T.-H.; Lee, S.-M.: The effects of ginseng total saponin, panaxadiol and panaxatriol. *Food Chem Toxicol.* **48** (2010) 1516–1520.
5. Wei, Y.; Ma, C. M.; Hattori, M.: Anti-HIV protease triterpenoids from the acid hydrolysate of Panax ginseng. *Phytochem. Lett.* **2** (2009) 63–66.
6. Jin, Y. H.; Choi, J.; Shin, S.; Lee, K. Y.; Park, J. H.; Lee, S. K.: Panaxadiol selectively inhibits cyclin A-associated Cdk2 activity by elevating p21WAF1/CIP1 protein levels in mammalian cells. *Carcinogenesis*. **24** (2003) 1767–1772.
7. Li, X. L.; Wang, C. Z.; Mehendale, S. R.; Sun, S.; Wang, Q.; Yuan, C. S.: Panaxadiol, a purified ginseng component, enhances the anti-cancer effects of 5-fluorouracil in human colorectal cancer cells. *Cancer Chemother. Pharmacol.* **64** (2009) 1097–1104.
8. Rodriguez, M.; Du, G.-J.; Wang, C.-Z.; Yuan, C.-S.: Letter to the editor panaxadiol's anticancer activity is enhanced by epicatechin. *Am. J. Chin. Med.* **38** (2010) 1233–1235.
9. Puff, H.; Friedrichs, E.; Habscheid, M.; Quante, G.: Panaxadiol and panaxatriol-monohydrat. *Acta Crystallogr.* **C42** (1986) 576–579.
10. Xu, Y.-R.; Yang, J.-J.; Liu, J.; Hou, G.-G.; Meng, Q.-G.: Synthesis and crystal structures of C24-epimeric 20(*R*)-ocotillol-type saponins. *Acta Crystallogr.* **C72** (2016) 498–503.
11. Liu, J.; Xu, Y.-R.; An, X.-S.; Hou, G.-G.; Meng, Q.-G.: Synthesis and crystal structures of a 3-acetylated (20*S*,24*S*)-ocotillol-type saponin and its C-24 epimer. *Acta Crystallogr.* **C73** (2017) 464–469.
12. Liu, Z.; Xu, Y.-R.; An, X.-S.; Yang, J.-J.; Meng, Q.-G.; Hou, G.-G.: Synthesis and crystal structure of ocotillol-type metabolites derived from (20*R*)-protopanaxadiol. *J. Chem. Research.* **41** (2017) 216–220.
13. Liu, H.; Wang, Y.: The crystal structure of (3*S*, 12*R*, 20*R*, 24*S*)-3,12-diacetyl-20,24-epoxy-dammarane-3,12,25-triol acetone solvate, $C_{34}H_{56}O_6$. *Z. Kristallogr. NCS* **233** (2018) 437–439.