Mei Zhang, Qing-Guo Meng, Gui-Ge Hou, Sheng Jiang, Yong-Sheng Jin and Yue Gao*

Crystal structure of (8*R*,10*R*,14*R*, *Z*)-2-((3-Fluoropyridin-4-yl) methylene)-12-hydroxy-4,4,8,10,14-pentamethyl-17-((*R*)-2,6,6-trimethyltetrahydro-2*H*-pyran-2-yl) hexadecahydro-3*H*-cyclopenta[*a*] phenanthren-3-one, C₃₆H₅₂FNO₃

*Corresponding author: Yue Gao, Department of Lab Teaching, School of Pharmacy, Naval Medical University, Shanghai, 200433, P. R. China, E-mail: gaoyue2000@hotmail.com

Mei Zhang and Qing-Guo Meng, School of Pharmacy, Collaborative Innovation Center of Advanced Drug Delivery System and Biotech Drugs in Universities of Shandong, Key Laboratory of Molecular Pharmacology and Drug Evaluation (Yantai University), Ministry of Education, Yantai University, Yantai, P. R. China

Gui-Ge Hou, School of Pharmacy, The Key Laboratory of Prescription Effect and Clinical Evaluation of State Administration of Traditional Chinese Medicine of China, Binzhou Medical University, Yantai, 264003, P. R. China

Sheng Jiang, Shandong Wendeng Jizhen American Ginseng Industry Co., Ltd., Shandong, 264400, P. R. China

Yong-Sheng Jin, Department of Organic Chemistry, School of Pharmacy, Naval Medical University, Shanghai, 200433, P. R. China

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Abstract

C₃₆H₅₂FNO₃, orthorhombic, *P*2₁2₁2₁ (no. 19), *a* = 7.8016(7) Å, *b* = 13.1609(10) Å, *c* = 30.536(2) Å, *V* = 3135.3(4) Å³, *Z* = 4, *R*_{gt}(*F*) = 0.0657, *wR*_{ref}(*F*²) = 0.1435, *T* = 100 K.

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The molecular structure is shown in the figure. Displacement ellipsoids are drawn at the 30% probability level. Table 1 contains crystallographic data and Table 2 contains

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.13 × 0.12 × 0.10 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.08 mm ⁻¹
Diffractometer, scan mode:	SuperNova,
$\theta_{\max}$, completeness:	25.0°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	14226, 5509, 0.095
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 3824
$N(\text{param})_{\text{refined}}$:	379
Programs:	CrysAlis ^{PRO} [1], SHELX [2–4]

the list of the atoms including atomic coordinates and displacement parameters.

Source of material

The title compound was synthesized by three-step chemical reactions in turn. First, ginsenoside of stems and leaves (GSL) was degraded by 10% sulfuric acid ethanol solution and purified by silica gel column chromatography. After recrystallization in ethyl acetate and CH₂Cl₂, the pure white crystalline product panaxadiol (PD; systematic name: (3S, 5R, 8R, 9R, 10R, 12R, 13R, 14R, 17S)-4, 4, 8, 10, 14-pentamethyl-17-((R)-2, 6, 6-trimethyltetrahydro-2H-pyran-2-yl) hexadecahydro-1H-cyclopenta[a]phen-anthrene-3, 12-diol)-was obtained. Second, panaxadiol and PCC were dissolved in 25 ml dichloromethane(methylene chloride) solution and stirred for 4 h at room temperature. The product 3-oxo-panaxadiol was purified by silica gel column chromatography. Finally, in a representative experiment 0.72 mL (25%) of sodium hydroxide aqueous solution was added dropwise to the mixture of 3-oxo-panaxadiol (100 mg; 0.218 mmol) and 3-fluoropyridine-4-formaldehyde (0.022 ml; 0.218 mmol) in 1.4 mL methanol and stirred at room temperature for 2.5 h. The in process-control was monitored by silica gel thin layer chromatography (TLC, 254 nm), the developing solvent is petroleum ether and ethyl acetate. When the reaction was finished, the reaction system was extracted twice with appropriate amount of water and ethyl acetate, and the third time with brine and ethyl acetate. The crude yellow oil was obtained by vacuum distillation of the organic phase and the title compound was purified by silica gel column chromatography. Suitable crystals of the title compound were obtained by recrystallization in ethyl acetate system and dried under vacuo at 65 °C for 5 h.

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

Atom	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.2876 (6)	0.7168 (3)	0.60218 (14)	0.0267 (11)
H1A	0.391895	0.711210	0.585065	0.032*
H1B	0.201292	0.674928	0.588127	0.032*
C2	0.2280 (6)	0.8262 (3)	0.60106 (14)	0.0271 (11)
C3	0.1648 (6)	0.8737 (3)	0.64248 (15)	0.0270 (11)
C4	0.1101 (6)	0.8075 (3)	0.68105 (13)	0.0245 (11)
C5	0.1568 (6)	0.6943 (3)	0.67499 (13)	0.0241 (10)
H5	0.063715	0.666078	0.657200	0.029*
C6	0.1523 (7)	0.6339 (4)	0.71757 (15)	0.0344 (12)
H6A	0.247982	0.654206	0.735862	0.041*
H6B	0.047317	0.649423	0.733223	0.041*
C7	0.1616 (7)	0.5208 (4)	0.70934 (15)	0.0367 (13)
H7A	0.061956	0.500185	0.692562	0.044*
H7B	0.157977	0.485487	0.737197	0.044*
C8	0.3249 (6)	0.4888 (3)	0.68446 (14)	0.0275 (11)
C9	0.3439 (6)	0.5559 (3)	0.64300 (14)	0.0237 (10)
H9	0.248135	0.535487	0.624201	0.028*
C10	0.3222 (6)	0.6738 (3)	0.64821 (14)	0.0234 (10)
C11	0.5050 (6)	0.5247 (3)	0.61719 (17)	0.0342 (12)
H11A	0.512165	0.565863	0.590916	0.041*
H11B	0.605323	0.539177	0.634859	0.041*
C12	0.5085 (7)	0.4125 (4)	0.60404 (16)	0.0360 (13)
H12	0.420024	0.400024	0.581915	0.043*
C13	0.4765 (6)	0.3444 (3)	0.64334 (15)	0.0272 (11)
H13	0.572895	0.354512	0.663464	0.033*
C14	0.3121 (6)	0.3757 (3)	0.66842 (14)	0.0262 (11)
C15	0.3062 (8)	0.2928 (4)	0.70371 (16)	0.0412 (14)
H15A	0.381189	0.309854	0.727964	0.049*
H15B	0.190522	0.284310	0.714747	0.049*
C16	0.3676 (6)	0.1958 (4)	0.68072 (15)	0.0355 (13)
H16A	0.271161	0.151548	0.674560	0.043*
H16B	0.447942	0.159411	0.699215	0.043*
C17	0.4566 (6)	0.2288 (3)	0.63713 (14)	0.0248 (11)
H17	0.373820	0.218237	0.613419	0.030*
C18	0.4772 (7)	0.5014 (4)	0.71648 (16)	0.0406 (14)
H18A	0.484252	0.570963	0.725801	0.061*
H18B	0.581699	0.482664	0.701979	0.061*
H18C	0.460133	0.458459	0.741503	0.061*
C19	0.4816 (6)	0.7281 (4)	0.66655 (17)	0.0336 (12)
H19A	0.581300	0.706522	0.650655	0.050*
H19B	0.494925	0.711423	0.696960	0.050*
H19C	0.467863	0.800246	0.663459	0.050*
C20	0.6169 (6)	0.1648 (3)	0.62624 (14)	0.0259 (11)
C21	0.7709 (6)	0.1363 (3)	0.55358 (14)	0.0278 (11)
C22	0.7212 (7)	0.0240 (3)	0.55536 (15)	0.0334 (12)
H22A	0.614124	0.014163	0.539798	0.040*
H22B	0.808645	-0.015991	0.540749	0.040*
C23	0.7014 (7)	-0.0131 (3)	0.60216 (17)	0.0370 (13)
H23A	0.664489	-0.083511	0.602121	0.044*
H23B	0.810835	-0.009248	0.617123	0.044*
C24	0.5703 (6)	0.0516 (3)	0.62608 (16)	0.0314 (12)
H24A	0.560877	0.027979	0.656078	0.038*
H24B	0.459356	0.042988	0.612253	0.038*
C25	0.7660 (6)	0.1871 (4)	0.65689 (15)	0.0360 (13)

Table 2: (continued)

Atom	x	y	z	U_{iso}^*/U_{eq}
H25A	0.852674	0.136031	0.653322	0.054*
H25B	0.726081	0.186868	0.686630	0.054*
H25C	0.813223	0.252583	0.650055	0.054*
C26	0.7344 (7)	0.1796 (4)	0.50828 (15)	0.0427 (14)
H26A	0.614838	0.171870	0.501664	0.064*
H26B	0.801332	0.143779	0.486873	0.064*
H26C	0.764126	0.250339	0.507754	0.064*
C27	0.9583 (6)	0.1531 (4)	0.56523 (16)	0.0371 (13)
H27A	0.981809	0.224626	0.566207	0.056*
H27B	1.029718	0.121637	0.543501	0.056*
H27C	0.981740	0.123517	0.593348	0.056*
C28	0.1773 (7)	0.8549 (4)	0.72367 (15)	0.0385 (13)
H28A	0.299030	0.844937	0.725551	0.058*
H28B	0.122654	0.822938	0.748248	0.058*
H28C	0.152381	0.926278	0.723871	0.058*
C29	−0.0879 (6)	0.8160 (4)	0.68132 (15)	0.0298 (11)
H29A	−0.120492	0.884406	0.688456	0.045*
H29B	−0.134178	0.770291	0.702755	0.045*
H29C	−0.131715	0.798728	0.652905	0.045*
C30	0.1515 (6)	0.3583 (4)	0.63932 (18)	0.0409 (13)
H30A	0.138679	0.287031	0.633559	0.061*
H30B	0.165081	0.394166	0.612156	0.061*
H30C	0.051609	0.383047	0.654253	0.061*
C31	0.2241 (6)	0.8849 (4)	0.56523 (16)	0.0308 (12)
H31	0.183236	0.950435	0.569761	0.037*
C32	0.2741 (6)	0.8621 (3)	0.52005 (14)	0.0264 (11)
C33	0.3199 (6)	0.9395 (3)	0.49219 (16)	0.0283 (11)
C34	0.3694 (6)	0.9244 (4)	0.44913 (16)	0.0331 (12)
H34	0.399698	0.980146	0.432114	0.040*
C35	0.3272 (8)	0.7547 (4)	0.45781 (16)	0.0429 (14)
H35	0.328042	0.689437	0.446141	0.051*
C36	0.2773 (7)	0.7658 (4)	0.50100 (16)	0.0366 (12)
H36	0.245824	0.709137	0.517320	0.044*
F1	0.3172 (4)	1.03671 (18)	0.50736 (9)	0.0384 (7)
N1	0.3748 (5)	0.8318 (3)	0.43148 (13)	0.0357 (10)
O1	0.1510 (4)	0.9668 (2)	0.64495 (11)	0.0365 (8)
O2	0.6732 (6)	0.3964 (3)	0.58506 (16)	0.0782 (16)
H2	0.692325	0.335271	0.583501	0.117*
O3	0.6564 (4)	0.1952 (2)	0.58156 (9)	0.0262 (7)

Experimental details

The H atoms were placed in idealized positions and treated as riding on their parent atoms, with $d(C-H) = 0.97$ Å (methylene), $d(C-H) = 0.98$ Å (aromatic), $d(C-H) = 0.96$ Å (methyl), $d(C-H) = 0.93$ Å (alkenyl) and $d(O-H) = 0.82$ Å (−OH). The absolute configuration was derived from the synthesis and the configuration of the educts.

Comment

Ginsenoside are divided into two groups according to their glycosidic structures: dammarane and oleanane. There are two types of dammaranes: protopanaxadiol type [5, 6] and protopanaxatriol type sharing a tetrahydrofuran ring and a dammarane skeleton. Because these ginsenosides and their derivatives have a wide range of biological activities, such as anticancer, enhancing myocardial function [7], anti-inflammatory [8] and analgesic, their synthesis and biological activities have attracted extensive attention. At the same time the conformation of the compound will have a certain influence on the biological activity [9]. Our laboratory has done a lot of research work on panaxadiol derivatives [10, 11] and panaxatriol derivatives [12], and obtained crystal structures [13] with good data. The title compound is a PD derivative. It is possible to modify the structure of ginsenoside which is an important saponin in ginsenoside [14].

Single crystal X-ray structure analysis of the title compound revealed that the substituents are at on C(2), the structure of the title compound is similar to that of panaxadiol. In the crystal structure, the pyridine ring is planar, and the other six membered rings except the ring with the keto group have chair conformation. The bond lengths and angles are all in the expected ranges [12].

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Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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