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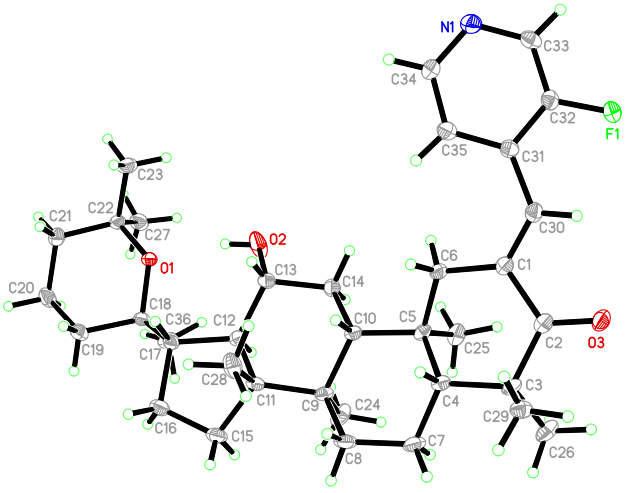
Crystal structure of (5*R*,8*R*,9*R*,10*R*,12*R*,13*R*,14*R*,17*S*,17*Z*)-2-((3-fluoropyridin-4-yl)methylene)-12-hydroxy-4,4,8,10,14-pentamethyl-17-((*R*)-2,6,6-trimethyltetrahydro-2*H*-pyran-2-yl) hexadecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one, $C_{36}H_{52}FNO_3$



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Abstract

$C_{36}H_{52}FNO_3$, orthorhombic, $P2_12_12_1$ (no. 19), a = 7.8101(5) Å, b = 13.1592(7) Å, c = 30.5721(15) Å, V = 3142.0(3) Å^3, Z = 4, $R_{gt}(F)$ = 0.0488, w$R_{ref}(F^2)$ = 0.1048, T = 293 K.

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Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.14 × 0.13 × 0.10 mm
Wavelength:	MoKα radiation (0.71073 Å)
μ:	0.08 mm^{-1}
Diffractometer, scan mode:	SuperNova
θ_{max}, completeness:	25.5°, >99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	14,083, 5656, 0.040
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 4598
$N(param)_{refined}$:	380
Programs:	CrysAlis^{Pro} [1], Shelx [2, 3]

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.

1 Source of material

Total saponins of ginseng stem and leaves were degraded by 18 % sulfuric acid in ethanol and refluxed for 4 h. Cooled to room temperature, the reaction solution was adjusted to neutral with appropriate amount of sodium carbonate, the residue was extracted with ethyl acetate, dried with anhydrous sodium sulfate, filtered, and concentrated under pressure to obtain the crude product, and the crude product was recrystallized with ethyl acetate to obtain the pure product of 20(*R*)-panaxadiol. 20(*R*)–Panaxadiol and PCC were dissolved in 25 mL of dichloromethane solution and purified by silica gel column chromatography after stirring at room temperature for 5 h to obtain 20(*R*)-3-oxopanaxadiol. 20(*R*)-3-Oxopanaxadiol (100 mg, 0.22 mmol) and 3-fluoropyridine-4-carboxaldehyde (0.02 mL, 0.22 mmol) were dissolved in 1.4 mL of methanol, 0.72 mL of 25 % aqueous sodium hydroxide solution was added and stirred at room temperature for 5 h. The response endpoint was detected by thin layer chromatography (TLC). At the end of the reaction, it was extracted with ethyl acetate and

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.2736 (4)	−0.3268 (2)	0.60107 (10)	0.0250 (7)
C2	0.3357 (4)	−0.3750 (2)	0.64263 (10)	0.0273 (7)
C3	0.3896 (4)	−0.3084 (2)	0.68110 (9)	0.0248 (7)
C4	0.3414 (4)	−0.1948 (2)	0.67523 (9)	0.0248 (7)
H4	0.434761	−0.166349	0.657657	0.030*
C5	0.1788 (4)	−0.1746 (2)	0.64796 (9)	0.0230 (7)
C6	0.2154 (4)	−0.2176 (2)	0.60193 (9)	0.0268 (7)
H6A	0.112144	−0.211619	0.584477	0.032*
H6B	0.302740	−0.175984	0.588209	0.032*
C7	0.3467 (5)	−0.1351 (2)	0.71759 (10)	0.0361 (9)
H7A	0.452246	−0.150402	0.732964	0.043*
H7B	0.251940	−0.155955	0.736044	0.043*
C8	0.3359 (5)	−0.0217 (3)	0.70952 (10)	0.0382 (9)
H8A	0.435606	−0.000437	0.692989	0.046*
H8B	0.338266	0.013350	0.737416	0.046*
C9	0.1737 (4)	0.0098 (2)	0.68452 (9)	0.0254 (7)
C10	0.1569 (4)	−0.0567 (2)	0.64259 (9)	0.0230 (7)
H10	0.253618	−0.035975	0.624202	0.028*
C11	0.1867 (4)	0.1231 (2)	0.66841 (9)	0.0262 (7)
C12	0.0233 (4)	0.1541 (2)	0.64317 (10)	0.0252 (7)
H12	−0.073750	0.142944	0.662913	0.030*
C13	−0.0052 (5)	0.0868 (3)	0.60347 (11)	0.0388 (9)
H13	0.084795	0.099753	0.581837	0.047*
C14	−0.0025 (5)	−0.0254 (2)	0.61640 (12)	0.0357 (9)
H14A	−0.008457	−0.066389	0.590070	0.043*
H14B	−0.103623	−0.040044	0.633713	0.043*
C15	0.1902 (5)	0.2064 (2)	0.70403 (11)	0.0399 (9)
H15A	0.113487	0.189292	0.727874	0.048*
H15B	0.304927	0.214836	0.715601	0.048*
C16	0.1307 (5)	0.3032 (2)	0.68082 (10)	0.0351 (8)
H16A	0.227824	0.346907	0.674720	0.042*
H16B	0.050710	0.340182	0.699141	0.042*
C17	0.0425 (4)	0.2707 (2)	0.63743 (10)	0.0242 (7)
H17	0.125563	0.281737	0.613869	0.029*
C18	−0.1180 (4)	0.3348 (2)	0.62630 (9)	0.0245 (7)
C19	−0.0723 (5)	0.4475 (2)	0.62659 (11)	0.0324 (8)
H19A	−0.063167	0.470455	0.656640	0.039*
H19B	0.038606	0.456517	0.612860	0.039*
C20	−0.2032 (5)	0.5125 (2)	0.60289 (11)	0.0375 (9)
H20A	−0.166269	0.582899	0.602909	0.045*
H20B	−0.312562	0.508568	0.617834	0.045*
C21	−0.2227 (5)	0.4751 (2)	0.55592 (11)	0.0342 (8)
H21A	−0.310335	0.514863	0.541353	0.041*
H21B	−0.115732	0.485559	0.540416	0.041*
C22	−0.2707 (4)	0.3631 (2)	0.55375 (10)	0.0271 (8)
C23	−0.2353 (5)	0.3204 (3)	0.50834 (10)	0.0407 (9)
H23A	−0.116555	0.329633	0.501283	0.061*
H23B	−0.304662	0.355371	0.487232	0.061*
H23C	−0.262421	0.249241	0.507876	0.061*
C24	0.0209 (5)	−0.0033 (3)	0.71602 (11)	0.0426 (10)
H24A	0.017282	−0.072198	0.726335	0.064*
H24B	−0.083650	0.012140	0.700903	0.064*
H24C	0.033974	0.041916	0.740428	0.064*
C25	0.0182 (4)	−0.2288 (2)	0.66558 (11)	0.0341 (8)
H25A	−0.080099	−0.207812	0.649044	0.051*
H25B	0.002056	−0.211505	0.695803	0.051*
H25C	0.032559	−0.301023	0.662878	0.051*
C26	0.3226 (5)	−0.3560 (3)	0.72356 (10)	0.0385 (9)
H26A	0.200502	−0.348153	0.724964	0.058*
H26B	0.374240	−0.322590	0.748169	0.058*
H26C	0.351060	−0.426917	0.724130	0.058*
C27	−0.4583 (5)	0.3454 (3)	0.56552 (11)	0.0378 (9)
H27A	−0.479512	0.273782	0.567913	0.057*
H27B	−0.530075	0.373634	0.543107	0.057*
H27C	−0.483262	0.377737	0.592940	0.057*
C28	0.3478 (4)	0.1416 (2)	0.64014 (12)	0.0391 (9)
H28A	0.357358	0.212725	0.633615	0.059*
H28B	0.338415	0.103850	0.613372	0.059*
H28C	0.447548	0.119693	0.655865	0.059*
C29	0.5871 (4)	−0.3165 (3)	0.68134 (10)	0.0302 (8)
H29A	0.620064	−0.385251	0.687705	0.045*
H29B	0.633022	−0.272005	0.703276	0.045*
H29C	0.630984	−0.297406	0.653180	0.045*
C30	0.2775 (4)	−0.3863 (2)	0.56560 (10)	0.0289 (8)
H30	0.316251	−0.452238	0.570331	0.035*
C31	0.2294 (4)	−0.3627 (2)	0.52022 (10)	0.0271 (8)
C32	0.1819 (4)	−0.4402 (2)	0.49228 (10)	0.0277 (7)
C33	0.1323 (4)	−0.4243 (3)	0.44958 (10)	0.0318 (8)
H33	0.099547	−0.479751	0.432689	0.038*
C34	0.1780 (6)	−0.2557 (3)	0.45767 (11)	0.0436 (10)
H34	0.178044	−0.190536	0.445946	0.052*
C35	0.2278 (5)	−0.2669 (3)	0.50075 (11)	0.0393 (9)
H35	0.260412	−0.210137	0.516866	0.047*
C36	−0.2667 (5)	0.3112 (3)	0.65699 (10)	0.0362 (9)
H36A	−0.351862	0.363485	0.654524	0.054*
H36B	−0.225632	0.308380	0.686570	0.054*
H36C	−0.316076	0.246914	0.649212	0.054*
F1	0.1806 (3)	−0.53701 (13)	0.50769 (6)	0.0389 (5)
N1	0.1299 (4)	−0.3320 (2)	0.43173 (9)	0.0384 (7)
O1	−0.1569 (3)	0.30433 (14)	0.58156 (6)	0.0254 (5)
O2	−0.1682 (5)	0.10256 (19)	0.58389 (12)	0.0840 (12)
H2	−0.183301	0.163538	0.579934	0.126*
O3	0.3489 (3)	−0.46721 (16)	0.64538 (7)	0.0382 (6)

washed with brine. The product was concentrated under reduced pressure and purified by silica gel column chromatography. The single crystal of the title compound was obtained by recrystallization with ethyl acetate solution.

2 Experimental details

The H atoms were placed in idealized positions and treated as riding on their parent atoms, with *d* (C–H) = 0.96 Å (methyl), U_{iso}(H) = 1.5U_{eq}(C), and *d*(C–H) = 0.97 Å (methylene), U_{iso}(H) = 1.2U_{eq}(C), and *d*(C–H) = 0.98 Å (methyne), U_{iso}(H) = 1.2U_{eq}(C), and *d*(C–H) = 0.93 Å (aromatic),

U_{iso}(H) = 1.2U_{eq}(C). H atoms on hydroxyl group were located in different maps and treated as riding.

3 Comment

Ginsenosides are divided into protopanoxadiol-type sapogenin, protopanoxatriol-type sapogenin and oleanolic acid type sapogenin [4]. The configuration of C_{20} of 20(*S*)-protopanoxadiol-type sapogenin is easily converted to *R* type when treated with an inorganic acid [5]. The synthesis and single crystal X-ray diffraction of 20(*S*)-propanaxanediol, 20(*R*)-propanaxanediol, 20(*R*)-panaxadiol and their derivatives have been studied in our group [6–10]. The title compound is the 20(*R*)-panaxadiol derivative.

The title compound has a dammarane type as the parent structure [11], with a pyridine ring structure attached to C(1). An *α*,*β*-unsaturated ketone group is formed between the pyridine group and the parent nucleus by the Claisen–Schmidt reaction effect. The angle of twist of C(30)=C(1)–C(2)=O(3) is −16.5(5)°. The bond length of C(30)=C(1) is 1.338(4) Å. The bond length of C(2)=O(3) is 1.221(4) Å. Formation of a *Z*-configuration between the pyridine ring and the carbonyl group [12]. In addition, the pyridinyl group is substituted with a fluorine atom and the C–F bond length is 1.359(3) Å. The presence of *α*,*β*-unsaturated ketone groups and fluorine atoms in the molecule facilitates the enhancement of the biological activity of the molecule [13]. The first ring contains a carbon-oxygen double bond and the bond length of C(2)–O(3) is 1.221(4) Å. The bond length of C(13)–O(2) is 1.422(4) Å. Bond length of C(22)–O(1), C(18)–O(1) in the tetrahydropyran ring are 1.455(3), 1.458(3) Å respectively. The molecules C(5), C(8), C(9), C(10), C(12), C(13), C(14), and C(17) are all chiral carbons, all of which are in the *R* conformation except C(17), which is in the *S* conformation. There is a pyran ring substitution at the C17 position, and the oxygen atom on the ring acts as a hydrogen bond acceptor to form an intramolecular O–H···O hydrogen bond. In the crystal structure, the pyridine ring has a planar conformation, and all the six-membered rings, except the ketone-containing ring, have a chair conformation with bond lengths and angles within the expected range.

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