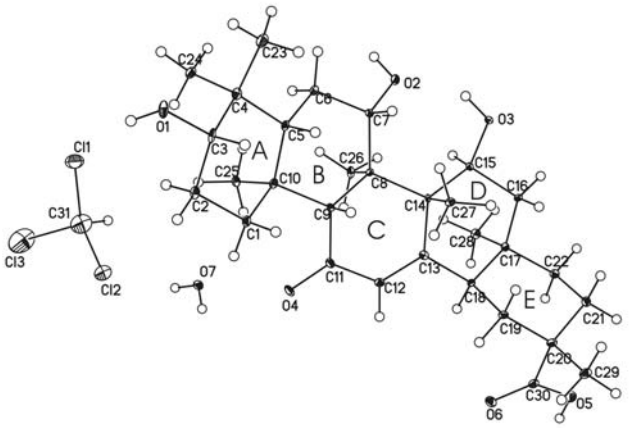
Crystal structure of 3β,7β,15α-trihydroxy-11-oxo-18β,20β-olean-12-en-30-oic acid — chloroform — water (1:1:1), $C_{30}H_{46}O_6 \cdot CHCl_3 \cdot H_2O$

Chao-Jun He[I,II], Hua Sun[I], Peng-Ju Li[I] and Min Wang[*,I]

[I] Tianjin University of Science and Technology, College of Biotechnology, Tianjin 300457, P. R. China
[II] Luoyang Normal University, Life Science Department, Luoyang 471022, Henan, P. R. China

Received February 13, 2011, accepted and available on-line April 10, 2011; CCDC no. 1267/3403



Abstract

$C_{31}H_{49}Cl_3O_7$, orthorhombic, $P2_12_12_1$ (no. 19), a = 11.828(1) Å, b = 13.213(2) Å, c = 19.606(2) Å, V = 3064.0 Å^3, Z = 4, $R_{gt}(F)$ = 0.067, $wR_{ref}(F^2)$ = 0.190, T = 113 K.

Source of material

Stock cultures of Absidia coerulea AC307 was stored on potato dextrose agar slants (PDA) at 4 °C. The spores of A. coerulea AC307 were gained by washing the slant agar using sterilized water. Then the suspension of certain spore concentration was transferred into the sterilized liquid medium. The composition of the medium was as follows (g/L): glucose 10.5, yeast extract 2.5, corn porridge 12.0, $(NH_4)_2SO_4$ 5.0. The experiment was conducted in 250 mL shake flasks containing 30 mL culture media inoculated with A. coerulea AC307. The flasks were shaken at 28 °C and 150 rpm for 19 h. Then the rotation speed was changed to 170 rpm for the rest of time. Glycyrrhetinic acid was dissolved in ethanol (100 g/L) and distributed among the flasks (0.2 g/L) and the reaction was allowed to proceed for 24 h. The mycelium was then removed by filtration, and the biomass was extracted with EtOAc (100 mL) for 5 min in an ultrasonic bath and filtered again. The broth was extracted with the same solvent (3 × 100 mL) and all extracts were combined and dried anhydrous Na_2SO_4. After filtration, the solvents were evaporated under reduced pressure. Controls were carried out in order to verify the action of the medium (without fungi) on the substrates and the presence of similar metabolites on the fungi cultures (without substrates). The crude extracts were purified by Si gel column using petroleum ether/acetone (9:2, *v*/*v*). The white powder was diffused with petroleum ether/chloroform (2:1, *v*/*v*) at room temperature. Colourless prismatic crystals suitable for X-ray analysis were obtained.

Experimental details

H atoms of water molecule were located from difference Fourier maps and refined freely. All H atoms bound to C atoms and on hydroxy O atoms were generated geometrically and refined as riding with d(C—H) = 0.93 - 0.97 Å, d(O—H) = 0.82 Å, and U_{iso}(H) = 1.2 U_{eq}(C) or 1.5 U_{eq}(O). The Flack paremeter of 0.06(13) is in agreement with the absolute configuration of the known absolute configuration.

Discussion

Glycyrrhetinic acid is a pentacyclic triterpenoid derivative of the β-amyrin type. Glycyrrhetinic acid and their derivatives have been used for a long time in traditional medicines for the treatment of hepatic ailments, pulmonary and allergies [1,2]. The broad spectrum comprises antioxidative, antiproliferative, antiulcer, cytotoxic, antiinflammatory and endocrine activities [3,4].

The asymmetric unit of the title crystal structure consists of one 7β,15α-dihydroxy-18β-glycyrrhetinic acid (3β,7β,15α-trihydroxy-11-oxo-18β,20β-olean-12-en-30-oic acid) molecule, one water molecule and one chloroform molecule. The 7β,15α-dihydroxy-18β-glycyrrhetinic acid has five fused six-membered rings (**A**/**B**/**C**/**D**/**E**). The cyclohexane rings **A**, **B** and **E** are in chair conformation, cyclohexene ring **C** is in an envelope conformation. The **D** and **E** rings are *cis*-fused. The other ring junctions are *trans*-fused. The torsion angle of C5–C6–C7–O2 (–176.3(2)°) indicates that the 7-hydroxy is β configuration. The 15-hydroxy is β configuration with the torsion angle C13–C14–C15–O3 of –158.6(2)°. The orientation of the carboxylic acid group with respect to cyclohexane ring **E** is indicated by the torsion angles ∠C19–C20–C30–O6 = –19.4(4)° and ∠C19–C20–C30–O5 = 161.6(2)°. The bond lengths and angles are within normal ranges [5-7].

There are two types of intermolecular hydrogen bonds contributing to the formation of 3D supramolecular structure: between water molecule and 7β,15α-dihydroxy-18β-glycyrrhetinic acid molecule, between 7β,15α-dihydroxy-18β-glycyrrhetinic acid molecule and adjacent 7β,15α-dihydroxy-18β-glycyrrhetinic acid molecule: O1–H1···O4^{i} (2.713(3) Å, 160.4°), O2–H2···O7^{ii} (2.893(3) Å, 156.2°) O5–H5···O7^{iii} (2.760(3) Å, 157.0°) O7–H7A···O1^{iv} (2.826(3) Å, 169(1)°) O7–H7B···O3^{v} (2.804(3) Å, 159(2)°) and O3–H3···O2 (2.609(3) Å, 147.1°); symmetry codes i: –x+1,y–1/2,–z+3/2; ii: x+1/2,–y+3/2,–z+2; iii: x+1/2,–y+5/2,–z+2; iv: –x+1,y+1/2,–z+3/2; v: x–1,y,z).

* Correspondence author (e-mail: minw@tust.edu.cn)

Table 1. Data collection and handling.

Crystal:	colorless prism, size 0.06 × 0.06 × 0.20 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	3.46 cm^{-1}
Diffractometer, scan mode:	Rigaku Saturn CCD, φ/ω
$2\theta_{max}$:	50.04°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	23397, 5408
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 5045
$N(param)_{refined}$:	389
Programs:	SHELXS-97, SHELXL-97 [8]

Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{iso}
H(1)	4*a*	0.5747	0.5449	0.6613	0.040
H(2)	4*a*	0.9026	0.6748	0.9903	0.034
H(3)	4*a*	1.0505	0.8173	0.9672	0.026
H(5)	4*a*	0.8933	1.4936	0.9874	0.039
H(1A)	4*a*	0.5561	0.8532	0.7560	0.021
H(1B)	4*a*	0.6811	0.8390	0.7262	0.021
H(2A)	4*a*	0.5164	0.6796	0.7368	0.022
H(2B)	4*a*	0.5545	0.7318	0.6667	0.022
H(3A)	4*a*	0.7397	0.6713	0.6834	0.023
H(5A)	4*a*	0.8147	0.7230	0.7912	0.017
H(6A)	4*a*	0.7411	0.6538	0.9210	0.020
H(6B)	4*a*	0.8503	0.6063	0.8846	0.020
H(7)	4*a*	0.9343	0.7651	0.8780	0.017
H(9)	4*a*	0.7872	0.8871	0.8146	0.015
H(12)	4*a*	0.6854	1.1172	0.8958	0.019
H(15)	4*a*	0.9428	0.9223	1.0194	0.016
H(16A)	4*a*	1.0867	1.0672	0.9532	0.017
H(16B)	4*a*	1.0918	1.0382	1.0323	0.017
H(18)	4*a*	0.8140	1.1906	0.9630	0.015
H(19A)	4*a*	0.9945	1.1645	0.8666	0.019
H(19B)	4*a*	0.8790	1.2239	0.8528	0.019
H(21A)	4*a*	1.1378	1.2379	0.9488	0.022
H(21B)	4*a*	1.1133	1.3458	0.9830	0.022
H(22A)	4*a*	0.9665	1.2778	1.0485	0.020
H(22B)	4*a*	1.0786	1.2134	1.0619	0.020
H(23A)	4*a*	0.8468	0.4990	0.8036	0.043
H(23B)	4*a*	0.8865	0.5794	0.7475	0.043
H(23C)	4*a*	0.8100	0.4849	0.7256	0.043
H(24A)	4*a*	0.6160	0.4694	0.7805	0.032
H(24B)	4*a*	0.5605	0.5658	0.8168	0.032
H(24C)	4*a*	0.6605	0.5053	0.8537	0.032
H(25A)	4*a*	0.5041	0.7178	0.8432	0.025
H(25B)	4*a*	0.5297	0.8152	0.8892	0.025
H(25C)	4*a*	0.5866	0.7088	0.9076	0.025
H(26A)	4*a*	0.6938	0.7932	0.9843	0.026
H(26B)	4*a*	0.6832	0.9138	0.9814	0.026
H(26C)	4*a*	0.7851	0.8625	1.0224	0.026
H(27A)	4*a*	0.9207	0.9898	0.8144	0.022
H(27B)	4*a*	0.9864	0.8886	0.8356	0.022
H(27C)	4*a*	1.0348	0.9967	0.8581	0.022
H(28A)	4*a*	0.8364	1.0441	1.0593	0.030
H(28B)	4*a*	0.8340	1.1601	1.0828	0.030
H(28C)	4*a*	0.9319	1.0865	1.1095	0.030
H(29A)	4*a*	1.1124	1.3133	0.8334	0.034
H(29B)	4*a*	1.0825	1.4223	0.8642	0.034
H(29C)	4*a*	0.9964	1.3679	0.8130	0.034
H(31A)	4*a*	0.2570	0.7094	0.8649	0.085
H(7A)	4*a*	0.310(1)	0.961(1)	0.9149(6)	0.027(9)
H(7B)	4*a*	0.2378(7)	0.911(2)	0.9640(9)	0.03(1)

Table 3. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1)	4*a*	0.6451(2)	0.5532(2)	0.6607(1)	0.021(1)	0.035(1)	0.023(1)	–0.009(1)	0.0020(9)	–0.0159(9)
O(2)	4*a*	0.9269(2)	0.7308(2)	0.9762(1)	0.022(1)	0.020(1)	0.026(1)	–0.0073(9)	–0.0134(9)	0.0104(8)
O(3)	4*a*	1.0734(2)	0.8770(1)	0.9622(1)	0.0129(8)	0.0124(9)	0.027(1)	0.0012(8)	–0.0063(8)	0.0011(8)
O(4)	4*a*	0.5689(2)	0.9794(2)	0.8395(1)	0.017(1)	0.026(1)	0.041(1)	0.0055(9)	–0.014(1)	–0.004(1)
O(5)	4*a*	0.9452(2)	1.4542(2)	0.9752(1)	0.024(1)	0.016(1)	0.037(1)	0.0022(9)	0.003(1)	–0.0059(9)
O(6)	4*a*	0.8027(2)	1.3750(2)	0.9232(1)	0.020(1)	0.023(1)	0.042(1)	0.0063(9)	–0.004(1)	–0.003(1)
C(1)	4*a*	0.6200(2)	0.8051(2)	0.7521(1)	0.019(1)	0.018(1)	0.016(1)	–0.006(1)	–0.005(1)	0.001(1)
C(2)	4*a*	0.5808(2)	0.7112(2)	0.7126(1)	0.020(1)	0.023(1)	0.013(1)	–0.007(1)	–0.001(1)	0.000(1)
C(3)	4*a*	0.6751(2)	0.6350(2)	0.7054(1)	0.020(1)	0.024(1)	0.013(1)	–0.014(1)	0.000(1)	–0.005(1)
C(4)	4*a*	0.7179(2)	0.5971(2)	0.7750(1)	0.015(1)	0.020(1)	0.018(1)	–0.003(1)	0.005(1)	–0.003(1)
C(5)	4*a*	0.7508(2)	0.6921(2)	0.8173(1)	0.014(1)	0.014(1)	0.015(1)	–0.006(1)	0.001(1)	0.004(1)
C(6)	4*a*	0.8024(2)	0.6676(2)	0.8879(1)	0.016(1)	0.014(1)	0.022(1)	–0.004(1)	0.001(1)	0.003(1)
C(7)	4*a*	0.8725(2)	0.7558(2)	0.9122(1)	0.013(1)	0.014(1)	0.015(1)	–0.000(1)	–0.003(1)	0.004(1)
C(8)	4*a*	0.8094(2)	0.8585(2)	0.9170(1)	0.013(1)	0.009(1)	0.015(1)	–0.002(1)	–0.003(1)	0.001(1)
C(9)	4*a*	0.7324(2)	0.8718(2)	0.8520(1)	0.014(1)	0.012(1)	0.011(1)	0.001(1)	–0.007(1)	–0.000(1)
C(10)	4*a*	0.6638(2)	0.7791(2)	0.8244(1)	0.015(1)	0.015(1)	0.016(1)	–0.004(1)	0.001(1)	0.002(1)
C(11)	4*a*	0.6664(2)	0.9701(2)	0.8607(2)	0.012(1)	0.021(1)	0.020(1)	0.001(1)	–0.001(1)	0.002(1)
C(12)	4*a*	0.7243(2)	1.0544(2)	0.8932(1)	0.017(1)	0.014(1)	0.018(1)	0.004(1)	0.001(1)	–0.002(1)
C(13)	4*a*	0.8274(2)	1.0500(2)	0.9196(1)	0.014(1)	0.018(1)	0.008(1)	0.002(1)	0.005(1)	0.000(1)
C(14)	4*a*	0.8962(2)	0.9517(2)	0.9168(1)	0.007(1)	0.012(1)	0.013(1)	–0.003(1)	–0.002(1)	–0.000(1)
C(15)	4*a*	0.9830(2)	0.9462(2)	0.9776(1)	0.011(1)	0.014(1)	0.015(1)	–0.001(1)	–0.003(1)	0.002(1)
C(16)	4*a*	1.0403(2)	1.0470(2)	0.9930(1)	0.016(1)	0.010(1)	0.016(1)	–0.001(1)	–0.003(1)	0.004(1)
C(17)	4*a*	0.9563(2)	1.1319(2)	1.0091(1)	0.017(1)	0.014(1)	0.013(1)	–0.002(1)	–0.006(1)	–0.000(1)
C(18)	4*a*	0.8787(2)	1.1481(2)	0.9469(1)	0.011(1)	0.010(1)	0.016(1)	0.000(1)	0.002(1)	0.001(1)
C(19)	4*a*	0.9365(2)	1.2081(2)	0.8880(1)	0.019(1)	0.014(1)	0.015(1)	0.002(1)	–0.002(1)	0.003(1)
C(20)	4*a*	0.9918(2)	1.3060(2)	0.9109(1)	0.020(1)	0.013(1)	0.019(1)	0.002(1)	0.002(1)	0.003(1)
C(21)	4*a*	1.0777(2)	1.2822(2)	0.9673(1)	0.015(1)	0.017(1)	0.023(1)	0.000(1)	–0.000(1)	–0.003(1)
C(22)	4*a*	1.0204(2)	1.2298(2)	1.0273(1)	0.019(1)	0.015(1)	0.016(1)	0.002(1)	–0.003(1)	–0.002(1)
C(23)	4*a*	0.8250(3)	0.5344(2)	0.7617(2)	0.021(2)	0.021(2)	0.043(2)	–0.003(1)	0.008(1)	–0.009(1)
C(24)	4*a*	0.6309(2)	0.5282(2)	0.8096(2)	0.021(1)	0.017(1)	0.026(2)	–0.004(1)	0.002(1)	–0.001(1)
C(25)	4*a*	0.5617(2)	0.7528(2)	0.8703(1)	0.013(1)	0.021(1)	0.017(1)	–0.003(1)	0.001(1)	–0.000(1)

Table 3. Continued.

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(26)	4*a*	0.7362(2)	0.8568(2)	0.9822(1)	0.015(1)	0.026(1)	0.012(1)	–0.009(1)	–0.001(1)	0.001(1)
C(27)	4*a*	0.9659(2)	0.9572(2)	0.8501(1)	0.019(1)	0.012(1)	0.013(1)	0.001(1)	–0.000(1)	0.001(1)
C(28)	4*a*	0.8830(3)	1.1030(2)	1.0708(1)	0.021(1)	0.021(1)	0.018(1)	0.000(1)	–0.001(1)	–0.001(1)
C(29)	4*a*	1.0512(3)	1.3570(2)	0.8498(2)	0.024(2)	0.019(1)	0.026(2)	0.002(1)	0.010(1)	0.006(1)
C(30)	4*a*	0.9017(2)	1.3804(2)	0.9366(1)	0.020(1)	0.015(1)	0.020(1)	0.001(1)	0.005(1)	0.003(1)
Cl(1)	4*a*	0.3101(1)	0.57280(9)	0.80231(8)	0.0486(6)	0.0411(5)	0.1032(9)	0.0053(5)	0.0002(6)	0.0166(6)
Cl(2)	4*a*	0.2753(1)	0.77712(9)	0.75990(9)	0.0847(8)	0.0419(6)	0.129(1)	–0.0108(6)	–0.0461(8)	0.0219(7)
Cl(3)	4*a*	0.0945(1)	0.6624(2)	0.8147(1)	0.0581(7)	0.092(1)	0.238(2)	0.0097(8)	0.068(1)	–0.017(1)
C(31)	4*a*	0.2373(5)	0.6852(4)	0.8180(3)	0.077(3)	0.068(3)	0.069(3)	0.005(3)	0.018(3)	–0.001(3)
O(7)	4*a*	0.3038(2)	0.9229(2)	0.9494(1)	0.0156(9)	0.023(1)	0.029(1)	0.0017(8)	0.0005(9)	0.0044(9)

Acknowledgment. This work was supported by the Natural Science Foundation of Tianjin (grant no. 08JCZDJC15200)

References

1. Kitagawa, I.: Licorice root. A natural sweetener and an important ingredient in Chinese medicine. Pure Appl. Chem. **74** (2002) 1189-1198.
2. Asl, M. N.; Hosseinzadeh, H.: Review of pharmacological effects of Glycyrrhiza sp and its bioactive compounds. Phytother. Res. **22** (2008) 709-724.
3. Subba Rao, G. S.; Kondaiah, P.; Singh, S. K.; Ravanan, P.; Sporn, M. B.: Chemical modifications of natural triterpenes-glycyrrhetinic and boswellic acids: evaluation of their biological activity. Tetrahedron **64** (2008) 11541-11548.
4. Chintharlapalli, S.; Papineni, S.; Jutooru, I.; McAlees, A.; Safe, S.: Structure-dependent activity of glycyrrhetinic acid derivatives as peroxisome proliferator-activated receptor {gamma} agonists in colon cancer cells. Mol. Cancer Ther. **6** (2007) 1588-1598.
5. Gzella, A.: Triterpenoide. XVIII. Kristallstrukturen von 2-Oxo- und 3-Oxo-18β-olean-12-en-28-säure-methylestern. Acta Crystallogr. **C55** (1999) 2153-2156.
6. Maartmann-Moe, K.; Bicknell, W.; Francis, G. W.: Structure of olean-12(13)-en-3β-yl acetate. Acta Crystallogr. **C43** (1987) 2362-2364.
7. Cai, Z.; Yu, Z. Y.; Ren, H.; Wang, X. Z.; Wang, J. W.: Synthesis and crystal structure of (*E*)-ethyl 3-keto-18β-glycyrrhetinate 3-oxime. Chinese J. Struct. Chem. **26** (2007) 1013-1016.
8. Sheldrick, G. M.: A short history of SHELX. Acta Crystallogr. **A64** (2008) 112-122.