Crystal structure of 5,19-bis(acetyloxy)-13-deoxy-10-deoxy-20-(ethylthio)-2,20-dihydro-(2α,5β,19*R*)-enmein, $C_{28}H_{38}O_{10}S$

H. Shi[I], Y.-W. Guo*[,I], J.-L. Yu[I] and J. Sun[II]

[I] Shanghai Institutes for Biological Sciences, Institute of Materia Medica, State Key Laboratory of Drug Research, Chinese Academy of Sciences, Shanghai, 201203 P. R. China

[II] Chinese Academy of Sciences, Institute of Organic Chemistry, Shanghai, 200032 P. R. China

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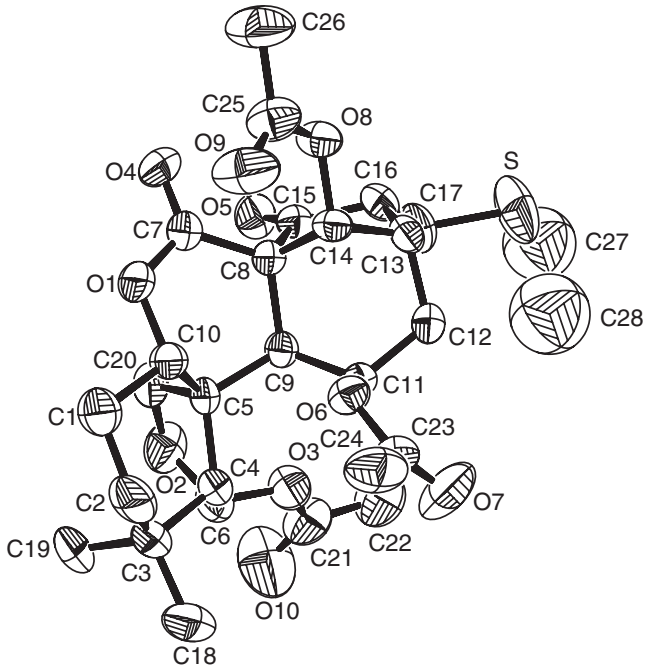

Abstract

$C_{28}H_{38}O_{10}S$, orthorhombic, $P2_12_12_1$ (No. 19), a = 9.1243(6) Å, b = 9.3896(7) Å, c = 33.962(2) Å, V = 2909.6 Å^3, Z = 4, $R_{gt}(F)$ = 0.058, $wR_{ref}(F^2)$ = 0.149, T = 293 K.

Source of material

The title compound, $C_{28}H_{38}O_{10}S$, was obtained in two-step syntheses. The macrocalyxin A (50 mg) was dissolved in a mixture of pyridine (1.5 ml) and acetic anhydride (1.5 ml) and the solution was left 24 h at room temperature, 5 ml MeOH was added to the mixture and the solution was concentrated in vacuo to give a residue that was purified by cc (solvent CH_2Cl_2:CH_3COCH_3 = 40:1) to give 5,19-bis(acetyloxy)-13-deoxy-10-acetate (5β,19*R*)-enmein (46.6 mg) (**I**). Into a solution of **I** (25 mg) in ethanol (50 ml) was added dropwise excess ethanethiol (0.5 ml). After being stirred at room temperature for 1 h, the mixture was concentrated in vacuo to give an oily residue, which was washed with 0.5 ml water, then crystallized in MeOH to afford the title compound as colourless crystals (23.7 mg). Crystals suitable for X-ray structure analysis were obtained by slow evaporation from an aqueous solution containing chloroform and methanol in a 1:1 ratio at room temperature.

Experimental details

All non-H atoms were refined anisotropically. The H atoms were proved initially from difference maps then refined by the SHELXL "nearest acceptor" method, except for those H atoms on methyl and ethyl, which were placed at calculated positions with C-H distance of 0.93 Å. Final difference Fourier maps showed the highest and lowest electron densities of 0.37 and –0.42 e/Å^{-3}, respectively.

Discussion

The title molecule is composed of three six-membered rings and two five-membered rings. The cyclohexane ring A (C1–C5/C10) adopt the chair conformation with puckering parameters [1] Q = 0.549(4) Å, θ = 22.4(4)° and φ = 42(1)°; the ring B (C10/O1/C7–C9/C5) exists in a distorted boat conformation (Q = 0.661(3) Å, θ = 110.0(3)° and φ = 93.2(3)°), ring C (C8/C9/C11–C14) adopts boat conformation (Q = 0.832(3) Å, θ = 77.9(2) and φ = 292.9(2)°). The two five-membered rings D (C13/C14/C8/C15/C16) and E (C4/C5/C20/O2/C6), adopt an envelope conformation with C14 and C4 displaced by 0.682(2) Å and 0.569(3) Å from the mean plane of the remaining four atoms. The stereochemistry of the A/B ring juncture is *trans*, and the B/C ring juncture is *cis*, C13 C14 and C15 located in ring C and ring D at the same time, to avoid the space is too crowded, only 2α configuration is taken in the additional reaction and no product which taken 2β configuration is observed. The main difference between title compound and macrocalyxin A [2], lies in ring D. In the molecule of macrocalyxin A, ring D is named conjugated α-methylenecyclopentanone, it has been found that the α-methylenecyclopentanone in the *Rabdosia diterpenes* is highly reactive toward sulfhydryl groups essential to enzyme function [3]. It is believed the steric strain within the five-member ring help to increase the reactivity of the conjugated double bond [4]. The steric strain within the five-member ring has been reduced, it can be observed through the bond angles ∠C16–C15–C8 change from 105.4(4)° into 108.0(2)° and ∠C15–C8–C14 change from 100.7(3)° into 102.3(2)°. The bond length of C15—C16 change from 1.484(6) Å into 1.529(4) Å, contributing to the release of the steric strain within ring D.

* Correspondence author (e-mail: ywguo@mail.shcnc.ac.cn)

Table 1. Data collection and handling.

Crystal:	colourless prism, size 0.395 × 0.400 × 0.411 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	1.65 cm^{-1}
Diffractometer, scan mode:	Bruker SMART CCD, φ/ω
$2\theta_{max}$:	56.52°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	17851, 6775
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 3909
$N(param)_{refined}$:	420
Programs:	SHELXS-97 [5], SHELXL-97 [6], OERTEP3 [7]

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

Atom	Site	*x*	*y*	*z*	U_{iso}
H(19)	4*a*	–0.1699	1.0399	0.8241	0.145
H(17)	4*a*	–0.0419	1.0099	0.8537	0.145
H(18)	4*a*	–0.2042	0.9771	0.8658	0.145
H(21)	4*a*	–0.3061	0.8394	0.7939	0.125
H(20)	4*a*	–0.3379	0.7764	0.8358	0.125
H(22)	4*a*	–0.2625	0.6818	0.8036	0.125
H(27)	4*a*	–0.1515	0.6368	1.0182	0.141
H(26)	4*a*	–0.0146	0.7089	0.9987	0.141
H(25)	4*a*	–0.0416	0.5451	0.9933	0.141
H(29)	4*a*	0.3032	1.0153	0.8323	0.112
H(30)	4*a*	0.4251	0.9020	0.8236	0.112
H(28)	4*a*	0.4586	1.0307	0.8515	0.112
H(32)	4*a*	0.6654	0.2819	0.7641	0.139
H(31)	4*a*	0.5269	0.1843	0.7684	0.139
H(33)	4*a*	0.6421	0.1925	0.8026	0.139
C(27)	4*a*	0.359(1)	0.264(1)	1.0415(2)	0.192(3)
H(34)	4*a*	0.2771	0.1989	1.0388	0.231
H(35)	4*a*	0.4254	0.2317	1.0619	0.231
C(28)	4*a*	0.317(1)	0.403(1)	1.0459(3)	0.230(5)
H(37)	4*a*	0.4013	0.4639	1.0442	0.345
H(36)	4*a*	0.2708	0.4154	1.0711	0.345
H(38)	4*a*	0.2487	0.4280	1.0255	0.345
H(1)	4*a*	0.086(5)	0.699(5)	0.753(1)	0.11(2)
H(2)	4*a*	–0.072(3)	0.637(3)	0.7678(8)	0.032(8)
H(3)	4*a*	–0.059(4)	0.893(4)	0.7743(9)	0.09(1)
H(4)	4*a*	0.086(2)	0.866(3)	0.8028(9)	0.06(1)
H(5)	4*a*	0.024(2)	0.790(2)	0.8715(7)	0.034(7)
H(6)	4*a*	–0.250(4)	0.725(3)	0.8974(9)	0.055(9)
H(7)	4*a*	0.091(3)	0.497(3)	0.8971(8)	0.038(8)
H(8)	4*a*	0.201(3)	0.655(3)	0.8089(8)	0.040(8)
H(9)	4*a*	0.181(3)	0.711(3)	0.9134(7)	0.044(8)
H(10)	4*a*	0.442(3)	0.649(3)	0.9233(8)	0.040(8)
H(11)	4*a*	0.335(4)	0.562(4)	0.947(1)	0.07(1)
H(12)	4*a*	0.537(3)	0.440(3)	0.9067(7)	0.030(6)
H(13)	4*a*	0.423(3)	0.544(3)	0.8473(8)	0.038(7)
H(14)	4*a*	0.423(3)	0.232(3)	0.9116(8)	0.042(8)
H(15)	4*a*	0.226(4)	0.351(4)	0.9613(9)	0.06(1)
H(16)	4*a*	0.274(3)	0.189(2)	0.9588(9)	0.049(9)
H(23)	4*a*	–0.155(3)	0.486(3)	0.8247(9)	0.050(9)
H(24)	4*a*	–0.078(3)	0.400(2)	0.8563(8)	0.049(9)

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}
S	4*a*	0.4589(1)	0.3055(2)	0.99078(3)	0.0767(7)	0.179(1)	0.0590(6)	0.0033(8)	–0.0222(6)	0.0266(7)
O(1)	4*a*	0.1186(3)	0.4575(2)	0.79340(6)	0.078(2)	0.064(1)	0.035(1)	0.021(1)	–0.016(1)	–0.012(1)
O(2)	4*a*	–0.2067(2)	0.5450(3)	0.87613(8)	0.048(1)	0.088(2)	0.071(2)	–0.018(1)	0.006(1)	–0.014(1)
O(3)	4*a*	–0.0917(2)	0.6605(3)	0.92770(6)	0.057(1)	0.086(2)	0.044(1)	0.012(1)	0.007(1)	–0.005(1)
O(4)	4*a*	0.2024(3)	0.2450(3)	0.80522(7)	0.092(2)	0.052(2)	0.067(2)	0.019(1)	–0.021(1)	–0.024(1)
O(5)	4*a*	0.1272(3)	0.2086(2)	0.88972(7)	0.062(1)	0.048(1)	0.073(2)	–0.012(1)	–0.010(1)	0.006(1)
O(6)	4*a*	0.3009(2)	0.7438(2)	0.86687(6)	0.052(1)	0.038(1)	0.045(1)	–0.000(1)	0.002(1)	–0.0016(9)
O(7)	4*a*	0.3254(4)	0.9195(3)	0.91030(9)	0.179(3)	0.051(2)	0.065(2)	–0.009(2)	–0.021(2)	–0.014(1)
O(8)	4*a*	0.4845(2)	0.3424(2)	0.83828(6)	0.053(1)	0.045(1)	0.049(1)	0.012(1)	0.007(1)	0.003(1)
O(9)	4*a*	0.4724(4)	0.4704(3)	0.78302(7)	0.126(2)	0.064(2)	0.058(2)	0.030(2)	0.025(2)	0.015(1)
O(10)	4*a*	–0.3020(3)	0.6871(6)	0.9581(1)	0.069(2)	0.256(5)	0.092(2)	0.025(3)	0.028(2)	–0.017(3)
C(1)	4*a*	0.0170(6)	0.6852(4)	0.7766(1)	0.087(3)	0.071(3)	0.039(2)	0.018(2)	–0.011(2)	0.005(2)
C(2)	4*a*	–0.0125(5)	0.8324(4)	0.7932(1)	0.091(3)	0.071(3)	0.051(2)	0.025(2)	–0.017(2)	0.018(2)
C(3)	4*a*	–0.1203(4)	0.8270(4)	0.8281(1)	0.070(2)	0.062(2)	0.057(2)	0.028(2)	–0.020(2)	–0.007(2)
C(4)	4*a*	–0.0499(3)	0.7342(3)	0.86115(9)	0.040(2)	0.048(2)	0.046(2)	0.007(1)	–0.009(1)	–0.005(1)
C(5)	4*a*	0.0257(3)	0.5946(3)	0.84786(8)	0.041(1)	0.045(2)	0.032(2)	0.004(1)	–0.009(1)	–0.002(1)
C(6)	4*a*	–0.1618(4)	0.6783(4)	0.8901(1)	0.043(2)	0.078(3)	0.053(2)	0.011(2)	–0.003(2)	–0.008(2)
C(7)	4*a*	0.1843(3)	0.3633(4)	0.81682(9)	0.052(2)	0.054(2)	0.042(2)	0.008(2)	–0.009(2)	–0.007(2)
C(8)	4*a*	0.2350(3)	0.4137(3)	0.85740(8)	0.041(2)	0.040(2)	0.036(2)	0.004(1)	–0.005(1)	–0.003(1)
C(9)	4*a*	0.1436(3)	0.5388(3)	0.87701(8)	0.042(2)	0.042(2)	0.031(2)	0.002(1)	–0.002(1)	0.001(1)
C(10)	4*a*	0.1004(4)	0.6020(3)	0.80752(8)	0.061(2)	0.047(2)	0.031(2)	0.015(2)	–0.005(1)	–0.001(1)
C(11)	4*a*	0.2442(3)	0.6488(3)	0.89698(8)	0.041(2)	0.039(2)	0.037(2)	0.007(1)	–0.004(1)	–0.005(1)
C(12)	4*a*	0.3671(4)	0.5813(3)	0.9205(1)	0.048(2)	0.048(2)	0.045(2)	0.000(2)	–0.013(2)	–0.006(2)
C(13)	4*a*	0.4315(3)	0.4437(3)	0.90220(9)	0.034(2)	0.049(2)	0.046(2)	0.004(1)	–0.007(1)	0.002(1)
C(14)	4*a*	0.3993(3)	0.4514(3)	0.85817(8)	0.043(2)	0.034(2)	0.043(2)	0.008(1)	0.003(1)	0.000(1)
C(15)	4*a*	0.2261(3)	0.2918(3)	0.88726(9)	0.048(2)	0.036(2)	0.043(2)	0.006(1)	–0.005(1)	–0.004(1)
C(16)	4*a*	0.3570(3)	0.3047(4)	0.91514(9)	0.043(2)	0.048(2)	0.047(2)	0.008(2)	–0.004(1)	0.010(2)
C(17)	4*a*	0.3068(4)	0.2843(5)	0.9569(1)	0.066(2)	0.074(3)	0.053(2)	–0.002(2)	–0.013(2)	0.018(2)
C(18)	4*a*	–0.1355(6)	0.9774(4)	0.8444(1)	0.126(4)	0.072(3)	0.091(3)	0.054(3)	–0.032(3)	–0.013(2)
C(19)	4*a*	–0.2707(4)	0.7764(5)	0.8140(1)	0.068(2)	0.098(3)	0.084(3)	0.036(2)	–0.038(2)	–0.013(2)
C(20)	4*a*	–0.1041(4)	0.4909(4)	0.8480(1)	0.050(2)	0.064(2)	0.048(2)	–0.005(2)	–0.009(2)	–0.003(2)
C(21)	4*a*	–0.1744(5)	0.6651(5)	0.9599(1)	0.071(3)	0.086(3)	0.053(2)	–0.004(2)	0.027(2)	–0.013(2)

Table 3. Continued.

Atom	Site	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(22)	4*a*	–0.0881(6)	0.6365(5)	0.9956(1)	0.112(3)	0.112(4)	0.058(3)	–0.003(3)	0.012(3)	–0.008(2)
C(23)	4*a*	0.3344(4)	0.8780(3)	0.8779(1)	0.063(2)	0.039(2)	0.069(2)	0.008(2)	–0.012(2)	–0.005(2)
C(24)	4*a*	0.3849(5)	0.9643(4)	0.8432(1)	0.080(2)	0.040(2)	0.104(3)	0.000(2)	0.011(3)	0.007(2)
C(25)	4*a*	0.5115(4)	0.3659(4)	0.8000(1)	0.074(2)	0.053(2)	0.052(2)	0.004(2)	0.018(2)	0.003(2)
C(26)	4*a*	0.5937(5)	0.2455(5)	0.7822(1)	0.108(3)	0.090(3)	0.080(3)	0.040(3)	0.032(3)	–0.007(2)

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References

1. Cremer, D.; Pople, J. A.: A General Definition of Ring Pukering Coordinates. J. Am. Chem. Soc. **97** (1975) 1354-1358.
2. Chen, Y. Z.; Yao, W. X.; Xu, B. J.: The crystal and molecular structure of macrocalyxin A. Kexue Tongbao (Foreign Lang. Edn.) **31** (1986) 950-955.
3. Yamaguchi, M.; Taniguchi, M.; Kubo, I.; Kubota, T.: Inhibitory effect of antibacterial and antitumor diterpenoids on oxidative phosphorylation in mitochondria isolated from rat liver. Agric. Biol. Chem. **41** (1977) 2475-2477.
4. Chen, Y. Z.; Wu, Z. W.; Cheng, P. Y.: Antitumor activity and internal stress of partially conjugated five and/or six-member rings of natural terpenoids. Chinese J. Org. Chem. **7** (1987) 21-28.
5. Sheldrick, G. M.: SHELXS-97. Program for the solution of crystal structures. University of Göttingen, Germany 1997.
6. Sheldrick, G. M.: SHELXL-97, a program for refining crystal structures. University of Göttingen, Germany 1997.
7. Farrugia, L. J.: ORTEP3 for Windows. University of Glasgow, Glasgow G12 8QQ, Scotland 1997.