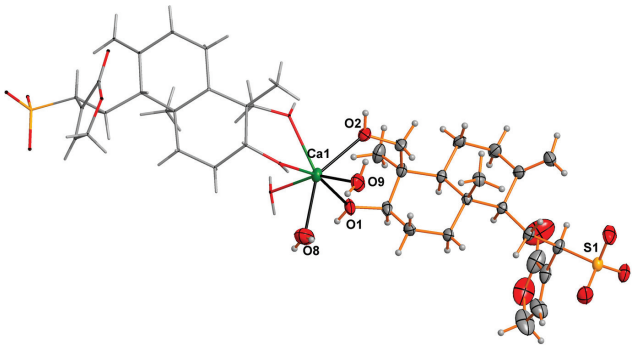
Yuan-Min Ding, Rui-Peng Li, Ying-Jie Chang, Jie Zhao, Hong-Min Liu and Wen Li*

Crystal structure of triaqua-bis(2-(6-hydroxy-5-(hydroxymethyl)-5,8*a*-dimethyl-2-methylenedecahydronaphthalen-1-yl)-1-(2-oxo-2,5-dihydrofuran-3-yl)ethane-1-sulfonato-κ^2*O*,*O*′)calcium(II) – ethanol (1/2), $C_{44}H_{76}CaO_{19}S_2$



https://doi.org/10.1515/ncrs-2019-0709
Received September 19, 2019; accepted December 20, 2019; available online January 25, 2020

Abstract

$C_{44}H_{76}CaO_{19}S_2$, monoclinic, *C*2 (no. 5), $a = 25.5446(14)$ Å, $b = 7.38025(19)$ Å, $c = 18.8450(10)$ Å, $\beta = 136.543(10)°$, $Z = 2$, $V = 2443.6(4)$ Å^3, $R_{gt}(F) = 0.0419$, $wR_{ref}(F^2) = 0.1161$, $T = 293(2)$ K.

CCDC no.: 1881358

The molecular structure is shown in the figure (The ethanol solvent was omitted for clarity). Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

***Corresponding author: Wen Li,** School of Pharmaceutical Sciences, Zhengzhou University, Zhengzhou 450001, P.R. China; and Henan Province and Key Laboratory of Technology of Drug Preparation, Collaborative Innovation Center of New Drug Research and Safety Evaluation and Ministry of Education and Key Laboratory of Henan Province for Drug Quality and Evaluation, Zhengzhou 450001, China, e-mail: liwen@zzu.edu.cn
Yuan-Min Ding and Jie Zhao: School of Chemical Engineering, Zhengzhou University, Zhengzhou 450001, P.R. China. https://orcid.org/0000-0001-6371-8755 (Y.-M. Ding)
Rui-Peng Li, Ying-Jie Chang and Hong-Min Liu: School of Pharmaceutical Sciences, Zhengzhou University, Zhengzhou 450001, P.R. China

Table 1: Data collection and handling.

Crystal:	Colourless prism
Size:	0.18 × 0.14 × 0.10 mm
Wavelength:	Cu *Kα* radiation (1.54184 Å)
μ:	2.54 mm^{-1}
Diffractometer, scan mode:	Xcalibur, ω
θ_{max}, completeness:	70.9°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	11865, 4221, 0.027
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 4143
$N(param)_{refined}$:	311
Programs:	Bruker [1], SHELX [2, 3]

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.78585(15)	0.2250(4)	0.9026(2)	0.0288(6)
H1A	0.7887	0.1530	0.9483	0.035*
H1B	0.8256	0.1835	0.9099	0.035*
C2	0.70815(18)	0.1944(5)	0.7908(2)	0.0360(7)
H2A	0.7028	0.0675	0.7730	0.043*
H2B	0.6680	0.2250	0.7845	0.043*
C3	0.70035(15)	0.3090(5)	0.7174(2)	0.0327(7)
H3	0.7428	0.2781	0.7276	0.039*
C4	0.70496(16)	0.5136(5)	0.7368(2)	0.0297(6)
C5	0.78410(15)	0.5426(4)	0.8521(2)	0.0249(6)
H5	0.8214	0.5003	0.8539	0.030*
C6	0.80399(17)	0.7421(5)	0.8829(2)	0.0334(6)
H6A	0.7716	0.7926	0.8877	0.040*
H6B	0.7949	0.8088	0.8304	0.040*
C7	0.88803(18)	0.7624(6)	0.9875(2)	0.0379(7)
H7A	0.9208	0.7231	0.9813	0.045*
H7B	0.8992	0.8884	1.0087	0.045*
C8	0.90234(16)	0.6491(5)	1.0661(2)	0.0306(6)
C9	0.88763(15)	0.4497(4)	1.0387(2)	0.0247(6)
H9	0.9156	0.4171	1.0231	0.030*
C10	0.80007(14)	0.4243(4)	0.9351(2)	0.0229(6)
C11	0.91789(15)	0.3265(5)	1.1279(2)	0.0290(6)
H11A	0.9020	0.2027	1.1033	0.035*
H11B	0.8962	0.3641	1.1515	0.035*
C12	1.00578(15)	0.3339(5)	1.2193(2)	0.0304(6)
H12	1.0207	0.4615	1.2299	0.037*
C13	1.04452(17)	0.2336(7)	1.1985(2)	0.0405(8)
C14	1.0565(3)	0.0604(8)	1.2002(4)	0.0602(12)
H14	1.0423	−0.0320	1.2170	0.072*
C15	1.0968(4)	0.0355(13)	1.1709(5)	0.096(3)
H15A	1.1461	−0.0210	1.2266	0.115*

Table 2 (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
H15B	1.0671	−0.0397	1.1098	0.115*
C16	1.0750(3)	0.3358(12)	1.1675(4)	0.0782(19)
C17	0.91799(19)	0.7221(6)	1.1440(3)	0.0422(8)
H17A	0.9204	0.8473	1.1512	0.051*
H17B	0.9266	0.6480	1.1916	0.051*
C18	0.7041(2)	0.6147(7)	0.6650(3)	0.0491(10)
H18A	0.7522	0.5992	0.6890	0.074*
H18B	0.6953	0.7413	0.6647	0.074*
H18C	0.6643	0.5670	0.5964	0.074*
C19	0.63904(17)	0.5824(5)	0.7186(2)	0.0351(7)
H19A	0.6348	0.5057	0.7560	0.042*
H19B	0.6504	0.7044	0.7458	0.042*
C20	0.75355(17)	0.4772(5)	0.9557(2)	0.0324(7)
H20A	0.7052	0.4167	0.9070	0.049*
H20B	0.7457	0.6059	0.9484	0.049*
H20C	0.7808	0.4418	1.0244	0.049*
Ca1	0.5000	0.31755(12)	0.5000	0.0289(2)
O1	0.63088(12)	0.2641(4)	0.61232(16)	0.0426(6)
H1	0.6416(13)	0.205(7)	0.586(2)	0.064*
O2	0.56760(12)	0.5829(4)	0.61114(18)	0.0411(6)
H2	0.5414(14)	0.672(4)	0.601(2)	0.062*
O3	1.1054(3)	0.2108(11)	1.1514(4)	0.112(2)
O4	1.0767(3)	0.4956(10)	1.1588(6)	0.126(2)
O5	1.12054(13)	0.2773(5)	1.41689(17)	0.0466(7)
O6	1.01488(19)	0.0681(5)	1.3185(2)	0.0534(7)
O7	1.00082(16)	0.3665(5)	1.3525(2)	0.0538(8)
O8	0.5000	−0.0089(7)	0.5000	0.0709(14)
H8	0.4809	−0.0490	0.5202	0.106*
O9	0.49635(17)	0.2524(5)	0.6170(2)	0.0502(7)
H9A	0.4649	0.1655	0.5938	0.075*
H9B	0.4819	0.3463	0.6260	0.075*
S1	1.03907(4)	0.25393(11)	1.33692(5)	0.0313(2)
C21	0.7247(4)	0.1840(13)	0.5369(6)	0.095(2)
H21A	0.7708	0.1194	0.5693	0.114*
H21B	0.7400	0.2987	0.5726	0.114*
C22	0.6819(5)	0.2215(16)	0.4299(7)	0.136(4)
H22A	0.6438	0.3115	0.4019	0.203*
H22B	0.6578	0.1123	0.3900	0.203*
H22C	0.7160	0.2653	0.4274	0.203*
O10	0.6855(3)	0.0798(7)	0.5523(4)	0.0866(14)
H10	0.6656	−0.0093	0.5145	0.130*

Source of material

Andrographolide calcium bisulfite (ACB) raw material was got from Jiangsu Jiuxu Pharmaceutical Com. Ltd. The crystals suitable for X-ray analysis were obtained from a mixture of water and ethanol by slow evaporation at room temperature after three days.

Experimental details

All H atoms were included in calculated positions and refined as riding atoms, with the d(C—H) = 0.90–0.97 Å. The U_{iso}(H) were set to 1.5 times U_{eq}(C) for the methyl H atoms, at 1.2 times U_{eq}(C) for all other H atoms. The Flack-Parsons-Wagner parameter x = 0.009(5) [3] was determined using 1606 quotients [(I+) − (I−)]/[(I+) + (I−)].

Comment

Andrographolide was isolated from traditional Chinese medicine Andrographis paniculata Nees, which has been widely used as an anti-inflammatory and anti-microbial drug for treatment of infectious diseases including malaria, HIV, bacterial dysentery, acute tonsillitis and pneumonia [4, 5]. Despite the wide-ranging therapeutic properties of andrographolide, the poor water solubility and instability leads to its low bioavailability and seriously limits its pharmacological function. Andrographolide sodium bisulfite is a water-soluble compound which is synthesized by andrographolide and sodium bisulfite and it has been used as a injection formulation in China for decades. Andrographolide calcium bisulfite is a related impurity of ASB which has been found by us in recent research.

The asymmetric unit contains one andrographolide bisulphite anion, one half of a calcium cation, ethanol molecules and 1.5 water molecules. Calcium cation is coordinated by four hydroxyl groups of the hydronaphthalene ring and three water molecules.

Ca—O bond distances [2.324(2), 2.440(3) Å] are within normal ranges and the value coincides with those observed in reported Ca complexes [6, 7]. In the molecules, two fused cyclohexane rings (C1—C10) adopt standard chair conformation and the dihedral angle between C6—C7—C9—C10 and C7—C8—C9 is 57.2(2)°, and the dihedral angle between C1—C2—C4—C5 and C1—C10—C5 is 45.4(1)°. Flack parameter of crystal structure was refined to 0.009(5), showing that atoms C3, C4, C9 and C12 are *R*, and atoms C5 and C10 are *S* configurated.

Acknowledgements: The authors are grateful to the Analysis and Testing Center of Zhengzhou University for use of the single-crystal X-ray diffraction facility. We thank the Science and Technology Bureau of Henan Province for the Cooperation Research Project Fund (No. 152107000041 for WL) and Jiangsu Jiuxu Pharmaceutical Com. Ltd for the financial support.

References

1. Bruker. APEX3, SAINT-Plus, XPREEP. Bruker AXS Inc., Madison, WI, USA (2017).
2. Sheldrick, G. M.: A short history of SHELX. Acta Crystallogr. **A64** (2008) 112–122.
3. Sheldrick, G. M.: Crystal structure refinement with SHELXL. Acta Crystallogr. **C71** (2015) 3–8.
4. Lee, J. C.; Tseng, C. K.; Young, K. C.; Sun, H.-Y.; Wang, S.-W.; Chen, W.-C.; Lin, C.-K.; Wu, Y.-H.: Andrographolide exerts anti-hepatitis C virus activity by up-regulating haeme oxygenase-1 *via* the p38 MAPK/Nrf2 pathway in human hepatoma cells. Br. J. Pharmacol. **171** (2014) 237–252.

5. Mishra, K.; Dash, A. P.; Swain, B. K.; Dey, N.: Anti-malarial activities of Andrographis paniculata and Hedyotis corymbosa extracts and their combination with curcumin. Malaria J. **8** (2009) 26.
6. Tai, X. S.; Wang, X.: Synthesis, structural characterization and antitumor activity of a Ca(II) coordination polymer based on 4-formyl-1,3-benzenedisulfonate-2-furoic acid hydrazide ligands. Crystallogr. Rep. **62** (2017) 242–245.
7. Tai, X. S.; Zhao, W. H.: Synthesis, crystal structure and antitumor activity of Ca(II) coordination polymer based on 1,5-naphthalenedisulfonate. J. Inorg. Organomet. Polym. **23** (2013) 1354–1357.