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The crystal structure of (6*aR*,6*bS*,8*aS*,8*bR*,9*S*,11*aS*,12*aS*,12*bS*)-10-(4-acetoxy-3-methylbutyl)-6*a*,8*a*,9-trimethyl-3,4,5,6,6*a*,6*b*,7,8,8*a*,8*b*,9,10,11*a*,12,12*a*,12*b*-hexadecahydro-1*H*-naphtho[2',1':4,5]indeno[2,1-*b*]furan-4-yl acetate, C₃₁H₄₈O₅

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Abstract

C₃₁H₄₈O₅, monoclinic, *P*2₁ (no. 4), *a* = 11.0421(3) Å, *b* = 6.49710(16) Å, *c* = 20.4687(4) Å, β = 97.922(2)°, *V* = 1454.45(6) Å³, *Z* = 2, *R*_{gt}(*F*) = 0.0382, *wR*_{ref}(*F*²) = 0.1024, *T* = 293(2) K.

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The molecular structure {systematic name: (6*aR*,6*bS*,8*aS*,8*bR*,9*S*,11*aS*,12*aS*,12*bS*)-10-(4-acetoxy-3-methylbutyl)-6*a*,8*a*,9-trimethyl-3,4,5,6,6*a*,6*b*,7,8,8*a*,8*b*,9,10,11*a*,12,12*a*,12*b*-hexadecahydro-1*H*-naphtho[2',1':4,5]indeno[2,1-*b*]furan-4-yl acetate} 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.

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.26 × 0.23 × 0.14 mm
Wavelength:	Cu Kα radiation (1.54184 Å)
μ:	0.60 mm ^{−1}
Diffractometer, scan mode:	Xcalibur, ω
θ _{max} , completeness:	66.9°, >99%
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} , <i>R</i> _{int} :	25745, 5109, 0.043
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	<i>I</i> _{obs} > 2 σ(<i>I</i> _{obs}), 4423
<i>N</i> (<i>param</i>) _{refined} :	332
Programs:	CrysAlis ^{PRO} [1], SHELX [2], SUPERFLIP [3], Olex2 [4]

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Source of material

All reagents and solvents were used as obtained without further purification. The mixture of diosgenin in dichloromethane was treated with acetic anhydride in the presence of 4-dimethylaminopyridine and pyridine at room temperature for 8 h to obtain the DG-3-acetate. DG-3-acetate was reduced by sodium cyanoborohydride and acetic acid in dichloromethane at room temperature for 24 h. After evaporation under vacuum, the residue was dissolved in dichloromethane, and the organic solution was washed with water and brine, and finally dried over anhydrous sodium sulfate. After filtration, the filtrate was evaporated to dryness.

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

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
O1	−1.0610(2)	−0.8190(5)	−1.04748(12)	0.0941(8)
C1	−1.1343(3)	−0.4935(5)	−0.83521(13)	0.0627(8)
H1A	−1.1844	−0.4057	−0.8115	0.075*
H1B	−1.0702	−0.4086	−0.8491	0.075*
O2	−1.21880(18)	−0.8012(4)	−0.99022(9)	0.0775(7)
C2	−1.2138(3)	−0.5773(6)	−0.89686(15)	0.0722(9)
H2A	−1.2833	−0.6509	−0.8841	0.087*
H2B	−1.2444	−0.4641	−0.9254	0.087*
O3	−0.63244(15)	−0.6521(3)	−0.48840(8)	0.0516(4)
C3	−1.1392(3)	−0.7192(5)	−0.93307(13)	0.0641(8)
H3	−1.0715	−0.6428	−0.9479	0.077*
O4	−0.5491(2)	−0.6407(4)	−0.16319(9)	0.0728(6)
C4	−1.0893(3)	−0.8967(5)	−0.88957(14)	0.0677(8)
H4A	−1.1566	−0.9788	−0.8780	0.081*
H4B	−1.0394	−0.9839	−0.9135	0.081*
O5	−0.4514(5)	−0.3693(7)	−0.12238(16)	0.176(2)
C5	−1.0133(2)	−0.8185(5)	−0.82735(13)	0.0568(6)
C6	−0.9006(3)	−0.8863(5)	−0.80981(13)	0.0648(8)
H6	−0.8701	−0.9808	−0.8375	0.078*
C7	−0.8183(2)	−0.8231(5)	−0.74900(13)	0.0616(7)
H7A	−0.7547	−0.7341	−0.7613	0.074*
H7B	−0.7793	−0.9446	−0.7281	0.074*
C8	−0.8861(2)	−0.7105(4)	−0.69948(11)	0.0483(6)
H8	−0.9319	−0.8116	−0.6771	0.058*
C9	−0.9770(2)	−0.5547(4)	−0.73555(12)	0.0483(6)
H9	−0.9289	−0.4650	−0.7606	0.058*
C10	−1.0742(2)	−0.6599(5)	−0.78726(12)	0.0518(6)
C11	−1.0340(2)	−0.4137(5)	−0.68766(13)	0.0616(7)
H11A	−1.0918	−0.4933	−0.6664	0.074*
H11B	−1.0793	−0.3052	−0.7128	0.074*
C12	−0.9402(2)	−0.3146(5)	−0.63399(13)	0.0582(7)
H12A	−0.8904	−0.2172	−0.6544	0.070*
H12B	−0.9832	−0.2396	−0.6032	0.070*
C13	−0.8578(2)	−0.4767(4)	−0.59653(11)	0.0451(5)
C14	−0.7977(2)	−0.5986(4)	−0.64806(11)	0.0476(6)
H14	−0.7568	−0.4959	−0.6724	0.057*
C15	−0.6950(2)	−0.7187(5)	−0.60656(12)	0.0577(7)
H15A	−0.7264	−0.8411	−0.5876	0.069*
H15B	−0.6320	−0.7582	−0.6328	0.069*
C16	−0.6465(2)	−0.5656(4)	−0.55340(12)	0.0515(6)
H16	−0.5686	−0.5081	−0.5627	0.062*
C17	−0.7427(2)	−0.3916(4)	−0.55291(12)	0.0470(6)
H17	−0.7139	−0.2688	−0.5740	0.056*
C18	−1.1727(3)	−0.7706(6)	−0.75361(16)	0.0731(9)
H18A	−1.1339	−0.8585	−0.7192	0.110*
H18B	−1.2235	−0.8518	−0.7856	0.110*
H18C	−1.2219	−0.6703	−0.7350	0.110*
C19	−0.9319(2)	−0.6175(5)	−0.55651(13)	0.0565(7)
H19A	−0.8776	−0.7100	−0.5302	0.085*
H19B	−0.9897	−0.6952	−0.5861	0.085*
H19C	−0.9748	−0.5351	−0.5282	0.085*
C20	−0.7443(2)	−0.3468(4)	−0.47912(12)	0.0479(6)
H20	−0.8215	−0.3972	−0.4666	0.057*
C21	−0.7294(3)	−0.1215(5)	−0.45982(16)	0.0663(7)

Table 2 (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
H21A	−0.7258	−0.1085	−0.4129	0.100*
H21B	−0.7977	−0.0444	−0.4813	0.100*
H21C	−0.6552	−0.0693	−0.4731	0.100*
C22	−0.6394(2)	−0.4810(4)	−0.44522(12)	0.0497(6)
H22	−0.5629	−0.4028	−0.4419	0.060*
C23	−0.6567(2)	−0.5585(5)	−0.37758(13)	0.0561(6)
H23B	−0.7332	−0.6336	−0.3810	0.067*
H23A	−0.6633	−0.4410	−0.3490	0.067*
C24	−0.5552(2)	−0.6966(5)	−0.34567(12)	0.0566(7)
H24A	−0.4778	−0.6260	−0.3457	0.068*
H24B	−0.5533	−0.8199	−0.3722	0.068*
C25	−0.5673(2)	−0.7601(4)	−0.27471(12)	0.0552(7)
H25	−0.6543	−0.7820	−0.2720	0.066*
C26	−0.5230(3)	−0.5880(5)	−0.22806(13)	0.0642(7)
H26A	−0.4357	−0.5686	−0.2273	0.077*
H26B	−0.5640	−0.4607	−0.2426	0.077*
C27	−0.5002(4)	−0.9599(6)	−0.25542(17)	0.0840(10)
H27A	−0.5315	−1.0669	−0.2854	0.126*
H27B	−0.5123	−0.9971	−0.2114	0.126*
H27C	−0.4145	−0.9418	−0.2573	0.126*
C28	−1.1675(3)	−0.8481(6)	−1.04357(14)	0.0723(8)
C29	−1.2551(4)	−0.9450(9)	−1.09621(18)	0.1149(16)
H29A	−1.2631	−1.0886	−1.0867	0.172*
H29C	−1.2256	−0.9296	−1.1379	0.172*
H29B	−1.3334	−0.8793	−1.0981	0.172*
C30	−0.5045(4)	−0.5205(6)	−0.11373(17)	0.0827(10)
C31	−0.5335(4)	−0.5951(7)	−0.04934(15)	0.0978(13)
H31A	−0.5993	−0.5152	−0.0364	0.147*
H31B	−0.4626	−0.5812	−0.0167	0.147*
H31C	−0.5572	−0.7372	−0.0531	0.147*

under vacuum and purified by silica-gel column chromatography (petroleum ether: ethyl acetate = 5:1, v/v). Suitable crystals of the title compound were obtained by recrystallization from petroleum ether and ethyl acetate. Suitable colourless crystals were obtained by recrystallization in ethanol.

Experimental details

All H atoms were included in calculated positions and refined as riding atoms, with C–H = 0.93–0.98 Å, with $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl H atoms and $1.2U_{eq}(C)$ for all other H atoms.

Comment

Diosgenin (DG), a steroid sapogenin, is the acid hydrolysate of the genus dioscorea. It has been reported that DG shows vasodilatory activity [5], renoprotective effects [6]. DG derivatives are known for the wide spectrum of biological activities, such as to prevent thrombosis effects [7], anti-inflammatory activity [8], anti-cancer activity [9]. Moreover, many steroid

sapogenins such as diosgenin, sisalagenin, neo-pentologenin and luvigenin have already been used in many aspects for the treatment of various diseases.

The title compound consists of three six-membered rings, a five-membered ring and a five-membered oxygen-containing heterocyclic ring. Two carbon-oxygen double bonds and carbon-oxygen bonds exist in the title compound which have been introduced by acetylation. As shown in figure, the asymmetric unit of the title compound contains one single target molecule. In this compound, the C—O bond distance (O4—C26) is 1.438(3) Å, (O4—C30) is 1.319(4) Å. The C—O double bond distance (O1—C28) is 1.204(4) Å, (O5—C30) is 1.170(5) Å. The distance of C—O bond (O3—C16) in furan ring is 1.433(3) Å. The C—C bond distance (C9—C10) is 1.558(4) Å, (C13—C17) is 1.551(3) Å, (C25—C27) is 1.520(4) Å. All bond lengths and angles are in the expected ranges [10].

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References

1. Rigaku Oxford Diffraction: CrysAlis^{PRO} Software system, version 1.171.39.32a. Rigaku Corporation, Oxford, UK (2017).
2. Sheldrick, G. M.: Crystal structure refinement with SHELXL. *Acta Crystallogr. C* **71** (2015) 3–8.
3. Palatinus, L.; Chapuis, G.: SUPERFLIP: a computer program for the solution of crystal structures by charge flipping in arbitrary dimensions. *J. Appl. Crystallogr.* **40** (2007) 786–790.
4. Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H.: OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Crystallogr.* **42** (2009) 339–341.
5. de Silva Morais, I. C. P.; Moura, I. J. L.; Sabino, C. K. B.; Nicolau, L. A. D.; de Moura Souza, F.; da Silva-Filho, J. C.; Oliveira, R. de C. M.; Medeiros, J. V. R.; de Lima, S. G.; de Oliveira, A. P.: Cardiovascular effect of diosgenin in ovariectomized rats. *J. Med. Food.* **22** (2019) 248–256.
6. Kanchan, D. M.; Somani, G. S.; Peshattiwar, V. V.; Kaikini, A. A.: Renoprotective effect of diosgenin in streptozotocin induced diabetic rats. *Pharmacol. Rep.* **432** (2015) 1–8.
7. Zheng, H.; Wei, Z.; Xin, G.; Ji, C.; Wen, L.; Xia, Q.; Niu, H.; Huang, W.: Preventive effect of a novel diosgenin derivative on arterial and venous thrombosis *in vivo*. *Bioorg. Med. Chem. Lett.* **26** (2016) 3364–3369.
8. Xin, G.; Wang, Y.; Guo, X.; Huang, B.; Du, D.; He, S.; Zhang, R.; Xing, Z.; Zhao, H.; Chen, Q.; Huang, W.; He, Y.: Synthesis of diosgenin-ibuprofen derivatives and their activities against insulin-dependent diabetes mellitus. *Chem. Pharm. Bull.* **61** (2013) 532–538.
9. Tan, Y.; Xiao, X.; Yao, J.; Han, F.; Luo, H.; Liang, G.; Ben-David, Y.; Pan, W.: Syntheses and anti-cancer activities of glycosylated derivatives of diosgenin. *Chem. Res. Chin. Univ.* **33** (2017) 80–86.
10. Benn, M.; Vohra, K. N.; Parvez, M.: 5a-Dihydrovespertilin acetate. *Acta Crystallogr. E* **66** (2010) o598.