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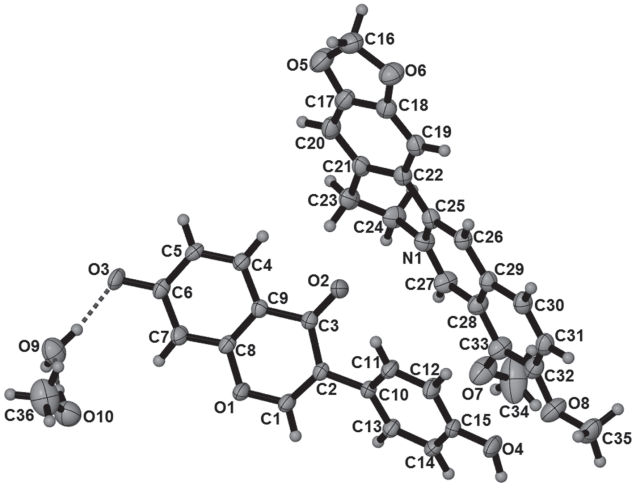
Crystal structure of 5,6-Dihydro-9,10-dimethoxy-benzo[*g*]-1,3-benzodioxolo[5,6-*a*]chinolizinium 3-(4-hydroxyphenyl)-4-oxo-4*H*-chromen-7-olate - methanol - water (1/1/1), $C_{36}H_{33}NO_{10}$



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Abstract

$C_{36}H_{33}NO_{10}$, monoclinic, $P2_1/c$ (no. 14), $a = 14.113(7)$ Å, $b = 17.883(9)$ Å, $c = 12.724(7)$ Å, $\beta = 108.218(9)°$, $V = 3050(3)$ Å^3, $Z = 4$, $R_{gt}(F) = 0.0788$, $wR_{ref}(F^2) = 0.1967$, $T = 293$ K.

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The asymmetric unit of the title crystal structure is shown in the figure. Tables 1 and 2 contain details of the measurement method and a list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Yellow needle
Size:	0.25 × 0.10 × 0.10 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	1.0 cm^{-1}
Diffractometer, scan mode:	Rigaku CCD, φ and ω
$2\theta_{max}$, completeness:	55°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	23917, 6962, 0.071
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 4866
$N(param)_{refined}$:	431
Programs:	SHELXL [1], SHELXS [2], CrystalClear [3]

Source of materials

A mixture of berberine chloride (370 mg, 1 mmol), NaOH (40 mg, 1 mmol) and daidzein (254 mg, 1 mmol) with 0.1 mL methanol added, was ground with a LAB WIZZ 320 ball mill in a 25 mL steel vessel for 15 min with a 15 mm steel ball at 30 Hz. The resulting powder was washed with water to remove the by-product NaCl and then re-crystallized in MeOH to give rise to yellow needle crystals.

Experimental details

The structure was solved by direct methods and refined on F^2 by full-matrix least-squares methods using SHELXL [2]. H atoms on C atoms were located geometrically with $U_{iso}(H) = 1.2\ U_{eq}(C)$ or $1.5\ U_{eq}(C)$. H atoms bonded to O were located by difference Fourier maps and the displacement factors were refined freely. Difference Fourier maps indicate disorder for one of the two methoxy groups, which could not be modelled satisfactorily against the available room-temperature data.

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

Atom	x	y	z	U_{iso}*/U_{eq}
O1	0.42164(12)	0.24512(12)	0.20957(14)	0.0518(5)
O2	0.30277(13)	0.17352(12)	0.44727(15)	0.0570(5)
O3	0.75058(12)	0.23520(12)	0.45429(16)	0.0564(5)
O4	−0.13952(12)	0.26680(13)	0.15280(17)	0.0621(6)
H4A	−0.1756	0.2696	0.0810	0.092(12)*
C1	0.32108(17)	0.24258(16)	0.1913(2)	0.0454(6)
H1	0.2791	0.2579	0.1206	0.055*
C2	0.27671(16)	0.22034(14)	0.2648(2)	0.0385(5)
C3	0.33839(17)	0.19745(14)	0.3758(2)	0.0403(6)
C4	0.51573(17)	0.19190(14)	0.5023(2)	0.0417(6)
H4	0.4927	0.1755	0.5610	0.050*
C5	0.61596(17)	0.20205(15)	0.5215(2)	0.0427(6)
H5	0.6608	0.1930	0.5935	0.051*
C6	0.65442(17)	0.22584(15)	0.4359(2)	0.0442(6)
C7	0.58559(18)	0.23823(16)	0.3308(2)	0.0487(7)
H7	0.6082	0.2531	0.2711	0.058*
C8	0.48414(17)	0.22872(15)	0.3143(2)	0.0419(6)
C9	0.44612(17)	0.20522(14)	0.3973(2)	0.0384(5)
C10	0.16589(16)	0.22497(14)	0.2352(2)	0.0389(5)
C11	0.12332(18)	0.25365(17)	0.3116(2)	0.0488(7)
H11	0.1645	0.2650	0.3845	0.059*
C12	0.02116(18)	0.26590(18)	0.2825(2)	0.0534(7)
H12	−0.0065	0.2851	0.3361	0.064*
C13	0.10216(17)	0.20658(15)	0.1306(2)	0.0437(6)
H13	0.1293	0.1852	0.0779	0.052*
C14	−0.00044(18)	0.21871(15)	0.1013(2)	0.0467(6)
H14	−0.0424	0.2051	0.0297	0.056*
C15	−0.04115(17)	0.25072(16)	0.1767(2)	0.0447(6)
O5	0.50105(17)	0.09294(15)	0.9663(2)	0.0802(7)
O6	0.33972(16)	0.11788(14)	0.96651(18)	0.0722(6)
O7	0.01155(19)	0.01491(17)	0.1700(2)	0.0910(8)
O8	−0.17746(16)	0.07326(14)	0.12883(19)	0.0785(7)
N1	0.20919(16)	0.01588(13)	0.48295(19)	0.0487(6)
C16	0.4423(3)	0.1162(2)	1.0327(3)	0.0743(9)
H16A	0.4635	0.1666	1.0633	0.089*
H16B	0.4514	0.0811	1.0952	0.089*
C17	0.4351(2)	0.07959(17)	0.8632(3)	0.0584(8)
C18	0.3385(2)	0.09456(16)	0.8629(2)	0.0530(7)
C19	0.2587(2)	0.08551(15)	0.7707(2)	0.0500(7)
H19	0.1929	0.0956	0.7715	0.060*
C20	0.4557(2)	0.05488(18)	0.7716(3)	0.0606(8)
H20	0.5222	0.0453	0.7728	0.073*
C21	0.37492(19)	0.04414(16)	0.6754(2)	0.0497(7)
C22	0.27708(18)	0.06057(14)	0.6739(2)	0.0453(6)
C25	0.19456(18)	0.05670(14)	0.5696(2)	0.0441(6)
C23	0.3903(2)	0.01558(19)	0.5707(3)	0.0604(8)
H23A	0.3999	0.0583	0.5256	0.073*
H23B	0.4511	−0.0158	0.5893	0.073*
C24	0.3019(2)	−0.02963(17)	0.5053(3)	0.0588(8)
H24A	0.3110	−0.0454	0.4345	0.071*
H24B	0.2963	−0.0751	0.5473	0.071*
C27	0.1423(2)	0.01343(18)	0.3836(2)	0.0581(8)
H27	0.1577	−0.0134	0.3265	0.070*
C28	0.0496(2)	0.04898(16)	0.3595(2)	0.0520(7)
C29	0.02849(18)	0.08746(14)	0.4468(2)	0.0457(6)
C26	0.10367(18)	0.09205(15)	0.5499(2)	0.0465(6)
H26	0.0915	0.1203	0.6075	0.056*
C30	−0.06731(19)	0.12009(16)	0.4241(3)	0.0525(7)
H30	−0.0842	0.1459	0.4810	0.063*
C31	−0.13543(19)	0.11472(16)	0.3212(2)	0.0537(7)
H31	−0.1994	0.1366	0.3081	0.064*
C32	−0.1137(2)	0.07769(17)	0.2339(3)	0.0568(7)
C33	−0.0209(2)	0.04545(19)	0.2525(3)	0.0625(8)
C34	−0.0362(4)	−0.0445(3)	0.1151(6)	0.150(3)
H34A	−0.0443	−0.0819	0.1679	0.225*
H34B	0.0024	−0.0659	0.0705	0.225*
H34C	−0.1020	−0.0292	0.0665	0.225*
C35	−0.2759(2)	0.1020(2)	0.1055(3)	0.0816(11)
H35A	−0.3108	0.0747	0.1491	0.122*
H35B	−0.3119	0.0958	0.0265	0.122*
H35C	−0.2727	0.1552	0.1247	0.122*
O10	0.6935(2)	0.46124(16)	0.2547(2)	0.0876(8)
H10A	0.7412	0.4202	0.2838	0.124(17)*
C36	0.7298(4)	0.5193(3)	0.3286(5)	0.1184(17)
H36A	0.7997	0.5289	0.3346	0.178*
H36B	0.7250	0.5056	0.4013	0.178*
H36C	0.6902	0.5645	0.3019	0.178*
O9	0.80292(17)	0.33679(14)	0.3239(2)	0.0793(7)
H9A	0.7806	0.3006	0.3601	0.129(18)*
H9B	0.8171	0.3167	0.2698	0.096(14)*

Comment

Flavonoids are a class of natural products with various pharmacological activities such as antioxidant and antitumor properties [4]. Multi-component crystals of flavonoids have been exploited recently [5]. Flavonoids have been also explored as cocrystal formers with other drug molecules [6].

Daidzein, 7-hydroxy-3-(4-hydroxyphenyl)-4*H*-1-benzopyran-4-one, is an isoflavone compound exhibiting a range of medicinal properties [7]. With two hydroxyl groups at opposite ends of the molecular structure it is a weak acid [8] capable of forming molecular salts and extended hydrogen-bonded structures. In this paper, we choose a basic natural product, berberine, as drug model. Daidzein crystallized in methanol with berberine to give rise to a 1:1:1 molecular salt hydrate, $[C_{20}H_{18}NO_4]^+[C_{15}H_9O_4]^-\cdot H_2O\cdot CH_4O$.

Difference Fourier maps show deprotonation of the 7-substituted hydroxyl group in the daidzein molecule. Hydrogen-bonded interactions between the resulting anion and 4′-substituted hydroxyl group [O4$\cdots$O3], give rise to a 1D hydrogen-bonded chain along the [2 0 1] direction. The dihedral angle between the phenyl ring (C10—C15) and pyran ring (O1/C1—C2—C3/C8—C9) of daidzein is 41.14(7)°. The water molecule is hydrogen bonded to methanol and to O3 and O4 of the daidzein anion, thereby connecting the 1D chain into a 2D hydrogen-bonded layer. Berberine cations are located in between the 2D layers to give the host-guest arrays .

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