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Crystal structure of 6-hydroxy-5-((2-hydroxy-6-oxocyclohex-1-en-1-yl)(4-methoxyphenyl)methyl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione,

$C_{20}H_{22}N_2O_6$

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Abstract

$C_{20}H_{22}N_2O_6$, monoclinic, $P2_1/c$ (no. 14), $a = 8.6657(6)$ Å, $b = 18.6201(14)$ Å, $c = 22.3583(18)$ Å, $\beta = 91.808(3)^\circ$, $V = 3605.9(5)$ Å³, $Z = 8$, $R_{\text{gt}}(F) = 0.067$, $wR_{\text{ref}}(F^2) = 0.177$, $T = 100(2)$ K.

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

Table 1: Data collection and handling.

Crystal:	Yellow block
Size:	$0.45 \times 0.24 \times 0.16$ mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ :	0.11 mm^{-1}
Diffractometer, scan mode:	APEX-II D8 venture, φ and ω
θ_{max} , completeness:	25.0° , >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	46796, 6354, 0.147
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 4039
$N(\text{param})_{\text{refined}}$:	523
Programs:	SHELX [12], Platon [13], Bruker [14]

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

Atom	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1A	−0.5150(3)	−0.78319(12)	−0.01258(11)	0.0213(6)
O2A	−0.4709(3)	−0.63355(13)	0.14814(12)	0.0322(7)
O3A	−0.0549(3)	−0.65660(13)	0.03302(12)	0.0240(6)
O4A	−0.3731(3)	−0.87855(13)	−0.07503(12)	0.0264(6)
O5A	0.0826(3)	−0.75653(13)	−0.02067(11)	0.0240(6)
O6A	−0.0056(3)	−0.51235(12)	−0.20770(11)	0.0248(6)
N1A	−0.4951(3)	−0.70691(15)	0.06716(13)	0.0224(7)
N2A	−0.2607(3)	−0.64919(15)	0.09156(13)	0.0222(7)
C1A	−0.4355(4)	−0.73787(18)	0.01569(16)	0.0185(8)
C2A	−0.6531(4)	−0.7223(2)	0.08251(18)	0.0294(9)
H2AA	−0.7074	−0.6780	0.0883	0.044*
H2AB	−0.6534	−0.7499	0.1187	0.044*
H2AC	−0.7030	−0.7490	0.0507	0.044*
C3A	−0.4123(5)	−0.66025(18)	0.10453(17)	0.0243(9)
C4A	−0.1622(5)	−0.6064(2)	0.13320(17)	0.0297(9)
H4AA	−0.2202	−0.5933	0.1674	0.045*
H4AB	−0.1284	−0.5638	0.1133	0.045*
H4AC	−0.0741	−0.6343	0.1459	0.045*
C5A	−0.1999(4)	−0.67452(17)	0.03947(15)	0.0177(8)
C6A	−0.2854(4)	−0.71471(17)	−0.00046(15)	0.0177(8)
C7A	−0.2326(4)	−0.73795(17)	−0.06183(15)	0.0164(8)
H7AA	−0.3285	−0.7485	−0.0846	0.020*
C8A	−0.1448(4)	−0.80876(17)	−0.06077(15)	0.0171(8)
C9A	−0.2208(4)	−0.87252(18)	−0.07060(16)	0.0211(9)

Table 2 (continued)

Atom	x	y	z	U_{iso}^*/U_{eq}
C10A	−0.1381(5)	−0.94220(18)	−0.07603(18)	0.0293(10)
H10A	−0.1872	−0.9702	−0.1079	0.035*
H10B	−0.1466	−0.9689	−0.0390	0.035*
C11A	0.0305(5)	−0.9322(2)	−0.0891(2)	0.0347(11)
H11A	0.0404	−0.9142	−0.1295	0.042*
H11B	0.0835	−0.9780	−0.0861	0.042*
C12A	0.1034(5)	−0.8795(2)	−0.04486(19)	0.0320(10)
H12A	0.1091	−0.9014	−0.0055	0.038*
H12B	0.2079	−0.8690	−0.0565	0.038*
C13A	0.0135(4)	−0.81078(19)	−0.04188(16)	0.0203(8)
C14A	−0.1554(4)	−0.67782(17)	−0.09778(15)	0.0161(8)
C15A	−0.0555(4)	−0.69252(18)	−0.14282(16)	0.0201(8)
H15A	−0.0235	−0.7397	−0.1484	0.024*
C16A	−0.0007(4)	−0.63912(18)	−0.18035(16)	0.0189(8)
H16A	0.0671	−0.6506	−0.2103	0.023*
C17A	−0.0480(4)	−0.56947(17)	−0.17261(15)	0.0182(8)
C18A	−0.1473(4)	−0.55318(18)	−0.12729(16)	0.0212(8)
H18A	−0.1777	−0.5059	−0.1214	0.025*
C19A	−0.2016(4)	−0.60662(18)	−0.09069(16)	0.0191(8)
H19A	−0.2700	−0.5950	−0.0609	0.023*
C20A	0.0980(5)	−0.5268(2)	−0.25458(17)	0.0313(10)
H20A	0.1236	−0.4828	−0.2742	0.047*
H20B	0.0497	−0.5590	−0.2830	0.047*
H20C	0.1904	−0.5485	−0.2381	0.047*
O1B	−0.8563(3)	−0.24511(13)	0.27567(11)	0.0233(6)
O2B	−0.7947(3)	−0.40041(14)	0.43112(12)	0.0358(7)
O3B	−0.3846(3)	−0.36567(13)	0.31292(11)	0.0265(6)
H3BA	−0.3435	−0.3308	0.2977	0.040*
O4B	−0.7290(3)	−0.14427(14)	0.21402(12)	0.0272(6)
O5B	−0.2581(3)	−0.25625(14)	0.26533(11)	0.0289(6)
O6B	−0.3101(3)	−0.47770(12)	0.05982(11)	0.0252(6)
N1B	−0.8271(3)	−0.32420(15)	0.35242(13)	0.0213(7)
N2B	−0.5902(4)	−0.38138(15)	0.37235(14)	0.0254(8)
C1B	−0.7700(4)	−0.29087(18)	0.30183(16)	0.0206(8)
C2B	−0.9866(4)	−0.3107(2)	0.36959(18)	0.0304(10)
H2BA	−1.0402	−0.3556	0.3730	0.046*
H2BB	−1.0378	−0.2815	0.3397	0.046*
H2BC	−0.9861	−0.2862	0.4074	0.046*
C3B	−0.7412(5)	−0.37122(19)	0.38752(17)	0.0268(9)
C4B	−0.4924(5)	−0.4252(2)	0.41304(18)	0.0358(11)
H4BA	−0.5136	−0.4132	0.4537	0.054*
H4BB	−0.3857	−0.4159	0.4057	0.054*
H4BC	−0.5141	−0.4751	0.4063	0.054*
C5B	−0.5287(4)	−0.35155(18)	0.32140(16)	0.0206(8)
C6B	−0.6214(4)	−0.31030(17)	0.28370(16)	0.0183(8)
C7B	−0.5721(4)	−0.28054(17)	0.22354(15)	0.0172(8)
H7BA	−0.6697	−0.2708	0.2017	0.021*
C8B	−0.4934(4)	−0.20745(18)	0.22776(15)	0.0191(8)
C9B	−0.5775(4)	−0.14515(19)	0.21885(16)	0.0230(9)
C10B	−0.5038(5)	−0.07294(18)	0.21613(18)	0.0305(10)
H10C	−0.5169	−0.0484	0.2539	0.037*
H10D	−0.5554	−0.0448	0.1850	0.037*
C11B	−0.3325(5)	−0.0774(2)	0.20361(19)	0.0376(11)
H11C	−0.3191	−0.0918	0.1624	0.045*
H11D	−0.2852	−0.0306	0.2094	0.045*
C12B	−0.2547(5)	−0.1314(2)	0.24516(19)	0.0352(11)

Table 2 (continued)

Atom	x	y	z	U_{iso}^*/U_{eq}
H12C	−0.1496	−0.1389	0.2328	0.042*
H12D	−0.2501	−0.1118	0.2854	0.042*
C13B	−0.3369(4)	−0.2026(2)	0.24594(17)	0.0255(9)
C14B	−0.4878(4)	−0.33341(17)	0.18305(15)	0.0165(8)
C15B	−0.5108(4)	−0.40751(18)	0.18682(16)	0.0208(8)
H15B	−0.5680	−0.4261	0.2177	0.025*
C16B	−0.4500(4)	−0.45356(18)	0.14549(16)	0.0211(8)
H16B	−0.4663	−0.5027	0.1490	0.025*
C17B	−0.3650(4)	−0.42744(17)	0.09881(16)	0.0188(8)
C18B	−0.3407(4)	−0.35433(18)	0.09401(16)	0.0194(8)
H18B	−0.2838	−0.3360	0.0629	0.023*
C19B	−0.4021(4)	−0.30853(17)	0.13610(15)	0.0176(8)
H19B	−0.3851	−0.2594	0.1326	0.021*
C20B	−0.2031(5)	−0.4528(2)	0.01710(18)	0.0321(10)
H20D	−0.1585	−0.4931	−0.0027	0.048*
H20E	−0.1229	−0.4256	0.0372	0.048*
H20F	−0.2560	−0.4229	−0.0119	0.048*
H40A	−0.424(6)	−0.837(3)	−0.055(2)	0.076(17)*
H30A	−0.012(7)	−0.687(3)	0.008(3)	0.10(2)*
H4B	−0.771(6)	−0.187(3)	0.230(2)	0.082(18)*

Source of material

To the reaction mixture of a barbituric acid derivative (2 mmol, 312.1 mg), 1,3-cyclohexandione (2 mmol, 428 mg) and 4-anisaldehyde (2 mmol) in 3 mL of water, Et₃NH (2.5 mmol) was added and stirred at rt for 12 h. After the reaction was completed as monitored by TLC, the precipitated product was collected by filtration, washed with 2 mL of water, and dried to give the desired compound; yield 90%. The NMR spectra were run in deuterated chloroform (CDCl₃) using a Jeol-400 NMR spectrometer. ¹H NMR (400 MHz, CDCl₃) δ: 8.25 (s, 1H, OH), 7.13 (s, 1H, OH), 6.99 (d, 2H, *J* = 7.32 Hz, Ph), 6.66 (d, 2H, *J* = 7.32 Hz, Ph), 5.09 (s, 1H, CHPh), 3.78 (s, 3H, OCH₃), 3.60 (s, 3H, NCH₃), 3.58 (s, 3H, NCH₃), 3.14 (d, 1H, *J* = 8.08 Hz, CH₂), 2.89 (d, 1H, *J* = 8.08 Hz, CH₂), 2.52 (m, 2H, CH₂), 2.18 (m, 2H, CH₂); ¹³C NMR (100 MHz, CDCl₃) δ: 196.3, 168.4, 167.8, 164.5, 163.4, 162.5, 137.7, 129.7, 128.9, 113.3, 112.8, 103.8, 55.7, 54.9, 36.4, 29.9, 28.6, 26.4, 19.9; IR (KBr, cm^{−1}) ν_{max} = 3500, 298, 1688, 1650, 1450, 1435, 1385, 1250; Anal. Calcd. for C₂₀H₂₂N₂O₆: C, 62.17; H, 5.74; N, 7.25; Found: C, 62.18; H, 5.74; N, 7.24; LC/MS (ESI, *m/z*): [M+], found 387.15, C₂₀H₂₂N₂O₆ for 386.15.

Comment

The barbiturates finding widest use as pharmaceuticals are the 5,5-disubstituted compounds. For examples: Pen-tothal, sodium [the sodium salt of 5-ethyl-5-(1-methylbuty)-2-thiobarbituric acid] which has been used clinically as an intravenous anesthetic. Many of its derivatives have been found to have a pronounced depressant action on the central nervous system and are, therefore, valuable as sedatives,

anesthetics, anxiolytic effects. During famous studies on the constitution of the barbiturates possessed as anti-epileptic drugs, GABA_A-ion receptor complex, anti-osteoporosis, radio-sensitization, anti-oxidant, anti-microbial, and anti-tumor activity, additionally, alpha-glucosidase diaminopimelate aminotransferase, tyrosinase inhibition, and death inducing agents [1–11]. We have demonstrated the reactivity of barbituric acid derivatives, cyclohexandione and 4-anisaldehyde in water as a green solvent. This multi-components approach (MCRs) has been applied to the synthesis of 6-hydroxy-5-((2-hydroxy-6-oxocyclohex-1-en-1-yl)(4-methoxyphenyl)methyl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione. The molecular structure of the target molecule was established by X-ray single crystal structure determination. Furthermore, the physico-spectroscopic property of the synthesized compound is reported.

The molecular structure (two crystallographically independent molecules) consists of a pyrimidine ring (C1/N1/C3/N2/C5/C6), cyclohexene moiety (C8/C9/C10/C11/C12/C13) and a phenyl ring (C14/C15/C16/C17/C18/C19) which are connected together through the carbon C7. The X-ray single crystal structure showed that the compounds exist in the enol form. The two double bonds between C5A–C6A, C5B–C6B, C8A–C9A, and C8B–C9B are 1.366(5), 1.380(5), 1.372(5) and 1.381(5) Å, respectively in molecules A and B. Bond lengths and angles are all in the expected ranges [13]. In the crystal structure, the molecules are packed with three non-classical hydrogen bonds between C–H...O along the *b* and *c* axes.

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