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Crystal structure of 3,7-dimethyl-1-(5-oxohexyl)-3,7-dihydro-1*H*-purine-2,6-dione 4-hydroxybenzoic acid, C₂₀H₂₄N₄O₆

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.12 × 0.13 × 0.12 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.11 mm ⁻¹
Diffractometer, scan mode:	SuperNova, ω -scans
$\theta_{\max}$, completeness:	29.5°, >84% (up to 25.3°, >99%)
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	8047, 4538, 0.026
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 3586
$N(\text{param})_{\text{refined}}$:	282
Programs:	SHELX [1, 2], CrysAlis ^{PRO} [3]

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Abstract

C₂₀H₂₄N₄O₆, triclinic, $P\bar{1}$ (no. 2), $a = 8.2441(5)$ Å, $b = 11.6409(6)$ Å, $c = 12.0107(9)$ Å, $\alpha = 64.328(6)^\circ$, $\beta = 70.778(6)^\circ$, $\gamma = 86.678(4)^\circ$, $V = 976.09(12)$ Å³, $Z = 2$, $R_{\text{gt}}(F) = 0.0671$, $wR_{\text{ref}}(F^2) = 0.1702$, $T = 100$ K.

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The crystal structure 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.

Source of material

Pentoxifylline (278 mg, 1 mmol) and 4-hydroxybenzoic acid (138 mg, 1 mmol) were dissolved in ethanol (30 mL). The colorless block crystals were obtained after several days.

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

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	1.1373(3)	1.4219(2)	−0.58966(19)	0.0361(5)
O2	0.6617(2)	0.86534(18)	−0.45472(17)	0.0262(4)
O3	0.6666(2)	0.89051(17)	−0.08677(17)	0.0210(4)
O4	0.6466(2)	0.88597(17)	0.14372(18)	0.0225(4)
O5	1.0450(2)	1.31397(18)	0.17545(19)	0.0277(4)
O6	1.1294(2)	1.38124(18)	−0.04199(18)	0.0247(4)
N1	0.6662(2)	0.87322(19)	−0.26895(19)	0.0170(4)
N2	0.4885(3)	0.7130(2)	−0.2588(2)	0.0195(5)
N3	0.3165(2)	0.56413(19)	−0.0393(2)	0.0179(4)
N4	0.4017(2)	0.64925(19)	0.06879(19)	0.0174(4)
C1	1.2065(4)	1.3783(3)	−0.3995(3)	0.0323(7)
H1A	1.308141	1.439458	−0.461065	0.048*
H1B	1.243194	1.298254	−0.344670	0.048*
H1C	1.130102	1.414469	−0.343534	0.048*
C2	1.1115(3)	1.3520(2)	−0.4749(3)	0.0234(6)
C3	0.9812(3)	1.2359(2)	−0.3988(2)	0.0225(5)
H3A	0.904541	1.239100	−0.317352	0.027*
H3B	1.043225	1.158389	−0.372915	0.027*
C4	0.8704(3)	1.2229(2)	−0.4726(3)	0.0241(6)
H4A	0.945919	1.212248	−0.550138	0.029*
H4B	0.815541	1.303161	−0.504745	0.029*
C5	0.7295(3)	1.1106(2)	−0.3903(2)	0.0218(5)
H5A	0.657092	1.118669	−0.310419	0.026*
H5B	0.654618	1.114734	−0.441360	0.026*
C6	0.8018(3)	0.9815(2)	−0.3501(2)	0.0200(5)
H6A	0.872604	0.972813	−0.429972	0.024*
H6B	0.878239	0.977906	−0.300299	0.024*
C7	0.6101(3)	0.8323(2)	−0.1333(2)	0.0164(5)

Table 2 (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
C8	0.6080(3)	0.8201(2)	−0.3352(2)	0.0189(5)
C9	0.4130(4)	0.6566(3)	−0.3208(3)	0.0257(6)
H9A	0.438476	0.567172	−0.294625	0.038*
H9B	0.462409	0.704772	−0.416428	0.038*
H9C	0.287679	0.660014	−0.292720	0.038*
C10	0.4318(3)	0.6666(2)	−0.1250(2)	0.0171(5)
C11	0.4890(3)	0.7223(2)	−0.0638(2)	0.0163(5)
C12	0.4164(3)	0.6694(2)	0.1767(2)	0.0216(5)
H12A	0.339001	0.604583	0.260097	0.032*
H12B	0.384479	0.754923	0.166495	0.032*
H12C	0.535715	0.662320	0.176097	0.032*
C13	0.3019(3)	0.5569(2)	0.0776(2)	0.0191(5)
H13	0.228429	0.492999	0.158459	0.023*
C14	0.7384(3)	0.9901(2)	0.1235(2)	0.0170(5)
C15	0.7373(3)	1.0035(2)	0.2335(2)	0.0182(5)
H15	0.670130	0.942674	0.318918	0.022*
C16	0.8342(3)	1.1055(2)	0.2178(2)	0.0182(5)
H16	0.833832	1.114261	0.292938	0.022*
C17	0.8342(3)	1.0812(2)	−0.0021(2)	0.0185(5)
H17	0.833066	1.073480	−0.077392	0.022*
C18	0.9304(3)	1.1825(2)	−0.0159(2)	0.0188(5)
H18	0.996326	1.244164	−0.101266	0.023*
C19	0.9326(3)	1.1959(2)	0.0931(2)	0.0176(5)
C20	1.0394(3)	1.3018(2)	0.0802(2)	0.0200(5)
H4	0.651(5)	0.885(4)	0.065(4)	0.064(12)*
H6	1.191(4)	1.445(3)	−0.042(3)	0.044(10)*

Experimental details

The structure was solved by direct methods and refined on F^2 by full-matrix least-squares methods using the SHELX program package [1,2]. H atoms on C atoms were located geometrically with $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{C})$ or $1.5 U_{\text{eq}}(\text{C})$. H atoms bonded to O were located by difference maps and refined freely.

Discussion

Pentoxifylline, 3,7-dimethyl-1-(5-oxohexyl)-3,7-dihydro-1H-purine-2,6-dione, is a cardiovascular drug which is formulated as sustained-release tablets [4]. Several cocrystals of pentoxifylline based on synthons between imidazole and carboxylic acids have been reported [5, 6]. There are four hydrogen-bond acceptors in molecular structure of pentoxifylline [7], which could result in various intermolecular interactions with different cocrystal formers. In this work, a cocrystal of pentoxifylline with 4-hydroxybenzoic acid, [C₁₃H₁₈N₄O₃]₂·[C₇H₆O₃]₂, was studied.

The cocrystal crystallized in the triclinic $P\bar{1}$ space group and contained one molecule of pentoxifylline and one molecule of 4-hydroxybenzoic acid in the asymmetric unit. There exist $R_2^2(7)$ synthon between the imidazole ring of

pentoxifylline and the carboxyl group of 4-hydroxybenzoic acid (O6–H6...N3 = 2.718(3) Å; C13–H13...O5 = 3.168(3) Å, $x - 1, y - 1, z$). There also exist hydrogen-bonded interactions between the purine moiety of pentoxifylline and the hydroxyl group of 4-hydroxybenzoic acid (O4–H4...O3 = 2.696(3) Å; C17–H17...O3 = 3.333(3) Å). As a result, 4-hydroxybenzoic acid and pentoxifylline are linked parallel to each other into a 1D hydrogen-bonded chain along the [1 1 0] direction. The purine rings of pentoxifylline are almost coplanar with 4-hydroxybenzoic acid within the chain.

The other two hydrogen-bond acceptors (O1 and O2) of pentoxifylline are involved in different weak C–H...O interactions. The –C=O in side chain of pentoxifylline is involved in C–H...O interactions with the imidazole ring of pentoxifylline (C12–H12A...O1 = 3.314(3) Å; C13–H13...O1 = 3.394(3) Å, $x - 1, y - 1, z + 1$). There also exist C–H...O interactions between the phenyl ring of 4-hydroxybenzoic acid and the C=O of purine (C15–H15...O2 = 3.218(3) Å, $x, y, z + 1$). There exist pi-pi interactions between imidazole groups with a centroid–centroid distance of 3.428 Å. The purine ring is also involved in pi-pi interactions with the phenyl ring of 4-hydroxybenzoic acid with a centroid–centroid distance of 3.506 Å. As a result, the various weak intermolecular interactions engineer the hydrogen-bonded chains into a structure with a density of 1.417 g/cm³.

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