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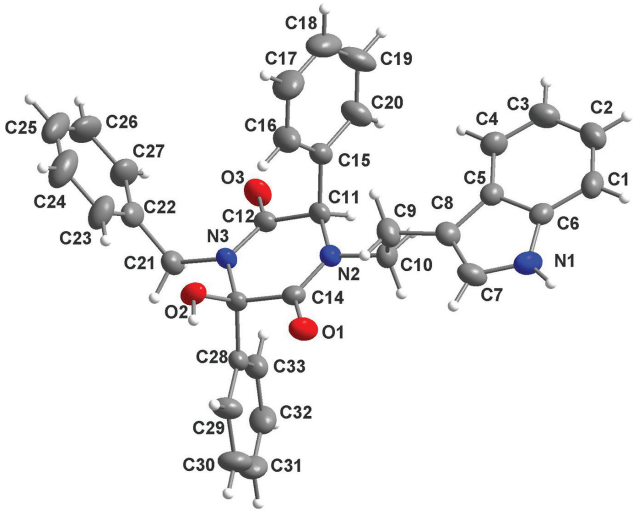
Crystal structure of 1-(2-(1*H*-indol-3-yl)ethyl)-4-benzyl-3-hydroxy-3,6-diphenylpiperazine-2,5-dione, $C_{33}H_{29}N_3O_3$



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Abstract

$C_{33}H_{29}N_3O_3$, triclinic, $P\bar{1}$ (no. 2), $a = 7.1229(8)$ Å, $b = 12.8851(13)$ Å, $c = 15.0472(15)$ Å, $\alpha = 92.354(2)°$, $\beta = 103.338(2)°$, $\gamma = 91.502(2)°$, $V = 1341.7(2)$ Å^3, $Z = 2$, $R_{gt}(F) = 0.0364$, $wR_{ref}(F^2) = 0.1074$, $T = 296(2)$ K.

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The molecular 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.

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Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.30 × 0.28 × 0.27 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.08 mm^{-1}
Diffractometer, scan mode:	Bruker Apex-II, φ and ω
θ_{max}, completeness:	25.0°, 99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	6862, 4688, 0.018
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 3871
$N(param)_{refined}$:	354
Programs:	Bruker [1], SHELX [2]

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
O1	1.05577(14)	0.31690(7)	0.19289(7)	0.0420(3)
O2	1.12495(12)	0.22906(8)	0.36611(6)	0.0360(2)
H2	1.2189	0.2281	0.3433	0.054*
O3	0.50126(13)	0.21694(8)	0.36264(7)	0.0430(3)
N1	0.81535(19)	0.69119(9)	−0.02533(8)	0.0431(3)
H1	0.8534	0.7118	−0.0721	0.052*
N2	0.76650(16)	0.35307(8)	0.22118(7)	0.0312(3)
N3	0.80410(14)	0.19376(8)	0.34729(7)	0.0276(2)
C1	0.5113(2)	0.79071(11)	−0.03781(9)	0.0413(4)
H1A	0.5184	0.8246	−0.0904	0.050*
C2	0.3618(2)	0.80656(12)	0.00410(11)	0.0470(4)
H2A	0.2649	0.8509	−0.0212	0.056*
C3	0.3525(2)	0.75725(12)	0.08416(11)	0.0488(4)
H3	0.2507	0.7704	0.1117	0.059*
C4	0.4913(2)	0.68950(11)	0.12308(10)	0.0412(3)
H4	0.4834	0.6570	0.1762	0.049*
C5	0.64436(19)	0.67045(10)	0.08126(9)	0.0320(3)
C6	0.6524(2)	0.72210(10)	0.00096(9)	0.0330(3)
C7	0.9074(2)	0.62201(11)	0.03528(11)	0.0429(4)
H7	1.0208	0.5898	0.0314	0.051*
C8	0.8100(2)	0.60677(10)	0.10202(9)	0.0360(3)
C9	0.8562(2)	0.53299(11)	0.17795(10)	0.0441(4)
H9A	0.8298	0.5648	0.2332	0.053*
H9B	0.9921	0.5178	0.1903	0.053*
C10	0.7342(2)	0.43218(10)	0.15125(9)	0.0369(3)
H10A	0.5989	0.4490	0.1379	0.044*
H10B	0.7610	0.4021	0.0955	0.044*
C11	0.61472(18)	0.33756(10)	0.27115(9)	0.0300(3)

Table 2 (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
H11	0.4927	0.3265	0.2253	0.036*
C12	0.63777(17)	0.24360(10)	0.32988(8)	0.0289(3)
C13	0.95630(17)	0.20753(9)	0.29776(8)	0.0262(3)
C14	0.92629(18)	0.29877(10)	0.23300(8)	0.0290(3)
C15	0.59419(19)	0.43426(10)	0.32943(9)	0.0338(3)
C16	0.7512(2)	0.47782(13)	0.39306(11)	0.0516(4)
H16	0.8710	0.4480	0.4006	0.062*
C17	0.7309(3)	0.56593(14)	0.44580(12)	0.0643(5)
H17	0.8370	0.5948	0.4886	0.077*
C18	0.5551(3)	0.61054(14)	0.43504(13)	0.0651(5)
H18	0.5418	0.6695	0.4705	0.078*
C19	0.3999(3)	0.56832(14)	0.37238(15)	0.0658(5)
H19	0.2807	0.5988	0.3651	0.079*
C20	0.4180(2)	0.47988(12)	0.31911(12)	0.0497(4)
H20	0.3111	0.4515	0.2765	0.060*
C21	0.8224(2)	0.10543(10)	0.40939(9)	0.0350(3)
H21A	0.9286	0.0637	0.4006	0.042*
H21B	0.7053	0.0619	0.3924	0.042*
C22	0.8565(2)	0.13885(11)	0.50956(10)	0.0432(4)
C23	1.0352(3)	0.17620(15)	0.55799(12)	0.0684(5)
H23	1.1358	0.1822	0.5284	0.082*
C24	1.0677(4)	0.20509(18)	0.65068(14)	0.0925(8)
H24	1.1893	0.2307	0.6821	0.111*
C25	0.9255(6)	0.19635(18)	0.69508(15)	0.0953(9)
H25	0.9485	0.2160	0.7569	0.114*
C26	0.7470(5)	0.1586(2)	0.64936(17)	0.0974(9)
H26	0.6488	0.1520	0.6804	0.117*
C27	0.7108(3)	0.12975(17)	0.55583(13)	0.0729(6)
H27	0.5887	0.1045	0.5250	0.087*
C28	0.96301(18)	0.11024(9)	0.23576(8)	0.0294(3)
C29	1.1305(2)	0.08695(12)	0.20803(11)	0.0438(4)
H29	1.2441	0.1257	0.2325	0.053*
C30	1.1293(3)	0.00591(13)	0.14382(12)	0.0551(4)
H30	1.2415	−0.0083	0.1247	0.066*
C31	0.9640(3)	−0.05317(12)	0.10855(11)	0.0529(4)
H31	0.9640	−0.1070	0.0654	0.063*
C32	0.7979(2)	−0.03254(12)	0.13726(10)	0.0486(4)
H32	0.6864	−0.0735	0.1146	0.058*
C33	0.7969(2)	0.04945(11)	0.20009(9)	0.0380(3)
H33	0.6838	0.0637	0.2184	0.046*

Source of material

Benzaldehyde (2.0 mmol), 2-(1*H*-indol-3-yl)ethan-1-amine (2.0 mmol), 2-oxo-2-phenylacetic acid (2.0 mmol) and (isocyanomethyl)benzene (2.0 mmol) were mixed and stirred overnight in CH_3OH (2.5 mL) at room temperature. The reaction mixture was monitored by TLC. When the reaction was completed, the solvent was removed under reduced pressure. Then the crude residue was subjected to diisopropylamine (2.0 equiv.) and CH_3CN (3.0 mL) solution under microwave irradiation condition at 140 °C for 10 min. After the microwave vial was cooled to room temperature, the residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0–100%) to afford the title product.

Experimental details

A suitable crystal was selected and collected on a Bruker APEX-II CCD. All hydrogen atoms were added using a riding model using the default parameters of the SHELX program (Table 2).

Comment

Piperazine-2,5-diones are widely employed in drug discovery and typically exhibit a wide range of important biological activities [3]. The Ugi four-component reaction (U-4CR), followed by various post-condensation transformations, is well known as a versatile and highly efficient synthetic strategy for the preparation of cyclic compounds [4, 5]. We previously reported the use of this strategy to achieve the construction of various pyrazine compounds.

The asymmetric unit of the title compound contains one molecule. The bond lengths and angles in both crystallographically independent molecules are in the normal ranges [6]. In conclusion, we have developed a facile process for the synthesis of 1-(2-(1*H*-indol-3-yl)ethyl)-4-benzyl-3-hydroxy-3,6-diphenylpiperazine-2,5-dione using a Ugi four-component reaction. This facile procedure can be readily used to synthesize a diverse range of compounds for high throughput screening in medicinal chemistry.

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