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Crystal structure of 7-(2-{4-[(4-bromophenyl)methyl]piperazin-1-yl}ethoxy)-2H-chromen-2-one, $C_{22}H_{23}BrN_2O_3$

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Abstract

$C_{22}H_{23}BrN_2O_3$, monoclinic, $P2_1/c$ (no. 14), $a = 5.9023(9)$ Å, $b = 14.554(2)$ Å, $c = 22.801(4)$ Å, $\beta = 90.801(2)^\circ$, $V = 1958.5(5)$ Å³, $Z = 4$, $R_{gt}(F) = 0.0388$, $wR_{ref}(F^2) = 0.0961$, $T = 100(2)$ K.

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Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of materials

7-Hydroxycoumarin (1.0 eq.) and K_2CO_3 (1.1 eq.) were suspended in 10 mL of acetone. 1,2-Dibromoethane (1.1 eq.) was slowly added and the mixture was reacted under reflux for 4 h. The resulting solution was dried *in vacuo*. Dichloromethane was added and the precipitate that formed was filtered out rendering 7-(2-bromoethoxy)-2H-chromen-2-one as a white solid that was used in the next step. Yield 59%; ¹H-NMR (400 MHz, $CDCl_3$) δ /p.p.m. = 7.65–7.61 (d, $J = 9.4$ Hz, 1H), 7.40–7.37 (d, $J = 8.8$, 1H), 6.87–6.84 (d, $J = 8.4$ Hz, 1H), 6.80 (s, 1H), 6.82–6.24 (d, $J = 9.6$ Hz, 1H), 4.36–4.32

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Table 1: Data collection and handling.

Crystal:	Colourless rod
Size:	$0.23 \times 0.11 \times 0.10$ mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ :	2.13 mm^{-1}
Diffractometer, scan mode:	Bruker APEX II DUO, φ and ω
$\theta_{\max}$, completeness:	28.4° , >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	38722, 4874, 0.036
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 4045
$N(\text{param})_{\text{refined}}$:	253
Programs:	Bruker [1], SHELX [3], X-Seed [3, 4], WinGX/ORTEP [5]

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

Atom	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
Br1	0.76860(5)	0.24905(2)	0.84133(2)	0.03223(9)
C2	0.1101(4)	0.50631(16)	0.09850(10)	0.0244(5)
C3	−0.1121(4)	0.54291(16)	0.08404(10)	0.0242(5)
H3	−0.152720	0.552887	0.044085	0.029*
C4	−0.2619(4)	0.56302(15)	0.12596(10)	0.0229(4)
H4	−0.406081	0.587222	0.115209	0.027*
C5	−0.3533(4)	0.56749(15)	0.23337(10)	0.0229(4)
H5	−0.497834	0.593586	0.225225	0.028*
C6	−0.2908(4)	0.54903(15)	0.29057(10)	0.0227(4)
H6	−0.391438	0.562693	0.321528	0.027*
C7	−0.0781(4)	0.50998(15)	0.30307(10)	0.0213(4)
C8	0.0720(4)	0.49083(15)	0.25835(10)	0.0213(4)
H8	0.216669	0.464876	0.266593	0.026*
C9	0.0038(4)	0.51089(15)	0.20086(9)	0.0202(4)
C10	−0.2070(4)	0.54841(15)	0.18681(10)	0.0207(4)
C11	0.1638(4)	0.44180(15)	0.37703(10)	0.0222(4)
H11A	0.303593	0.476193	0.367859	0.027*
H11B	0.166105	0.382223	0.356098	0.027*
C12	0.1435(4)	0.42735(15)	0.44266(9)	0.0221(4)
H12A	0.134736	0.487911	0.462256	0.027*
H12B	0.001243	0.393833	0.450583	0.027*
C13	0.3590(4)	0.39435(15)	0.53062(9)	0.0221(4)
H13A	0.219539	0.375473	0.551006	0.027*
H13B	0.381250	0.461035	0.537056	0.027*
C14	0.5601(4)	0.34196(15)	0.55555(10)	0.0228(4)
H14A	0.699677	0.361295	0.535381	0.027*
H14B	0.578647	0.356186	0.597803	0.027*
C15	0.5018(4)	0.22343(16)	0.48540(10)	0.0260(5)
H15A	0.476691	0.156732	0.479809	0.031*
H15B	0.642865	0.240415	0.465073	0.031*

Table 2 (continued)

Atom	x	y	z	U _{iso} */U _{eq}
C16	0.3038(4)	0.27639(15)	0.45873(10)	0.0236(5)
H16A	0.292190	0.262981	0.416234	0.028*
H16B	0.161250	0.256386	0.477194	0.028*
C17	0.7166(4)	0.19038(17)	0.57274(10)	0.0280(5)
H17A	0.859339	0.210558	0.554442	0.034*
H17B	0.694644	0.124446	0.563619	0.034*
C18	0.7354(4)	0.20272(15)	0.63836(10)	0.0222(4)
C19	0.5547(4)	0.17739(16)	0.67359(11)	0.0269(5)
H19	0.423346	0.150567	0.656151	0.032*
C20	0.5642(4)	0.19086(16)	0.73373(11)	0.0264(5)
H20	0.440023	0.173861	0.757484	0.032*
C21	0.7569(4)	0.22940(15)	0.75877(10)	0.0223(4)
C22	0.9400(4)	0.25468(16)	0.72513(11)	0.0260(5)
H22	1.071314	0.280982	0.742865	0.031*
C23	0.9277(4)	0.24079(16)	0.66470(11)	0.0265(5)
H23	1.052576	0.257552	0.641124	0.032*
N1	0.3342(3)	0.37579(12)	0.46753(8)	0.0205(4)
N2	0.5268(3)	0.24332(12)	0.54787(8)	0.0230(4)
O1	0.1582(3)	0.49123(11)	0.15792(7)	0.0226(3)
O2	0.2580(3)	0.48714(13)	0.06486(7)	0.0318(4)
O3	−0.0341(3)	0.49394(11)	0.36086(7)	0.0246(3)

(t, 2H), 3.68–3.64 (t, 2H). A solution of 7-(2-bromoethoxy)-2H-chromen-2-one (1.0 eq.) and 1-(4-bromobenzyl)-piperazine (1.0 eq) in acetonitrile (10 mL) was refluxed in the presence of anhydrous K₂CO₃ (1.1 mmol) for 8 h. The reaction mixture was dried *in vacuo*. The residue was purified by silica gel chromatography using CHCl₃/MeOH (50:1) as eluent to obtain the title compound as a light yellow viscous oil. Recrystallisation from ethanol rendered colourless rod crystals. Yield 32%; ¹H-NMR (400 MHz, CDCl₃) δ/p.p.m. = 7.63–7.60 (d, *J* = 9.6 Hz, 1H), 7.43–7.40 (d, *J* = 8.4 Hz, 2H), 7.36–7.33 (d, *J* = 8.6 Hz, 1H), 7.20–7.17 (d, *J* = 8.4 Hz, 2H), 6.84–6.81 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.80–6.79 (m, 1H), 6.25–6.22 (d, *J* = 9.6 Hz, 1H), 4.16–4.12 (t, 2H), 3.44 (s, 2H), 2.85–2.81 (t, 2H, Hz), 2.61–2.48 (m, 8H); ¹³C-NMR (100 MHz, CDCl₃) δ = 161.9, 161.2, 155.8, 143.3, 137.1, 131.3, 130.8, 128.7, 120.9, 113.2, 113.0, 112.6, 101.5, 66.5, 62.2, 56.8, 53.6, 52.9.

Experimental details

Data collection and reduction were carried out using the software package APEX3 [1]. The structure was solved and refined using SHELX-2016 [2] employed within X-Seed [3, 4]. Hydrogen atoms were placed in calculated positions using riding models. ORTEP-3 [5] was used to generate the publication material.

Comment

The title compound was studied as part of an ongoing project into the development of coumarin-donepezil hybrid

derivatives for the treatment of neurodegenerative disorders and/or tuberculosis [6–8]. Continued development of these coumarin-donepezil hybrids is motivated by their good biological activities exhibited, e.g. as cholinesterase inhibitors [6, 7], mono-amine oxidase inhibitors [6, 7], neuroprotectants and anti-tubercular abilities [8].

In the crystal structure the coumarin ring system is planar, as confirmed by the dihedral angles of 180.0(2)° and 178.8(2)° for C5–C10–C4–C3 and C8–C9–O1–C2, respectively. As in other coumarin compounds [9], there is asymmetry with respect to the O–C=O and C–C=O bond angles, with values of 116.3(2) and 127.1(2)°. In a similar way, the O1–C9–C8 and C5–C10–C4 angles at the junction of the two fused rings have values of 116.02(19) and 124.6(2)°, respectively. Electron localization is indicated by the C3–C4 bond with a length of 1.343(3) Å. The ether group at C7–O3–C11 is almost co-planar with the coumarin as shown by the dihedral angles of 179.5(2)° and 179.9(2)° for C5–C6–C7–O3 and C9–C8–C7–O3, respectively. The piperazine moiety that links the ethoxy-coumarin derivative with the 4-bromophenyl(methyl) moiety adopts a chair conformation. The parameters for the 4-bromophenyl(methyl) moiety are consistent with structures in the literature [10]. Two important dihedral angles at the tertiary amine groups of the piperazine structure t1 [N1–C12–C11–O3, −179.25(17)°] and t2 [N2–C17–C18–C19, 60.0(3)°] describe the conformation of the molecule.

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