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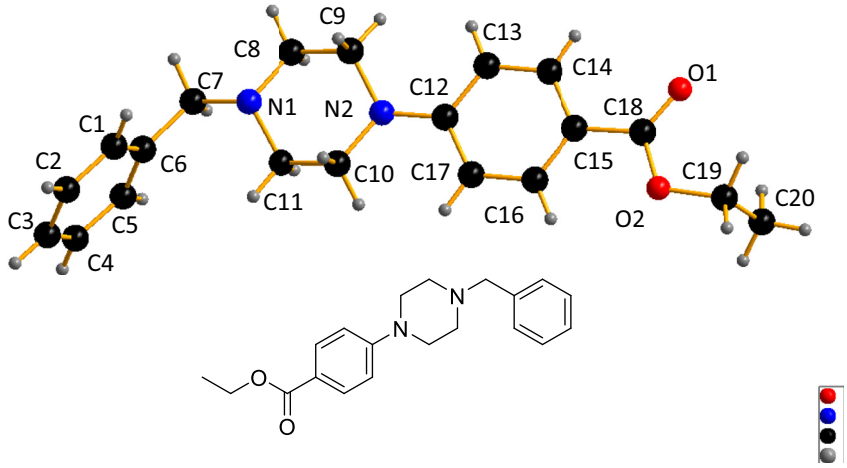
Crystal structure of ethyl 4-(4-benzylpiperazin-1-yl)benzoate, $C_{20}H_{24}N_2O_2$



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Abstract

$C_{20}H_{24}N_2O_2$, monoclinic, $P2_1$ (no. 4), a = 8.0021(9) Å, b = 5.9588(7) Å, c = 18.7274(19) Å, β = 93.546(7)°, V = 891.27(17) Å^3, Z = 2, $R_{gt}(F)$ = 0.0408, $wR_{ref}(F^2)$ = 0.1208, T = 300 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.

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.23 × 0.22 × 0.21 mm
Wavelength:	Cu $K\alpha$ radiation (1.54178 Å)
μ:	0.62 mm^{-1}
Diffractometer, scan mode:	φ and ω
θ_{max}, completeness:	68.3°, 99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	7,510, 2,770, 0.041
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 2,292
$N(param)_{refined}$:	218
Programs:	Olex2,[1] SHELX[2,3]

1 Source of material

Ethyl 4-(4-benzylpiperazin-1-yl)benzoate was prepared by the direct reaction between 1-benzylpiperazine hydrochloride and ethyl 4-fluorobenzoate. In detail, a solution of ethyl 4-fluorobenzoate (17.51 g, 0.104 mol) and 1-benzylpiperazine hydrochloride (44.3 g, 0.209 mol) in N,N-dimethylformamide (100 ml) was stirred and refluxed at 433 K for 16 h. The reaction mixture was allowed to reach room temperature and poured into 750 ml stirring water. The solid part was filtered off, washed with water, dried for 15 h at 32 K in vacuo, recrystallized with 150 ml isopropanol, filtered off, washed with isopropanol and dried for 48 h at 323 K in vacuo, producing 23.5 g of ethyl 4-(4-benzylpiperazin-1-yl)benzoate in 69.7 % yield.

2 Experimental details

Single crystals of ethyl 4-(4-benzylpiperazin-1-yl)benzoate were cultured in a mixed solvent of dichloromethane and

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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}
C1	0.2339 (3)	0.4615 (6)	0.09447 (14)	0.0683 (8)
H1	0.281723	0.324781	0.108242	0.082*
C2	0.3086 (4)	0.5949 (9)	0.04465 (17)	0.0890 (11)
H2	0.407239	0.547196	0.025666	0.107*
C3	0.2398 (4)	0.7941 (7)	0.02325 (16)	0.0849 (11)
H3	0.290095	0.881266	−0.010591	0.102*
C4	0.0973 (4)	0.8647 (7)	0.05164 (15)	0.0784 (9)
H4	0.049878	1.001178	0.037272	0.094*
C5	0.0218 (4)	0.7356 (6)	0.10173 (14)	0.0655 (8)
H5	−0.075535	0.786963	0.121017	0.079*
C6	0.0884 (3)	0.5322 (5)	0.12351 (12)	0.0525 (6)
C7	0.0021 (3)	0.3866 (5)	0.17591 (12)	0.0552 (7)
H7A	−0.098953	0.461656	0.189169	0.066*
H7B	−0.030690	0.246659	0.152607	0.066*
C8	0.1475 (3)	0.5400 (5)	0.28145 (12)	0.0558 (7)
H8A	0.044884	0.610385	0.295029	0.067*
H8B	0.204349	0.644421	0.251474	0.067*
C9	0.2582 (3)	0.4896 (5)	0.34794 (13)	0.0606 (7)
H9A	0.362961	0.425160	0.334403	0.073*
H9B	0.283304	0.627819	0.373783	0.073*
C10	0.1214 (3)	0.1310 (5)	0.35537 (13)	0.0558 (6)
H10A	0.055511	0.038775	0.385768	0.067*
H10B	0.219030	0.045201	0.343691	0.067*
C11	0.0179 (3)	0.1866 (5)	0.28711 (12)	0.0537 (6)
H11A	−0.009801	0.048942	0.261396	0.064*
H11B	−0.085945	0.257022	0.299132	0.064*
C12	0.2285 (3)	0.3200 (5)	0.46605 (12)	0.0465 (5)
C13	0.3301 (3)	0.4845 (6)	0.49972 (13)	0.0610 (7)
H13	0.368937	0.601828	0.472506	0.073*
C14	0.3746(3)	0.4780(6)	0.57195(13)	0.0610(7)
H14	0.440465	0.592379	0.592437	0.073*
C15	0.3233(3)	0.3051(5)	0.61451(12)	0.0520(6)
C16	0.2251(3)	0.1401(5)	0.58155(13)	0.0630(8)
H16	0.189499	0.020901	0.608852	0.076*
C17	0.1780 (3)	0.1461 (5)	0.50973 (14)	0.0605 (7)
H17	0.111138	0.031811	0.489820	0.073*
C18	0.3705 (3)	0.2914 (5)	0.69206 (13)	0.0588 (7)
C19	0.5317 (3)	0.4551 (7)	0.78971 (13)	0.0687 (8)
H19A	0.643144	0.518911	0.796007	0.082*
H19B	0.535932	0.303394	0.808528	0.082*
C20	0.4138 (4)	0.5908 (8)	0.82984 (17)	0.0885 (11)
H20A	0.406809	0.739571	0.810174	0.133*
H20B	0.453280	0.598593	0.879244	0.133*
H20C	0.305068	0.522326	0.826101	0.133*
N1	0.1070 (2)	0.3364 (4)	0.24113 (10)	0.0503 (5)
N2	0.1751 (2)	0.3332 (3)	0.39408 (10)	0.0504 (5)
O1	0.3198 (3)	0.1503 (5)	0.73111 (11)	0.0947 (9)
O2	0.4799 (2)	0.4492 (4)	0.71423 (9)	0.0695 (6)

methol (20:1, v/v) for 3 days. Using Olex2,[1] the structure was solved with the ShelXT[2] structure solution program and refined with the ShelXL[3] refinement package. All hydrogen atoms were placed in their geometrically idealized positions and constrained to ride on their parent atoms.

3 Comment

Ethyl 4-(4-benzylpiperazin-1-yl)benzoate is a key inermediate for the synthesis of diacylglycerol acyltransferase (DGAT) inhibitors, in particular a DGAT1 inhibitor.[4] DGAT is a microsomal enzyme that can be classified into four types based on structural and localization differences: DGAT1, DGAT2, bifunctional enzyme (wax ester synthase, WS/DGAT), and cytosolic DGAT (CytoDGAT).[5] Piperidine or piperazine derivatives exhibiting inhibitory activity against DGAT, particularly DGAT1.[6] Here, ethyl 4-(4-benzylpiperazin-1-yl) benzoate is the main starting material for the synthesis of piperazine derivatives. In the molecules forming the title crystal structure, the key bond lengths and angles are within normal ranges. The C–N bonds are confirmed by the distance of N1–C7, N2–C12. Their lengths are 1.469(3) Å, and 1.391(3) Å, respectively. Additionally, the lengths of C18–O1 and C18–O2 are 1.201(3) Å and 1.334(4) Å, which are consistent with the ester group. The bond angles of C8–N1–C11 and C9–N2–C10 measures 107.78(18) Å and 111.39(19) Å, respectively, which is attributed to the bond angles characteristic of piperazine. These results indicated the structure of ethyl 4-(4-benzylpiperazin-1-yl)benzoate.

Author contributions: Xue Zeng drafted most parts of the manuscript and conducted the experiments of crystal analysis. Wenwu Zhong and Yuanfang Hou cultured the crystal of compound. Yuanjiao Feng contributed to the analysis of results. All authors agreed to the final version of the manuscript. All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

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Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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