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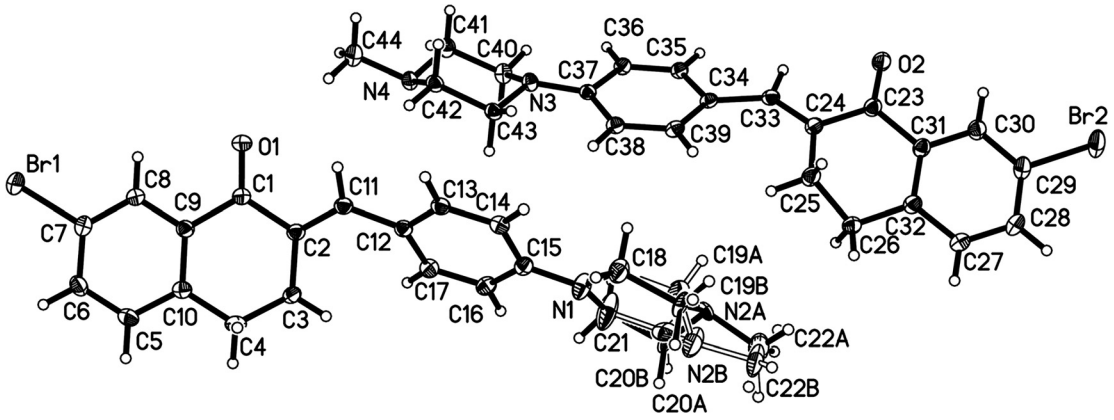
Crystal structure of (*E*)-7-bromo-2-(4-(4-methylpiperazin-1-yl)benzylidene)-3,4-dihydronaphthalen-1(2*H*)-one, $C_{22}H_{23}BrN_2O$



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Abstract

$C_{22}H_{23}BrN_2O$, triclinic, $P\bar{1}$ (no. 2), a = 10.0543(1) Å, b = 11.4893(1) Å, c = 16.5853(1) Å, α = 93.152(1)°, β = 91.877(1)°, γ = 97.097(1)°, V = 1896.81(3) Å^3, Z = 4, $R_{gt}(F)$ = 0.0318, $wR_{ref}(F^2)$ = 0.0840, T = 293 K.

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The asymmetric unit of the title crystal structure is shown in the figure. Displacement ellipsoids are drawn at the 30% probability level. 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:	Yellow block
Size:	0.15 × 0.12 × 0.10 mm
Wavelength:	Cu *K*α radiation (1.54178 Å)
μ:	3.05 mm^{-1}
Diffractometer, scan mode:	XtaLAB AFC12 (RINC)
θ_{max}, completeness:	71.6°, 99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	19,658, 7178, 0.019
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 6731
$N(param)_{refined}$:	509
Programs:	CrysAlis^{PRO} [1], SHELX [2, 3]

Source of material

Referring to the literature synthesis [4], 7-bromo-3,4-dihydronaphthalen-1(2*H*)-one was synthesized with succinic anhydride with the aid of Friedel–Crafts reaction, reduction reaction by hydrazine hydrate, and dehydration condensation. In a round bottom flask, 7-bromo-3,4-dihydronaphthalen-1(2*H*)-one (0.90 g, 4.00 mmol) and 4-(4-methylpiperazin-1-yl)benzaldehyde (0.82 g, 4.00 mmol) were dissolved in 10 mL of methanol. The mixture stirred in an ice-cold brine bath at 268 K until clarified. Then 5 mL of 25% sodium hydroxide solution was added and the reaction was switched to room temperature and stirred for 1.5 h. The entire reaction was monitored by using thin layer chromatography (TLC). After the reaction, the solvent was removed by filtration, while the filter residue was passed through silica gel column chromatography (dichloromethane: methanol = 40:1), (v/v) to acquire the yellow title compound. The title compound was recrystallized from 30 mL of dichloromethane and 15 mL of methanol at room temperature to get yellow crystals, (*E*)-7-bromo-2-(4-(4-methylpiperazin-1-yl)benzylidene)-3,4-dihydronaphthalen-1(2*H*)-one.

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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}
Br1	0.55109 (3)	1.18181 (3)	0.02866 (2)	0.05807 (10)
Br2	0.98301 (3)	−0.33930 (2)	1.00966 (2)	0.04605 (9)
C1	0.65254 (17)	0.91681 (15)	0.27152 (11)	0.0258 (4)
C2	0.61538 (17)	0.86870 (15)	0.35041 (10)	0.0242 (3)
C3	0.48203 (18)	0.89444 (16)	0.38236 (11)	0.0278 (4)
H3A	0.477650	0.876015	0.438667	0.033*
H3B	0.409750	0.845210	0.352255	0.033*
C4	0.46444 (18)	1.02330 (16)	0.37466 (11)	0.0279 (4)
H4A	0.375762	1.036487	0.391487	0.033*
H4B	0.529869	1.071903	0.410271	0.033*
C5	0.41138 (18)	1.14445 (15)	0.25819 (12)	0.0287 (4)
H5	0.349990	1.178107	0.289899	0.034*
C6	0.43130 (19)	1.18046 (16)	0.18076 (12)	0.0317 (4)
H6	0.384206	1.237978	0.160513	0.038*
C7	0.5224 (2)	1.12948 (17)	0.13400 (12)	0.0342 (4)
C8	0.59297 (19)	1.04367 (17)	0.16270 (12)	0.0315 (4)
H8	0.653526	1.010116	0.130286	0.038*
C9	0.57262 (17)	1.00781 (15)	0.24064 (11)	0.0248 (4)
C10	0.48152 (17)	1.05876 (15)	0.28957 (11)	0.0239 (3)
C11	0.70590 (17)	0.81238 (14)	0.38886 (11)	0.0245 (3)
H11	0.787415	0.812126	0.363954	0.029*
C12	0.69554 (17)	0.75157 (14)	0.46378 (11)	0.0235 (3)
C13	0.81137 (17)	0.74359 (14)	0.51098 (11)	0.0241 (3)
H13	0.893045	0.779068	0.493998	0.029*
C14	0.81014 (17)	0.68541 (15)	0.58170 (11)	0.0250 (4)
H14	0.889597	0.684606	0.611874	0.030*
C15	0.68908 (17)	0.62714 (15)	0.60850 (11)	0.0251 (4)
C16	0.57304 (17)	0.63223 (16)	0.56006 (11)	0.0275 (4)
H16	0.491809	0.593575	0.575349	0.033*
C17	0.57584 (18)	0.69270 (16)	0.49063 (11)	0.0271 (4)
H17	0.496350	0.694616	0.460724	0.032*
C18	0.7992 (2)	0.5779 (2)	0.73218 (13)	0.0414 (5)
H18A	0.836956	0.659919	0.738093	0.050*
H18B	0.864601	0.535397	0.705583	0.050*
C21	0.5734 (2)	0.4857 (3)	0.69326 (18)	0.0707 (10)
H21A	0.578453	0.418691	0.655733	0.085*
H21B	0.493066	0.519253	0.677891	0.085*
C23	0.95557 (18)	−0.06368 (16)	0.76427 (11)	0.0270 (4)
C24	0.91578 (17)	0.04370 (15)	0.72836 (11)	0.0250 (4)
C25	0.8890 (2)	0.14180 (16)	0.78761 (11)	0.0308 (4)
H25A	0.844630	0.198734	0.759194	0.037*
H25B	0.973622	0.181329	0.810651	0.037*
C26	0.80134 (19)	0.09647 (16)	0.85566 (11)	0.0293 (4)
H26A	0.799132	0.159607	0.896710	0.035*
H26B	0.710399	0.073599	0.834189	0.035*
C27	0.8179 (2)	−0.03271 (18)	0.97274 (12)	0.0329 (4)
H27	0.769151	0.017114	1.002460	0.040*
C28	0.8562 (2)	−0.13082 (18)	1.00763 (12)	0.0345 (4)
H28	0.832600	−0.147769	1.059853	0.041*
C29	0.9303 (2)	−0.20305 (16)	0.96294 (11)	0.0323 (4)
C30	0.96656 (19)	−0.17964 (16)	0.88581 (11)	0.0300 (4)
H30	1.017861	−0.228574	0.857250	0.036*
C31	0.92545 (18)	−0.08132 (15)	0.85067 (10)	0.0256 (4)
C32	0.85062 (18)	−0.00689 (16)	0.89425 (11)	0.0268 (4)
C33	0.90671 (17)	0.04022 (15)	0.64704 (11)	0.0237 (3)
H33	0.924816	−0.030888	0.623029	0.028*
C34	0.87460 (16)	0.12394 (14)	0.58833 (10)	0.0220 (3)
C35	0.85196 (17)	0.07993 (14)	0.50764 (10)	0.0233 (3)
H35	0.851856	−0.000215	0.496104	0.028*
C36	0.83000 (17)	0.14948 (14)	0.44499 (10)	0.0234 (3)
H36	0.814541	0.115373	0.392837	0.028*
C37	0.83051 (15)	0.27195 (14)	0.45854 (10)	0.0211 (3)
C38	0.84667 (17)	0.31645 (14)	0.53973 (10)	0.0235 (3)
H38	0.842108	0.395852	0.551721	0.028*
C39	0.86916 (17)	0.24485 (15)	0.60212 (10)	0.0242 (3)
H39	0.881005	0.277959	0.654702	0.029*
C40	0.74615 (18)	0.29786 (15)	0.32088 (11)	0.0268 (4)
H40A	0.651304	0.296433	0.330408	0.032*
H40B	0.763227	0.217815	0.307961	0.032*
C41	0.78164 (19)	0.37181 (16)	0.25002 (11)	0.0287 (4)
H41A	0.873826	0.366010	0.236517	0.034*
H41B	0.724365	0.341837	0.203382	0.034*
C42	0.85447 (17)	0.53768 (15)	0.33753 (11)	0.0261 (4)
H42A	0.847342	0.620188	0.349648	0.031*
H42B	0.946332	0.530849	0.323790	0.031*
C43	0.82172 (17)	0.47027 (14)	0.41166 (11)	0.0242 (3)
H43A	0.886430	0.498392	0.455203	0.029*
H43B	0.733480	0.483802	0.429093	0.029*
C44	0.7981 (2)	0.56460 (18)	0.19939 (13)	0.0381 (4)
H44A	0.784488	0.644673	0.212151	0.057*
H44B	0.741262	0.533660	0.153610	0.057*
H44C	0.890217	0.561393	0.186883	0.057*
N1	0.68307 (17)	0.56910 (15)	0.68005 (10)	0.0360 (4)
N3	0.82436 (14)	0.34417 (12)	0.39443 (9)	0.0229 (3)
N4	0.76539 (15)	0.49481 (13)	0.26860 (9)	0.0275 (3)
O1	0.74353 (14)	0.88416 (13)	0.23240 (8)	0.0373 (3)
O2	1.00634 (16)	−0.13885 (12)	0.72495 (8)	0.0383 (3)
C19A[a]	0.7819 (19)	0.5324 (12)	0.8181 (8)	0.029 (2)
H19A[a]	0.867941	0.517453	0.840712	0.034*
H19B[a]	0.747554	0.591051	0.853209	0.034*
C20A[a]	0.5523 (15)	0.4385 (11)	0.7762 (7)	0.030 (2)
H20A[a]	0.511887	0.494453	0.810483	0.036*
H20B[a]	0.492372	0.365313	0.771448	0.036*
C22A[a]	0.657 (2)	0.3853 (13)	0.8932 (12)	0.056 (3)
H22A[a]	0.617403	0.446233	0.921887	0.084*
H22B[a]	0.739593	0.373672	0.920605	0.084*
H22C[a]	0.596551	0.313586	0.890969	0.084*
N2A[a]	0.6838 (3)	0.4187 (3)	0.8122 (2)	0.0253 (7)
C19B[a]	0.784 (2)	0.5149 (14)	0.8018 (9)	0.039 (3)
H19C[a]	0.819060	0.441234	0.790176	0.047*
H19D[a]	0.843351	0.558132	0.843288	0.047*
C20B[a]	0.5780 (15)	0.4368 (10)	0.7692 (8)	0.039 (4)
H20C[a]	0.598050	0.356948	0.759292	0.047*
H20D[a]	0.487472	0.430909	0.788437	0.047*
C22B[a]	0.6623 (19)	0.4215 (13)	0.9087 (11)	0.059 (4)
H22D[a]	0.688385	0.345148	0.896070	0.089*
H22E[a]	0.573048	0.413056	0.928303	0.089*
H22F[a]	0.723231	0.462582	0.949415	0.089*
N2B[a]	0.6656 (4)	0.4875 (5)	0.8363 (3)	0.0575 (12)

[a]Occupancy: 0.5.

Experimental details

The H atoms were placed in idealized positions and treated as riding on their parent atoms, with *d*(C–H) = 0.96 Å (methyl), U_{iso}(H) = 1.5U_{eq}(C), *d*(C–H) = 0.97 Å (methylene), U_{iso}(H) = 1.2U_{eq}(C), and *d*(C–H) = 0.93 Å (aromatic), U_{iso}(H) = 1.2U_{eq}(C).

Comment

In recent years, some heterocyclic anti-inflammatory agents, such as (*E*)-4-(4-ethylbenzylidene)-6,8-dimethoxy-3,4-dihydrobenzo[b]oxepin-5(2*H*)-one [5], and (*E*)-7-methoxy-2-(4-methoxy-3-(trifluoromethyl) benzylidene)-3, 4-dihydronaphthalen-1(2*H*)-one [6] have been reported and possessed the positive anti-inflammatory and anti-tumor activities with low toxicity. Some *meta*–CF_3 and *para*–OMe substituted 3,4-dihydronaphthalen-1(2*H*)-one (DHN) derivatives showed more potential anti-neuroinflammatory actions through inhibiting the activation of NF-**kappa**B signaling pathway [7]. In order to study the substituent effect, 7-substitute of DHN was replaced by an electron-withdrawing substitute (–Br), while the 2-aromatic ring was replaced by a great electron-donating substitute, such as 4-(4-methylpiperazin-1-yl)benzylidene group.

Single-crystal structure analysis reveals that there are two DHN molecules in the asymmetric unit (*cf*. the Figure). Bond lengths and angles are all in the expected ranges [8–11]. The pharmacophore of the title compound is 3,4-dihydronaphthalen-1 (2*H*)-one, with bromine substitution at the 7^{th} position and 4-methylpiperazine substitution at the 2-aromatic ring. In a molecule, 4-methylpiperazine group has a mixed order structurally. Therefore, the 4-methylpiperazine exhibits two types of “chair” conformation and “boat” conformation [8]. In another molecule, 4-methylpiperazine only exhibits “chair” conformation. Both DHN molecules adopt the *E* stereochemistry of the olefinic double bond [9, 10]. Bond length of C(2) = C(11) is 1.344(3) Å, while bond length of C(24) = C(33) is 1.347(3) Å. The entire molecule forms a linear structure under the action of the olefin bond. In pharmacophore, two methylene groups affect the molecular coplanarity. So, the 2-aromatic ring and the 3,4-dihydronaphthalen-1(2*H*)-one moiety are not coplanar with each other, and the dihedral angles are about 56.04(4)° and 34.86(2)°, respecitvely. In addition, some active groups, such as carbonyl, *α*,*β*-unsaturated keto, and 4-methylpiperazine of the title compound may contribute to the anti-inflammatory activity.

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