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2-Chloro-1-[4-(2,4-difluorobenzyl)-piperazin-1-yl]ethanone

Bo Zhang, Guri L. V. Damu, Jing-Song Lv and Cheng-He Zhou*

Laboratory of Bioorganic & Medicinal Chemistry, School of Chemistry and Chemical Engineering, Southwest University, Chongqing 400715, People's Republic of China
Correspondence e-mail: zhouch@swu.edu.cn

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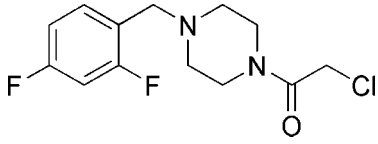
Key indicators: single-crystal X-ray study; T = 296 K; mean σ(C–C) = 0.003 Å; R factor = 0.031; wR factor = 0.086; data-to-parameter ratio = 10.6.

In the title molecule, $C_{13}H_{15}ClF_2N_2O$, the piperazine ring is in a chair conformation with the 2,4-difluorobenzyl and chloroacetyl substituents in equatorial positions.

Related literature

For the synthesis, see: Gan *et al.* (2010). For applications of piperazine derivatives, see: Gan, Cai & Zhou (2009); Cai *et al.* (2009); Gan, Lu, & Zhou (2009).



Experimental

Crystal data

$C_{13}H_{15}ClF_2N_2O$
M_r = 288.72
Orthorhombic, $P2_12_12_1$
a = 7.895 (2) Å
b = 8.512 (2) Å
c = 19.884 (5) Å
V = 1336.2 (6) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.30 mm^{-1}
T = 296 K
0.30 × 0.25 × 0.24 mm

Data collection

Bruker SMART CCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.915, T_{max} = 0.931
5743 measured reflections
2324 independent reflections
2238 reflections with $I > 2\sigma(I)$
R_{int} = 0.026

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.086
S = 1.07
2324 reflections
220 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.37 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}
Absolute structure: Flack (1983), 938 Friedel pairs
Flack parameter: 0.05 (7)

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXTL* (Sheldrick, 2008).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: LH5389).

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supporting information

Acta Cryst. (2012). E**68**, o70 [doi:10.1107/S1600536811052597]

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S1. Comment

The piperazine ring is present in many clinical drugs (Cai *et al.*, 2009). The incorporation of a piperazine moiety gernerally improves physicochemical properties, and thereby enhances biological activities (Gan, Cai & Zhou, 2009). The piperazine moiety is extensively employed to construct various bioactive molecules (Gan, Lu & Zhou, 2009). Our interest is to develop azole-containing piperazine derivatives as medicinal agents (Gan *et al.*, 2010). Herein we report the crystal structure of the title compound (I).

In the molecular structure (Fig. 1) of (I) the piperazine ring is in a chair conformation, in which the 2,4-difluorobenzyl and chloroacetyl groups are located in equatorial positions.

S2. Experimental

Compound (I) was synthesized according to the procedure of Gan *et al.* (2010). Single crystals suitable for X-ray diffraction analysis were grown in a mixed solution petroleum ether and ethyl acetate by slow evaporation at room temperature.

S3. Refinement

The hydrogen atoms attached to the benzene ring were placed in calculated positions with C—H = 0.93 Å and U_{iso}(H) = 1.2U_{eq}(C). All other H atoms were refined independently with isotropic displacement parameters.

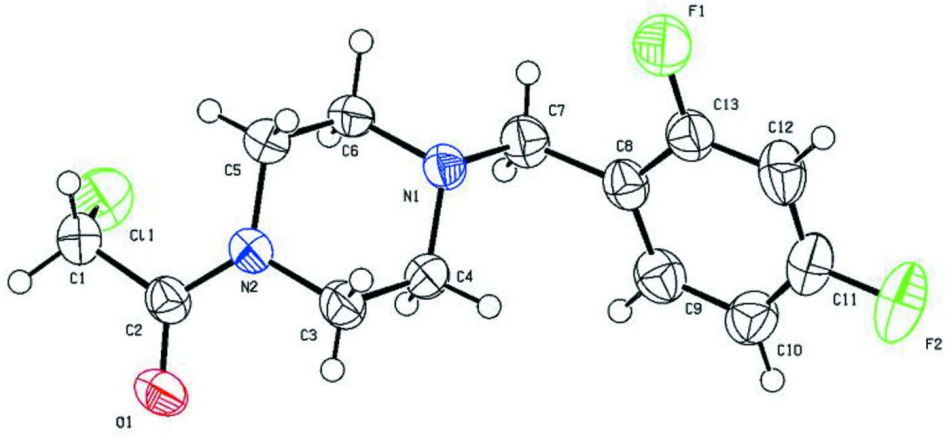

Figure 1

The molecular structure of the title compound showing 50% ellipsoids.

2-Chloro-1-[4-(2,4-difluorobenzyl)piperazin-1-yl]ethanone

Crystal data

$C_{13}H_{15}ClF_2N_2O$
$M_r = 288.72$
Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab
$a = 7.895$ (2) Å
$b = 8.512$ (2) Å
$c = 19.884$ (5) Å
$V = 1336.2$ (6) Å^3
$Z = 4$
$F(000) = 600$
$D_x = 1.435$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 4078 reflections
$\theta = 3.2$–$27.4°$
$\mu = 0.30$ mm^{-1}
$T = 296$ K
Block, colorless
0.30 × 0.25 × 0.24 mm

Data collection

Bruker SMART CCD diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min} = 0.915$, $T_{max} = 0.931$
5743 measured reflections
2324 independent reflections
2238 reflections with $I > 2\sigma(I)$
$R_{int} = 0.026$
$\theta_{max} = 25.0°$, $\theta_{min} = 2.1°$
$h = -9 \rightarrow 8$
$k = -8 \rightarrow 10$
$l = -21 \rightarrow 23$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.031$
$wR(F^2) = 0.086$
$S = 1.07$
2324 reflections
220 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0501P)^2 + 0.1826P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.37$ e Å^{-3}
$\Delta\rho_{min} = -0.18$ e Å^{-3}
Absolute structure: Flack (1983), 938 Friedel pairs
Absolute structure parameter: 0.05 (7)

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

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

	x	y	z	U_{iso}*/U_{eq}
Cl1	0.26806 (8)	1.41412 (7)	0.14714 (3)	0.06679 (19)
N1	0.53726 (18)	0.88254 (16)	0.14628 (8)	0.0392 (3)
F1	0.86597 (19)	0.62487 (19)	0.15098 (7)	0.0786 (4)

N2	0.25240 (19)	1.04611 (18)	0.20166 (8)	0.0441 (4)
C7	0.6577 (3)	0.8543 (2)	0.09087 (11)	0.0466 (4)
C2	0.1248 (2)	1.1492 (2)	0.19486 (9)	0.0397 (4)
C4	0.3630 (2)	0.8503 (2)	0.12429 (10)	0.0437 (4)
C6	0.5486 (2)	1.0480 (2)	0.16685 (11)	0.0458 (4)
O1	−0.01636 (16)	1.11102 (17)	0.17464 (8)	0.0559 (4)
C3	0.2357 (3)	0.8832 (2)	0.17911 (11)	0.0482 (4)
F2	0.6783 (2)	0.21756 (16)	0.01314 (7)	0.0834 (5)
C1	0.1573 (3)	1.3191 (2)	0.21356 (10)	0.0474 (4)
C13	0.7660 (2)	0.5758 (2)	0.10072 (9)	0.0477 (4)
C9	0.5670 (3)	0.6280 (2)	0.01646 (10)	0.0504 (5)
H9	0.4984	0.6980	−0.0070	0.061*
C5	0.4260 (2)	1.0821 (3)	0.22316 (11)	0.0509 (5)
C8	0.6638 (2)	0.6844 (2)	0.06941 (8)	0.0416 (4)
C10	0.5682 (3)	0.4712 (3)	−0.00294 (10)	0.0539 (5)
H10	0.5005	0.4354	−0.0380	0.065*
C11	0.6726 (3)	0.3717 (2)	0.03146 (10)	0.0540 (5)
C12	0.7734 (3)	0.4185 (2)	0.08374 (10)	0.0576 (5)
H12	0.8430	0.3483	0.1066	0.069*
H2M	0.219 (3)	1.327 (3)	0.2523 (10)	0.049 (6)*
H1M	0.049 (3)	1.374 (3)	0.2171 (10)	0.048 (5)*
H9M	0.451 (3)	1.011 (3)	0.2616 (12)	0.056 (6)*
H5M	0.328 (2)	0.920 (2)	0.0833 (9)	0.038 (5)*
H4M	0.265 (3)	0.814 (3)	0.2201 (11)	0.064 (6)*
H10M	0.432 (3)	1.185 (3)	0.2347 (12)	0.064 (7)*
H7M	0.665 (3)	1.071 (2)	0.1839 (9)	0.045 (5)*
H6M	0.362 (3)	0.745 (3)	0.1093 (11)	0.062 (7)*
H8M	0.524 (3)	1.123 (2)	0.1293 (10)	0.048 (5)*
H3M	0.134 (3)	0.868 (3)	0.1630 (11)	0.057 (6)*
H11M	0.761 (3)	0.886 (3)	0.1060 (10)	0.051 (5)*
H12M	0.619 (3)	0.919 (3)	0.0531 (13)	0.061 (6)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0769 (4)	0.0526 (3)	0.0708 (3)	−0.0112 (3)	0.0027 (3)	0.0112 (2)
N1	0.0336 (7)	0.0325 (7)	0.0514 (8)	0.0009 (6)	0.0024 (6)	−0.0012 (6)
F1	0.0775 (9)	0.0846 (10)	0.0737 (8)	0.0243 (8)	−0.0276 (7)	−0.0206 (8)
N2	0.0328 (7)	0.0415 (8)	0.0581 (8)	0.0027 (7)	−0.0002 (7)	−0.0081 (7)
C7	0.0422 (10)	0.0400 (10)	0.0577 (11)	−0.0014 (8)	0.0096 (9)	0.0031 (9)
C2	0.0351 (8)	0.0415 (9)	0.0424 (8)	0.0014 (8)	0.0052 (7)	0.0008 (7)
C4	0.0375 (9)	0.0323 (9)	0.0611 (11)	−0.0029 (8)	−0.0004 (8)	−0.0060 (8)
C6	0.0321 (9)	0.0385 (10)	0.0667 (12)	−0.0006 (7)	−0.0065 (8)	−0.0067 (9)
O1	0.0328 (6)	0.0533 (8)	0.0815 (9)	0.0013 (6)	−0.0034 (6)	−0.0032 (7)
C3	0.0361 (9)	0.0376 (9)	0.0710 (12)	−0.0001 (8)	0.0047 (9)	−0.0024 (9)
F2	0.1251 (14)	0.0440 (7)	0.0812 (9)	0.0043 (8)	0.0120 (9)	−0.0143 (7)
C1	0.0461 (10)	0.0431 (10)	0.0532 (11)	0.0057 (9)	0.0024 (9)	−0.0072 (9)
C13	0.0456 (9)	0.0524 (11)	0.0451 (9)	0.0064 (10)	−0.0002 (8)	−0.0044 (8)

C9	0.0508 (10)	0.0531 (12)	0.0474 (10)	0.0074 (9)	−0.0017 (8)	0.0041 (9)
C5	0.0394 (10)	0.0492 (12)	0.0643 (12)	0.0064 (9)	−0.0108 (9)	−0.0151 (10)
C8	0.0386 (9)	0.0418 (10)	0.0444 (9)	0.0017 (8)	0.0096 (7)	0.0030 (8)
C10	0.0562 (12)	0.0567 (12)	0.0487 (10)	−0.0027 (10)	0.0024 (9)	−0.0083 (9)
C11	0.0689 (13)	0.0396 (10)	0.0535 (10)	−0.0009 (10)	0.0147 (9)	−0.0055 (9)
C12	0.0688 (13)	0.0498 (11)	0.0542 (11)	0.0208 (11)	0.0009 (10)	0.0031 (9)

Geometric parameters (Å, º)

Cl1—C1	1.778 (2)	C6—H8M	1.00 (2)
N1—C4	1.469 (2)	C3—H4M	1.03 (2)
N1—C6	1.469 (2)	C3—H3M	0.88 (3)
N1—C7	1.475 (2)	F2—C11	1.362 (2)
F1—C13	1.340 (2)	C1—H2M	0.91 (2)
N2—C2	1.343 (2)	C1—H1M	0.98 (2)
N2—C3	1.463 (2)	C13—C8	1.376 (3)
N2—C5	1.468 (2)	C13—C12	1.382 (3)
C7—C8	1.509 (3)	C9—C8	1.387 (3)
C7—H11M	0.91 (2)	C9—C10	1.389 (3)
C7—H12M	0.98 (3)	C9—H9	0.9300
C2—O1	1.228 (2)	C5—H9M	1.00 (2)
C2—C1	1.516 (3)	C5—H10M	0.90 (3)
C4—C3	1.509 (3)	C10—C11	1.365 (3)
C4—H5M	1.046 (19)	C10—H10	0.9300
C4—H6M	0.94 (3)	C11—C12	1.368 (3)
C6—C5	1.508 (3)	C12—H12	0.9300
C6—H7M	1.00 (2)		
C4—N1—C6	108.60 (14)	H4M—C3—H3M	114 (2)
C4—N1—C7	110.54 (15)	C2—C1—Cl1	109.57 (13)
C6—N1—C7	108.94 (14)	C2—C1—H2M	111.4 (14)
C2—N2—C3	121.37 (16)	Cl1—C1—H2M	109.4 (13)
C2—N2—C5	126.42 (16)	C2—C1—H1M	108.8 (13)
C3—N2—C5	111.78 (15)	Cl1—C1—H1M	105.6 (12)
N1—C7—C8	112.82 (15)	H2M—C1—H1M	111.9 (18)
N1—C7—H11M	106.6 (13)	F1—C13—C8	118.23 (17)
C8—C7—H11M	110.3 (14)	F1—C13—C12	117.35 (17)
N1—C7—H12M	106.2 (14)	C8—C13—C12	124.42 (18)
C8—C7—H12M	109.6 (14)	C8—C9—C10	122.64 (19)
H11M—C7—H12M	111.4 (19)	C8—C9—H9	118.7
O1—C2—N2	122.76 (17)	C10—C9—H9	118.7
O1—C2—C1	119.10 (16)	N2—C5—C6	110.06 (16)
N2—C2—C1	118.14 (16)	N2—C5—H9M	106.3 (14)
N1—C4—C3	111.97 (16)	C6—C5—H9M	109.0 (13)
N1—C4—H5M	112.1 (10)	N2—C5—H10M	108.9 (16)
C3—C4—H5M	106.2 (10)	C6—C5—H10M	109.9 (16)
N1—C4—H6M	106.0 (15)	H9M—C5—H10M	113 (2)
C3—C4—H6M	113.6 (14)	C13—C8—C9	115.72 (18)

H5M—C4—H6M	106.9 (17)	C13—C8—C7	122.34 (17)
N1—C6—C5	110.60 (17)	C9—C8—C7	121.95 (17)
N1—C6—H7M	109.5 (12)	C11—C10—C9	117.5 (2)
C5—C6—H7M	107.6 (11)	C11—C10—H10	121.3
N1—C6—H8M	112.9 (11)	C9—C10—H10	121.3
C5—C6—H8M	107.8 (12)	F2—C11—C10	118.9 (2)
H7M—C6—H8M	108.2 (17)	F2—C11—C12	117.6 (2)
N2—C3—C4	109.69 (15)	C10—C11—C12	123.4 (2)
N2—C3—H4M	106.1 (13)	C11—C12—C13	116.28 (19)
C4—C3—H4M	108.3 (14)	C11—C12—H12	121.9
N2—C3—H3M	109.5 (15)	C13—C12—H12	121.9
C4—C3—H3M	108.7 (15)		

C4—N1—C7—C8	−64.7 (2)	N1—C6—C5—N2	−58.6 (2)
C6—N1—C7—C8	176.09 (16)	F1—C13—C8—C9	178.12 (17)
C3—N2—C2—O1	6.0 (3)	C12—C13—C8—C9	−1.7 (3)
C5—N2—C2—O1	177.8 (2)	F1—C13—C8—C7	−1.6 (3)
C3—N2—C2—C1	−174.52 (18)	C12—C13—C8—C7	178.66 (19)
C5—N2—C2—C1	−2.7 (3)	C10—C9—C8—C13	1.8 (3)
C6—N1—C4—C3	−58.6 (2)	C10—C9—C8—C7	−178.50 (18)
C7—N1—C4—C3	−178.10 (15)	N1—C7—C8—C13	−85.7 (2)
C4—N1—C6—C5	59.1 (2)	N1—C7—C8—C9	94.6 (2)
C7—N1—C6—C5	179.51 (16)	C8—C9—C10—C11	−1.3 (3)
C2—N2—C3—C4	117.63 (19)	C9—C10—C11—F2	−179.20 (19)
C5—N2—C3—C4	−55.3 (2)	C9—C10—C11—C12	0.5 (3)
N1—C4—C3—N2	56.8 (2)	F2—C11—C12—C13	179.39 (19)
O1—C2—C1—Cl1	−101.22 (18)	C10—C11—C12—C13	−0.4 (3)
N2—C2—C1—Cl1	79.24 (19)	F1—C13—C12—C11	−178.81 (18)
C2—N2—C5—C6	−115.8 (2)	C8—C13—C12—C11	1.0 (3)
C3—N2—C5—C6	56.7 (2)		