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3-[4-(2-Chlorophenyl)piperazinomethyl]-5-methyl-1-benzoxazolin-2(3*H*)-one

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.003 Å
R factor = 0.040
wR factor = 0.127
Data-to-parameter ratio = 14.1

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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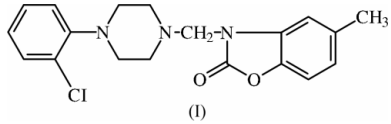
The title compound, $C_{19}H_{20}ClN_3O_2$, is composed of an essentially planar benzoxazolinone ring system, a chlorophenyl group and a central piperazine ring. The benzoxazolinone ring system is nearly perpendicular to the piperazine ring, which displays an almost perfect chair conformation.

Comment

Benzoxazolinones have been investigated primarily for their medicinal value as central nervous system depressants which exhibit analgesic, antipyretic, anticonvulsant, hypnotic and skeletal muscle-relaxant activity (Sam & Valentine, 1969). In addition, many investigations of benzoxazolin-2-ones showed that compounds with this structure have anti-inflammatory, antineoplastic and antimicrobial activities (Clark & Pessolano, 1953; Varma & Nobles, 1986; Gökhan *et al.*, 1996; Vaccher *et al.*, 1986; Varma & Kapoor, 1979; Erol *et al.*, 1989; Kalcheva *et al.*, 1990; Köksal *et al.*, 2002). The useful medicinal value of these derivatives prompted us to synthesize 3-substituted benzoxazolin-2-ones and elucidate their structures. The pharmacological results obtained indicate that the title compound, (I), possesses good analgesic activity coupled with notable anti-inflammatory properties and, moreover, remarkable gastric tolerance.



(I)

To obtain information about the stereochemistry of the molecule and to confirm the assigned structure, an X-ray analysis of (I) was undertaken. It was found that the phenyl group contains a Cl atom in the *ortho* position, with a C—Cl distance of 1.738 (2) Å. This is in agreement with values in a related structure reported in the literature (Capuano *et al.*, 2000). The benzoxazolinone ring system is planar, with a maximum deviation from planarity of 0.02 (1) Å for atom C18. The plane through the C atoms of the piperazine ring makes a dihedral angle of 81.01 (5)° with benzoxazolinone ring. The benzoxazolinone ring system is nearly perpendicular to the piperazine ring, with a dihedral angle of 81.44 (4)°. The piperazine ring itself has an almost perfect chair conformation.

Experimental

3-Substituted 5-methyl-benzoxazolin-2-ones were prepared according to the Mannich reaction using arylpiperazine derivatives, formaldehyde and 5-methyl-2-benzoxazolinone, obtained from 4-methyl-2-aminophenol by fusion with urea. The structures of the compounds were deduced from IR, ^{1}H NMR and elemental analyses.

5-Methyl-2-benzoxazolinone was prepared by a modification of the procedure described by Bywater *et al.* (1945), using 0.1 mol 4-methyl-2-aminophenol and 0.12 mol urea. The mixture was fused at 418–423 K for 4 h in a preheated oil bath. The residue was recrystallized from water. Yield: 59.69%, m.p = 394–395 K. The title compound, (I), and derivatives with other substituents on the piperazine ring were prepared by vigorously stirring a solution of 0.1 mol of the substituted piperazine derivative and 0.1 mol 5-methyl-2-benzoxazolinone in methanol. 0.12 mol of formalin (37%, *w*/*v*) was added and the mixture refluxed in a water bath for 1 h. The reaction mixture was then poured on to crushed ice and the resulting solid mass separated by filtration, dried and crystallized from ethanol–water. For (I), yield 74.76%; m.p = 432–433 K. Calculated: C 63.77, H 5.63, O 11.74%; found: C 63.64, H 5.40, O 11.57%. IR data (KBr/cm^{-1}): 3200, 2917 (C—H), 1774 (C═O). ^{1}H NMR ($CDCl_3$): 7.4–6.8 (*m*, 7H), 4.7 (*s*, 2H), 3.3–3.0 (*s*, 4H), 3.0–2.8 (*s*, 4H), 2.4 (*s*,3H).

Crystal data

$C_{19}H_{20}ClN_3O_2$	$Z = 2$
$M_r = 357.84$	$D_x = 1.370$ Mg m^{-3}
Triclinic, $P\overline{1}$	Mo $K\alpha$ radiation
$a = 6.2122$ (7) Å	Cell parameters from 8369 reflections
$b = 10.8899$ (12) Å	$\theta = 0.0$–$29.5°$
$c = 13.0580$ (14) Å	$\mu = 0.24$ mm^{-1}
$\alpha = 84.042$ (8)°	$T = 293$ (2) K
$\beta = 84.028$ (9)°	Prism, colourless
$\gamma = 82.499$ (9)°	0.70 × 0.57 × 0.35 mm
$V = 867.41$ (17) Å^3	

Data collection

Stoe IPDS-2 diffractometer	2762 reflections with $I > 2\sigma(I)$
ω scans	$R_{int} = 0.041$
Absorption correction: spherical (*X-RED*32; Stoe & Cie, 2002)	$\theta_{max} = 26.0°$
6303 measured reflections	$h = -7 \rightarrow 7$
3201 independent reflections	$k = -13 \rightarrow 13$
	$l = -16 \rightarrow 16$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.067P)^2 + 0.1P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.040$	$(\Delta/\sigma)_{max} = 0.001$
$wR(F^2) = 0.128$	$\Delta\rho_{max} = 0.35$ e Å^{-3}
$S = 1.13$	$\Delta\rho_{min} = -0.36$ e Å^{-3}
3201 reflections	Extinction correction: *SHELXL*97
227 parameters	Extinction coefficient: 0.010 (3)
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

Cl1—C2	1.7384 (19)	N1—C7	1.455 (2)
N2—C11	1.457 (2)	N1—C10	1.4616 (19)
N2—C9	1.459 (2)	N3—C12	1.367 (2)
N2—C8	1.4639 (19)	N3—C14	1.395 (2)
N1—C1	1.417 (2)	N3—C11	1.445 (2)
C9—N2—C11—N3	58.53 (16)	C8—N2—C11—N3	179.65 (12)

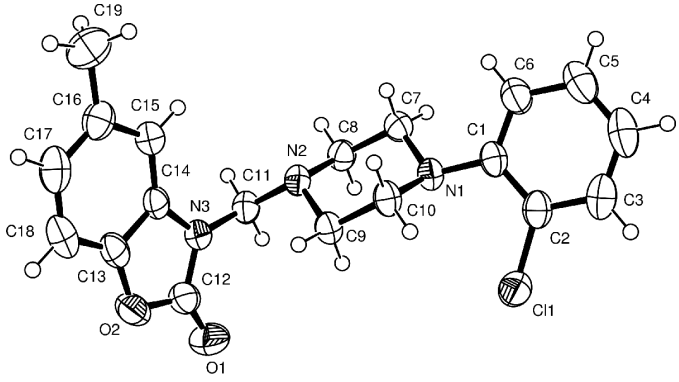


Figure 1
The structure of title compound, (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme.

H atoms were included in calculated positions and refined using a riding model; C—H(aromatic) = 0.93 Å, CH_2 C—H = 0.97 Å with U_{iso}(H) = 1.2U_{eq}(parent C atom), and CH_3 C—H = 0.96 Å, with U_{iso}(H) = 1.5U_{eq}(parent C-atom).

Data collection: *X-AREA* (Stoe & Cie, 2002); cell refinement: *X-AREA*; data reduction: *X-RED*32 (Stoe & Cie, 2002); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97; molecular graphics: *ORTEP*III (Burnett & Johnson, 1996); software used to prepare material for publication: *WinGX* (Farrugia, 1999) and *PARST* (Nardelli, 1995).

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