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1-(2-Chlorophenyl)-*N*-methyl-*N*-(1-methylpropyl)-isoquinoline-3-carboxamide

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.005 Å
Disorder in main residue
R factor = 0.069
wR factor = 0.164
Data-to-parameter ratio = 12.3

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

The quinoline fragment of the title compound, $C_{21}H_{21}ClN_2O$ (PK11195), is planar; the dihedral angle between this plane and the chlorophenyl plane is 78.6 (1)°. In the crystal structure, there are two disordered alternative molecules that have different relative stereochemistry of the disordered parts.

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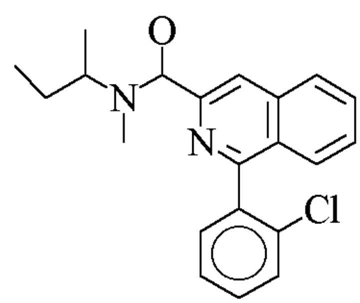
Comment

The title compound, PK11195 [(I) in Scheme below], is the first specific non-benzodiazepine ligand which was found to bind the peripheral benzodiazepine receptors with nanomolar affinity (Dubroeucq *et al.*, 1984; LeFur, Perrier *et al.*, 1983; LeFur, Guilloux *et al.*, 1983), and is commonly used as the radioligand for these receptors. Structural, conformational and electronic requirements for recognition and binding processes were widely studied (for example, Cappelli *et al.*, 1997, and references therein).



(I)

Here, we report the results of X-ray crystallographic studies of PK11195. Unfortunately, the crystal structure is highly disordered: the methylpropyl substituent was found in two different positions (hereinafter denoted as *A* and *B*, Fig. 1) with site-occupation factors of 0.62 (1) and 0.38 (1) for the *A* and *B* fragments, respectively. Moreover, the Cl substituent in the chlorophenyl fragment was also found in two positions (2′ and 6′), with site-occupation factors of 0.94 (1) and 0.06 (1), respectively.

Both disordered methylpropyl fragments define different relative stereochemistry of the chiral C33 atom. Attempts to refine the structure in a chiral space group $P2_1$ gave no significant improvement; the structure could be solved with two different molecules in the asymmetric part of the unit cell, but the refinement was unstable and, what is more important, both independent molecules also showed significant disorder.

Fig. 1 shows a perspective view of the molecule *A*. The quinoline moiety and the phenyl ring are planar, the maximum deviations from their least-squares planes are 0.019 (3) Å for the former and 0.012 (3) Å for the latter. The dihedral angle

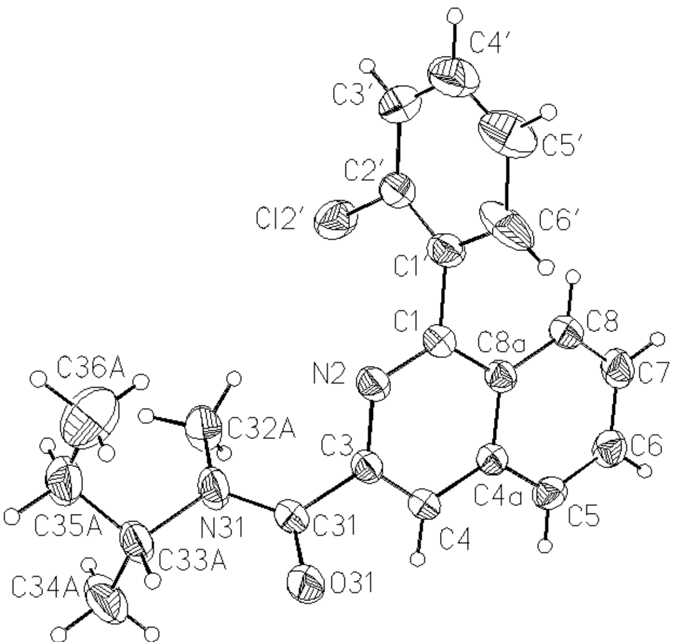


Figure 1
A perspective view of the molecule with the atom-numbering scheme (Siemens, 1989). Displacement ellipsoids are drawn at the 33% probability level and H atoms are depicted as spheres of arbitrary radii. Only the molecule of higher occupancy is shown.

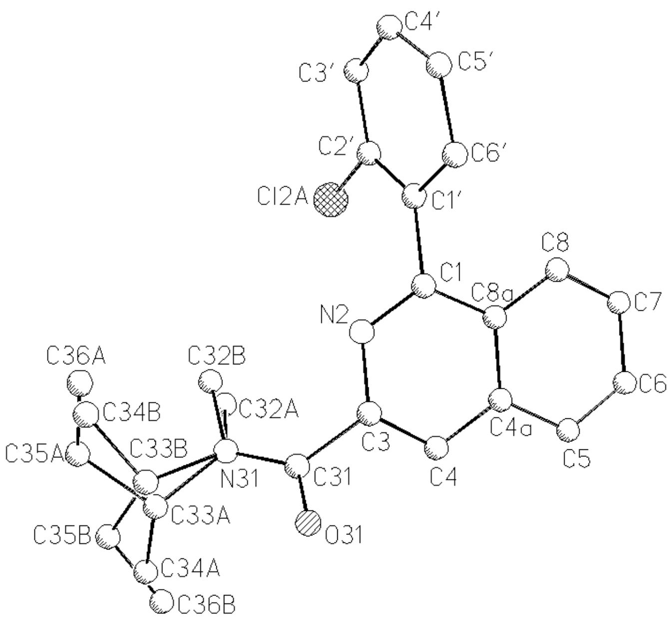


Figure 2
Comparison of the disordered fragments (Siemens, 1989). H atoms have been omitted for clarity.

between these planes is 78.63 (12)°, close to the value of 74.6° found by molecular mechanics for the receptor-bound molecule (Fiorini *et al.*, 1994). The amide plane C3/C31/O31/N31 makes a dihedral angle of 58.40 (12)° with the quinoline plane.

The crystal packing is mainly determined by van der Waals forces and very weak C—H···Cl and C—H···O interactions.

Experimental

Colourless crystals were grown from an acetone solution by slow evaporation.

Crystal data

$C_{21}H_{21}ClN_2O$
M_r = 352.85
Monoclinic, $P2_1/c$
a = 10.365 (2) Å
b = 15.529 (4) Å
c = 11.767 (3) Å
β = 93.33 (2)°
V = 1890.8 (8) Å^3
Z = 4
D_x = 1.240 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 11–23°
μ = 1.86 mm^{-1}
T = 293 (2) K
Block, colourless
0.15 × 0.10 × 0.10 mm

Data collection

CAD-4*F* four-circle diffractometer
$\omega/2\theta$ scans
7214 measured reflections
3385 independent reflections
2278 reflections with $I > 2\sigma(I)$
R_{int} = 0.074
θ_{max} = 67.5°
$h = 0 \rightarrow 12$
$k = -14 \rightarrow 18$
$l = -12 \rightarrow 14$
2 standard reflections
frequency: 33 min
intensity decay: 5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.069
$wR(F^2)$ = 0.164
S = 1.29
3385 reflections
276 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.005P)^2 + 0.5P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.003
$\Delta\rho_{max}$ = 0.64 e Å^{-3}
$\Delta\rho_{min}$ = −0.51 e Å^{-3}

Table 1
Selected torsion angles (°).

N2—C1—C1′—C2′	−78.3 (4)	C32*A*—N31—C33*A*—C35*A*	−64 (1)
C8a—C1—C1′—C2′	103.5 (4)	N31—C33*A*—C35*A*—C36*A*	−54 (1)
N2—C1—C1′—C6′	100.9 (3)	C34*A*—C33*A*—C35*A*—C36*A*	177 (1)
C8a—C1—C1′—C6′	−77.3 (4)	C31—N31—C33*B*—C34*B*	112 (2)
C4—C3—C31—N31	−124.0 (3)	C31—N31—C33*B*—C35*B*	−123 (1)
N2—C3—C31—N31	60.5 (4)	C34*B*—C33*B*—C35*B*—C36*B*	−178 (2)
C3—C31—N31—C33*A*	174.9 (4)	N31—C33*B*—C35*B*—C36*B*	55 (2)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C4—H4···Cl2*A*^{i}	0.93	3.03	3.891 (3)	154
C5—H5···Cl2*A*^{i}	0.93	3.25	4.064 (3)	147
C6—H6···O31^{ii}	0.93	2.78	3.560 (4)	142
C7—H7···O31^{iii}	0.93	2.60	3.468 (4)	155

Symmetry codes: (i) $2-x, \frac{1}{2}+y, \frac{1}{2}-z$; (ii) $2-x, 1-y, 1-z$; (iii) $x-1, y, z$.

The sum of the site-occupancy factors for the disordered fragments was constrained to unity. The Cl atom of lower occupancy was refined isotropically. Constraints were applied to the geometry (bond lengths and angles), as well as to the anisotropic displacement parameters of the fragments of lower occupancy.

Data collection and cell refinement: *CAD*-4 *Software* (Enraf–Nonius, 1989); data reduction: *ENPROC* (Rettig, 1978); structure solution: *SHELXS*97 (Sheldrick, 1990); structure refinement: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *Stereochemical Workstation Operation Manual* (Siemens, 1989).

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