Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

N-(3-Chlorophenyl)-2-(4-isobutylphenyl)-propanamide

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.006 Å
R factor = 0.091
wR factor = 0.256
Data-to-parameter ratio = 19.9

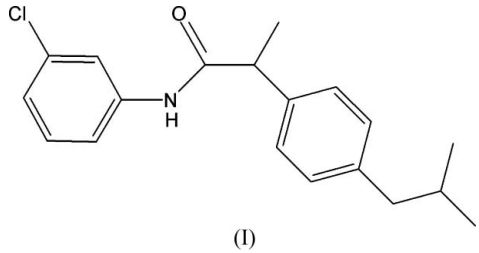
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 23 August 2006
Accepted 30 August 2006

The asymmetric unit of the title compound, $C_{19}H_{22}ClNO$, contains two independent molecules with different conformations of the isobutyl group. The benzene rings in the two molecules make dihedral angles of 71.7 (1) and 76.6 (1)°. Intermolecular N—H···O hydrogen bonds link the molecules into infinite chains along [100].

Comment

Amides are a well known class of drugs having radio- and chemosensitizing properties (Pero *et al.*, 1998) and are used in the treatment of psychiatric patients (Racagni *et al.*, 2004). Iodobenzamide is the radiopharmaceutical imaging agent for the detection of melanoma and its metastases (Moins *et al.*, 2002). Substituted benzamides are potential antipsychotic agents with antidopaminergic properties (Högberg *et al.*, 1991) and inhibitors of steroid-5-reductase (Picard & Hartmann, 2002). Ibuprofen [2-(4-isobutylphenyl)propanoic acid], like naproxen, fenoprofen and benoxaprofen, is a classical non-steroidal anti-inflammatory drug (NSAID) which inhibits the formation of prostaglandins, but a serious side effect is its gastrointestinal toxicity. A number of attempts to prepare derivatives with reduced side effects have been reported. Thus, ibuprofen sugar derivatives showed better anti-inflammatory activity than ibuprofen itself (Song *et al.*, 2004). NSAIDs obtained by linking ibuprofen to furoxan and furazan groups exhibit anti-inflammatory activity comparable with that of ibuprofen, but with much reduced acute gastrotoxicity. The masking of the ibuprofen-free carboxylic group seems to be principally the basis of this reduced topical irritant action (Lolli *et al.*, 2001). Ester and amide prodrugs of ibuprofen are significantly less irritating to the gastric mucosa than ibuprofen (Shanbhag *et al.*, 1992). Amide derivatives of ibuprofen showed improved enantiomer separation using a chiral stationary phase in HPLC (Nicoll-Griffith, 1987). The title compound, (I), was prepared in the above context to obtain more effective NSAIDS with fewer side effects.



(I)

The asymmetric unit of (I) contains two independent molecules (Fig. 1), having similar geometric parameters (Table 1),

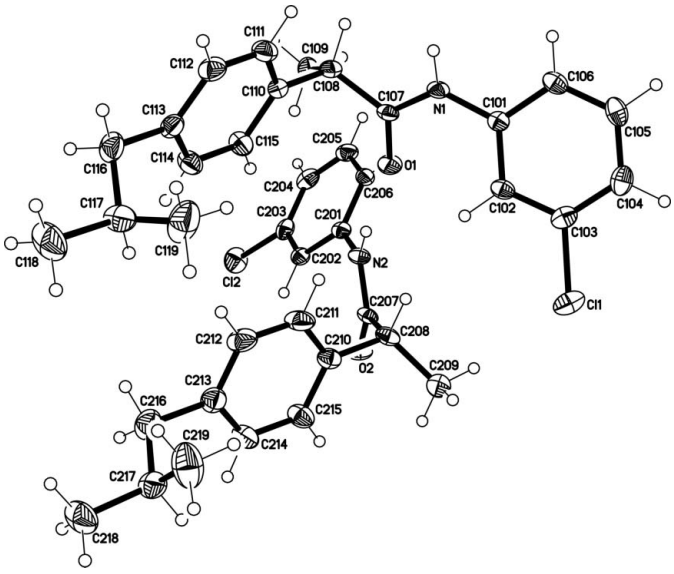


Figure 1
The asymmetric unit of the title compound, showing the atomic labelling and displacement ellipsoids drawn at the 50% probability level.

but differing in the orientation of the isobutyl group. In one molecule this group is positioned *trans* to the methyl group, while in the other molecule a *cis* arrangement is realized. The C112—C113—C116—C117 and C212—C213—C216—C217 torsion angles are −114.6 (5) and −107.9 (5)°, respectively. The mean planes of C101/N1/C107/O1/C108 and the chlorophenyl group make a dihedral angle of 32.6 (1)° [37.8 (1)° for the second molecule], and the two benzene rings make a dihedral angle of 71.7 (1)° [76.6 (1)° in the second molecule]. Intermolecular N—H···O hydrogen bonds (Table 2) link alternate independent molecules into infinite chains along [100], with the isobutylphenyl units oriented in parallel planes (Fig. 2).

Experimental

A solution of 2-(4-isobutylphenyl)propanoyl chloride (2.24 g, 10 mmol) in acetone (75 ml) was added dropwise to a solution of 3-bromoaniline (10 mmol) in acetone (10 ml) and the resulting mixture refluxed for 1 h. The reaction mixture was poured into cold water, whereupon the amide was precipitated as a solid. Repeated recrystallization attempts from ethanol provided colourless crystals (3.6 g, 8.1 mmol, 81%) of only very poor quality. The crystal finally selected for data collection was the best out of seven specimens investigated.

Crystal data

$C_{19}H_{22}ClNO$
M_r = 315.83
Monoclinic, $P2_1/c$
a = 9.8140 (16) Å
b = 32.640 (5) Å
c = 10.7522 (18) Å
β = 91.276 (4)°
V = 3443.3 (10) Å^3
Z = 8
D_x = 1.218 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.22 mm^{-1}
T = 120 (2) K
Prism, colourless
0.42 × 0.39 × 0.28 mm

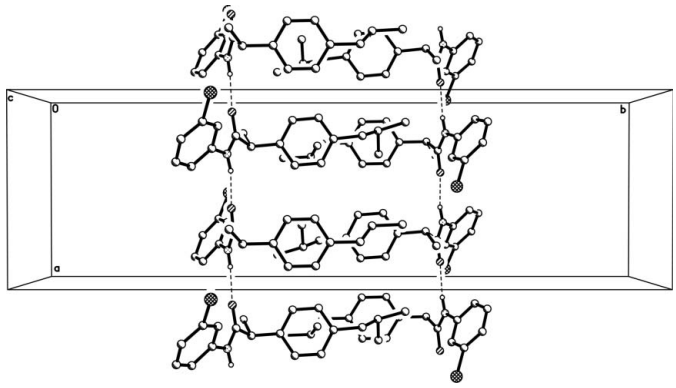


Figure 2
The crystal packing, viewed down the c axis, with intermolecular hydrogen bonds indicated by dashed lines. H atoms not involved in hydrogen bonding have been omitted.

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2002)
T_{min} = 0.922, T_{max} = 0.943
32978 measured reflections
7885 independent reflections
4890 reflections with $I > 2\sigma(I)$
R_{int} = 0.127
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.091
$wR(F^2)$ = 0.256
S = 1.09
7885 reflections
397 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1172P)^2 + 1.5681P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.79 e Å^{-3}
$\Delta\rho_{min}$ = −0.74 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

Cl1—C103	1.735 (4)	Cl2—C203	1.738 (4)
O1—C107	1.229 (4)	O2—C207	1.232 (4)
N1—C107	1.355 (5)	N2—C207	1.344 (5)
N1—C101	1.402 (5)	N2—C201	1.419 (5)
C107—C108	1.506 (5)	C207—C208	1.520 (5)
C108—C110	1.517 (5)	C208—C210	1.518 (5)
C108—C109	1.529 (5)	C208—C209	1.524 (6)
C107—N1—C101	126.4 (3)	C207—N2—C201	125.1 (3)
N1—C107—C108	115.7 (3)	N2—C207—C208	115.5 (3)
C107—C108—C110	109.6 (3)	C210—C208—C207	108.0 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···O2^{i}	0.88	1.95	2.821 (4)	169
N2—H2A···O1	0.88	1.93	2.800 (4)	168

Symmetry code: (i) $x+1, y, z$.

H atoms were located in difference maps and refined in idealized positions riding on the C (C—H = 0.95–0.99 Å) or N (N—H = 0.88 Å) atoms, with U_{iso}(H) = 1.2U_{eq}(C,N) and 1.5U_{eq}(methyl C). Methyl H atoms were refined on the basis of rigid groups allowed to rotate but not tip.

Data collection: *SMART* (Bruker, 2002); cell refinement: *SAINT* (Bruker, 2002); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Bruker, 2002); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

AS gratefully acknowledges a research grant from the Quaid-I-Azam University Islamabad Research Fund (project No. DFNS/ 2006-382).

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