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1-(3-Bromophenyl)-3-[3-(4-isobutylphenyl)-propanoyl]thiourea

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.002 Å
R factor = 0.034
wR factor = 0.087
Data-to-parameter ratio = 20.8

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

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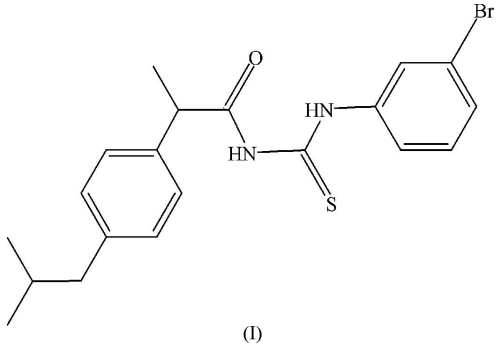
In the crystal structure of the title compound, $C_{20}H_{23}BrN_2OS$, the dihedral angle between the two aromatic rings is 72.51 (6)°. The crystal packing shows dimers formed by intermolecular N—H···S hydrogen bonds.

Comment

1,3-Disubstituted thioureas are extremely versatile building blocks for the synthesis of a variety of heterocyclic compounds and exhibit a wide spectrum of bioactivities. *N*,*N*-Dialkyl-*N*-aroylthioureas are efficient ligands for the separation of platinum group metals (Koch, 2001). 1,3-Dialkyl- or diarylthioureas have shown significant antifungal activity against plant pathogens (Krishnamurthy *et al.*, 1999). *N*-Aryl-*N*-phenylthioureas have been developed as an anion-binding site in a hydrogen-bonding receptor (Nie *et al.* 2004), calix[4]arenes containing thioureas as neutral receptors towards α,α-dicarboxylate anions (Zlatuskova *et al.*, 2004), and others as vanilloid receptor ligands (Park *et al.*, 2004). 1-Benzoyl-3-(4,6-disubstituted-pyrimidine-2-yl)thioureas have shown excellent herbicidal activity (Sijia *et al.*, 2003). 1-Aroyl-3-arylthioureas have recently been used in the synthesis of imidazole-2-thiones (Zeng *et al.*, 2003) and 1,3-thiazolines (Saeed & Pervez, 2006), and have been shown to exhibit excellent phytotoxic, antifungal and antibacterial activities. Ibuprofen [2-(4-isobutyl phenyl)propanoic acid] is a well known nonsteroidal anti-inflammatory drug (NSAID) used to treat the symptoms of



(I)

rheumatism and arthritis. These drugs relieve pain and swelling and reduce inflammation by inhibiting the formation of prostaglandins. Classical NSAIDs, such as ibuprofen, inhibit both isoforms of cyclooxygenase COX-1 and COX-2 involved in the first step of the arachidonic acid cascade. Long term use of NSAIDs results in an increased risk of gastrointestinal ulceration and resulting complications, such as bleeding and perforation (Griswold & Adams, 1996). Inhibition of COX-1 rather than of COX-2 underlies this gastrointestinal toxicity (Wallace & Granger, 1996). Thus, various ibuprofen deriva-

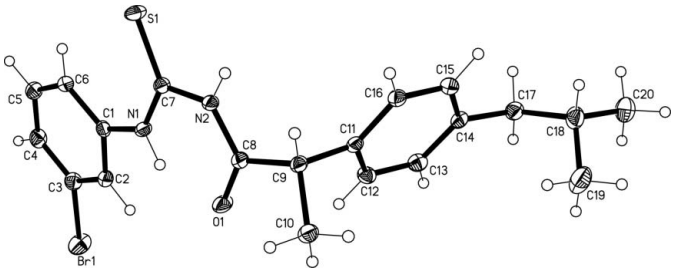


Figure 1
The molecular structure of (I). Displacement ellipsoids are drawn at the 50% probability level.

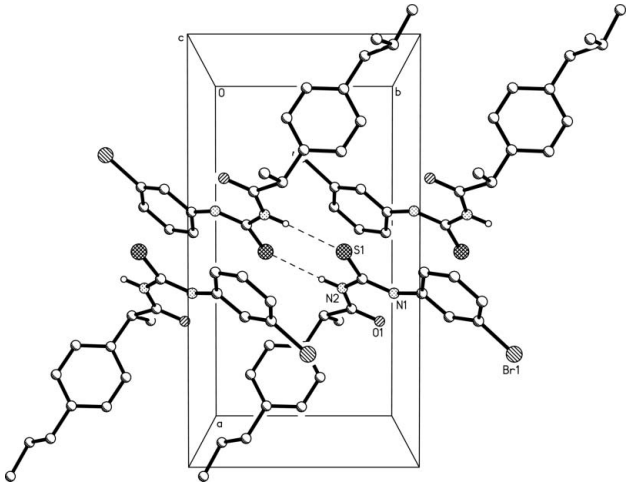


Figure 2
The crystal packing, viewed along [001], with the intermolecular hydrogen-bonding pattern indicated as dashed lines. H atoms not involved in these interactions have been omitted.

tives have been prepared in order to decrease these side-effects. For example, sugar, ester and amide derivatives have shown anti-inflammatory activity comparable with that of ibuprofen, but with 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). In this context, the synthesis of the title ibuprofenyl-arylthiourea, (I), has been carried out.

Compound (I) (Fig. 1) shows the typical thiourea C═S and C═O double bonds as well as shortened C—N bond lengths (Table 1). The thiocarbonyl and carbonyl groups are almost coplanar with the bromophenyl ring, as reflected by the torsion angles C7–N2–C8–O1 [−3.6 (3)°] and C8–N2–C7–N1 [−0.1 (3)°]. This is associated with the expected typical thiourea intramolecular N—H···O hydrogen bond (Table 2). The dihedral angle formed by the two benzene ring planes is 72.51 (6)°. Other geometric parameters present no unusual features.

The crystal packing shows intermolecular N—H···S hydrogen bonds (Table 2, Fig. 2), forming dimers. The Br atom is not involved in any hydrogen bonds.

Experimental

A solution of 2-(4-isobutylphenyl)propanoyl chloride (2.24 g, 10 mmol) in acetone (75 ml) was added dropwise to a suspension of potassium thiocyanate (0.97 g, 10 mmol) in acetone (30 ml) and the reaction mixture was refluxed for 30 min. After cooling to room temperature, a solution of 3-bromoaniline (10 mmol) in acetone (10 ml) was added and the resulting mixture refluxed for 2 h. The reaction mixture was poured into cold water and the thiourea was precipitated as a solid. It was recrystallized from ethanol as colourless crystals (yield 3.6 g, 8.6 mmol, 86%). Spectroscopic analysis: IR (KBr, ν, cm^{-1}): 3351 (free NH), 3200 (assoc. NH), 1667 (CO), 1610 (arom.), 1529 (thioureido I) 1325 II, 1160 III, 744, 762; ^{1}H NMR ($CDCl_3$, δ, p.p.m.): 93 [6H, *d*, $(CH_3)_2CH$, J = 6.6 Hz], 1.58 (3H, *d*, $ArCHCH_3$, J = 7.2 Hz), 1.84–1.90 (1H, *p*, $ArCH_3CH$, J = 6.9 Hz), 2.49 [2H, *d*, $(CH_3)_2CHCH_2Ar$, J = 7.2 Hz], 3.66–3.73 [1H, *q*, $(CH_3)_2CH$, J = 6.9 Hz], 7.1–7.29 (5H, *m*, arom.), 7.74 (1H, *s*, arom.), 7.6 (1H, *s*, arom.), 8.69 (1H, *s*, broad, NH), 12.43 (1H, *s*, broad, NH). Analysis, calculated for $C_{20}H_{23}BrN_2OS$: C 57.28, H 5.53, N 6.68, S 7.65%; found: C 57.28, H 5.53, N 6.68, S 7.65%.

Crystal data

$C_{20}H_{23}BrN_2OS$
M_r = 419.37
Monoclinic, $P2_1/c$
a = 14.4471 (8) Å
b = 7.7226 (4) Å
c = 17.4659 (10) Å
β = 92.406 (1)°
V = 1946.94 (18) Å^3
Z = 4
D_x = 1.431 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 2.23 mm^{-1}
T = 120 (2) K
Prism, colourless
0.42 × 0.40 × 0.28 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2002)
T_{min} = 0.423, T_{max} = 0.534
18926 measured reflections
4711 independent reflections
4100 reflections with $I > 2\sigma(I)$
R_{int} = 0.029
θ_{max} = 28.1°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.034
$wR(F^2)$ = 0.087
S = 1.05
4711 reflections
226 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0454P)^2 + 1.0691P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.98 e Å^{-3}
$\Delta\rho_{min}$ = −0.92 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

Br1—C3	1.8930 (19)	N1—C1	1.415 (2)
S1—C7	1.6699 (18)	N2—C8	1.378 (2)
O1—C8	1.225 (2)	N2—C7	1.390 (2)
N1—C7	1.335 (2)		
C7—N1—C1	132.37 (16)	N1—C7—N2	114.32 (15)
C8—N2—C7	128.34 (15)	N2—C8—C9	115.34 (15)
C8—N2—C7—N1	−0.1 (3)	C7—N2—C8—O1	−3.6 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1	0.88	1.85	2.605 (2)	143
N2—H2A···S1^{i}	0.88	2.56	3.4209 (15)	168

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

H atoms were located in difference syntheses, refined in idealized positions riding on their parent atoms, with C—H = 0.95–1.0 Å and N—H = 0.88 Å and with U_{iso}(H) = 1.2U_{eq}(C,N) or 1.5U_{eq}(methyl-C).

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*.

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