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2-Amino-4-(4-chloro-3-methylphenyl)-5-propyl-1,3-thiazolium iodide

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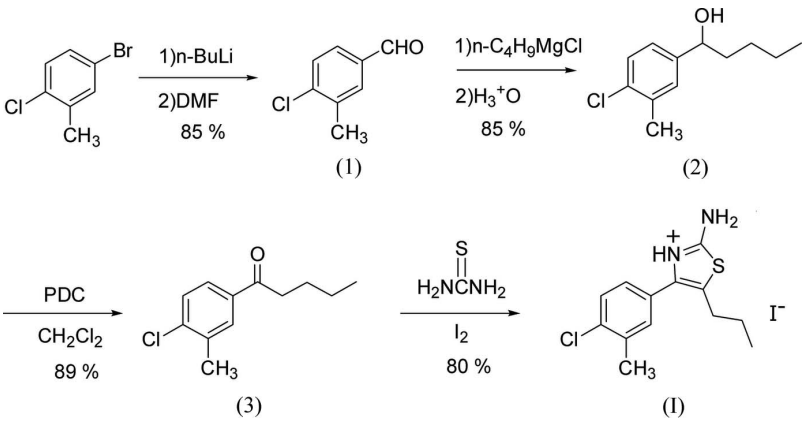
In the crystal structure of the title compound, $C_{13}H_{16}ClN_2S^+\cdot I^-$, the molecule of 2-amino-4-(4-chloro-3-methylphenyl)-5-propyl-1,3-thiazole is protonated on the ring N atom. The angle between the planes formed by the 1,3-thiazole and benzene rings is 39.3 (1)°, and this conformation is caused by the presence of the propyl group in position 5 of the heterocyclic ring. The packing in the crystal structure is mainly stabilized by $^+NH\cdots I^-$ and $NH\cdots I^-$ hydrogen bonds and stacking of 2-amino-4-(4-chloro-3-methylphenyl)-5-propyl-1,3-thiazolium cations.

Comment

Thiazole derivatives have found application not only in industry as corrosion inhibitors (Form *et al.*, 1974; Quraishi & Sharma, 2005) but also as pharmacologically active substances (Nakamura *et al.*, 1995; Au-Alvarez *et al.*, 1999; van Tilburg *et al.*, 2001; Kennedy *et al.*, 2004). The thiazole ring is a building block of many naturally occurring molecules that are involved in different biological activities and is used as the building block in organic syntheses (Arcadi *et al.*, 1999; Masquelin & Obrecht, 2001; Sadigova *et al.*, 2004). The title compound, (I), was synthesized as a novel analog in an anticancer drug discovery program and belongs to a group of 2-amino-4-phenyl-1,3-thiazole derivatives (Au-Alvarez *et al.*, 1999) that have 12 representatives (assuming a lack of substitution of the amino group) in the Cambridge Structural Database (CSD; Allen, 2002) as of November 2006. There are two additional compounds that have a naphthyl group instead of the benzene ring. Most of these structures were analyzed in terms of hydrogen-bonding networks, because the 2-amino-1,3-thiazole group can be a donor for two and an acceptor for three hydrogen bonds (Lynch *et al.*, 2002; Lynch & McClenaghan, 2004).



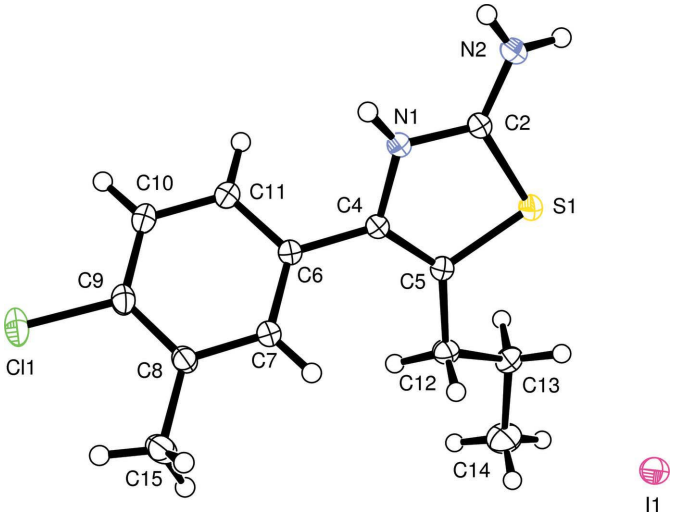


Figure 1
The molecular structure of the title compound. Displacement ellipsoids are drawn at the 50% probability level and H atoms are drawn as spheres of an arbitrary radius.

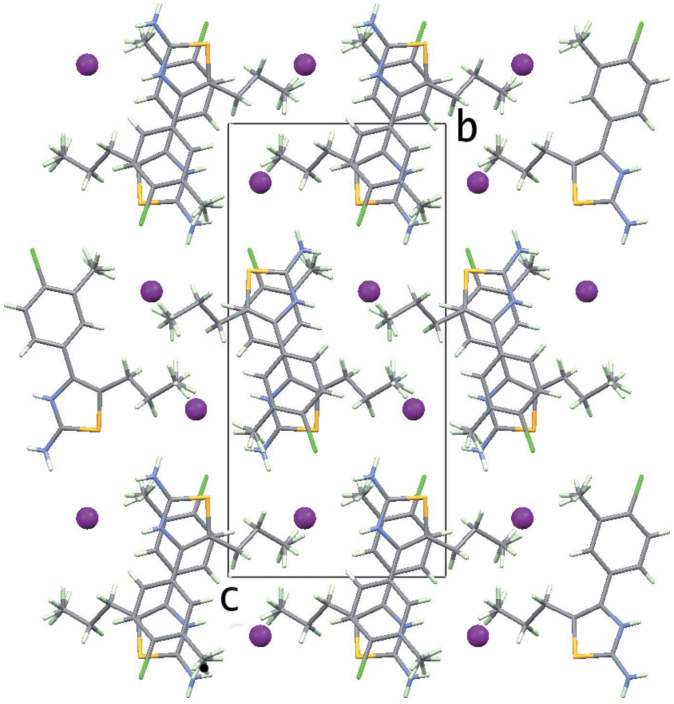


Figure 2
The crystal packing of (I), shown along [100]. H atoms are shown in light green and iodide ions are drawn as purple spheres.

The angle between the ring planes is 39.3 (1)°, while the torsion angle C11—C6—C4—N1 has value 36.9 (1)° (Table 1). If compared with the other 12 structures (refcodes APTZOL, HIYLOQ, PAJQIB, TAHWUV, UFEBAI, WAKJAU, XEGWAH, XUNJUL, XUNKAS, XUNKEW, XUNKIA and XUNKOG) from this family reported in the CSD, only in four is the angle larger (refcodes UFEBAI, WAKJAU, XUNJUL and XEGWAH). The range for the angle between the rings is 5.1–51.5°. The twist is mainly caused by bulky groups attached to position 5 of the 1,3-thiazole ring or to the *ortho* position of the benzene ring. However, the compound with the smallest twist between the rings has a hydroxyl group in the *ortho* position (XUNKEW). In this case the intramolecular hydrogen bond between the hydroxy group and the N atom from the 1,3-thiazole ring causes the molecule to be almost planar (Lynch *et al.*, 2002).

The delocalization of the double bond in the N1—C2—N2 system of the title compound is very similar to delocalization observed in the case of 2-amino-4-*p*-tolyl-1,3-thiazolium chloride dihydrate (Lynch & McClenaghan, 2004). In (I), the C2—N2 bond length (Table 1) is shorter than the average [1.344 (2) Å] for the other 12 members of the family in the CSD. The N1—C2 bond is longer than the average [1.317 (1) Å] for the same group. Delocalization also extends to the C2—S1 bond, which in the case of (I) is shorter than the average [1.75 (3) Å] for the same group.

The network of hydrogen bonds and stacking of the cations are the most important interactions for the crystal packing. In (I), the 2-amino-4-(4-chloro-3-methylphenyl)-5-propyl-1,3-thiazolium cations stack in columns that are parallel to the [100] direction. The cations in the columns are arranged in an alternating pattern. Similar columns are also observed in three (PAJQIB, WAKJAU and XUNKIA) of the 12 previously mentioned members of the family of 2-amino-4-phenyl-1,3-thiazole derivatives found in the CSD. Three hydrogen bonds (Table 2) are found in the crystal structure of (I) and in all of them the I^- anion is the acceptor, while the amino group and the protonated N atom from the 1,3-thiazole ring are the donors of H atoms. The network of hydrogen bonds extends along the [010] direction, perpendicular to the stacks of protonated 2-amino-4-(4-chloro-3-methylphenyl)-5-propyl-1,3-thiazole molecules.

All cations in the crystal structure of (I) possess the same axial chirality. The synthetic compound was used for crystallization, which evidently spontaneously formed chirally pure crystals. Interestingly three (HIYLOQ, PAJQIB and WAKJAU) of the 12 2-amino-4-phenyl-1,3-thiazole derivatives reported in the CSD also have axial chirality and create chiral crystals.

Experimental

To a cold solution (195 K) of 4-bromo-1-chloro-2methylbenzene (5.0 g, 24.3 mmol) in THF (40 ml) was added slowly *n*-BuLi (18.3 ml, 29.2 mmol, 1.6 *M* in hexane). The reaction mixture was warmed naturally to 283 K for about 3 h and then recooled to 195 K. DMF (3.77 ml, 24.2 mmol) was added slowly to the reaction mixture, which was allowed to warm naturally and was stirred overnight, quenched with saturated NH_4Cl (20 ml), extracted with diethyl ether, dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography to give 4-chloro-3-methylbenzaldehyde, (1), as a pale-yellow oil (3.21 g, 85%).

Compound (1) (1.5 g, 9.70 mmol) was added to a solution of butylmagnesium chloride (5.82 ml, 11.64 mmol, 2.0 *M* in diethyl ether) in THF (30 ml). The mixture was stirred at room temperature for 1 h, quenched with saturated NH_4Cl (20 ml), extracted with

diethyl ether, dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography to give 1-(4-chloro-3-methylphenyl)pentan-1-ol, (2), as a clear oil (1.75 g, 85%).

To a solution of (2) (1.5 g, 7.05 mmol) in CH_2Cl_2 (20 ml) was added pyridinium dichromate (3.98 g, 10.6 mmol) and 4 Å molecular sieves (1.0 g, powder). The mixture was stirred at room temperature overnight, filtered and concentrated. The residue was purified by column chromatography to give 1-(4-chloro-3-methylphenyl)pentan-1-one, (3), as a sticky oil (1.32 g, 89%).

To a stirred solution of (3) (0.54 g, 2.56 mmol) in absolute ethanol (10 ml) was added thiourea (0.78 g, 10.25 mmol) and iodine (0.72 g, 2.84 mmol). The mixture was heated at 383 K for 2 h in an open vessel (extra ethanol was added if the mixture was dry) and cooled to room temperature. Water was added to the crude residue; the precipitate was collected by filtration and washed with diethyl ether and water to afford (I) as a pink solid (0.80 g, 79%). M.p. 447–449 K. Analysis calculated for $C_{13}H_{16}ClIN_2S$: C 39.56, H 4.09, N 7.10%; found: C 39.64, H 4.14, N 7.06%.

The crystal for data collection was obtained at room temperature by slow evaporation of 2-amino-4-(4-chloro-3-methylphenyl)-5-propyl-1,3-thiazolium iodide solution in methanol.

Crystal data

$C_{13}H_{16}ClN_2S^+\cdot I^-$
M_r = 394.69
Orthorhombic, $P2_12_12_1$
a = 7.761 (1) Å
b = 9.659 (1) Å
c = 20.145 (1) Å
V = 1510.1 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 2.42 mm^{-1}
T = 103 K
0.53 × 0.26 × 0.26 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
Absorption correction: multi-scan (Otwinowski *et al.*, 2003)
T_{min} = 0.47, T_{max} = 0.53
107797 measured reflections
16521 independent reflections
14434 reflections with $I > 2\sigma(I)$
R_{int} = 0.037

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.027
$wR(F^2)$ = 0.072
S = 1.01
16517 reflections
176 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 1.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.98 e Å^{-3}
Absolute structure: Flack (1983), 7019 Friedel pairs
Flack parameter: 0.001 (6)

Table 1
Selected geometric parameters (Å, °).

S1—C2	1.719 (1)	C5—C4	1.359 (1)
S1—C5	1.755 (1)	C6—C4	1.473 (1)
N1—C2	1.337 (1)	C2—N2	1.322 (1)
N1—C4	1.403 (1)		
C2—S1—C5	91.33 (4)	N1—C4—C6	117.82 (7)
C4—C5—S1	110.30 (6)	N2—C2—N1	123.64 (8)
C12—C5—S1	119.34 (6)	N2—C2—S1	125.34 (7)
C5—C4—N1	112.43 (7)	N1—C2—S1	111.02 (6)
C5—C4—C6	129.74 (7)		
C7—C6—C4—C5	40.3 (1)	C7—C6—C4—N1	−141.0 (1)
C11—C6—C4—C5	−141.9 (1)	C11—C6—C4—N1	36.9 (1)

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···I1^{i}	0.84 (2)	2.77 (2)	3.529 (1)	153 (2)
N2—H2···I1^{i}	0.78 (2)	2.88 (2)	3.585 (1)	152 (2)
N2—H3···I1^{ii}	0.87 (2)	2.71 (2)	3.531 (1)	158 (2)

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

The H atoms attached to N atoms were located in a difference map and all their parameters were refined. Methyl groups were refined as disordered, each over two sites of equal occupancy, with C—H distances of 0.96 Å and U_{iso}(H) = 1.5U_{eq}(C). All other H atoms bound to C atoms were placed in geometric positions and treated as riding with C—H = 0.93 or 0.97 Å and U_{iso}(H) = 1.2U_{eq}(C). The highest residual electron density peak is located 0.85 Å from the I1 atom.

Data collection: *HKL-2000* (Otwinowski & Minor, 1997); cell refinement: *HKL-2000*; data reduction: *HKL-2000*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990) and *HKL-3000SM* (Minor *et al.*, 2006); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997) and *HKL-3000SM*; molecular graphics: *HKL-3000SM*, *ORTEPIII* (Burnett & Johnson, 1996), *ORTEP-3* (Farrugia, 1997) and *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *HKL-3000SM*.

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