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3-(4-Chlorophenyl)-5-methyl-2-propylamino-8,9,10,11-tetrahydro-2-benzothieno[2′,3′;2,3]-pyrido[4,5-*d*]pyrimidin-4(3*H*)-one

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Key indicators

Single-crystal X-ray study
T = 292 K
Mean σ(C–C) = 0.003 Å
Disorder in main residue
R factor = 0.052
wR factor = 0.156
Data-to-parameter ratio = 17.2

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

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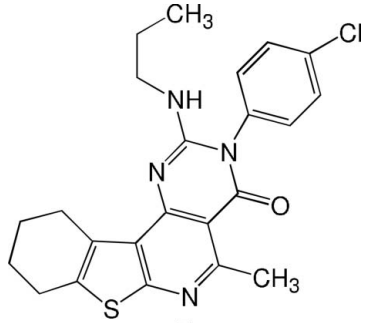
The asymmetric unit of the title compound, $C_{23}H_{23}ClN_4OS$, contains two crystallographically independent molecules in which the orientations of the propylamine group and chlorophenyl rings with respect to the fused ring system are different. The terminal cyclohexene ring adopts a half-chair conformation. The crystal packing is stabilized by N—H···O, N—H···N and C—H···O hydrogen bonds and π–π interactions.

Comment

Many pyridopyrimidines exhibit pharmaceutical and germicidal activities (Anderson & Broom, 1977). Over two hundred tetrahydro- and octahydropyrido[4,3-*d*]pyrimidines have been synthesized as potential diuretic, antirheumatic and bacteriostatic drugs, but only a few fully aromatic pyrido[4,3-*d*]pyri-]pyrimidines are known. An important synthetic route for pyrido[4,3-*d*]pyrimidine is the condensation reaction of 4-aminonicotinic acid and amines (Ismail & Wibberley, 1967). However, this method often requires long reaction times. Recently, we have developed a new and facile regioselective annulation process, which proceeded smoothly under mild conditions *via* a tandem aza-Wittig and cyclization reaction, to synthesize novel pyridopyrimidine derivatives (Zhou *et al.*, 2005). In this paper, we report the structure of the title compound, (I).



(I)

The asymmetric unit contains two crystallographically independent molecules in which the orientations of the propylamine group and chlorophenyl rings with respect to the fused ring system are different (Fig. 1). The bond lengths and angles in the thieno[2,3-*b*]pyridine ring system (Table 1) are in agreement with the corresponding values observed in a similar compound (Patel *et al.*, 2003). The C—S bond lengths are longer than the values observed in both free thiophene (1.714 Å; Bonham & Momany, 1963), measured using electron diffraction, and thieno[2,3-*c*]pyridine [1.728 (1) and

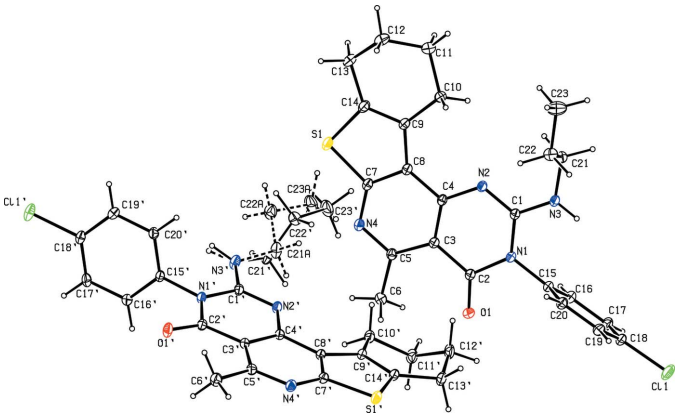


Figure 1
The asymmetric unit of (I), showing 50% probability displacement ellipsoids. Both components of the disordered propylamine group are shown.

1.731 (1) Å; Nerenz *et al.*, 1997]. The C7—S1—C14 angle is narrower than that observed in free thiophene [92.2 (2)°]. The C5—N4—C7 angles are smaller than 120° (Ghosh & Simonsen, 1993). The C=N bond lengths (Table 1) are longer than the typical C=N distance of 1.28 Å (Zhao *et al.*, 2005). In both independent molecules, the central aromatic ring system consisting of thiophene, pyridine and pyrimidine rings is essentially planar, and the terminal cyclohexene ring adopts a half-chair conformation. The crystal packing is stabilized by N—H···O, N—H···N and C—H···O hydrogen bonds (Table 2). The C15′–C20′ ring and the N4/C3–C5/C7–C8 ring of the inversion-related molecule at $(1-x, 1-y, 1-z)$ are stacked with a centroid–centroid distance of 3.754 (1) Å, indicating a weak π–π stacking interaction.

Experimental

6-Methyl-4-amino-5-ethoxycarbonyltetrahydrobenzo[4,5]thieno-[3,2;5,6]pyridine was prepared according to the literature procedure (Veronese *et al.*, 1995) in 64% yield. Iminophosphorane was also synthesized according to a literature method (Wamhoff *et al.*, 1993) in 93% yield. To a solution of iminophosphorane (0.525 g, 1 mmol) in anhydrous CH_2Cl_2 (10 ml) was added 4-chlorophenyl isocyanate (1.1 mmol) under N_2 atmosphere at room temperature. The reaction mixture was left unstirred for 5 h, and then the solvent was removed under reduced pressure and Et_2O/petroleum ether was added to precipitate triphenylphosphine oxide. Removal of the solvent gave carbodiimide, which was used directly without further purification. To the solution of the carbodiimide prepared above in CH_2Cl_2 (10 ml) was added *n*-propylamine (1.1 mmol). The reaction mixture was stirred for 30 min, and then the solvent was removed and anhydrous ethanol (10 ml) with several drops of CH_3CH_2ONa in CH_3CH_2OH was added. The mixture was stirred for 11 h at room temperature, the solution was condensed and the residue was recrystallized from CH_3CH_2OH to give the title compound. Single crystals were obtained by evaporation of a methanol solution (m.p. 501–503 K). Analysis calculated for $C_{23}H_{23}ClN_4OS$: C 62.93, H 5.28, N 12.76%; found: C 63.26, H 5.23, N 12.45%. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz): δ 0.91 (*t*, *J* = 7.2 Hz, 3H, CH_3), 1.62 (*q*, *J* = 7.2 Hz, 2H, CH_2), 1.92 (*s*, 4H, $2CH_2$), 2.87 (*s*, 2H, CH_2), 2.94 (*s*, 3H, CH_3 of pyridyl), 3.29 (*s*, 2H, CH_2), 3.44 (*m*, 2H, NCH_2), 4.41 (*s*, 1H, NH), 7.27–7.60 (*m*, 4H, Ar—H). MS (EI, *m*/*z*, %): 439 (M^++1 35.14), 438 (100), 398 (14.08), 396 (17.21), 395 (24.23), 110 (15.44).

Crystal data

$C_{23}H_{23}ClN_4OS$
M_r = 438.96
Triclinic, $P\overline{1}$
a = 11.8884 (6) Å
b = 13.3784 (7) Å
c = 15.7892 (8) Å
α = 114.054 (1)°
β = 98.926 (1)°
γ = 101.335 (1)°
V = 2169.42 (19) Å^3
Z = 4
D_x = 1.344 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3870 reflections
θ = 2.3–26.9°
μ = 0.30 mm^{-1}
T = 292 (2) K
Block, colourless
0.40 × 0.30 × 0.30 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.891, T_{max} = 0.917
25134 measured reflections
9849 independent reflections
6468 reflections with $I > 2\sigma(I)$
R_{int} = 0.040
θ_{max} = 27.5°
$h = -15 \rightarrow 15$
$k = -17 \rightarrow 17$
$l = -20 \rightarrow 20$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.053
$wR(F^2)$ = 0.156
S = 1.03
9849 reflections
574 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0778P)^2 + 0.1323P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.32 e Å^{-3}
$\Delta\rho_{min}$ = −0.21 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

S1—C7	1.737 (2)	S1′—C7′	1.734 (2)
S1—C14	1.738 (3)	S1′—C14′	1.735 (3)
O1—C2	1.209 (2)	O1′—C2′	1.220 (2)
N2—C1	1.308 (2)	N2′—C1′	1.307 (2)
N2—C4	1.367 (3)	N2′—C4′	1.369 (3)
N4—C5	1.334 (3)	N4′—C5′	1.327 (3)
N4—C7	1.349 (3)	N4′—C7′	1.343 (3)
C7—S1—C14	91.00 (11)	C7′—S1′—C14′	91.06 (10)
C1—N2—C4	118.07 (18)	C1′—N2′—C4′	117.71 (17)
C5—N4—C7	116.82 (18)	C5′—N4′—C7′	116.56 (18)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3′—H3′*B*···N4^{i}	0.90	2.30	3.072 (3)	144
N3—H3···O1′^{ii}	0.86	2.22	2.912 (2)	138
C13′—H13*C*···O1^{iii}	0.97	2.38	3.285 (3)	154

Symmetry codes: (i) $-x+1, -y+1, -z+1$; (ii) $x, y, z-1$; (iii) $-x+1, -y, -z$.

In one of the independent molecules, the propylamine group is disordered over two orientations with occupancies of 0.515 (8) and 0.485 (8). The disorder was modelled with C—C and C···C distances restrained to 1.54 (1) and 2.51 (1) Å, respectively. All the H atoms were placed in idealized positions and constrained to ride on their parent atoms, with N—H = 0.86 and 0.90 Å, C—H = 0.93–0.97 Å, and with U_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms and 1.2U_{eq}(C,N) for other H atoms.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT* (Bruker, 1998); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997*a*); program(s) used to refine

structure: *SHELXL97* (Sheldrick, 1997*a*); molecular graphics: *SHELXTL* (Sheldrick, 1997*b*); software used to prepare material for publication: *SHELXTL*.

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