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2-[(*E*)-(4-Chlorophenyl)methyleneamino]-*N*-(*X*-methylphenyl)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxamide, where *X* = 2 and 3

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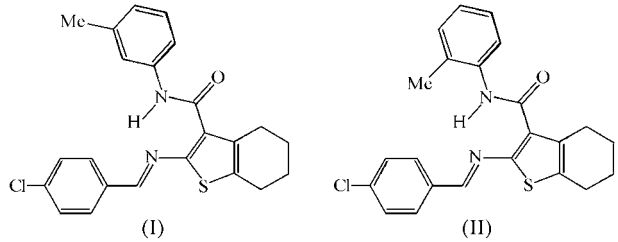
The title compounds, both $C_{23}H_{21}ClN_2OS$, are isomeric, with (I) and (II) being the *N*-3-methylphenyl and *N*-2-methylphenyl derivatives, respectively. The dihedral angle between the 4-chlorophenyl group and the thiophene ring in (II) [38.1 (1)°] is larger than that in (I) [7.1 (1)°], indicating steric repulsion between the chlorophenyl and *o*-toluidine groups in (II). In both compounds, an intramolecular N—H···N hydrogen bond forms a pseudo-six-membered ring, thus locking the molecular conformation. In the crystal structures, molecules are connected *via* N—H···O hydrogen bonds, forming chains along the *b* axis in (I) and along the *c* axis in (II). Intermolecular C—H···O/S and π–π interactions are also observed in (II), but not in (I).

Comment

The design and synthesis of compounds which possess important pharmacological properties, such as antibacterial, anticancer, anti-inflamatory and antitoxic properties, is an area of research with widespread potential application in medicine (Pellis & West, 1968; Cohen *et al.*, 1977; Csaszar & Morvay, 1983; Lakshmi *et al.*, 1985), and in this regard we have selected thiophene derivatives (El-Maghraby *et al.*, 1984; Dzhurayev *et al.*, 1992; Gewald *et al.*, 1966), which have been found to exhibit these activities. In this context, S-containing Schiff bases are most effective. We have already reported the crystal structures of biologically active thiophene-3-carboxamide derivatives (Vasu *et al.*, 2003, 2004). In this paper, structure analyses are presented for the two title compounds, (I) and (II), which show antibacterial and antifungal activities (Mohan & Saravanan, 2002, 2003). The compounds are isomers of each other, differing only in the position of attachment of the methyl at the *meta* and *ortho* positions.

Compounds (I) (Fig. 1 and Table 1) and (II) (Fig. 2 and Table 3) contain three different structural moieties and these will be discussed separately. The thiophene ring is essentially planar. The six-membered cyclohexene ring adopts a half-chair conformation, with atoms C6 and C7 deviating from the C5/C3/C4/C8 plane by −0.246 (7) and 0.218 (7) Å, respectively, in (I), and by −0.249 (5) and 0.320 (1) Å, respectively, in (II). The puckering parameters (Cremer & Pople, 1975) generated by *PLATON* (Spek, 1990) for the cyclohexene ring are q_2 = 0.138 (4) Å, φ_2 = −151. (2)° and τ = 25 (1)° in (I), with corresponding values of 0.126 (3) Å, −131 (2)° and 26 (1)° in (II).



The bond angles in the toluidine ring, C20—C21—C22 in (I) [118.6 (1)°] and C17—C22—C21 in (II) [117.6 (2)°], deviate significantly from the ideal value of 120°. This deviation is due to the electron-donating inductive effect of the methyl group (Vasu *et al.*, 2003, 2004). The angle between the mean planes of the *m*-toluidine and thiophene rings is 18.4 (1)° in (I), whereas that between the *o*-toluidine and thiophene rings is 12.9 (1)° in (II). The C16—N2—C17—C18 torsion angle is 11.4 (5)° in (I) and 27.4 (4)° in (II), indicating that the presence of a methyl group in the *ortho* position in (II) causes rotation about the N2—C17 bond to minimize steric repulsion with the amino H atom. An intramolecular N—H···N hydrogen bond (Tables 2 and 4) in each structure locks the molecule into a rigid pseudo-six-membered ring conformation and removes the conformational flexibility.

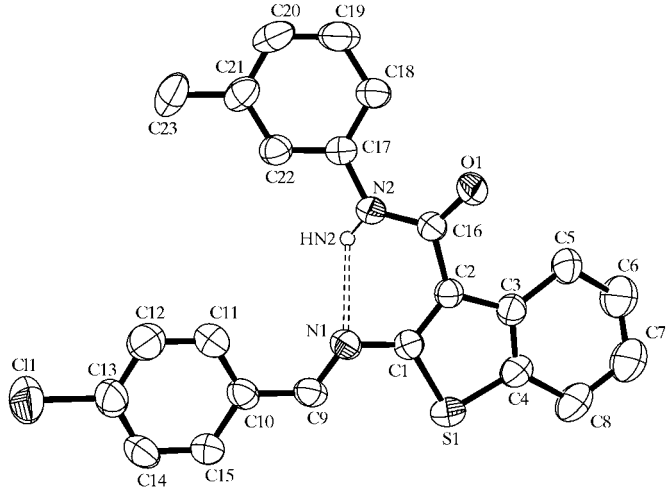


Figure 1
The molecular structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms not involved in hydrogen bonding have been omitted for clarity. The broken lines show the N—H···N intramolecular hydrogen bond.

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The amino H atom is also involved in an intermolecular N—H···O hydrogen bond, and molecular chains are formed. In (I), these chains are along the *b* axis, related by a *b*-glide plane ($\frac{1}{2}-x, \frac{1}{2}+y, z$) orthogonal to the *a* axis (Fig. 3). In (II), the chains are along the *b* axis, related by a *c*-glide plane ($x, \frac{1}{2}-y, z+\frac{1}{2}$) orthogonal to the *b* axis (Fig. 4). There are no intermolecular C—H···O/S or π–π interactions in (I). On the other hand, in (II), the chlorophenyl rings are oriented in a manner that facilitates intermolecular π–π interactions, the centre-to-centre distance between the chlorophenyl rings being 3.863 Å. In (II), there are also intermolecular C—H···O/S interactions (Fig. 4 and Table 4).

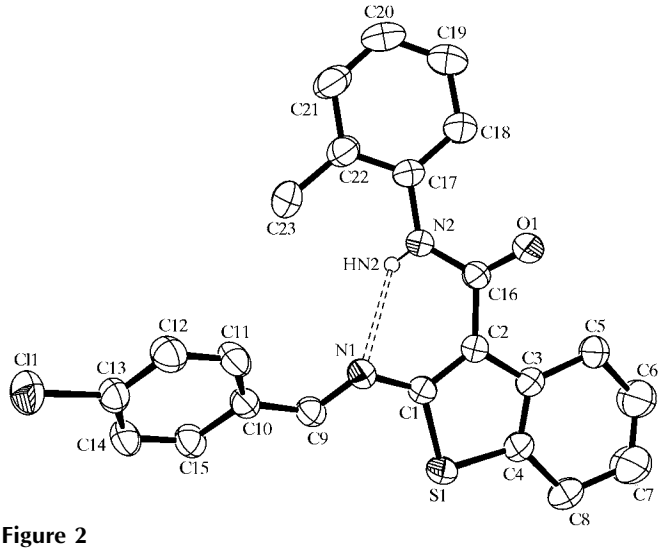

Figure 2
The molecular structure of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms not involved in hydrogen bonding have been omitted for clarity. The broken lines show the N—H···N intramolecular hydrogen bond.

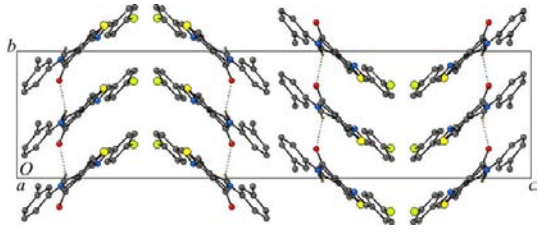

Figure 3
A packing diagram for (I). The dotted lines show the formation of N—H···O hydrogen-bonded chains.

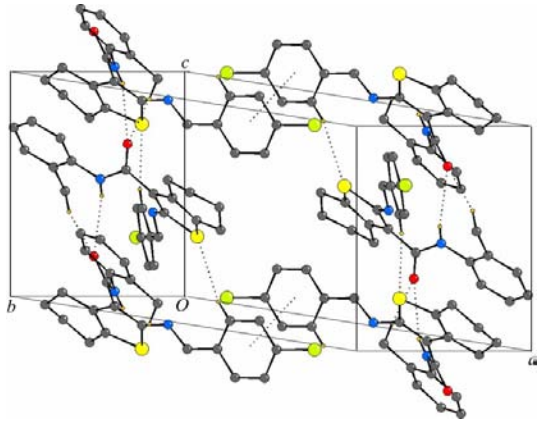

Figure 4
A packing diagram for (II). The dotted lines show N—H···O hydrogen bonds, and C—H···O, C—H···S and π–π interactions.

Experimental

The title compounds were synthesized using the Gewald reaction (Gewald *et al.*, 1966). For compound (I), *m*-cyanotoluidine was refluxed with cyclohexanone in the presence of sulfur, dimethylamine and ethanol at 313–323 K for 1 h. The resulting product was then treated with 4-chlorobenzaldehyde in an equimolar ratio in the presence of ethanol, which yielded (I). This was then recrystallized from a mixture of dichloromethane and ethyl acetate (1:2) by slow evaporation. Yellow crystals of (I) were obtained after four weeks and used for single-crystal data collection. For compound (II), a similar procedure was followed using *o*-cyanotoluidine, and later 4-chlorobenzaldehyde was added. The compound was purified and crystallized using the same procedure as for (I).

Compound (I)

Crystal data

$C_{23}H_{21}ClN_2OS$
$M_r = 408.93$
Orthorhombic, *Pbca*
$a = 13.785\ (11)$ Å
$b = 8.554\ (7)$ Å
$c = 34.74\ (3)$ Å
$V = 4096\ (6)$ Å^3
$Z = 8$
$D_x = 1.326$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 650 reflections
$\theta = 1.6$–$26.4°$
$\mu = 0.31$ mm^{-1}
$T = 293\ (2)$ K
Block, yellow
0.30 × 0.25 × 0.15 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min} = 0.908$, $T_{max} = 0.956$
29 534 measured reflections
4113 independent reflections
2436 reflections with $I > 2\sigma(I)$
$R_{int} = 0.069$
$\theta_{max} = 26.4°$
$h = -16 \rightarrow 15$
$k = -10 \rightarrow 10$
$l = -42 \rightarrow 42$

Refinement

Refinement on F^2
$R(F) = 0.060$
$wR(F^2) = 0.136$
$S = 1.02$
4113 reflections
262 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0454P)^2 + 2.7373P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.29$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °) for (I).

N2—C16	1.350 (4)	N1—C9	1.274 (3)
N2—C17	1.411 (4)	N1—C1	1.382 (4)
C21—C22—C17	121.5 (3)	C22—C21—C20	118.6 (3)
C9—N1—C1—S1	−11.1 (4)	C16—N2—C17—C18	11.4 (5)
C1—C2—C16—N2	−28.7 (4)	C11—C10—C9—N1	4.4 (4)

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—HN2···N1	0.85 (3)	2.32 (3)	2.887 (4)	125 (3)
N2—HN2···O1^{i}	0.85 (3)	2.26 (3)	3.009 (4)	147 (3)

Symmetry code: (i) $\frac{3}{2}-x,\frac{1}{2}+y,z$.

Compound (II)

Crystal data

$C_{23}H_{21}ClN_2OS$
M_r = 408.94
Monoclinic, $P2_1/c$
a = 17.511 (4) Å
b = 12.519 (3) Å
c = 9.232 (2) Å
β = 97.406 (4)°
V = 2006.9 (8) Å^3
Z = 4
D_x = 1.354 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 725 reflections
θ = 1.7–25.4°
μ = 0.31 mm^{-1}
T = 293 (2) K
Block, yellow
0.30 × 0.15 × 0.10 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.921, T_{max} = 0.970
15 187 measured reflections
3994 independent reflections
3307 reflections with $I > 2\sigma(I)$
R_{int} = 0.018
θ_{max} = 26.4°
$h = -21 \rightarrow 21$
$k = -15 \rightarrow 15$
$l = -11 \rightarrow 11$

Refinement

Refinement on F^2
$R(F)$ = 0.048
$wR(F^2)$ = 0.157
S = 0.91
3994 reflections
262 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.1224P)^2 + 0.6875P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.43 e Å^{-3}
$\Delta\rho_{min}$ = −0.42 e Å^{-3}

Table 3
Selected geometric parameters (Å, °) for (II).

N2—C16	1.336 (3)	N1—C9	1.281 (2)
N2—C17	1.421 (3)	N1—C1	1.389 (3)
C17—C22—C21	117.6 (2)	C20—C21—C22	122.3 (2)
N2—C16—C2—C1	−38.2 (3)	C16—N2—C17—C18	27.4 (4)
C9—N1—C1—S1	−25.1 (2)	C11—C10—C9—N1	−11.1 (3)

Table 4
Hydrogen-bonding geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2N···N1	0.77 (3)	2.52 (3)	2.985 (3)	121 (2)
N2—H2N···O1^{i}	0.77 (3)	2.52 (3)	3.250 (3)	159 (3)
C11—H11···S1^{ii}	0.93	2.84	3.747 (2)	166
C23—H23*C*···O1^{i}	0.96	2.48	3.406 (3)	163

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

For both compounds, amino atom H2N and atom H9 (bonded to C9) were located from difference Fourier maps and were refined isotropically. All other H atoms were constrained to ride on their parent atoms, with C—H = 0.93–0.97 Å and U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(C_{methyl}). The methyl groups were allowed to rotate freely about their C—C bond. In both compounds, the C6—C7 bond length is shorter than the expected value. These C atoms of the cyclohexene moiety have a large vibrational degree of freedom and this is reflected in the large atomic displacement parameters, resulting in the short C—C bond length.

For both compounds, data collection: *SMART* (Bruker, 1998); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 1998); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1993); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997) and *CAMERON* (Watkin *et al.*, 1993); software used to prepare material for publication: *PLATON* (Spek, 2003).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: OB1203). Services for accessing these data are described at the back of the journal.

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