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Two biologically active thiophene-3-carboxamide derivatives

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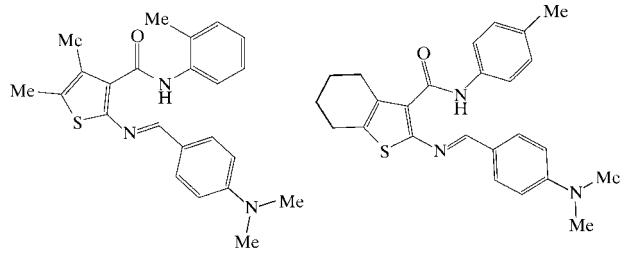
The two title compounds, 2-({(1*Z*)-[4-(dimethylamino)-phenyl]methylene}amino)-4,5-dimethyl-*N*-(2-methylphenyl)-thiophene-3-carboxamide, $C_{23}H_{25}N_3OS$, (I), and 2-({(1*E*)-[4-(dimethylamino)phenyl]methylene}amino)-*N*-(4-methylphenyl)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxamide, $C_{25}H_{27}N_3OS$, (II), show antibacterial and antifungal activities. The asymmetric unit of (II) contains two crystallographically independent molecules. The *o*-toluidine ring in (I) lies *gauche* with respect to the thiophene ring. In (II), the *p*-toluidine ring is coplanar with the thiophene ring in one molecule, but is tilted from it in the other molecule. Neither structure exhibits any significant intermolecular interactions, but in both, an intramolecular N—H···N hydrogen bond forms a pseudo-six-membered ring, thus locking the molecular conformation and removing conformational flexibility.

Comment

Most Schiff bases (Pellis & West, 1968; Cohen *et al.*, 1977; Csaszar & Morvay, 1983; Lakshmi *et al.*, 1985) and their thiophene derivatives (El-Maghraby *et al.*, 1984; Dzhurayev *et al.*, 1992; Gewald *et al.*, 1966) possess antibacterial, antitubercular and antifungal activities. Sulfur-containing Schiff bases are particularly effective. The two title compounds, 2-({(1*Z*)-[4-(dimethylamino)phenyl]methylene}amino)-4,5-dimethyl-*N*-(2-methylphenyl)thiophene-3-carboxamide, (I), and 2-({(1*E*)-[4-(dimethylamino)phenyl]methylene}amino)-*N*-(4-methylphenyl)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxamide, (II), belong to the same series of compounds and show antibacterial and antifungal activities (Mohan & Saravanan, 2002, 2003).

Compound (I) contains three different structural moieties which will be discussed separately (Fig. 1). The thiophene ring exhibits normal geometry and is planar, with a maximum deviation of 0.0166 (4) Å for atom C4. The *o*-toluidine group is in a *gauche* conformation with respect to the plane of the thiophene ring, as indicated by the C7—N1—C8—C9 torsion angle of −137.4 (4)°. The angle between the mean planes of the *o*-toluidine and thiophene rings is 56.44 (11)°.



The dimethylamino group is coplanar with its attached phenyl ring [C20—C19—N3—C22 = −1.1 (5)°]. The *p*-(dimethylamino)phenyl moiety is also coplanar with the thiophene ring, the angle between the two planes being 3.25 (15)°. It is interesting to note that the angles C18—C19—C20 [116.4 (4)°] and C17—C16—C21 [115.9 (4)°] deviate significantly from the ideal value of 120° for a phenyl ring. This deviation is due to the electron-donating effect of the *p*-(dimethylamino)phenyl group attached to C19.

Compound (II) crystallizes with two crystallographically independent molecules (*A* and *B*) in the asymmetric unit (Fig. 2). This compound also contains three different structural moieties. The thiophene ring exhibits normal geometry in both symmetry-independent molecules. The *p*-toluidine group is coplanar with the thiophene ring in molecule *A* [C7—N1—C8—C9 = −179.0 (3)°], while it is tilted from the thiophene ring in molecule *B* [C32—N4—C33—C34 = −151.6 (3)°]. The

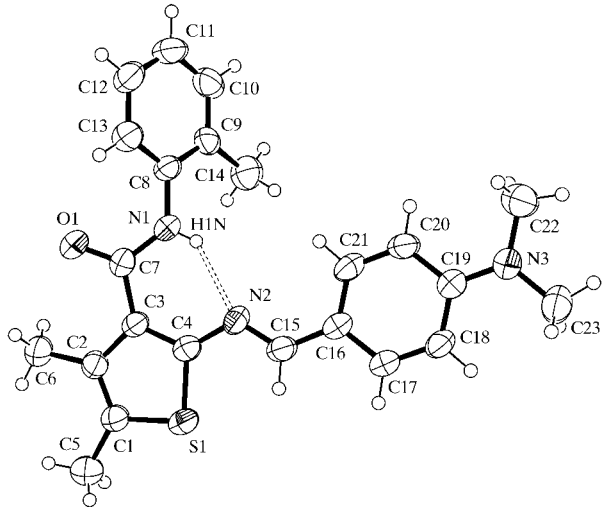


Figure 1
View of the molecule of compound (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are represented by circles of arbitrary size.

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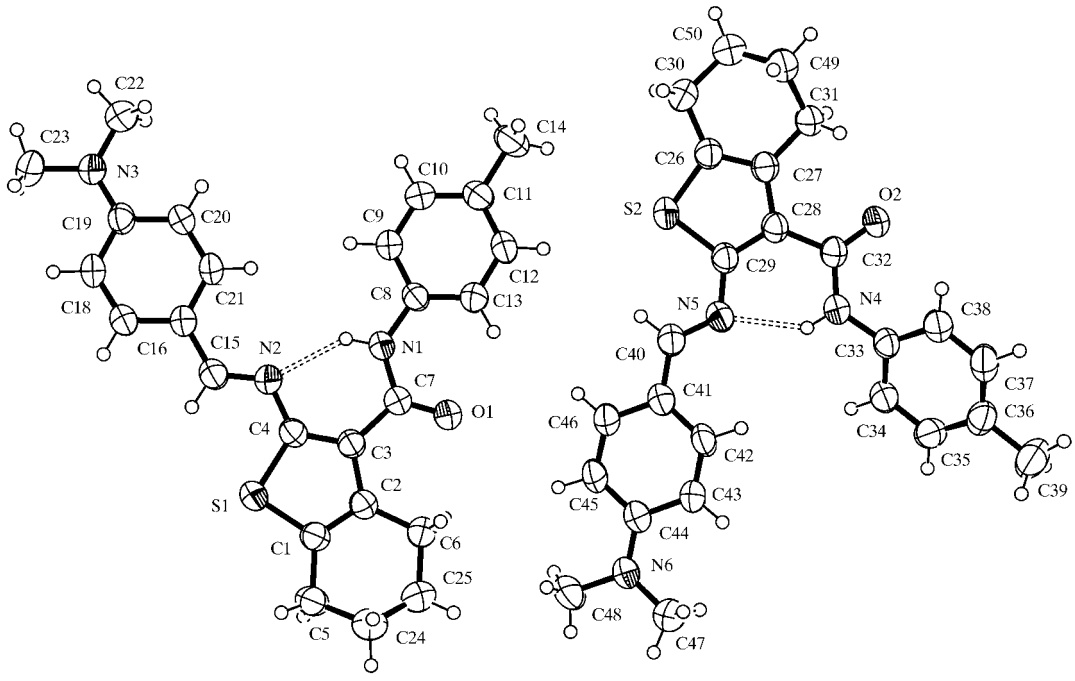

Figure 2
View of the asymmetric unit of compound (II), showing the two symmetry-independent molecules and the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are represented by circles of arbitrary size.

angles between the mean planes of the *p*-toluidine and thiophene rings in molecules *A* and *B* are 2.96 (8) and 25.18 (8)°, respectively.

The dimethylamino group is coplanar with its attached phenyl ring in molecule *A* [C20—C19—N3—C22 = 0.9 (4)°], whereas in molecule *B*, it is slightly tilted [C43—C44—N6—C47 = 7.4 (4)°]. The dimethylamino moiety is essentially coplanar with the thiophene ring; the angles between the mean planes of these moieties in molecules *A* and *B* are 2.48 (8) and 9.38 (8)°, respectively. The angles C18—C19—C20 [117.0 (2)°] and C17—C16—C21 [116.7 (2)°] in molecule *A*, and C43—C44—C45 [116.6 (2)°] and C42—C41—C46 [117.0 (2)°] in molecule *B* again deviate significantly from the ideal value of 120° for a phenyl ring, as was observed in the case of compound (I).

There are no significant intermolecular hydrogen-bonding interactions in the packing of compounds (I) and (II). The packing is essentially stabilized *via* weak van der Waals forces. However, there is a significant intramolecular N—H···N hydrogen-bonding interaction in each structure which locks the molecule into a rigid pseudo-six-membered ring conformation and removes the conformational flexibility (Figs. 1 and 2, and Tables 1 and 2). Hence, the free N—H group is not available to participate in intermolecular interactions.

Experimental

The title compounds were synthesized using the Gewald reaction (Gewald *et al.*, 1966). For compound (I), *o*-cyanotoluidine was refluxed with ethyl methyl ketone in the presence of sulfur, dimethylamine and ethanol at 313–323 K for 1 h. The product was then reacted with *p*-(dimethylamino)benzaldehyde in an equimolar ratio in the presence of ethanol, which yielded (I). This was then purified and crystallized from a solution in *N*,*N*-dimethylformamide and ethanol (1:2) by slow evaporation. Crystals (m.p. 419 K) were obtained after three weeks and were used for single-crystal data collection. For compound (II), a similar procedure was followed using cyclohexanone in place of ethyl methyl ketone and *p*-cyanotoluidine in place of *o*-cyanotoluidine. The product obtained was purified and crystallized using the same procedure as followed for (I) (m.p. 497 K).

Compound (I)

Crystal data

$C_{23}H_{25}N_3OS$
M_r = 391.53
Triclinic, $P\overline{1}$
a = 7.8352 (9) Å
b = 10.7300 (13) Å
c = 13.1342 (15) Å
α = 94.222 (2)°
β = 99.965 (2)°
γ = 108.593 (2)°
V = 1020.9 (2) Å^3
Z = 2
D_x = 1.274 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 835 reflections
θ = 2.3–21.2°
μ = 0.18 mm^{-1}
T = 293 (2) K
Prism, red
0.20 × 0.20 × 0.20 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1997)
T_{min} = 0.908, T_{max} = 0.966
10 235 measured reflections
3725 independent reflections
1678 reflections with $I > 2\sigma(I)$
R_{int} = 0.086
θ_{max} = 25.4°
$h = -9 \rightarrow 9$
$k = -12 \rightarrow 12$
$l = -15 \rightarrow 15$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0417P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$R(F) = 0.066$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.128$	$\Delta\rho_{max} = 0.20$ e Å^{-3}
$S = 0.94$	$\Delta\rho_{min} = -0.19$ e Å^{-3}
3725 reflections	
262 parameters	
H atoms: see below	

Table 1
Hydrogen-bonding geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1N···N2	0.77 (3)	2.12 (3)	2.766 (5)	143 (3)

Compound (II)

Crystal data

$C_{25}H_{27}N_3OS$	$D_x = 1.283$ Mg m^{-3}
$M_r = 417.57$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/n$	Cell parameters from 839 reflections
$a = 8.016$ (2) Å	$\theta = 2.6$–$21.4°$
$b = 21.255$ (6) Å	$\mu = 0.17$ mm^{-1}
$c = 25.651$ (7) Å	$T = 293$ (2) K
$\beta = 98.378$ (5)°	Prism, yellow
$V = 4324$ (2) Å^3	0.40 × 0.35 × 0.30 mm
$Z = 8$	

Data collection

Bruker SMART CCD area-detector diffractometer	8756 independent reflections
	6163 reflections with $I > 2\sigma(I)$
φ and ω scans	$R_{int} = 0.034$
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1997)	$\theta_{max} = 26.4°$
	$h = -10 \rightarrow 10$
$T_{min} = 0.925$, $T_{max} = 0.950$	$k = -24 \rightarrow 26$
33 520 measured reflections	$l = -31 \rightarrow 31$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.067P)^2 + 2.0342P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R(F) = 0.059$	$(\Delta/\sigma)_{max} = 0.002$
$wR(F^2) = 0.165$	$\Delta\rho_{max} = 0.49$ e Å^{-3}
$S = 1.06$	$\Delta\rho_{min} = -0.24$ e Å^{-3}
8756 reflections	
555 parameters	
H atoms: see below	

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1N···N2	0.86 (3)	2.06 (3)	2.780 (3)	141 (3)
N4—H4N···N5	0.82 (3)	2.07 (3)	2.765 (3)	141 (3)

For both compounds, the position of the amide H atom was located from a difference Fourier map and was refined freely along with an isotropic displacement parameter. The methyl H atoms were constrained to an ideal geometry [C—H = 0.96 Å and U_{iso} = $1.5U_{eq}$(C)], but were allowed to rotate freely about the C—C bond. All remaining H atoms were placed in idealized positions and constrained to ride on their parent atoms [C—H = 0.93–0.97 Å and U_{iso}(H) = $1.2U_{eq}$(C)].

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); 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: LN1181). Services for accessing these data are described at the back of the journal.

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