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N-(*X*-Methylphenyl)-2-{(*Z*)-[(2,3,4-trimethoxyphenyl)methylidene]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxamide, where *X* = 2 and 3

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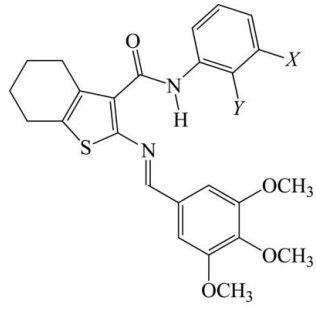
The title isomers, *viz*. the *N*-(3-methylphenyl)-, (I), and *N*-(2-methylphenyl)-, (II), derivatives, both $C_{26}H_{28}N_2O_4S$, adopt an *E* configuration that places the thiophene and trimethoxyphenyl groups on opposite sides of the C=N double bond, providing a suitable orientation for formation of an intramolecular N—H···N hydrogen bond. However, while the molecule in (I) is close to being planar, the *N*-methylphenyl group in (II) is twisted significantly from the plane of the remainder of the molecule. Both crystal structures are essentially layered and there are no intermolecular N—H···O hydrogen bonds. Compound (I) has a significantly higher calculated density than (II) (1.340 *cf* 1.305 Mg m^{-3}), indicating that the molecular packing in the *meta* isomer is overall more efficient than that in the *ortho* isomer.

Comment

Thiophene derivatives have recently been incorporated into new pharmaceutical and chemical compounds tested as anti-inflammatory agents (Pillai *et al.*, 2004, 2005). The double functionality of carboxamide/thiophene derivatives drives the study of the structural properties of both 2-thiophenecarboxamides and 2-thiophenecarbamates, in an attempt to elucidate the structure–activity relationships involved in their pharmacological activity (Ribeiro da Silva *et al.*, 2007). Various ligands based on the benzo[*b*]thiophene molecular framework, in an appropriately substituted form, have demonstrated moderate to strong binding affinity for the oestrogen receptor (Jones *et al.*, 1984; Pinney & Katzenellenbogen, 1991; Pinney *et al.*, 1991; Palkowitz *et al.*, 1997). In view of the clinical applications of these classes of compounds, single-crystal structure determinations have been performed on a series of biologically active thiophene-3-carboxamide derivatives (Vasu *et al.*, 2003, 2004*a*,*b*, 2005, 2008). In the majority of these structures, the invariant molecular skeleton comprises the *N*-phenyl-2-{[(1*E*)-phenylmethylidene]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxamide unit. This molecular skeleton is divided into three parts, namely the cyclohexene fused thiophene part, the *N*-phenyl ring and the benzylideneamine unit. Most of the reported structure determinations involve various substituents on the *N*-phenyl and benzylideneamine parts. The title compounds contain a methyl group in the *meta* [for (I)] or *ortho* [for (II)] position of the *N*-phenyl ring, and three methoxy groups on the benzylideneamine unit.



(I) X = CH_3, Y = H
(II) X = H, Y = CH_3

Compounds (I) and (II) crystallize in the space groups $P\overline{1}$ and *Pbca*, respectively, in both cases with one molecule in the asymmetric unit. For both structures, atoms C24 and C25 of the cyclohexene ring were modelled as disordered, with refined site occupancies of 0.686 (7):0.314 (7) for the two disorder components in (I), and 0.501 (10):0.499 (10) for the two components in (II). All of the disorder components for the cyclohexene ring correspond to a half-chair conformation. The C1–C4/S1 thiophene ring is planar in both structures, with the maximum deviations from the least-squares planes being −0.007 (2) and 0.009 (2) Å for atom C4 in (I) and (II), respectively.

The bond angle C9—C10—C11 in (I) and C6—C7—C8 in (II) are 118.16 (17) and 116.98 (18)°, respectively, which deviate from the ideal value of 120° on account of the electron-releasing inductive effect of the methyl group. Similar variations in bond angles have been observed in 2-[(*E*)-(4-chlorophenyl)methyleneamino]-*N*-(*X*-methylphenyl)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxamide, where *X* = 2 or 3 (Vasu *et al.*, 2004*a*), and in 2-{[(*E*)-(4-methoxyphenyl)-methylene]amino}-*N*-(3-methylphenyl)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxamide and *N*-(4-methylphenyl)-2-{[(*E*)-(4-methylphenyl)methylene]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxamide (Vasu *et al.*, 2004*b*). Similarly, the bond angles C4—N2—C13 (around the imine N atom) and C5—N1—C6 (around the amide N atom) are 119.94 (13) and 127.79 (14)°, respectively, in (I), and 121.83 (14) and 123.96 (13)°, respectively, in (II). This implies delocalization of the lone pair of electrons on N over the thiophene and *N*-phenyl rings in both compounds. This is further corroborated by the fact that the bond lengths corre-

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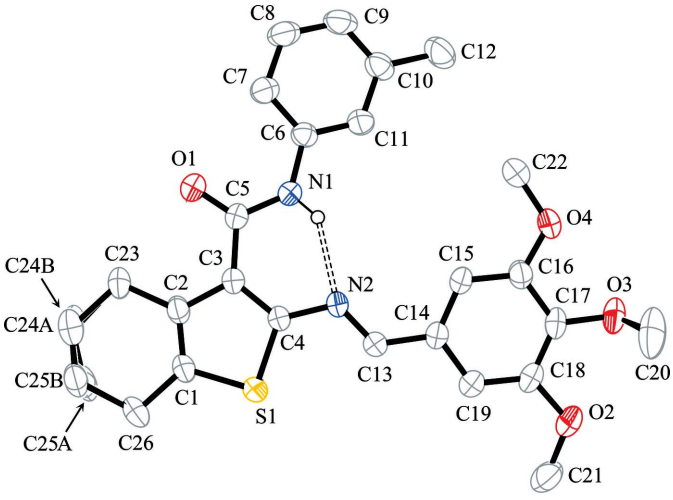

Figure 1
The molecular structure of (I), showing the atom-numbering scheme and the disorder of the cyclohexene ring. Displacement ellipsoids are drawn at the 50% probability level. H atoms have been omitted, except for that involved in the intramolecular hydrogen bond, which is indicated by dashed lines.

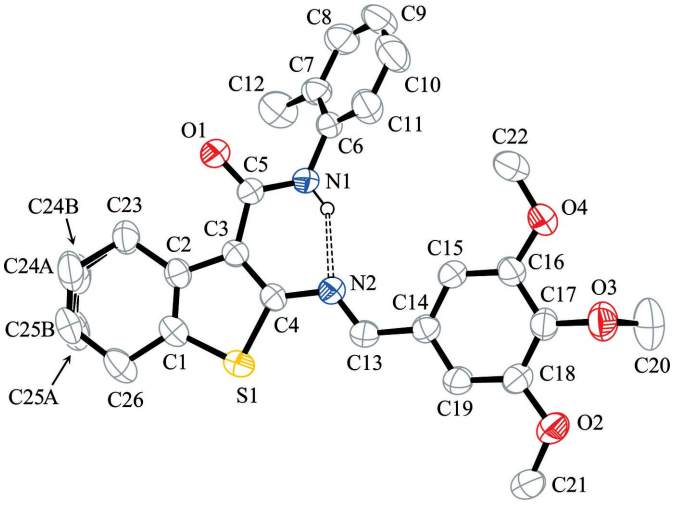

Figure 2
The molecular structure of (II), showing the atom-numbering scheme and the disorder of the cyclohexene ring. Displacement ellipsoids are drawn at the 50% probability level. H atoms have been omitted, except for that involved in the intramolecular hydrogen bond, which is indicated by dashed lines.

sponding to the imine and carboxamide groups are significantly different: in (I), the C5—N1, C4—N2 and C13—N2 bond lengths are 1.351 (2), 1.3889 (18) and 1.2770 (19) Å, respectively, while in (II) the corresponding values are 1.355 (2), 1.389 (2) and 1.274 (2) Å. Similar bond lengths have been reported for analogous systems (Vasu *et al.*, 2003, 2004*a*,*b*; Kumar *et al.*, 2005). The dihedral angles formed by the *m*-toluidine ring in (I) and *o*-toluidine ring in (II) with the plane of the thiophene ring are 11.39 (6) and 48.74 (6)° for (I) and (II), respectively. It is noteworthy that the distortion from planarity is considerably larger for (II) than for (I).

In the 2,3,4-tris(methoxyphenyl)- group, all bond lengths and angles are comparable with standard literature values

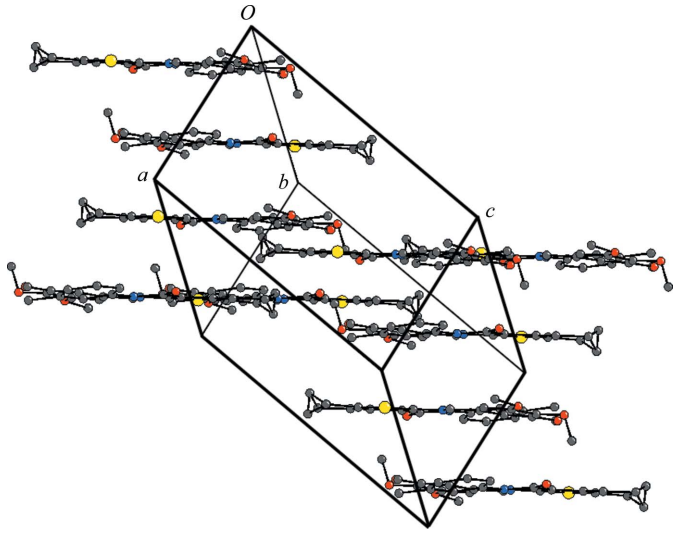

Figure 3
A packing diagram for (I), projected approximately on to the (1$\bar{2}$2) plane, depicting the layered-type structure. H atoms have been omitted.

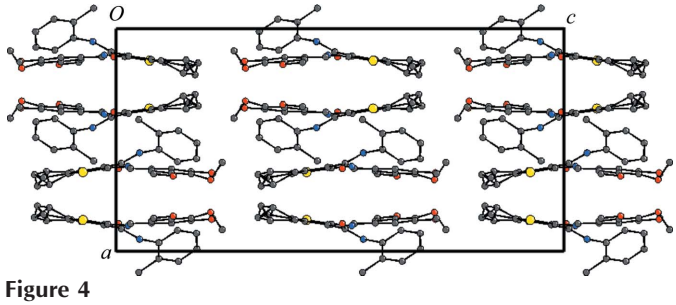

Figure 4
A packing diagram for (II), viewed along the *b* axis, depicting the layered-type structure. H atoms have been omitted.

(Allen *et al.*, 1987). The C16—O4, C17—O3 and C21—O2 bond lengths suggest some double-bond character due to resonance delocalization of the O-atom lone pairs with the benzene ring. In both structures, two of the methyl groups lie essentially in the plane of the benzene ring, with the C22—O4—C16—C17 and C21—O2—C18—C17 torsion angles being 174.72 (16) and −175.55 (15)°, respectively, for (I), and 171.42 (19) and −175.88 (16)°, respectively, for (II). The third methyl group lies out of the plane of the benzene ring in both structures, with the C20—O3—C17—C18 torsion angle being −74.3 (2) and 86.6 (2)° in (I) and (II), respectively.

An intramolecular N—H···N hydrogen bond is present in both structures (Table 1; Figs. 1 and 2), in spite of the presence of the carbonyl group. The absence of any intermolecular N—H···O=C hydrogen bond is based on the fact that there is restricted rotation about the C13=N2 double bond. The observed *E* configuration places the bulky thiophene and trimethoxyphenyl groups on opposite sides of the double bond, thereby placing the lone pair on atom N2 in a suitable orientation for formation of the intramolecular hydrogen bond. The hydrogen bond in (II) is significantly distorted compared with that in (I), on account of the twist of the *N*-phenyl ring from the plane of the remainder of the mol-

ecule. There are no primary intermolecular interactions that obviously dictate the crystal packing in (I) and (II). The structures of both compounds are essentially layered, with the molecular planes lying approximately parallel within the planes of the layers (Figs. 3 and 4). Compound (I) has a significantly higher calculated density than (II) [1.340 *cf* 1.305 Mg m^{-3}], indicating that the molecular packing in the *meta* isomer is overall more efficient than in the *ortho* isomer.

Experimental

Compounds (I) and (II) were synthesized using a Gewald reaction (Gewald *et al.*, 1966). *m*-Cyanotoluidine [for (I)] or *o*-cyanotoluidine [for (II)] (0.04 mol) was refluxed with ethyl methyl ketone in the presence of sulfur at 313–323 K for 1 h. The products were then reacted with trimethoxybenzaldehyde in an equimolar ratio in the presence of ethanol to yield either (I) or (II), in both cases with *ca* 70% yield. Both compounds were recrystallized by slow evaporation from ethyl acetate to yield yellow needle-shaped crystals [m.p.: 451 K for (I) and 446 K for (II)].

Compound (I)

Crystal data

$C_{26}H_{28}N_2O_4S$
M_r = 464.57
Triclinic, $P\overline{1}$
a = 8.7346 (17) Å
b = 10.187 (2) Å
c = 14.253 (3) Å
α = 70.790 (3)°
β = 76.059 (3)°
γ = 78.143 (4)°
V = 1151.3 (4) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.18 mm^{-1}
T = 290 K
0.32 × 0.12 × 0.11 mm

Data collection

Bruker SMART CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.950, T_{max} = 0.981
9094 measured reflections
4468 independent reflections
3431 reflections with $I > 2\sigma(I)$
R_{int} = 0.034

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.115
S = 1.02
4468 reflections
321 parameters
6 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.18 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

Compound (II)

Crystal data

$C_{26}H_{28}N_2O_4S$
M_r = 464.56
Orthorhombic, *Pbca*
a = 13.437 (5) Å
b = 12.993 (5) Å
c = 27.088 (10) Å
V = 4729 (3) Å^3
Z = 8
Mo $K\alpha$ radiation
μ = 0.17 mm^{-1}
T = 290 K
0.20 × 0.10 × 0.02 mm

Data collection

Bruker SMART CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.991, T_{max} = 0.997
34929 measured reflections
4639 independent reflections
3186 reflections with $I > 2\sigma(I)$
R_{int} = 0.105

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···N2	0.86	2.10	2.8169 (18)	141

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···N2	0.86	2.20	2.793 (2)	126

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.045
$wR(F^2)$ = 0.123
S = 0.94
4639 reflections
321 parameters
6 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.21 e Å^{-3}

For both (I) and (II), atoms C24 and C25 of the cyclohexene ring exhibited disorder and were split into two components, with site-occupancy factors constrained to sum to unity. Atoms C24*A* and C25*A* belong to one disorder component, while C24*B* and C25*B* belong to the other; the refined site occupancies were 0.686 (7) and 0.314 (7), respectively, for (I), and 0.501 (10) and 0.499 (10), respectively, for (II). In both cases, the six C—C bond distances involving the disordered C atoms were restrained to 1.54 (1) Å. H atoms were placed in geometric positions on all disordered C atoms, with site-occupancy factors constrained to those of the parent C atoms and with U_{iso}(H) = 1.2U_{eq}(C). H atoms associated with atoms C23 and C26 were also modelled as disordered, in geometric positions consistent with the two disorder components. All other C-bound H atoms were positioned geometrically and refined as riding, with C—H = 0.93 (aromatic), 0.96 (methyl) or 0.97 Å (methylene), and with U_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms or 1.2U_{eq}(C) otherwise. The amine H atoms were placed geometrically, with N—H = 0.86 Å, and refined as riding, with U_{iso}(H) = 1.2U_{eq}(N). All methyl groups were allowed to rotate about their local threefold axis.

For both compounds, data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997) and *CAMERON* (Watkin *et al.*, 1993); software used to prepare material for publication: *PLATON* (Spek, 2009).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BI3001). Services for accessing these data are described at the back of the journal.

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