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(*Z*)-3-(1*H*-Indol-3-yl)-2-(3-thienyl)-acrylonitrile and (*Z*)-3-[1-(4-*tert*-butylbenzyl)-1*H*-indol-3-yl]-2-(3-thienyl)acrylonitrile

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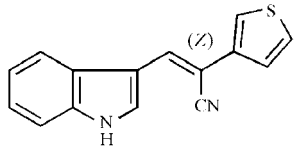
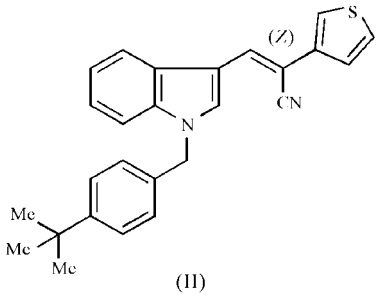
(*Z*)-3-(1*H*-Indol-3-yl)-2-(3-thienyl)acrylonitrile, $C_{15}H_{10}N_2S$, (I), and (*Z*)-3-[1-(4-*tert*-butylbenzyl)-1*H*-indol-3-yl]-2-(3-thienyl)acrylonitrile, $C_{26}H_{24}N_2S$, (II), were prepared by base-catalyzed reactions of the corresponding indole-3-carboxaldehyde with thiophene-3-acetonitrile. $^1H/^{13}C$ NMR spectral data and X-ray crystal structures of compounds (I) and (II) are presented. The olefinic bond connecting the indole and thiophene moieties has *Z* geometry in both cases, and the molecules crystallize in space groups $P2_1/c$ and $C2/c$ for (I) and (II), respectively. Slight thienyl ring-flip disorder (*ca* 5.6%) was observed and modeled for (I).

Comment

Acrylonitriles represent an interesting class of biologically active compound. 3-Aryl-substituted 2-[1*H*(2*H*)-benzotriazol-1(2)-yl]acrylonitriles have been shown to possess tuberculostatic activity (Sanna *et al.*, 2000), and (*E*)-3-(3-amino-4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)acrylonitrile and its analogs show potent antitumor activity (Ohsumi *et al.*, 1998). We have synthesized a series of novel substituted aryl/heteroaryl 2-(thiophen-3-yl)acrylonitriles and evaluated them for antitubercular activity against *Mycobacterium tuberculosis* $H37R_v$ and for anticancer activity. X-ray crystal analysis of one representative compound showed that the olefinic bond had a *Z* geometry (Sonar *et al.*, 2004). The present study is aimed at establishing the effect of bulkier substituents at the 1-position of the indole ring on the geometry of the molecule. The title compounds were synthesized by the base-catalyzed condensation reaction of indole-3-carboxaldehyde and 1-(*tert*-butylbenzyl)indole-3-caboxaldehyde with thiophene-3-acetonitrile to afford compounds (I) and (II), respectively. The structures of these products were initially identified by NMR spectroscopy. In order to confirm the olefinic bond geometry in these compounds and to obtain more detailed information of the structural conformation of the molecules, their X-ray structures were determined.



(I)



(II)

X-ray analysis confirmed the molecular structures and atom connectivities for (I) and (II), as illustrated in Figs. 1 and 2. Selected geometric parameters are presented in Tables 1 and

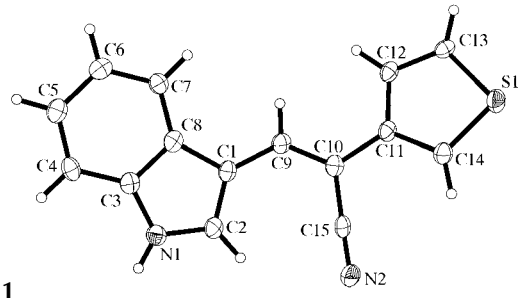


Figure 1
A view of the molecule of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The thienyl ring is disordered and only the ring with the major occupancy [0.944 (2)] is shown.

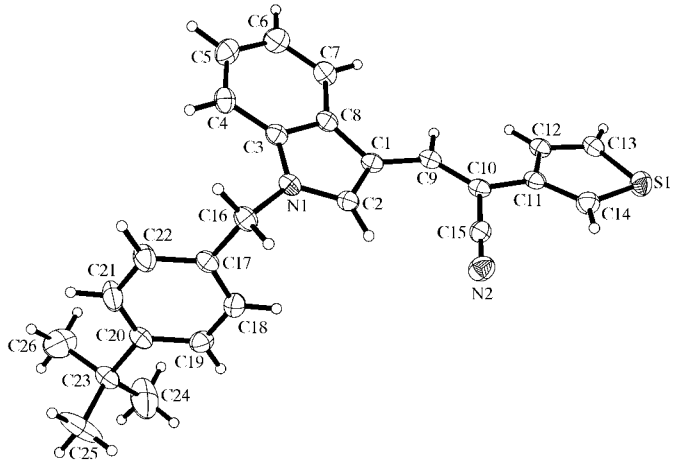


Figure 2
A view of the molecule of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The methyl groups of the *tert*-butyl moiety are disordered over two orientations and only the groups with the major occupancy [0.668 (6)] are shown.

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3. For each structure, the indole ring is planar, with bond distances and angles comparable to those reported for other indole derivatives (Mason *et al.*, 2003). In compound (II), the benzene ring of the 4-*tert*-butylbenzyl group is orthogonal to the indole ring system, forming a dihedral angle of 75.16 (4)°, and the *tert*-butyl group is disordered. In both molecules, the olefinic bond connecting the indole and thiophene moieties has a *Z* geometry. Deviations from the ideal bond-angle geometry around the Csp^2 atoms of the double bond are observed. In both molecules, the C9═C10—C15, C9═C10—C11 and C14═C11—C10 bond angles [120.07 (19)/119.79 (14), 124.4 (2)/124.71 (14) and 124.2 (2)/123.76 (14)°, respectively, in (I)/(II)] are close to the ideal geometry (120°); however, the C2═C1—C9, C10═C9—C1 and C15═C10—C11 angles [130.43 (19)/130.42 (15), 130.2 (2)/129.60 (15) and 115.4 (2)/115.49 (13)°, respectively, in (I)/(II)] are distorted because of strain induced by the double bond linking the indole and thiophene rings. The vinyl group bearing the indole and thiophene rings and the nitrile group in compounds (I) and (II) has a double-bond length of 1.356 (3) Å and is significantly longer than that observed in the disubstituted vinyl group of 2-styrylbenzimidazoles [1.304 (4) Å; Bacelo *et al.*, 1997]. This fact is evidence of some delocalization in the bridging units of these molecules. Furthermore, the C1—C9, C10—C11 and C10—C15 bond lengths [1.433 (3)/1.440 (2), 1.485 (3)/1.467 (2) and 1.438 (3)/1.439 (2) Å, respectively, in compounds (I)/(II)] are slightly shorter than a C_{ar}—Csp^2 single bond (Wilson, 1992). The C2═C1—C9═C10, C1—C9═C10—C11 and C9═C10—C11═C14 torsion angles in (I)/(II) are −7.4 (4)/−6.8 (3), −174.7 (3)/−178.88 (14) and 168.7 (3)/169.61 (16)°, respectively; these values suggest that the indole and thiophene ring planes do not deviate much from the plane of the double bond, facilitating continuous conjugation between the indole and thiophene ring π-electron systems. There is also extensive conjugation beginning at atom C15 and extending to the indole ring. A very small amount of thienyl ring-flip disorder (*ca* 5.6%) for (I) was observed and modeled, but no such disorder was seen for (II).

The mode of packing of (I), along the *b* direction, is illustrated in Fig. 3. The H atom attached to atom N1 is involved in an intermolecular hydrogen bond [2.970 (3) Å] with atom N2 of an inversion-related molecule (Table 2), thus forming an infinite chain. In addition to weak non-bonded interactions, van der Waals forces contribute to the stabilization of the crystal structures of (I) and (II).

From the present investigation, it is evident that, irrespective of the size of the substituent on the indole 1-position, the base-catalyzed reaction between thiophene-3-acetonitrile and indole-3-carboxaldehyde leads to the formation of the *Z* isomer.

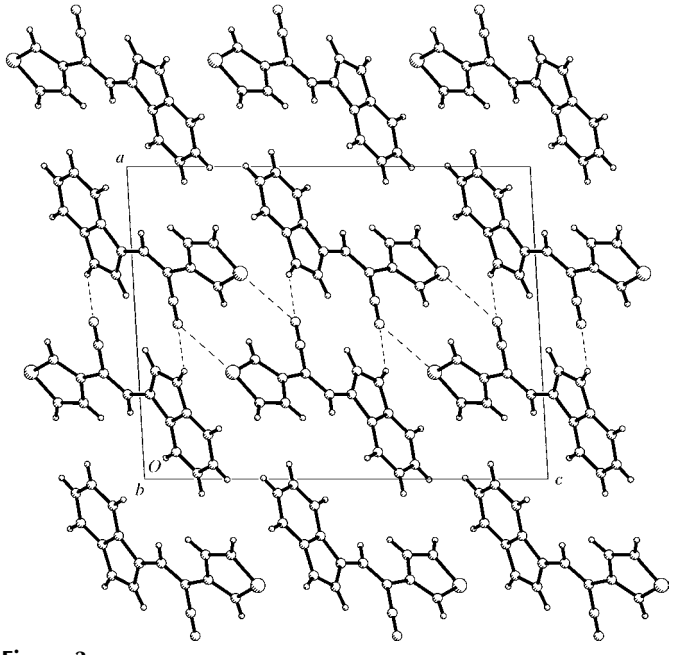

Figure 3
A packing diagram of (I), viewed down the *b* axis, showing hydrogen-bonding interactions (dashed lines).

Experimental

A mixture of indole-3-carboxaldehyde (0.290 g, 2 mmol) and thiophene-3-acetonitrile (0.247 g, 2 mmol) was dissolved in piperidine (5 ml) and the solution was refluxed for 5 h. The cooled reaction mixture was poured on to crushed ice (50 g), and the yellow solid that separated was collected by filtration, washed with water and dried. Crystallization from methanol gave (I) as yellow flakes suitable for X-ray analysis. ^{1}H NMR ($CDCl_3$): δ 7.16–7.26 (*m*, 2H), 7.51 (*d*, 1H), 7.68–7.70 (*m*, 3H), 8.55 (*d*, 1H), 8.16 (*s*, 1H), 8.30 (*s*, 1H), 12.00 (*s*, 1H). ^{13}C NMR ($CDCl_3$): δ 98.5, 110.3, 112.1, 118.6, 119.6, 120.3, 120.9, 122.5, 124.6, 126.4, 126.9, 127.8, 133.2, 135.6, 136.5. A mixture of 1-(4-*tert*-butylbenzyl)indole-3-carboxaldehyde (0.583 g, 2 mmol) and thiophene-3-acetonitrile (0.247 g, 2 mmol) was dissolved in 5% sodium methoxide in methanol (10 ml), and the solution was refluxed for 2 h. The cooled reaction mixture was poured on to crushed ice and the yellow solid that separated was collected by filtration and dried. Crystallization from methanol afforded yellow needles of (II) suitable for X-ray analysis. ^{1}H NMR ($CDCl_3$): δ 1.29 (*s*, 9H), 5.38 (*s*, 2H), 7.12 (*d*, 2H), 7.25–7.38 (*m*, 5H), 7.40 (*d*, 2H), 7.47 (*t*, 1H), 7.76–7.79 (*m*, 2H), 8.37 (*s*, 1H). ^{13}C NMR ($CDCl_3$): δ 31.6, 34.8, 50.9, 100.3, 110.9, 118.3, 120.1, 121.2, 121.3, 123.3, 124.2, 125.9, 126.7, 127.2, 128.3, 129.9, 131.9, 133.3, 136.2, 137.1, 151.1.

Compound (I)

Crystal data

$C_{15}H_{10}N_2S$
M_r = 250.31
Monoclinic, $P2_1/c$
a = 12.8530 (2) Å
b = 5.6020 (6) Å
c = 16.5980 (8) Å
β = 93.241 (2)°
V = 1193.19 (14) Å^3
Z = 4
D_x = 1.393 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5185 reflections
θ = 1.0–27.5°
μ = 0.25 mm^{-1}
T = 90.0 (2) K
Thin plate, yellow
0.40 × 0.15 × 0.02 mm

Data collection

Nonius KappaCCD diffractometer
ω scans at fixed χ = 55°
Absorption correction: multi-scan (*SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.894, T_{max} = 0.995
9660 measured reflections
2713 independent reflections
1853 reflections with $I > 2\sigma(I)$
R_{int} = 0.087
θ_{max} = 27.4°
$h = -16 \rightarrow 16$
$k = -7 \rightarrow 7$
$l = -21 \rightarrow 21$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0528P)^2 + 0.2991P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.047$	$(\Delta/\sigma)_{max} = 0.016$
$wR(F^2) = 0.116$	$\Delta\rho_{max} = 0.38$ e Å^{-3}
$S = 1.03$	$\Delta\rho_{min} = -0.28$ e Å^{-3}
2713 reflections	
189 parameters	
H-atom parameters constrained	

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

C1—C9	1.433 (3)	C10—C11	1.485 (3)
C2—N1	1.359 (3)	C13—S1	1.748 (3)
C9—C10	1.356 (3)	S1—C14	1.693 (2)
C10—C15	1.438 (3)	C15—N2	1.147 (3)
C2—C1—C9	130.43 (19)	C9—C10—C11	124.4 (2)
C10—C9—C1	130.2 (2)	C15—C10—C11	115.4 (2)
C9—C10—C15	120.07 (19)	C14—C11—C10	124.2 (2)
C9—C1—C2—N1	175.73 (19)	C1—C9—C10—C11	−174.7 (3)
C2—C1—C9—C10	−7.4 (4)	C9—C10—C11—C14	168.7 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···N2^{i}	0.88	2.23	2.971 (3)	141

Symmetry code: (i) $1-x, 1-y, 1-z$.

Compound (II)

Crystal data

$C_{26}H_{24}N_2S$	$D_x = 1.212$ Mg m^{-3}
$M_r = 396.53$	Cu $K\alpha$ radiation
Monoclinic, $C2/c$	Cell parameters from 6982 reflections
$a = 25.4535$ (4) Å	$\theta = 1.0$–$68.1°$
$b = 6.2152$ (1) Å	$\mu = 1.41$ mm^{-1}
$c = 28.1787$ (4) Å	$T = 90.0$ K
$\beta = 102.797$ (1)°	Lath, yellow
$V = 4347.10$ (12) Å^3	0.25 × 0.10 × 0.02 mm
$Z = 8$	

Data collection

Nonius KappaCCD diffractometer	3478 reflections with $I > 2\sigma(I)$
ω and φ scans	$R_{int} = 0.044$
Absorption correction: multi-scan (*APEX2*; Bruker–Nonius, 2004)	$\theta_{max} = 68.1°$
$T_{min} = 0.660$, $T_{max} = 0.972$	$h = -24 \rightarrow 30$
15 461 measured reflections	$k = -7 \rightarrow 5$
3907 independent reflections	$l = -33 \rightarrow 31$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0599P)^2 + 3.3516P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.043$	$(\Delta/\sigma)_{max} = 0.001$
$wR(F^2) = 0.116$	$\Delta\rho_{max} = 0.31$ e Å^{-3}
$S = 1.04$	$\Delta\rho_{min} = -0.32$ e Å^{-3}
3907 reflections	Extinction correction: *SHELXL97*
311 parameters	Extinction coefficient: 0.00033 (6)
H atoms treated by a mixture of independent and constrained refinement	

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

S1—C14	1.7117 (18)	C1—C9	1.440 (2)
S1—C13	1.7161 (18)	C9—C10	1.356 (2)
N1—C2	1.361 (2)	C10—C15	1.439 (2)
N2—C15	1.150 (2)	C10—C11	1.467 (2)
C2—C1—C9	130.42 (15)	C9—C10—C11	124.71 (14)
C10—C9—C1	129.60 (15)	C15—C10—C11	115.49 (13)
C9—C10—C15	119.79 (14)	C14—C11—C10	123.76 (14)
C9—C1—C2—N1	173.82 (14)	C1—C9—C10—C11	−178.88 (14)
C2—C1—C9—C10	−6.8 (3)	C9—C10—C11—C14	169.61 (16)

H atoms were found in difference Fourier maps, and were subsequently positioned geometrically and treated with appropriate riding models. For (I), distances to parent atoms of 0.95 and 0.88 Å for C—H and N—H bonds, respectively, were used. In (II), C—H bonds in the disordered *tert*-butyl group were fixed at 0.98 Å, while for non-disordered parts of the molecule, the H-atom positions were allowed to refine along the riding-model C—H vector.

For compound (I), data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO–SMN* (Otwinowski & Minor, 1997). For compound (II), data collection: *APEX2* (Bruker–Nonius, 2004); cell refinement: *APEX2*; data reduction: *APEX2*. For both compounds, program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *XP* (Sheldrick, 1995); software used to prepare material for publication: *SHELXL97* and local programs.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1789). Services for accessing these data are described at the back of the journal.

References

Bacelo, D. E., Cox, O., Rivera, L. A., Cordero, M. & Huang, S. D. (1997). *Acta Cryst.* C**53**, 907–909.
Bruker–Nonius (2004). *APEX2*. Bruker–Nonius Inc., Madison, Wisconsin, USA.
Mason, M. R., Barnard, T. S., Segla, M. F., Xie, B. & Kirschbaum, K. (2003). *J. Chem. Crystallogr.* **33**, 531–540.
Nonius (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.
Ohsumi, K., Nakagawa, R., Fukuda, Y., Hatanaka, T., Morinaga, Y., Nihei, Y., Ohishi, K., Suga, Y., Akiyama, Y. & Tsuji, T. (1998). *J. Med. Chem.* **41**, 3022–3032.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Sanna, P., Carta, A. & Nikookar, M. E. R. (2000). *Eur. J. Med. Chem.* **35**, 535–543.
Sheldrick (1995). *XP* in *SHELXTL/PC*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Sonar, V. N., Parkin, S. & Crooks, P. A. (2004). *Acta Cryst.* C**60**, o217–o218.
Wilson, A. J. C. (1992). *International Tables for Crystallography*, Vol. C, Table 9.5.1.1. Dordrecht: Kluwer Academic Publishers.