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Key indicators

Single-crystal X-ray study
T = 90 K
Mean $\sigma(\text{C}-\text{C}) = 0.003 \text{ \AA}$
Disorder in main residue
R factor = 0.040
wR factor = 0.087
Data-to-parameter ratio = 15.9For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.**(Z)-2-(3-Thienyl)-3-(3,4,5-trimethoxyphenyl)-acrylonitrile**The title compound, $\text{C}_{16}\text{H}_{15}\text{NO}_3\text{S}$, was prepared by base-catalyzed reaction of 3,4,5-trimethoxybenzaldehyde with thiophene-3-acetonitrile. The olefinic bond has *Z* geometry and thiophene ring flip disorder is observed.

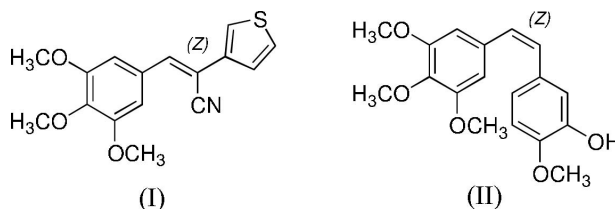
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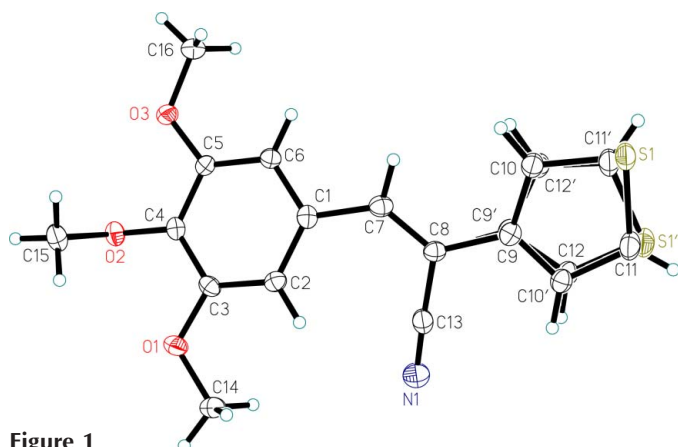
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Comment

Combretastatins are mitotic agents isolated from the bark of the South African tree *Combretum caffrum* (Pettit *et al.*, 1989; Hamel & Lin, 1983). The most potent of these is combretastatin A-4, (II), which has been found to be a potent cytotoxic agent and which strongly inhibits the polymerization of brain tubulin by binding to the colchicine site. Compound (II) shows potent cytotoxicity against a wide variety of human cancer cell lines, including MDR cancer cell lines (El-Zayat *et al.*, 1993). Compound (II) is thus attractive as a lead compound for the development of anticancer drugs. The title compound, (I), was designed as an analog of (II) in which the 3-hydroxy-4-methoxyphenyl moiety is replaced by a thiophene moiety and an olefinic bond-carrying nitrile group. The present investigation of (I) is a continuation of our work on the synthesis and X-ray structure of 3-aryl/heteroaryl-2-thiophen-3-ylacrylonitriles (Sonar *et al.*, 2004). In order to confirm the olefinic bond geometry, the X-ray structure determination of (I) was carried out.



The molecular structure and atom-numbering scheme of (I) are shown in Fig. 1, and selected bond lengths and angles are listed in Table 1. In (I), the olefinic bond connecting the 3,4,5-trimethoxyphenyl and thiophene rings has *Z* geometry. Significant deviations from the ideal bond-angle geometry around the Csp^2 atoms of the double bond are observed. The bond angles $\text{C1}-\text{C7}=\text{C8}$, $\text{C7}=\text{C8}-\text{C9}$ and $\text{C13}-\text{C8}-\text{C9}$ [$129.74(18)$, $125.7(19)$ and $113.1(18)^\circ$, respectively] are distorted, due to steric hindrance of the double bond linking the two ring systems. The olefinic double bond bearing the three conjugated substituents in (I) has a double-bond length of $1.353(3) \text{ \AA}$, slightly larger than that observed in the disubstituted olefinic group of 2-styrylbenzimidazole [$1.304(4) \text{ \AA}$; Bacelo *et al.*, 1997], suggesting some delocalization in the unsaturated bridging units. The value of the


Figure 1

A view of the molecule of (I), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. Both disorder components are shown.

C2=C1—C7=C8 torsion angle [21.3 (3)°] indicates deviation of the 3,4,5-trimethoxyphenyl ring from the plane of the olefinic double bond. However, the C1—C7 and C8—C9 bond lengths [1.465 (3) and 1.481 (9) Å, respectively] are slightly shorter in comparison with the C_{ar} — C_{sp^2} single bond (Wilson, 1992), suggesting extensive conjugation between the π -electron systems of the 3,4,5-trimethoxyphenyl and thiophene moieties.

In the crystal structure of (I), molecules are linked into two-dimensional layers by weak C—H···O and C—H···N interactions (Table 2 and Fig. 2).

Experimental

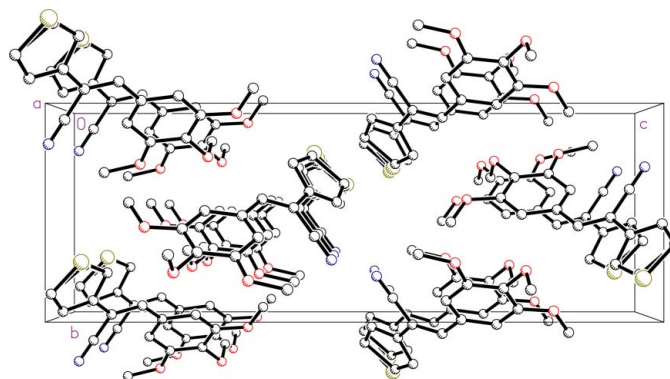
A mixture of 3,4,5-trimethoxybenzaldehyde (0.392 g, 2 mmol) and thiophene-3-acetonitrile (0.247 g, 2 mmol) was dissolved in 5% sodium methoxide in methanol (10 ml) and the solution was refluxed for 2 h. The cooled reaction mixture was poured on to crushed ice (50 g) and the pale-yellow solid that separated was collected by filtration, washed with water and air-dried. Crystallization from methanol gave (I) as pale-yellow blocks, which were suitable for X-ray analysis. $^1\text{H NMR}$ (CDCl_3 , δ , p.p.m.): 3.92 (s, 3H), 3.93 (s, 6H), 7.15 (s, 2H), 7.35–7.40 (m, 3H), 7.58 (q, 1H).

Crystal data

$\text{C}_{16}\text{H}_{15}\text{NO}_3\text{S}$	Mo $K\alpha$ radiation
$M_r = 301.35$	Cell parameters from 1966 reflections
Orthorhombic, $P2_12_12_1$	$\theta = 1.0$ – 27.5°
$a = 6.9281$ (2) Å	$\mu = 0.23$ mm $^{-1}$
$b = 8.6629$ (2) Å	$T = 90.0$ (2) K
$c = 24.3962$ (7) Å	Block, pale yellow
$V = 1464.20$ (7) Å 3	$0.32 \times 0.25 \times 0.15$ mm
$Z = 4$	
$D_x = 1.367$ Mg m $^{-3}$	

Data collection

Nonius KappaCCD area-detector diffractometer	3337 independent reflections
ω scans	2787 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (SCALEPACK; Otwinowski & Minor, 1997)	$R_{\text{int}} = 0.047$
$T_{\text{min}} = 0.910$, $T_{\text{max}} = 0.966$	$\theta_{\text{max}} = 27.5^\circ$
11 185 measured reflections	$h = -8 \rightarrow 8$
	$k = -11 \rightarrow 11$
	$l = -31 \rightarrow 31$


Figure 2

A packing diagram for (I), viewed down the b axis. Hydrogen bonds are shown as dashed lines.

Refinement

Refinement on F^2	$(\Delta/\sigma)_{\text{max}} = 0.001$
$R[F^2 > 2\sigma(F^2)] = 0.040$	$\Delta\rho_{\text{max}} = 0.22$ e Å $^{-3}$
$wR(F^2) = 0.087$	$\Delta\rho_{\text{min}} = -0.22$ e Å $^{-3}$
$S = 1.04$	Extinction correction: SHELXL97 (Sheldrick, 1997)
3337 reflections	Extinction coefficient: 0.0151 (18)
210 parameters	Absolute structure: Flack (1983), with 1386 Friedel pairs
H-atom parameters constrained	Flack parameter: 0.00 (7)
$w = 1/[\sigma^2(F_o^2) + (0.0293P)^2 + 0.6118P]$	
where $P = (F_o^2 + 2F_c^2)/3$	

Table 1

Selected geometric parameters (Å, °).

O1—C3	1.371 (2)	C8—C9	1.481 (9)
O2—C4	1.377 (2)	C10—S1	1.739 (15)
O3—C5	1.370 (2)	S1—C11	1.752 (12)
C1—C7	1.465 (3)	C13—N1	1.148 (3)
C7—C8	1.353 (3)		
C2—C1—C7	123.86 (17)	C13—C8—C9	113.1 (18)
C8—C7—C1	129.74 (18)	C10—C9—C8	120 (3)
C7—C8—C13	121.11 (18)	C10—S1—C11	90.4 (7)
C7—C8—C9	125.7 (19)	N1—C13—C8	177.1 (2)
C2—C1—C7—C8	21.3 (3)	C7—C8—C9—C12	−169 (4)
C6—C1—C7—C8	−155.28 (19)	C7—C8—C9—C10	7 (7)

Table 2

Hydrogen-bond geometry (Å, °).

$D\text{—}H\cdots A$	$D\text{—}H$	$H\cdots A$	$D\cdots A$	$D\text{—}H\cdots A$
C10—H10···O2 ⁱ	0.95	2.59	3.35 (2)	137
C10—H10···O3 ⁱ	0.95	2.47	3.380 (19)	160
C12—H12···N1 ⁱⁱ	0.95	2.58	3.422 (19)	148

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

All H atoms were placed in calculated positions, with C—H distances of 0.95 Å [0.98 Å for methyl], and included in the refinement in the riding-model approximation, with $U_{\text{iso}}(\text{H}) = 1.2$ (1.5 for methyl) times $U_{\text{eq}}(\text{C})$. The Flack (1983) parameter was refined explicitly, with both TWIN and BASF parameters. Disorder of the thiophene ring is common in these sorts of molecules. The geometries of the two PARTs was kept similar using the SAME restraint and displacement parameters in these disordered pieces were restrained using both ISOR and SIMU. In addition, the components of anisotropic displacement for disordered atoms occupying approximately the same site were made equal using the EADP constraint.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO-SMN* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *XP* in *SHELXTL* (Sheldrick, 1995); software used to prepare material for publication: *SHELXL97* and local programs.

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