

(E)-3-(Benzo[*b*]thiophen-2-yl)-2-(3,4,5-trimethoxyphenyl)acrylonitrile and (Z)-3-(benzo[*b*]thiophen-2-yl)-2-(3,4-dimethoxyphenyl)acrylonitrileVijayakumar N. Sonar,^a Sean Parkin^b and Peter A. Crooks^{a*}^aDepartment of Pharmaceutical Sciences, College of Pharmacy, University of Kentucky, Lexington, KY 40536, USA, and ^bDepartment of Chemistry, University of Kentucky, Lexington, KY 40506, USA

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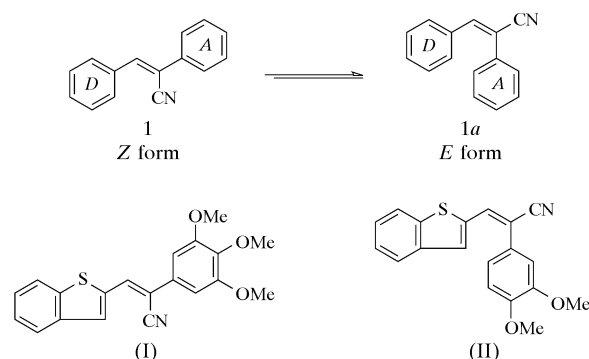
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The title compounds, C₂₀H₁₇NO₃S, (I), and C₁₉H₁₅NO₂S, (II), were prepared by the reaction of benzo[*b*]thiophene-2-carbaldehyde with (3,4,5-trimethoxyphenyl)acetonitrile and (3,4-dimethoxyphenyl)acetonitrile, respectively, in the presence of methanolic potassium hydroxide. In (I), the C=C bond linking the benzo[*b*]thiophene and the 3,4,5-trimethoxyphenyl units has *E* geometry, with dihedral angles between the plane of the bridging unit and the planes of the two adjacent ring systems of 5.2 (3) and 13.1 (2)°, respectively. However, in (II), the C=C bond has *Z* geometry, with dihedral angles between the plane of the bridging unit and the planes of the adjacent benzo[*b*]thiophene and 3,4-dimethoxyphenyl units of 4.84 (17) and 76.09 (7)°, respectively. There are no significant intermolecular hydrogen-bonding interactions in the packing of (I) and (II). The packing is essentially stabilized *via* van der Waals forces.

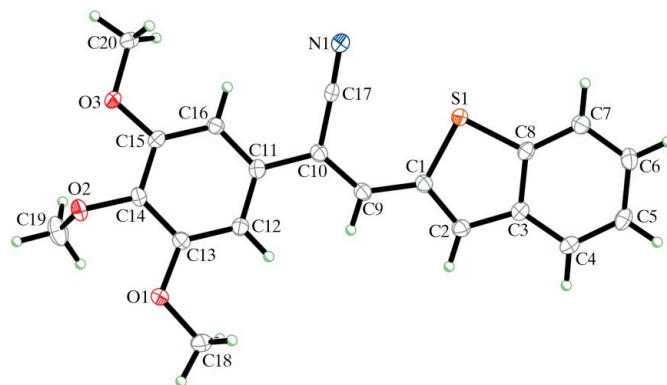
Comment

2,3-Diarylacrylonitriles are very important synthons for the synthesis of a wide spectrum of biologically active molecules (Loupy *et al.*, 2005). These compounds have been shown to possess spasmolytic, estrogenic, hypotensive, antioxidative, tuberculostatic, antitrichomonal, insecticidal and cytotoxic activities (Saczewski *et al.*, 2004). Compounds of general structure 1 (see scheme) undergo interconversion to the corresponding *E* isomer in solution under certain conditions; the behavior of such compounds is dependent on the nature of the two groups linked across the double bond carrying the nitrile group, *i.e.* whether π -excessive (donating) or π -deficient (accepting). Normally, base-catalyzed condensation of aryl/heteroarylaldehydes with aryl/heteroarylacetonitriles leads to the formation of the *Z* isomer, but isomerism to the *E* form can be readily monitored by NMR studies. In connection with our ongoing research, we have undertaken the synthesis of a

series of novel substituted aryl/heteroarylacrylonitriles. Compounds (I) and (II) were prepared by the reaction of benzo[*b*]thiophene-2-carboxaldehyde with (3,4,5-trimethoxyphenyl)acetonitrile and (3,4-dimethoxyphenyl)acetonitrile in the presence of methanolic potassium hydroxide under reflux. In order to obtain detailed information on the structural conformation of these molecules and to confirm the geometry, their X-ray structure determination has been carried out. Recrystallization from ethyl acetate afforded yellow needles of (I) that were suitable for X-ray analysis, but (II) afforded yellow silky needles that were not suitable for X-ray analysis. Furthermore, when (II) was crystallized from a mixture of ethyl acetate and chloroform by slow evaporation at room temperature over a period of one week, a mixture of yellow crystals (fine silky crystals as well as crystalline hexagons) was obtained.



The molecular structure and the atom-numbering scheme of (I) are shown in Fig. 1; selected bond lengths and angles are listed in Table 1. In (I), the olefinic bond connecting the 3,4,5-trimethoxyphenyl and benzo[*b*]thiophene ring systems has *E* geometry. Significant deviations from the ideal bond-angle geometry around the *Csp*² atoms of the double bond are observed. The C11—C10—C17, C10=C9—C1, and C9—C1—S1 bond angles [115.92 (16), 130.57 (17), and 125.51 (14)°, respectively] are distorted owing to steric hindrance of the double bond linking the two ring systems. Neither the benzo[*b*]thiophene ring nor the benzene ring of the 3,4,5-trimethoxyphenyl group is coplanar with the vinyl double bond,

**Figure 1**

A view of the asymmetric unit of (I), with displacement ellipsoids drawn at the 50% probability level and H atoms shown as small spheres of arbitrary radii.

making dihedral angles of 5.2 (3) and 13.1 (2)°, respectively. The C9=C10 double bond [1.366 (2) Å] in (I) is slightly longer than that observed in the disubstituted olefinic group of 2-styrylbenzimidazole [1.304 (4) Å; Bacelo *et al.*, 1997], suggesting some delocalization in the unsaturated bridging units. This fact is further supported by the C1—C9 bond length [1.443 (2) Å], which is slightly shorter than a C_{ar}—Csp² single bond (Wilson, 1992), suggesting extensive conjugation between the π-electron system of the benzo[*b*]thiophene system and the central double bond.

The observed O—C bond lengths are in agreement with values found for the aromatic methoxy group. There is an asymmetry of the exocyclic angles at atoms C13 and C15 [O1—C13—C12/C14 = 124.09 (16)/115.20 (15)° and O3—C15—C16/C14 = 124.20 (16)/115.42 (15)°]. This is caused by the tendency of the methoxy group to be coplanar with the benzene ring, owing to conjugation of the O1 and O3 lone pairs with the benzene ring (Domiano *et al.*, 1979). However, the exocyclic angles [C15—C14—O2/C13—C14—O2 = 120.21 (16)/120.61 (16)°] at atom C14 are symmetric because of the influence of the adjacent methoxy groups; these force the O—C bond of the central methoxy group out of the plane of the aromatic ring at an angle that is approximately perpendicular to the plane of the aromatic ring, affording an almost symmetrical structure. This is contrary to what is observed with a single methoxy substituent at this position on the aromatic ring (Sonar *et al.*, 2006), where the O—C bond of the methoxy group is coplanar with the aromatic ring, resulting in asymmetry in the aromatic ring and a consequent difference in the exocyclic angles adjacent to the methoxy group.

Fig. 2 shows an ellipsoid plot of (II), and selected geometric parameters are presented in Table 2. The olefinic bond connecting the 3,4-dimethoxyphenyl and benzo[*b*]thiophene ring systems in compound (II) has *Z* geometry. The bond angles around the Csp² atoms are distorted from the standard value (120°). The C11—C10—C17, C10=C9—C1, and C9—C10—C11 bond angles [116.69 (18), 129.9 (2), and 125.2 (2)° respectively] are distorted owing to steric hindrance of the double bond linking the two ring systems. The plane of the 3,4-

dimethoxyphenyl ring is twisted with respect to the plane of the benzo[*b*]thiophene ring system. The 3,4-dimethoxyphenyl and benzo[*b*]thiophene planes make dihedral angles of 76.09 (7) and 4.84 (17)°, respectively, with the plane of the central vinyl unit. In (II), the bridging unit C9=C10 [1.346 (3) Å] is slightly longer than reported [1.304 (4) Å; Bacelo *et al.*, 1997]. However, the C1—C9 bond length [1.443 (2) Å] is slightly shorter than a typical C_{ar}—Csp² single bond (Wilson, 1992), suggesting extensive conjugation between the π-electron system of the benzo[*b*]thiophene system and the central double bond.

The observed O—C bond lengths are in agreement with values found for anisoles. There is an asymmetry of the exocyclic angles at C13 and C14 [O1—C13—C12/O1—C13—C14 = 124.98 (18)/115.58 (17)° and O2—C14—C15/O2—C14—C13 = 124.73 (19)/115.23 (18)°]. This is caused by the tendency of the methoxy group to be coplanar with the benzene ring, owing to conjugation of the O1 and O2 lone pairs with the benzene ring (Domiano *et al.*, 1979).

There are no significant intermolecular hydrogen-bonding interactions in the packing of (I) and (II). The packing is essentially stabilized *via* van der Waals forces.

Experimental

The title compounds were prepared according to the previously reported procedure of Sonar *et al.* (2004). Recrystallization from ethyl acetate afforded yellow needles of (I), which were suitable for X-ray analysis; compound (II) was crystallized from a mixture of ethyl acetate and chloroform by slow evaporation over a period of one week affording pale-yellow crystals. For (I): ¹H NMR (DMSO-*d*₆): δ 3.72 (*s*, 3H), 3.88 (*s*, 6H), 7.04 (*s*, 2H), 7.43–7.52 (*m*, 2H), 7.99 (*dd*, 1H), 8.03 (*s*, 1H), 8.09 (*dd*, 1H), 8.40 (*s*, 1H); ¹³C NMR (DMSO-*d*₆): δ 56.12, 60.18, 103.25, 108.75, 117.66, 122.67, 124.69, 125.18, 126.70, 128.67, 131.48, 135.52, 137.30, 138.01, 138.42, 140.17, 153.11. For (II): ¹H NMR (DMSO-*d*₆): δ 3.76 (*s*, 3H), 3.85 (*s*, 3H), 7.02–7.13 (*m*, 3H), 7.33–7.39 (sextet, 2H), 7.82–7.89 (*m*, 3H), 8.01 (*s*, 1H); ¹³C NMR (DMSO-*d*₆): δ 55.53, 55.62, 110.87, 112.16, 119.97, 121.84, 122.31, 123.43, 124.48, 124.86, 126.52, 132.27, 136.55, 137.28, 138.01, 140.85, 149.02, 150.00.

Compound (I)

Crystal data

C₂₀H₁₇NO₃S
M_r = 351.41
 Monoclinic, *P*2₁/*c*
a = 7.4136 (1) Å
b = 23.4782 (3) Å
c = 10.3932 (2) Å
 β = 110.3689 (6)°

V = 1695.90 (5) Å³
Z = 4
 Mo *K*α radiation
 μ = 0.21 mm⁻¹
T = 90.0 (2) K
 0.40 × 0.15 × 0.15 mm

Data collection

Nonius KappaCCD diffractometer
 Absorption correction: multi-scan
 (SCALEPACK; Otwinowski &
 Minor, 1997)
T_{min} = 0.921, *T_{max}* = 0.969

7649 measured reflections
 3894 independent reflections
 2800 reflections with *I* > 2σ(*I*)
R_{int} = 0.037

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.045$
 $wR(F^2) = 0.127$
S = 1.07
 3894 reflections

229 parameters
 H-atom parameters constrained
 $\Delta\rho_{\max} = 0.65 \text{ e } \text{Å}^{-3}$
 $\Delta\rho_{\min} = -0.29 \text{ e } \text{Å}^{-3}$

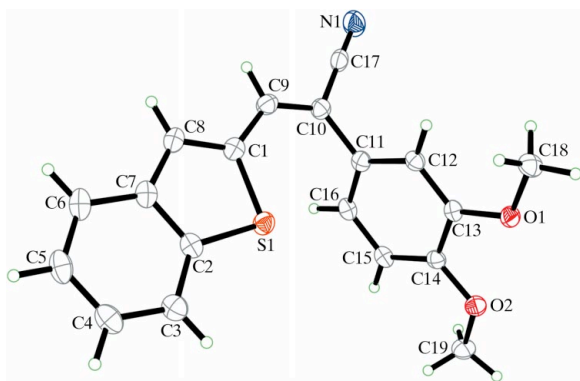


Figure 2

A view of the asymmetric unit of (II), with displacement ellipsoids drawn at the 50% probability level and H atoms shown as small spheres of arbitrary radii.

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

C1—S1	1.7519 (18)	C15—O3	1.368 (2)
C8—S1	1.7328 (19)	C17—N1	1.149 (2)
C10—C17	1.437 (2)	C19—O2	1.426 (2)
C10—C11	1.480 (2)	C20—O3	1.431 (2)
C14—O2	1.376 (2)		
C9—C10—C17	119.79 (16)	C14—O2—C19	113.83 (14)
O2—C14—C13	120.61 (16)	C15—O3—C20	116.82 (14)
N1—C17—C10	177.9 (2)	C8—S1—C1	91.12 (9)
C2—C1—C9—C10	175.25 (18)	C1—C9—C10—C17	2.2 (3)
S1—C1—C9—C10	-2.3 (3)	C1—C9—C10—C11	-174.59 (18)

Compound (II)*Crystal data*

C ₁₉ H ₁₅ NO ₂ S	V = 1541.25 (6) Å ³
M _r = 321.38	Z = 4
Monoclinic, P2 ₁ /n	Mo Kα radiation
a = 9.2958 (2) Å	μ = 0.22 mm ⁻¹
b = 6.0830 (1) Å	T = 90.0 (2) K
c = 27.2763 (7) Å	0.27 × 0.22 × 0.06 mm
β = 92.1871 (10)°	

Data collection

Nonius KappaCCD diffractometer	6626 measured reflections
Absorption correction: multi-scan (SCALEPACK; Otwinowski & Minor, 1997)	3528 independent reflections
T _{min} = 0.943, T _{max} = 0.987	2288 reflections with I > 2σ(I)
	R _{int} = 0.052

Refinement

R[F ² > 2σ(F ²)] = 0.047	210 parameters
wR(F ²) = 0.127	H-atom parameters constrained
S = 1.00	Δρ _{max} = 0.42 e Å ⁻³
3528 reflections	Δρ _{min} = -0.31 e Å ⁻³

H atoms were found in difference Fourier maps and subsequently placed in idealized positions, with constrained C—H distances of 0.98 Å for methyl H atoms and 0.95 Å for all other H atoms. U_{iso}(H) values were set at either 1.5U_{eq} of the attached methyl C atom or 1.2U_{eq}(C) for all other H atoms.

For both compounds, data collection: COLLECT (Nonius, 1999); cell refinement: DENZO-SMN (Otwinowski & Minor, 1997) for (I) and SCALEPACK (Otwinowski & Minor, 1997) for (II); data reduction: DENZO-SMN; program(s) used to solve structure:

Table 2
Selected geometric parameters (Å, °) for (II).

S1—C2	1.737 (2)	C14—O2	1.366 (2)
S1—C1	1.756 (2)	C17—N1	1.153 (3)
C10—C17	1.441 (3)	O2—C19	1.432 (2)
C10—C11	1.490 (3)		
C2—S1—C1	91.18 (10)	C13—O1—C18	116.63 (15)
C9—C10—C17	118.05 (19)	C14—O2—C19	117.29 (16)
N1—C17—C10	179.2 (2)		
C8—C1—C9—C10	-176.5 (2)	C1—C9—C10—C17	178.7 (2)
S1—C1—C9—C10	3.3 (3)	C1—C9—C10—C11	-0.5 (4)

SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: XP in SHELXTL/PC (Sheldrick, 1995); software used to prepare material for publication: SHELXL97 and local procedures.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: HJ3056). Services for accessing these data are described at the back of the journal.

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