

# The Crystal and Molecular Structure of 2-(Benzothiazol-2-yl)-3-[2-ethoxycarbonyl-1-(ethoxycarbonylmethyl)pyrrol-4-yl]propenenitrile

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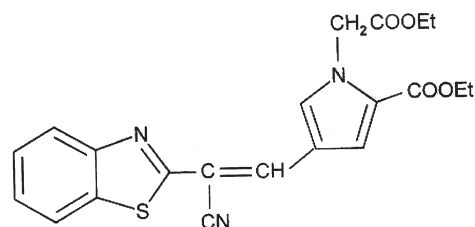
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The crystal and molecular structure of the title compound, C<sub>21</sub>H<sub>19</sub>N<sub>3</sub>O<sub>4</sub>S, which belongs to a broad class of nitrogen heterocycles widely used in medicinal chemistry as well as the pharmaceutical and chemical industries, was determined in order to elucidate the conformation of the substituents bonded to the pyrrole ring and the extent of  $\pi$ -electron delocalization. The compound crystallizes in the monoclinic space group C2/c with  $a = 30.266(7)$  Å,  $b = 9.403(6)$  Å,  $c = 15.881(9)$  Å,  $\beta = 120.35(6)^\circ$ , and  $Z = 8$ . The structure was refined by the least-squares procedure to  $R = 0.049$  for 2561 observed reflections. As indicated by the planarity of the molecule and the bond-lengths pattern, the  $\pi$ -electron delocalization extends over the whole molecule except for the ethoxycarbonylmethyl group. As expected, the arrangement of the benzothiazole and pyrrole moieties at the ethylenic double bond is *trans*.

In the last years, 2-alkoxycarbonylpyrrole derivatives have attracted considerable interest as they display a broad spectrum of biological activities, the analgesic, morphine agonist, spasmolytic, antipyretic, and antiinflammatory activities being some of the most important [1]. It has also been reported that introduction of additional alkoxycarbonyl and/or heteroaryl group(s) to the 1- and 4-positions of the pyrrole ring has a favourable effect to the spasmolytic activity. Therefore, our strategy was to incorporate extra ethoxycarbonylmethyl and 2-(2-benzothiazole)-2-cyanovinyl substituents in the 1- and 4-positions of the parent 2-ethoxycarbonylpyrrole in order to develop novel compound possessing spasmolytic and possibly other type of biological activity. Moreover, the title molecule can also be regarded as a push-pull ethylene, a class of compounds exhibiting a various degree of conjugation across the C=C double bond and hence polarization of the molecule which is responsible for unique properties of the compounds (*e.g.* absorption in the near-ultraviolet and visible regions). Thus, the purpose of this X-ray structural analysis was twofold: 1. to determine the spatial distribution of the functional groups as one of the main determinants of the biological activity and 2. to assess the extent of conjugation for the future study of the relationship between



the electronic and physicochemical properties of this class of compounds.

Crystal data and the data collection parameters are summarized in Table 1. The final atomic coordinates are given in Table 2, selected interatomic distances and bond angles in Table 3, and selected torsion angles in Table 4.

As shown in Fig. 1, which is an ORTEP [2] drawing of the molecule, the benzothiazole and pyrrole rings are *trans* positioned at the C10=C13 double bond. This bond (1.331(6) Å) is somewhat longer than that reported for unsubstituted ethylene [3] but fits well with values generally observed for weakly to moderately polarized ethylenes [4, 5]. Much stronger conju-

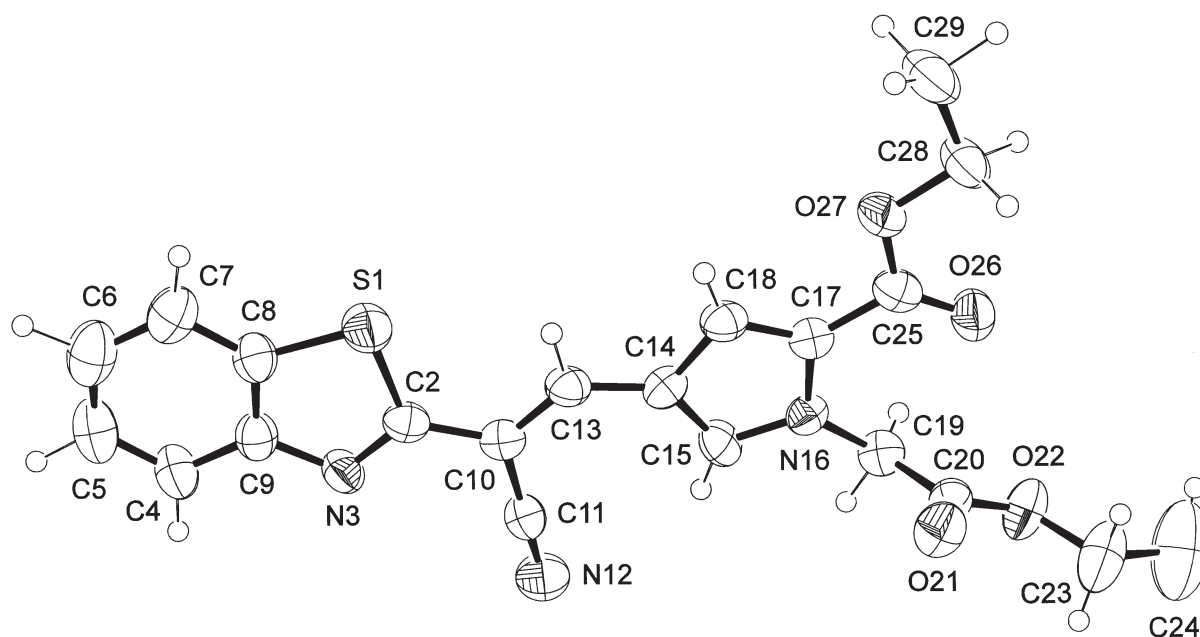
**Table 1.** Crystal Data and Structure Refinement for the Title Compound

Empirical formula	C <sub>21</sub> H <sub>19</sub> N <sub>3</sub> O <sub>4</sub> S
Relative molecular mass	409.45
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, C2/c
Unit cell dimensions	$a = 30.266(7)$ Å, $\alpha = 90^\circ$ $b = 9.403(6)$ Å, $\beta = 120.35(6)^\circ$ $c = 15.881(9)$ Å, $\gamma = 90^\circ$
Volume/Å <sup>3</sup>	3900(3)
$Z$ , calculated density	8, 1.395 Mg m <sup>-3</sup>
Measured density	1.40(1) Mg m <sup>-3</sup>
Absorption coefficient	0.20 mm <sup>-1</sup>
$F(000)$	1712
Crystal size	0.40 mm × 0.25 mm × 0.20 mm
$\theta$ range for data collection	1.56 to 23.56°
Reflections collected/unique	3023/2561 ( $R(\text{int}) = 0.035$ )
Refinement method	Full-matrix least-squares on $F^2$
Data/restraints/parameters	2561/0/263
Goodness-of-fit on $F^2$	0.994
Final $R$ indices ( $I > 2\sigma(I)$ )	$R1 = 0.0492$ , $wR2 = 0.1120$
$R$ indices (all data)	$R1 = 0.1184$ , $wR2 = 0.1460$

gation push-pull effect across the ethylenic bond and hence much larger C=C bond distance (1.37–1.38 Å) was observed for compounds possessing a strong  $\pi$ -electron donating function (*viz.* amine or imine nitrogen) bonded directly to the C=C bond [6, 7].

As expected, the benzothiazole and pyrrole rings are planar to within experimental error (r.m.s. deviations 0.005 and 0.002 Å, respectively) and are nearly coplanar with the plane of the ethylenic double bond

(atoms C2, C10, C11, C14, C13, H13, where H13 is the hydrogen atom bonded to C13), the dihedral angle being 1.9(3)° and 4.9(3)°, respectively. The twist about the C=C bond, as measured by the angle between the planes through C2, C10, C11 and C13, H13, C14 is 3.45(3)°. The conjugation in the molecule can also be observed in the C2—C10, C10—C11, and C13—C14 bond distances which are shorter than the values reported for C(*sp*<sup>2</sup>)—C(*sp*<sup>2</sup>) or C(*sp*<sup>2</sup>)—C(*sp*) single bonds [8, 9]. The two C—S bond distances in the benzothiazole ring (1.710(5) Å and 1.729(5) Å) are comparable with those found in thiophene [10] but are shorter than those reported for 2-amino-4-nitrobenzothiazole [11]. The difference (0.019 Å) between the two C—S bonds and the value for the C—S—C valence angle (90.2(2)°) are commonly observed in substituted benzothiazole derivatives [12–14]. Due to the equivalency of the two C—S bonds it is apparent that the lone pair on the sulfur contributes to the conjugation only within the ring system, with the  $\pi$ -density being not transferred further out of the ring. In contrast, the pyrrole ring is substantially distorted from C<sub>2v</sub> symmetry [15], the two N—C bond lengths differing by a highly significant amount of 0.045(5) Å. Obviously, this reflects the conjugation effect of the 2-ethoxycarbonyl substituent (at C17) and the push-pull effect of the ethylenic bond (at C14). The 2-ethoxycarbonyl group is roughly coplanar with the mean plane of the pyrrole ring (dihedral angle 4.6(6)°). The second ethoxycarbonyl group of the molecule is rotated around the N16—C19 and C19—C20 bonds so that it makes an angle of 79.8(4)° with the pyrrole plane. Thus, the overall planarity of

**Fig. 1.** A view of the title molecule showing the labelling of the non-H atoms. Displacement ellipsoids are shown at the 35 % probability level and H atoms are drawn as small circles of arbitrary radii.

**Table 2.** Final Positional Parameters and  $U_{eq}(U_{iso})$  with e.s.d.'s in Parentheses.  $U_{eq} = (1/3) \sum_i \sum_j U_{ij} a_i^* a_j^* a_i \cdot a_j$ 

Atom	$x/a$	$y/b$	$z/c$	$U_{eq}(U_{iso})/\text{\AA}^2$
S1	0.15932(5)	0.24269(15)	0.38416(9)	0.0556(5)
C2	0.1796(2)	0.3091(5)	0.3077(3)	0.0417(12)
N3	0.15613(15)	0.2575(4)	0.2197(3)	0.0455(10)
C4	0.0877(2)	0.0852(6)	0.1253(3)	0.0563(15)
C5	0.0538(2)	−0.0100(6)	0.1263(4)	0.067(2)
C6	0.0506(2)	−0.0316(6)	0.2079(5)	0.072(2)
C7	0.0815(2)	0.0426(6)	0.2918(4)	0.063(2)
C8	0.1158(2)	0.1366(5)	0.2920(3)	0.0470(13)
C9	0.1195(2)	0.1581(5)	0.2095(4)	0.0458(13)
C10	0.2193(2)	0.4139(5)	0.3419(3)	0.0403(12)
C11	0.2332(2)	0.4610(5)	0.2724(4)	0.0489(14)
N12	0.2443(2)	0.4975(5)	0.2177(3)	0.0684(15)
C13	0.2417(2)	0.4676(5)	0.4317(3)	0.0428(13)
C14	0.2790(2)	0.5759(5)	0.4787(3)	0.0391(12)
C15	0.3020(2)	0.6642(5)	0.4436(3)	0.0452(13)
N16	0.33272(13)	0.7547(4)	0.5143(2)	0.0387(9)
C17	0.3296(2)	0.7267(5)	0.5968(3)	0.0385(12)
C18	0.2969(2)	0.6176(5)	0.5753(3)	0.0433(12)
C19	0.3616(2)	0.8689(5)	0.5030(3)	0.0479(13)
C20	0.4175(2)	0.8472(6)	0.5610(3)	0.0446(13)
O21	0.43854(13)	0.7355(4)	0.5925(3)	0.0597(10)
O22	0.44068(13)	0.9683(4)	0.5691(2)	0.0620(11)
C23	0.4963(2)	0.9637(7)	0.6233(5)	0.085(2)
C24	0.5163(3)	1.1092(9)	0.6367(6)	0.139(3)
C25	0.3586(2)	0.8054(6)	0.6868(4)	0.0451(13)
O26	0.38998(13)	0.8951(4)	0.7020(2)	0.0582(10)
O27	0.34650(12)	0.7615(4)	0.7516(2)	0.0532(9)
C28	0.3759(2)	0.8224(6)	0.8473(3)	0.0567(14)
C29	0.3565(2)	0.7567(6)	0.9079(4)	0.072(2)
H4	0.0953	0.0864	0.0734	0.070
H5	0.0328	−0.0711	0.0652	0.083
H6	0.0265	−0.1187	0.2090	0.090
H7	0.0829	0.0343	0.3571	0.077
H13	0.2328	0.4323	0.4785	0.052
H15	0.2956	0.6685	0.3787	0.056
H18	0.2867	0.5784	0.6141	0.053
H19A	0.3513	0.8496	0.4324	0.060
H19B	0.3512	0.9373	0.5152	0.060
H23A	0.5029	0.9447	0.6870	0.102
H23B	0.5016	0.9213	0.5713	0.102
H24A	0.5064	1.1481	0.6800	0.158
H24B	0.4851	1.1730	0.5900	0.158
H24C	0.5089	1.1531	0.5700	0.158
H28A	0.3769	0.9516	0.8500	0.074
H28B	0.4138	0.7933	0.8755	0.074
H29A	0.3784	0.8029	0.9821	0.092
H29B	0.3125	0.7879	0.8774	0.092
H29C	0.3566	0.6622	0.9156	0.092

the molecule is only perturbed by the ethoxycarbonyl-methyl substituent.

## EXPERIMENTAL

### Synthesis

A solution of 2-ethoxycarbonyl-1-(ethoxycarbonylmethyl)pyrrole-4-carbaldehyde (0.51 g; 2 mmol) [16] in ethanol (10 cm<sup>3</sup>) and 10 % ethanolic sodium ethoxide (3–4 drops) were added to a hot solution of benzothiazol-2-ylacetonitrile (0.34 g; 2 mmol) [17] in

the same solvent (10 cm<sup>3</sup>) while stirring. The reaction mixture was refluxed during 30 min, whereupon it was gradually cooled to room temperature with stirring. The solid portion was filtered off and recrystallized from ethanol, the yield being 0.8 g (56 %), m.p. = 86–88°C.

### X-Ray Structural Analysis

The crystal used for the data collection was obtained by recrystallization from ethanol–water ( $\varphi_r = 1 : 1$ ) mixture. The density of crystals was mea-

**Table 3.** Selected Bond Lengths and Bond Angles with e.s.d.'s in Parentheses

Bond	Bond length/Å	Bond	Bond length/Å
S1—C8	1.710(5)	C11—N12	1.133(6)
S1—C2	1.729(5)	C13—C14	1.419(6)
C2—N3	1.300(6)	C14—C15	1.372(6)
N3—C9	1.396(6)	C14—C18	1.400(6)
C2—C10	1.433(6)	C15—N16	1.339(5)
C8—C9	1.385(6)	N16—C17	1.384(5)
C10—C13	1.331(6)	N16—C19	1.452(6)
C10—C11	1.435(7)	C17—C25	1.447(7)
Atoms	Angle/°	Atoms	Angle/°
C8—S1—C2	90.2(2)	C10—C13—C14	132.5(4)
N3—C2—C10	124.1(4)	C15—C14—C18	106.3(4)
N3—C2—S1	115.2(4)	C15—C14—C13	130.7(4)
C2—N3—C9	110.1(4)	C18—C14—C13	122.9(4)
C10—C2—S1	120.6(4)	N16—C15—C14	108.9(4)
C13—C10—C11	121.2(5)	C15—N16—C17	108.9(4)
C13—C10—C2	122.9(4)	C15—N16—C19	124.9(4)
C11—C10—C2	115.9(4)	C17—N16—C19	126.1(4)
N12—C11—C10	179.6(5)	C18—C17—N16	107.3(4)
C17—C18—C14	108.7(4)		

**Table 4.** Selected Torsion Angles with e.s.d.'s in Parentheses

Atoms	Angle/°
S1—C2—C10—C13	−1.4(6)
S1—C2—C10—C11	179.7(3)
C2—C10—C13—C14	−175.8(4)
C10—C13—C14—C15	3.2(9)
C19—N16—C17—C25	−4.3(6)
C15—N16—C19—C20	−113.6(5)
N16—C19—C20—O21	20.4(7)
C19—C20—O22—C23	−179.0(4)
C18—C17—C25—O26	174.3(5)
C17—C25—O27—C28	174.8(4)

sured by flotation in a bromoform—cyclohexane solution. Approximate values of lattice parameters found from Weissenberg photographs were refined by least-squares method using 15 precisely centred reflections on a Syntex P2<sub>1</sub> diffractometer (interval of 2 $\theta$  angles 13—22°). Integral intensities were collected at room temperature on a Syntex P2<sub>1</sub> diffractometer using graphite-monochromated MoK $\alpha$  radiation and the  $\Theta$  – 2 $\Theta$  scan technique. To check stability of the apparatus, two reference reflections were measured after every 100 measured reflections; no systematic decrease of the reference reflections during the measurement was observed. Only reflections classified as observed according to the criterion  $I > 2\sigma(I)$  were included in the refinement of the structure. All intensities were corrected for Lorentz and polarization factors using the local program XP21 [18]. The structure was solved by direct methods and refined by the full-matrix least-

squares method using the SHELXS-86 and SHELXL-93 program packages, respectively [19, 20]. The hydrogen atoms were located from a difference Fourier map but were not refined with  $U_{\text{iso}}$  set to 1.20  $U_{\text{eq}}$  of the parent atom.

Tables of the anisotropic thermal parameters for the nonhydrogen atoms ( $U_{ij}$ ), bond lengths involving the hydrogen atoms, and  $F_o$ ,  $F_c$  values were deposited as “supplementary material” at one of the authors (V. K.).

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