Thiophene 1-Oxides. V [1], [2], [3], [4]. Comparison of the Crystal Structures and Thiophene Ring Aromaticity of 2,5-Diphenylthiophene, its Sulfoxide and Sulfone

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The detailed preparation of 2,5-diphenylthiophene 1-oxide (2) is reported as well as the comparative study of the crystal structures of 2,5-diphenylthiophene, 1, its sulfoxide 2 and sulfone 3 obtained by X-ray diffraction. This work represents the first experimental study of a complete heterocyclic series, including a thiophene derivative, and the corresponding sulfoxide and sulfone. On the basis of the geometrical parameters, the first unequivocal experimental parameters obtained for a thiophene 1-oxide derivative, we have also examined the evolution of the aromatic character of the thiophene ring when oxidizing the sulfur atom to the sulfoxide and the sulfone. Paolini's bond orders and Julg and François's aromaticity indices have also been calculated for the three compounds and compared to those previously calculated for related thiophene derivatives by semi-empirical or *ab initio* methods [6], [7]. All the data examined showed that, in spite of its non planarity, the thiophene ring of 2,5-diphenylthiophene 1-oxide 2 could still exhibit some delocalization of its π electrons indicating a certain degree of aromaticity lower than in thiophene 1 but higher than in the sulfone 3.

Intoduction.

Recent results suggest that thiophene 1-oxides could often be formed as primary reactive metabolites from thiophene derivatives *in vivo* [2]. Thus, mercaptates derived from the reaction of glutathione with thiophene 1-oxide have been identified as the major urinary metabolites of thiophene itself in rats. Moreover, a thiophene sulfoxide derived from the cytochrome P450-catalyzed oxidation of a 3-aroylthiophene compound in rat liver microsomes has been trapped by reaction with thiol nucleophiles and mercaptates derived from the reaction of this thiophene sulfoxide with glutathione have been found in the urine of rats treated with the 3-aroylthiophene [1], [4]. Finally, the toxic effects of a 2-aroylthiophene drug, thienylic acid (Ticrynafen), as well as its ability to act as a suicide substrate of human liver P450 2C9 [8], have been attributed to the intermediate formation of a thiophene sulfoxide metabolite. However, such thiophene *S*-oxides which appear to play important roles in drug metabolism and toxicology, are generally incompletly known in chemistry. Only two of them bearing two bulky substituents at positions 2 and 5 have been prepared in low yields (5%), by chemical oxidation of the corresponding thiophenes, and characterized by uv and nmr spectroscopy in solution [9]. Other thiophene 1-oxides have been produced as transient species and only characterized at the level of their complexes with transition metals [10] or their adducts with Diels-Alder dienophiles [11].

In order to understand the formation and biological consequences of thiophene *S*-oxides, it is necessary to better understand the chemical structure and reactivity of these species, and hence to find good preparative methods for their formation. Quite recently, we have reported preliminary results about a selective method of *S*-oxidation of some thiophene and benzothiophene derivatives, and its application to the synthesis of 2,5-diphenylthiophene 1-oxide (2). Also reported were the first results about the solid state structure of 2 [3]. In fact, a search through the Cambridge Structural Database [12] revealed that only two crystal structures of thiophene sulfoxide derivatives were available (if one exclude benzothiophene derivatives). However, the first instance is concerned with a rhodium complex of tetramethylthiophene 1-oxide [10]. The second case involves the structure of tetraphenylthiophene 1-oxide for which there is an indetermination on the S and O positions caused by local disorder in the crystal [13]. Thus, since the crystal structure of 2,5-diphenylthiophene 1-oxide provided the first complete structure characterization of a thiophene 1-oxide, it appeared interesting to compare its structural characteristics with those of the corresponding thiophene and thiophene sulfone derivatives. In fact, although some properties of thiophenes, such as their degree of aromaticity, have been compared to those of the corresponding sulfoxide and sulfone using semi-empirical and *ab initio* calculation, no such comparison of the crystal structures has ever been reported. Actually, only three structures of thiophene 1,1-dioxides have been published.

In this paper, we describe the preparation of 2,5-diphenylthiophene, **1**, and of its sulfoxide **2** and sulfone **3** and present the comparative study of the X-ray structures of these three compounds, the first complete series, including a thiophene derivative and the corresponding sulfoxide and sulfone.

EXPERIMENTAL

Melting points were determined with a Kofler hot stage and were uncorrected. Mass spectra were recorded on a Nermag R10-10 spectrometer at the Ecole Normale Supérieure de Paris. Infrared spectra were taken on a Perkin Elmer 783 spectrophotometer. The intensity of each vibration is indicated between brakets using the following abbreviations: w (weak), m (medium), s (strong). The ^{1}H- and ^{13}C-nmr spectra were recorded on a Bruker ARX 250 spectrometer. Chemical shifts are reported in δ relative to the signal of tetramethylsilane taken as an internal standard. uv-visible spectra were recorded on a Kontron-Uvikon 810 (or 820) spectrophotometer. Neutral aluminium oxide used for flash chromatography was obtained from Aldrich (Brockmann standard grade 1, ca 150 mesh). Dibenzoylethane was purchased from Lancaster; the Lawesson's reagent and trifluoroacetic acid from Janssen Chimica and hydrogen peroxide (30% in water) from Prolabo.

Synthesis.

2,5-Diphenylthiophene (**1**).

Following the procedure of Schridhar [14], 5 g (21 mmoles) of 1,2-dibenzoylethane and 10.2 g (25 mmoles) of Lawesson's reagent in 100 ml of toluene yielded, after recrystallization in hot isopropyl alcohol, 2.1 g (45%) of purified 2,5-diphenylthiophene, mp 147° (lit 152-153° [12]). Its ^{1}H nmr was identical to that previously published.

2,5-Diphenylthiophene 1-Oxide (**2**).

This compound was obtained by dissolving 236 mg (1 mmole) of **1** and 4.6 ml (60 mmoles) of trifluoroacetic acid in 10 ml of dichloromethane. Hydrogen peroxide (0.3 ml, 3 mmoles) was added to the reaction mixture maintained in an ice bath. The reaction was monitored by tlc (Merck aluminium oxide plates 60F$_{250}$, type E), 0.25 mm, dichloromethane: Rf = 0.9 (thiophene); Rf = 0.6 (sulfoxide). After completion of the reaction (4 hours), the reaction mixture was neutralized with a saturated solution of sodium bicarbonate and the dichloromethane layers were washed with brine. The product was isolated and purified by flash chromatography over deactivated aluminium oxide (6% water) and eluted with dichloromethane, yielding 107 mg (42%) of yellow crystals of the 2,5-diphenylthiophene 1-oxide (**2**), mp 124-126° dec (from dichloromethane/hexane). The neutralization, isolation and purification steps must be done quickly because the crude sulfoxide decomposes rapidly. ^{1}H nmr (deuteriodichloromethane): δ 7.70 (4H, m, *ortho* H), 7.30-7.50 (6H, m, *para* H, *meta* H), 6.96 ppm (2H, s, H3, H4); ^{13}C nmr (deuteriochloroform): δ 152.2 (C2, C5), 130.8 (C6, C6'), 129.3 (*para* C), 129.2 (*meta* C), 126.6 (*ortho* C), 123.6 ppm (C3, C4); ms: (70 eV, electron impact) m/z 252 (M$^+$, 18), 236 (M$^+$-16, 100); ms: (chemical ionization, ammonia) m/z 270 (M$^+$+18, 3), 253 (M$^+$+1, 16); 237 (M$^+$-16+1, 95), 236 (M$^+$-16, 100); ir (potassium bromide): ν 3060 (w), 3020 (w), 2960 (m), 2920 (s), 2850 (m),

1595 (w), 1490, 1495 (m), 1316 (w), **1050 (s, SO)**, 855, 840 (w), 760, 755, 690 (s) cm^{-1}; uv (acetonitrile): λ max 230 nm (shoulder), 266 nm (shoulder), 305 nm (ε 25,000); hmrs Calcd. for C$_{16}$H$_{12}$OS: 252.0611. Found: 252.0609 (M$^+$).

Anal. Calcd. for C$_{16}$H$_{12}$OS: C, 76.2; H, 4.8; S, 12.7. Found: C, 76.42; H,4.92; S, 12.95.

2,5-Diphenylthiophene 1,1-Dioxide (**3**).

Following the procedure of Miyahara for the oxidation of thiophene derivatives [15], the reaction of 100 mg (0.42 mmole) of **1** with 10 ml (0.84 mmole) of an acetone solution of dimethyldioxirane [16] (0.084 mole.l^{-1}) in 35 ml of dichloromethane yielded, after flash chromatography (deactivated aluminium oxide (4% water), dichloromethane/cyclohexane (70/30)), 93 mg (83%) of a yellow powder of 2,5-diphenylthiophene 1,1-dioxide (**3**), mp 179° (lit 179-180° [15]). The ^{1}H nmr was identical to that previously published [17].

Preparation of crystaline Products **1, 2, 3**.

Crystals of **1** and **3** suitable for X-ray investigation were grown from a minimun amount of ethyl acetate. This mixture was warmed and a small amount of toluene was added until complete dissolution. This mixture was then kept overnight at room temperature. Crystals which separated were washed with a small amount of ethyl acetate and dried. Crystals of **2** suitable for X-ray investigation were grown from a minimum amount of hot toluene. This mixture was then kept overnight at room temperature. Crystals of X-ray quality were separated, washed with little toluene and dried.

Crystal data for **1** is: C$_{16}$H$_{12}$S, M_r = 236.32, monoclinic, a = 27.372(11), b = 5.818(2), c = 7.617(3) Å, β = 98.16(4)°, V = 1200.7(8) Å^3 (from accurate 2θ values for 25 reflections with 41 ≤2θ ≤52°, λ = 1.5418 Å), space group $P2_1/n$, Z = 4, Dx = 1.307 g.cm^{-3}, T = 293 K; colorless tablets; μ (Cu-Kα) = 2.137 mm^{-1}.

Crystal data for **2** is: C$_{16}$H$_{12}$SO, M_r = 252.32, orthorhombic, a = 6.631(3), b = 7.270(3), c = 26.081(10) Å, V = 1257.3(9) Å^3 (from accurate 2θ values for 23 reflections with 27 ≤2θ ≤43°, λ = 1.5418 Å), space group $Pnam$, Z = 4, Dx = 1.333 g.cm^{-3}, T = 293 K; bright yellow tablets; μ (Cu-Kα) = 2.138 mm^{-1}.

Crystal data for **3** is: C$_{16}$H$_{12}$SO$_2$, M_r = 268.32, orthorhombic, a = 7.273(3), b = 14.811(6), c = 12.195(5) Å, V = 1313.6(9) Å^3 (from accurate 2θ values for 25 reflections with 20 ≤2θ ≤41°, λ = 1.5418 Å), space group $P2_12_12_1$, Z = 4, Dx = 1.357 g.cm^{-3}, T = 293 K; green yellow tablets; μ (Cu-Kα = 2.139 mm^{-1}.

Data Collection and Processing.

Diffraction data were collected on a Philips PW1100 Diffractometer; maximum 2θ of 53.28° with -31 ≤h ≤31, 0 ≤k ≤6, 0 ≤l ≤8 for crystalline **1**, 67.02° with 0 ≤h ≤7, 0 ≤k ≤8, 0 ≤l ≤31 for crystalline **2** and 60.08° with 0 ≤h ≤8, 0 ≤k ≤16, 0 ≤l ≤13 for crystalline **3**. Of the 1512 (crystalline **1**) and 1148 (crystalline **3**) unique reflections measured for each crystalline substance, respectively, only the 1244 (**1**) and 929 (**3**) reflections with (F ≥ 6σ(F)) were used in the solution and refinement of the structures. For crystalline **2**, 1138 data were collected and used in all calculations. Three standard reflexions were collected every 60 minutes; the maximum drift correction was 1.1% for crystalline **1**, 1.4% for crystalline **2** and 3.5% for crystalline **3**.

Structures Analysis and Refinement.

The structures were solved by direct methods using SHELXS-86 [18] and refined using SHELXL-93 [19]. Approximate

positions of all non-hydrogen atoms were found in the first Fourier map. For structures **1** and **2**, all hydrogen atoms were found by difference synthesis and refined isotropically; for structure **3**, all hydrogen atoms were generated geometrically with C-H = 0.93 Å and Ueq equal 1.2 times that of the parent atom. No absorption correction was made. At final convergence with refinement method of Full-matrix least-squares on F^2, R = 0.078, wR2 = 0.208, S = 1.21 for 202 parameters, $(\Delta\rho)max/(\Delta\rho)min$ = 0.59/-0.43 eÅ^{-3} for structure **1**, R = 0.052, wR2 = 0.156, S = 1.07 for 110 parameters, $(\Delta\rho)max/(\Delta\rho)min$ = 0.32/-0.33 eÅ^{-3} for structure **2** and R = 0.058, wR2 = 0.150, S = 1.16 for 173 parameters, $(\Delta\rho)max/(\Delta\rho)min$ = 0.35/-0.36 eÅ^{-3} for structure **3**. The weighting scheme is w = 1/[σ^2(Fo^2) + (0.0888P)^2 + 2.9697P] for structure **1**, w = 1/[σ^2(Fo^2) + (0.0882P)^2 + 1.2942P] for structure **2** and w = 1/[σ^2(Fo^2) + (0.1174P)^2 + 0.1936P] for structure **3**, where P = (Fo^2 + 2Fc^2)/3 and in the final cycle $(\Delta/\sigma)max$ = 0.036 (**1**), 0.001 (**2**) and 0.001 (**3**). Tables of bond lengths and angles are given in Tables 1 to 6, fractional coordinates and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre and are available as supplementary material. The atom numbering is given in Scheme 1. Plots of the structure are shown in Figures 1 and 2. All calculations were done on IBM RS6000 cluster at IDRIS.

either to the sulfone **3** or to an opened-ring compound, 1,4-diphenylbut-2-ene-1,4-dione (**4**).

In the crystal structure of 2,5-diphenylthiophene, the thiophene ring is planar with the sulfur atom being in the mean plane of the four carbon atoms. Dihedral angles of 8.3(2)° and 8.7(2)° are found between the phenyl rings and the central thiophene ring (Figure 1). The bond distances and angles obtained for the thiophene ring are comparable to those previously reported for other thiophene derivatives [12]. The molecule found in the crystal structure of 2,5-diphenylthiophene 1-oxide has a mirror plane defined by S, O and the mid-point of C(3)-C(4). The heterocycle is not planar; the sulfur atom lies outside the plane formed by the four thiophene carbon atoms by 0.278 Å whereas the oxygen atom lies outside this plane in the opposite direction by 0.746 Å (Figure 2). A dihedral angle of -12.5(1)° is found between the phenyl rings and the central thiophene ring. In the crystal structure of 2,5-diphenylthiophene 1,1-dioxide, the heterocycle is planar with the S atom being in the mean plane of the four carbon atoms. The SO$_2$ moiety was found to lie in a plane perpendicular to the thiophene ring. The two oxygen atoms are located outside
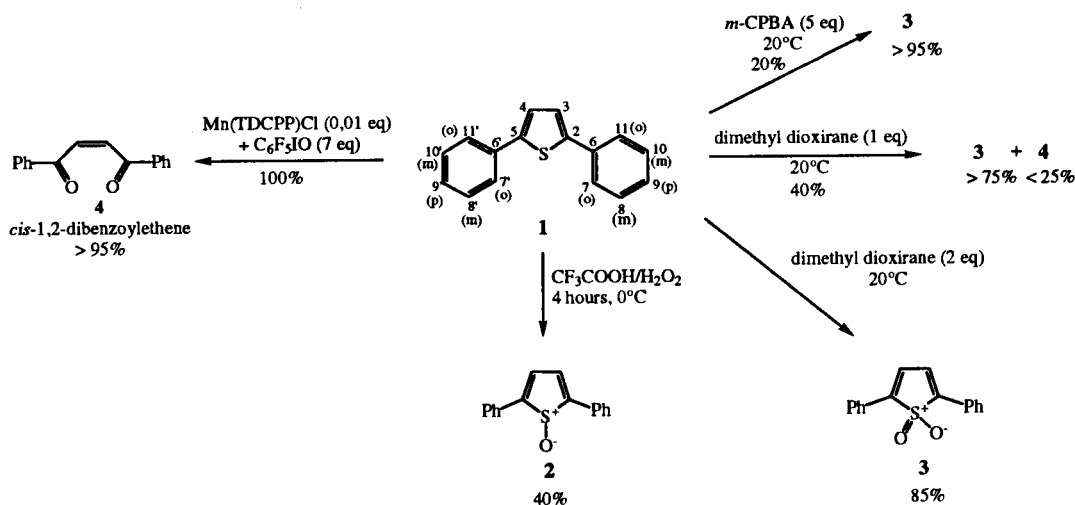
m-CPBA = meta-chloroperbenzoic acid; TDCPP = meso-tetra-(2,6-dichlorophenyl)porphyrin

Results.

2,5-Diphenylthiophene 1-oxide was prepared by oxidation of 2,5-diphenylthiophene with a mixture of hydrogen peroxide and trifluoroacetic acid (Scheme 1). This oxidative system was first used to prepare benzo[b]thiophene 1-oxide [1], which had never before been described in the literature, and appeared to be very useful to prepare some thiophene S-oxides with rather good yields [3]. Among the different chemical oxidative systems we tried, the trifluoroacetic adid/hydrogen peroxide system was the only one which selectively gave sulfoxide **2** (Scheme 1). Other systems such as meta-chloroperbenzoic acid, dimethyldioxirane or iodosobenzene in the presence of a Mn(II) porphyrin, led

this plane, on opposite sides, by distances respectively of -1.21(1) Å and 1.21(1) Å (Figure 2). Dihedral angles of 7.4(2)° and -39.1(2)° are found between the two benzene rings and the central thiophene ring.

Bond distances and bond angles for the three compounds under investigation are listed in Tables 1 to 6 with estimated standard deviations in parentheses.

The S-O distances found in the sulfoxide and in the sulfones are respectively 1.484(3) Å (**2**), 1.418(5) Å and 1.427(5) Å (**3**). These bond lengths as well as the shorter distance found for the S-O bond of **3** when compared to **2** are in agreement with what has already been reported for other aliphatic acyclic or cyclic sulfoxides or sulfones [12], [20].
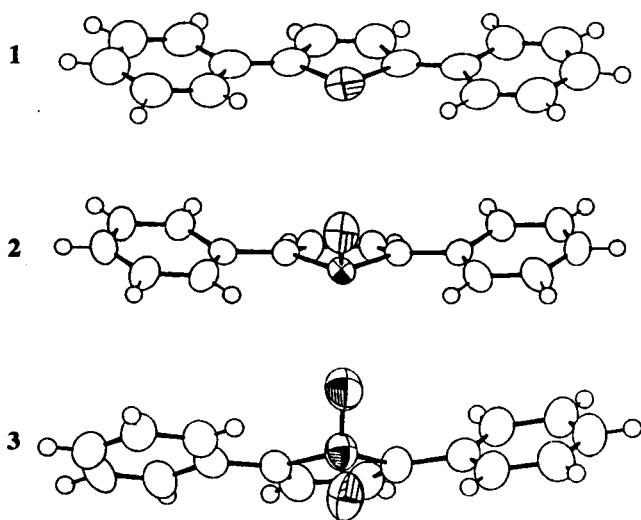
1

2

3

Figure 1. ORTEP structures of compounds **1**, **2** and **3** (molecules A and B) front views.
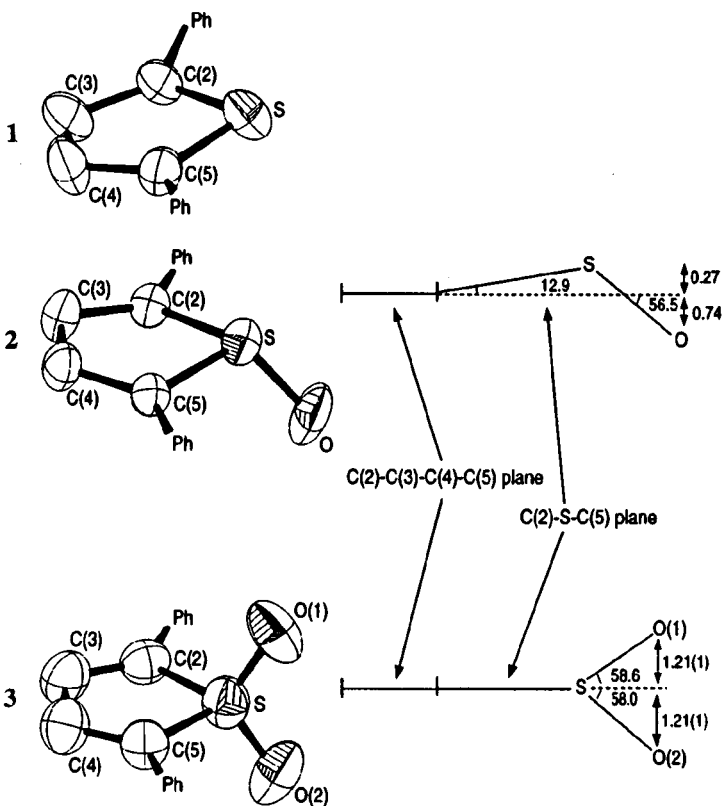
1

2

3

Figure 2: ORTEP structures of compounds **1**, **2** and **3** (molecules A and B) side views.

Discussion.

The planarity, sulfur atom bonding characteristics and geometry of the carbon atom framework of the thiophene

ring of compounds **1**, **2** and **3** have been examined in order to characterize the effects of the binding of one or two

Table 1

Bond Lengths (Å) of 2,5-Diphenylthiophene (**1**).

S-C(2)	1.718 (6)	C(9)-H(9)	0.99 (7)
S-C(5)	1.726 (6)	C(10)-C(11)	1.334 (10)
C(4)-C(5)	1.380 (9)	C(10)-H(10)	0.95 (7)
C(5)-C(6')	1.418 (8)	C(11)-H(11)	1.00 (8)
C(3)-C(4)	1.361 (11)	C(6')-C(11')	1.427 (9)
C(4)-H(4)	0.75 (9)	C(6')-C(7')	1.428 (9)
C(2)-C(3)	1.386 (9)	C(7')-C(8')	1.363 (10)
C(3)-H(3)	0.78 (5)	C(7')-H(7')	0.85 (8)
C(2)-C(6)	1.440 (8)	C(8')-C(9')	1.357 (10)
C(6)-C(11)	1.414 (9)	C(8')-H(8')	1.03 (8)
C(6)-C(7)	1.408 (9)	C(9')-C(10')	1.401 (10)
C(7)-C(8)	1.345 (10)	C(9')-H(9')	0.99 (5)
C(7)-H(7)	0.98 (6)	C(10')-C(11')	1.330 (10)
C(8)-C(9)	1.374 (11)	C(10')-H(10')	0.97 (8)
C(8)-H(8)	0.80 (8)	C(11')-H(11')	0.92 (8)
C(9)-C(10)	1.407 (10)		

Table 2

Bond Angles (degree) of 2,5-Diphenylthiophene (**1**).

C(5)-S-C(2)	93.7 (3)	C(11)-C(10)-C(9)	120.6 (8)
C(3)-C(2)-C(6)	129.4 (6)	C(11)-C(10)-H(10)	131 (5)
C(3)-C(2)-S	108.7 (5)	C(9)-C(10)-H(10)	108 (5)
C(6)-C(2)-S	121.7 (4)	C(10)-C(11)-C(6)	123.0 (7)
C(4)-C(3)-C(2)	114.3 (6)	C(10)-C(11)-H(11)	124 (4)
C(4)-C(3)-H(3)	137 (4)	C(6)-C(11)-H(11)	113 (4)
C(2)-C(3)-H(3)	108 (4)	C(5)-C(6')-C(7')	123.3 (6)
C(3)-C(4)-C(5)	114.9 (6)	C(5)-C(6')-C(11')	123.2 (6)
C(3)-C(4)-H(4)	128 (7)	C(7')-C(6')-C(11')	113.5 (7)
C(5)-C(4)-H(4)	116 (7)	C(8')-C(7')-C(6')	121.9 (7)
C(4)-C(5)-C(6')	129.7 (6)	C(8')-C(7')-H(7')	125 (6)
C(4)-C(5)-S	108.4 (5)	C(6')-C(7')-H(7')	112 (6)
C(6')-C(5)-S	121.7 (4)	C(9')-C(8')-C(7')	122.0 (8)
C(7)-C(6)-C(11)	115.1 (6)	C(9')-C(8')-H(8')	119 (4)
C(7)-C(6)-C(5)	123.1 (6)	C(7')-C(8')-H(8')	118 (4)
C(11)-C(6)-C(5)	121.8 (6)	C(8')-C(9')-C(10')	118.1 (8)
C(8)-C(7)-C(6)	121.5 (7)	C(8')-C(9')-H(9')	126 (3)
C(8)-C(7)-H(7)	124 (3)	C(10')-C(9')-H(9')	116 (3)
C(6)-C(7)-H(7)	114 (3)	C(11')-C(10')-C(9')	120.8 (7)
C(7)-C(8)-C(9)	122.5 (8)	C(11')-C(10')-H(10')	133 (5)
C(7)-C(8)-H(8)	135 (6)	C(9')-C(10')-H(10')	106 (5)
C(9)-C(8)-H(8)	101 (6)	C(10')-C(11')-C(6')	123.7 (7)
C(8)-C(9)-C(10)	117.2 (8)	C(10')-C(11')-H(11')	126 (5)
C(8)-C(9)-H(9)	128 (4)	C(6')-C(11')-H(11')	110 (5)
C(10)-C(9)-H(9)	114 (4)		

oxygen atoms to a thiophene sulfur atom. For that purpose, selected bond lengths, bond angles and torsion angles are reported in Table 7. These data are compared with theoretical predictions made on thiophene 1-oxide itself from semi-empirical MNDO [6] or *ab initio* [7], [21] calculations. An interesting question related to that comparison is concerned with the degree of aromaticity of the thiophene ring in **1**, **2** and **3**. The concept of aromaticity is considered as one of the most important general concept for the general under-standing of organic chemistry and heterocyclic chemistry. Its complexity is emphasised by the writting of Katritzky:

Table 3

Bond Lengths (Å) of 2,5-Diphenylthiophene-S-oxide (2)

S-O	1.484 (3)	C(7)-H(7)	0.93 (4)
S-C(2)	1.781 (2)	C(8)-C(9)	1.370 (5)
C(2)-C(3)	1.345 (4)	C(8)-H(8)	0.97 (5)
C(2)-C(6)	1.462 (3)	C(9)-C(10)	1.368 (5)
C(3)-C(3i)	1.433 (5)	C(9)-H(9)	0.94 (4)
C(3)-H(3)	0.88 (4)	C(10)-C(11)	1.381 (4)
C(6)-C(11)	1.393 (4)	C(10)-H(10)	0.89 (4)
C(6)-C(7)	1.392 (4)	C(11)-H(11)	0.98 (3)
C(7)-C(8)	1.390 (4)		

Symmetry codes: (i) x, y, -z+3/2

Table 4

Bond Angles (degree) of 2,5-Diphenylthiophene-S-oxide (2)

O-S-C(2)	112.66 (12)	C(6)-C(7)-H(7)	119 (2)
O-S-C(2i)	112.65 (12)	C(9)-C(8)-C(7)	120.5 (3)
C(2)-S-C(2i)	91.3 (2)	C(9)-C(8)-H(8)	123 (2)
C(3)-C(2)-C(6)	130.2 (2)	C(7)-C(8)-H(8)	116 (2)
C(3)-C(2)-S	108.9 (2)	C(10)-C(9)-C(8)	119.6 (3)
C(6)-C(2)-S	120.7 (2)	C(8)-C(9)-H(9)	122 (2)
C(2)-C(3)-C(3i)	114.5 (2)	C(9)-C(10)-C(11)	120.9 (3)
C(3i)-C(3)-H(3)	123 (2)	C(10)-C(9)-H(9)	118 (2)
C(2)-C(3)-H(3)	122 (2)	C(11)-C(10)-H(10)	120 (3)
C(7)-C(6)-C(2)	121.7 (2)	C(9)-C(10)-H(10)	119 (3)
C(11)-C(6)-C(2)	119.9 (2)	C(10)-C(11)-C(6)	120.3 (3)
C(11)-C(6)-C(7)	118.3 (3)	C(10)-C(11)-H(11)	121 (2)
C(8)-C(7)-C(6)	120.3 (3)	C(6)-C(11)-H(11)	119 (2)
C(8)-C(7)-H(7)	120 (2)		

Symmetry codes: (i) x, y, -z+3/2. For more ease in the comparison of the different crystal structures, the atoms C(2i), C(3i) and C(6i) will be refered in the discussion and in the summary Tables (Tables 7, 8 and 9) as respectively the atoms C(5), C(4) and C(6').

Table 5

Bond Lengths (Å) of 2,5-Diphenylthiophene-1,1-Dioxide (3)

S-O(1)	1.418 (5)	C(7')-C(8')	1.396 (9)
S-O(2)	1.427 (5)	C(8')-C(9')	1.356 (10)
S-C(2)	1.780 (6)	C(9')-C(10')	1.368 (10)
S-C(5)	1.770 (6)	C(10')-C(11')	1.398 (9)
C(2)-C(3)	1.324 (9)	C(6)-C(11)	1.389 (9)
C(2)-C(6)	1.476 (8)	C(6)-C(7)	1.373 (9)
C(3)-C(4)	1.497 (9)	C(7)-C(8)	1.394 (10)
C(4)-C(5)	1.316 (8)	C(8)-C(9)	1.367 (11)
C(5)-C(6')	1.482 (8)	C(9)-C(10)	1.372 (12)
C(6')-C(11')	1.380 (8)	C(10)-C(11)	1.383 (10)
C(6')-C(7')	1.372 (9)		

Table 6

Bond Angles (degrees) of 2,5-Diphenylthiophene-1,1-Dioxide (3).

O(1)-S-O(2)	116.6 (3)	C(7')-C(6')-C(5)	121.8 (6)
O(1)-S-C(2)	110.3 (3)	C(11')-C(6')-C(5)	118.3 (6)
O(2)-S-C(2)	111.6 (3)	C(6')-C(7')-C(8')	119.7 (6)
O(1)-S-C(5)	112.3 (3)	C(9')-C(8')-C(7')	120.1 (7)
O(2)-S-C(5)	109.7 (3)	C(8')-C(9')-C(10')	121.1 (7)
C(5)-S-C(2)	94.2 (3)	C(9')-C(10')-C(11')	119.2 (7)
C(3)-C(2)-C(6)	132.0 (6)	C(6')-C(11')-C(10')	120.1 (7)
C(3)-C(2)-S	107.4 (5)	C(7)-C(6)-C(2)	121.3 (5)
C(6)-C(2)-S	120.6 (4)	C(11)-C(6)-C(2)	119.5 (6)
C(2)-C(3)-C(4)	115.5 (6)	C(7)-C(6)-C(11)	119.2 (6)
C(5)-C(4)-C(3)	114.0 (6)	C(6)-C(7)-C(8)	119.9 (7)
C(4)-C(5)-C(6')	129.7 (5)	C(9)-C(8)-C(7)	120.4 (8)
C(4)-C(5)-S	108.9 (4)	C(8)-C(9)-C(10)	120.3 (7)
C(6')-C(5)-S	121.3 (4)	C(9)-C(10)-C(11)	119.6 (7)
C(7')-C(6')-C(11')	119.8 (6)	C(6)-C(11)-C(10)	120.6 (7)

maximizes the overlap of the p-orbitals involved in the π-system; (ii) cyclic conjugation leads to a levelling out of the differences in bond length between formal double and single bonds. In that context, a molecule can be considered as aromatic when the lengths of its carbon-carbon bonds are close to the value of 1.397 Å found in benzene [22].

Regarding the first notion of planarity, the thiophene ring of 1 is clearly planar whereas that of 2 is not. The nonplanarity of S-oxides of sulfur-containing heterocycles has been previously observed [21], [23]. It has also been predicted from theoretical calculations for thiophene 1-oxide itself [6], [7], and it has been proposed that this could be due to the pyramidal geometry of the sulfur atom which is more difficult to accomodate in a five-membered ring because it introduces stress in the molecule [7]. A similar pyramidal geometry has been proposed for 2,5-di-*tert*-octylthiophene 1-oxide on the basis of nmr spectroscopic studies which showed the existence of two pyramidal conformations of the molecule in fast exchange at room temperature [9]. However, the deviation from planarity of sulfoxide 2 is small contrary to what was observed for a tetramethylthiophene 1-oxide Rhodium complex [10]. In the sulfoxide 2, the sulfur and oxygen atoms are displaced on opposite sides of the mean plane of the thiophene ring resulting in a structure in which some π-delocalisation could still exist (Figure 2).

Regarding the notion of cyclic conjugation with mean C-C bonds intermediate between single and double bonds, Table 7 shows that there is a lengthening of the C(3)-C(4) bond as well as a shortening of the C(2)-C(3) and C(4)-C(5) bonds when passing from 1 which is clearly aromatic to 2. This feature results in a more pronounced alternation between double and single C-C bonds in the thiophene ring of 2 (1.386 (9), 1.380(9) and 1.361(11) Å in 1 instead of 1.345(4) and 1.433(5) Å in 2 for the C-C double and single bonds). This bond alternation is even more marked in sulfone 3 (Table 7). The carbon-sulfur bond distances found in the three derivatives

"aromaticity is not merely a yes/no concept" [22]. During the last ten years, the concept of heteroaromaticity has been fully discussed, the most recent review being written by Simkin *et al.* [23]. These authors concluded that there was no general parameters able to give a quantitative scale of aromaticity. However geometrical criteria may be used to evaluate quantitative variations of aromaticity in a series of similar, comparable molecules. Inherent in the definition of aromaticity are the two following notions: (i) a planar ring

Table 7

Characteristic Bond Lengths (Å) Bond Angles (degree) and Torsion Angles (degrees) of 2,5-Diphenylthiophene (1), 2,5-Diphenylthiophene 1-Oxide (2) [a] and 2,5-Diphenylthiophene-1,1-dioxide (3) from the Crystal Structures Obtained from X-ray Analysis: Comparison with those Reported for the Thiophene 1-Oxide from MNDO Optimized Geometries [6, 7]

	1	2	3	[b]	[c]	[d]	[e]
bond length							
S-O(1)	/	1.484 (3)	1.418 (5)	1.516	1.487	1.516	1.510
S-O(2)	/	/	1.427 (5)	/	/	/	/
S-C(2)	1.718 (6)	1.781 (2)	1.780 (6)	1.776	1.782	1.786	1.673
S-C(5)	1.726 (6)	1.781 (2)	1.770 (6)	[a]	[a]	[a]	[a]
C(2)-C(3)	1.386 (9)	1.345 (4)	1.324 (9)	1.351	1.322	1.324	1.372
C(3)-C(4)	1.361 (11)	1.433 (5)	1.497 (9)	1.477	1.484	1.475	1.409
C(4)-C(5)	1.380 (9)	1.345 (4)	1.316 (8)	[a]	[a]	[a]	[a]
C(2)-C(6)	1.440 (8)	1.462 (3)	1.476 (8)	/	/	/	/
C(5)-C(6')	1.418 (8)	1.462 (3)	1.482 (8)	/	/	/	/
bond angle							
C(2)-S-C(5)	93.7 (3)	91.3 (2)	94.2 (3)	90.9	/	89.4	97.5
S-C(2)-C(3)	108.7 (5)	108.9 (2)	107.4 (5)	111.8	/	112.2	107.5
C(2)-C(3)-C(4)	114.3 (6)	114.5 (2)	115.5 (6)	112.6	/	113.1	113.8
C(3)-C(4)-C(5)	114.9 (6)	114;5 (2)	114.0 (6)	[a]	/	[a]	[a]
C(4)-C(5)-S	108.4 (5)	108.9 (2)	108.9 (4)	[a]	/	[a]	[a]
dihedral angle							
phenyl 1 - thienyle	8.3 (2)	-12.5 (1)	7.4 (2)	/	/	/	/
phenyl 2- thienyle	8.7 (2)	-12.5 (1)	-39.1 (2)	/	/	/	/
α	/	12.9 (1)	/	-4.3	-6.3	/	/
β	/	56.5 (1)	/	64.3	46.2	/	/

[a] symmetrical molecule: α and β represent the angle of respectively the sulfur and oxygen atom with the C(2)-C(3)-C(4)-C(5) plane. [b] Optimized geometry used by Hashmall *et al.* [6] for thiophene oxide. [c] Optimized geometry calculated by Rozas [7] for thiophene 1-oxide. [d] Optimized geometry for thiophene 1-oxide calculated by Amato *et al.* [21] in the pyramidal structure. [e] Optimized geometry for thiophene 1-oxide calculated by Amato *et al.* [21] in the planar structure.

Table 8

Bond Orders Obtained for Compounds 1, 2 [a], 3 and related compounds [b]

bond	1	2	3	thiophene [c]	thiophene 1-oxide [c]	thiophene-1,1-dioxide [c]
C(2)-C(3)	1.73	1.96	2.10	1.94	2.11	2.16
C(3)-C(4)	1.87	1.47	1.18	1.46	1.23	1.15
C(4)-C(5)	1.76	1.96	2.15	1.94	2.11	2.16
C(2)-S	1.40	1.12	1.12	1.53	1.11	1.01
C(5)-S	1.36	1.12	1.16	1.53	1.11	1.01

[a] symmetrical molecule. [b] Calculated by using the Paolini's formula [24] $L_p = L_l - 0.78(\rho_P^{0.33} - 1)$, where L_p = individual bond length, L_l = pure single C-C (1.54 Å) or C-S (1.81 Å) single bond and ρ_P = Paolini bond order. [c] Values calculated by Rozas [7].

Table 9

A Indices [a] for Compounds 1, 2, 3 and Related Structures.

No.	compound	Entire Structure	5-membered Ring
1	2,5-diphenylthiophene	0.87	0.99
2	2,5-diphenylthiophene-S-oxide	0.87	0.79
3	2,5-diphenylthiophene-S,S-dioxide	0.72	0.18
	thiophene [b]	0.93	0.93
	thiophene-S-oxide [c]	0.69	0.69
	dibenzothiophene [27]	0.96	0.97
	dibenzothiophene-S-oxide [4]	0.91	0.75
	fluorene [28]	0.92	0.87
	benzene	1.00	/

[a] Calculated by using the Julg and François' formula [27] $A = 1 - (225/n)\Sigma_{rs}(1-(d_{rs}/d))^2$, where n=number of CC bond, d_{rs} = individual C-C bond length, d = averaged bond length for all C-C bonds for the structure under consideration. [b] Bond length used from microwave spectra [28]. [c] Used bond length for calculations by the semiempirical MNDO method [6].

are in good agreement with those proposed for thiophene itself and its sulfoxide and sulfone [7]. They are significantly longer in **2** and **3** than in **1** (1.781(2) Å for **2**, 1.770(6) and 1.780(6) Å for **3**, compared to 1.718(6) and 1.726(6) Å for **1**). Considering now the junction bonds C(2)-C(6) and C(5)-C(6') between the benzene rings and the central heterocycle, it appears that there is a sort of levelling out of the C-C bond lengths of the whole

molecule in **1** (1.376 Å for the average thiophene C-C bond, 1.418 Å and 1.440 Å for the juntion bonds and 1.38 Å for the average benzene C-C bond). By comparison there is more pronounced alternation of double and single bonds on the whole molecules of **2** and **3**.

This increase in bond alternation, including the elongation of the C-S bonds, is indicative of a decrease in π-delocalization in the thiophene ring when passing from 1 to 2 and 3, this trend being more accentuated in 3 than in 2.

Recently, Jenks et al. have published a computational study of the effects of conjugation and aromaticity on the bond dissociation energies and geometry of a number of sulfoxides, including thiophene 1-oxide itself, benzo[b]thiophene 1-oxide and dibenzothiophene 1-oxide [25]. In particular, they have noticed that the variation of the C-S and C(3)-C(4) bonds due to benzannulation was minimal compared to the sulfide series. They proposed that this trend could be consistent with a substantial loss in aromaticity in the sulfoxide compounds. They have also showed that, if the corresponding sulfide is aromatic, then the bond dissociation energy diminishes dramatically. The sulfoxidic bond dissociation energy for thiophene 1-oxide, for instance, is estimated to lie in the range of 61-65 kcal/mol, compared to 87 kcal/mol for dimethyl sulfoxide and 89 kcal/mol for diphenyl sulfoxide. The explanation given for this observation was that the aromaticity of the sulfides could be disrupted by oxidation of the sulfur, the sulfoxides being significantly less aromatic than the sulfides.

Another way to evaluate the aromatic character of 1, 2 and 3 was to calculate the bond orders of bonds in the thiophene ring. An aromatic compound should exhibit a certain degree of uniformity in the bond orders of the ring. The Paolini's bond order-bond length relationship [26] was chosen for the present study, in order to compare the results obtained for our experimental investigation to the results given by Rozas using theoretical bond lengths calculated for thiophene 1-oxide and thiophene 1,1-dioxide [7]. The results are given in Table 8. As expected, the values found for 1 are in agreement with an aromatic thiophene ring. The values calculated for 2 and 3 confirm that there is more bond alternation between double and single C-C bonds in these two compounds. Nevertheless, the alternation in bond orders is much more accentuated in the sulfone 3 than in the sulfoxide 2.

Finally, a third approach in the evaluation of the aromaticity of the thiophene ring in the three compounds was to determine the A indices defined by Julg and François [27] for the entire carbon atom framework and for the heterocyclic fragment alone. Large values of A indicate relatively small bond alternation and correspondingly large delocalization, while small values of A indicate considerable bond alternation and correspondingly small delocalization. The results are reported in Table 9. They are compared with the values reported by Hashmall et al. [6] for thiophene 1-oxide by using C-C bond distances calculated by the MNDO method. Also included are the values calculated by Hashmall et al. [6] for thiophene, dibenzothiophene and related compounds (fluorene, dibenzothiophene) by using experimental C-C

bond distances. The A indices for the entire structures are identical for 2,5-diphenylthiophene and 2,5-diphenylthiophene 1-oxide. Nevertheless, if we consider the A indices for the heterocyclic ring alone, there is a significant decrease of A when passing from 1 to 2. This could be due to the fact that the two benzene rings are distorted in 2,5-diphenylthiophene whereas they are not in the symetrical sulfoxide 2 (A indices for the phenyl fragments alone are as follows: A = 0.88 and 0.84 (1), A = 0.99 (2)). Moreover, it is noteworthy that the A values calculated for 2 for the entire carbon atom framework as well as for the heterocyclic ring alone are markedly higher than those reported for thiophene 1-oxide (for the thiophene ring 0.79 for 2 and 0.69 for thiophene 1-oxide) [6]. This could be due to the influence of the two phenyl groups on the structure of the thiophene ring.

Therefore, even though the A values found for the five-membered ring of 2 are lower to those calculated for 1, fluorene and dibenzothiophene, they are much higher than those found for sulfone 3.

Altogether, the aforementioned data show that, in spite of its non planarity, the thiophene ring of 2,5-diphenylthiophene 1-oxide 2 exhibits some delocalization of its π electrons indicating a certain degree of lower aromaticity than in thiophene 1 but much higher than in the sulfone 3.

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