

2.09

Thiophenes and their Benzo Derivatives: Structure

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2.09.1 INTRODUCTION

Heterocyclic compounds are divided into heteroaromatic and heteroalicyclic derivatives. In heteroaromatic compounds (as in carbocyclic aromatics), each atom in the ring is in the same plane and each ring is associated with $(4n + 2)\pi$ -electrons.

Thiophene is an aromatic compound. Its structure can be assumed to be derived from benzene by replacement of two annular CH groups with sulfur. The sulfur atom in this five-membered ring acts as an electron donating heteroatom by contributing two electrons to the aromatic sextet and thiophene is thus considered to be an electron-rich heterocycle. The chemistry of thiophene and other five-membered heterocycles, for example pyrrole and furan, are consequently dominated by this effect.

The fact that the lone pair on sulfur contributes to the aromaticity is seen in the lower dipole moment of thiophene as compared to its saturated analogue tetrahydrothiophene (0.52 D vs 1.90 D) [\(72JA8854\)](#). In thiophene, as in most of the other five-membered heterocycles and their saturated analogues, the dipole is directed from the ring towards the heteroatom. The only exceptions to this are pyrrole and *N*-alkylpyrroles where the nitrogen atom is the positive end of the dipole.

Although thiophene is aromatic and assumed to be derived from benzene, the bond length equivalence seen for the C—C and C—H bonds in benzene is not found here. In thiophene, as will be discussed later, the C—S and C—C bonds are all different in length as are the C—H bonds.

The numbering in thiophene (**1**) starts at the sulfur atom and continues around the ring. This numbering system will generally be followed throughout the text. The C_2 and C_5 carbon atoms are also designated as C_α ; the C_3 and C_4 carbons as C_β . Substituted thiophenes are named similarly to substituted benzenes. Some of the more common radicals (**2–5**) are shown in Figure 1. Protonation of thiophene leads to three cationic species (**6–8**) none of which are aromatic. There are two dihydro derivatives, 2,3- (**9**) and 2,5-dihydrothiophene (**10**) and a single tetrahydrothiophene (**11**). Alternatively, (**9**) and (**10**) are also known as Δ^2 - and Δ^3 -dihydrothiophene or 2- and 3-thiolane where the number indicates the position of the double bond. The benzo derivatives benzo[*b*]- (**12**) and benzo[*c*]-thiophene (**13**) are considered analogues of naphthalene while dibenzothiophene (**14**) is related to phenanthrene.

Thiophene was first discovered in 1882 by Victor Meyer. It is a colorless liquid with a boiling point of 84.4°C (760 torr) and a melting point of –38.3°C [\(83KO\(22\)965\)](#). Although it is generally thought of to have an odor similar to benzene, pure thiophene, when distilled from copper (II) chloride is practically odorless. It is highly flammable, moderately toxic, immiscible with water and soluble in organic solvents. Some of the physical properties of thiophene have been listed in Table 1.

Thiophene was first synthesized by Meyer [\(B-1888MI 209-01, 83KO\(22\)965\)](#) by ring closure of succinic acid with phosphorus pentasulfide. Although thiophene is found in deposits of lignite, coal, and crude oils, its extraction from these sources is not feasible. A summary on the investigation of thiophene and thiophene derivatives occurring in petroleum, oil shales, and coals has been covered by Galpern in *Thiophene and Its Derivatives* [\(85HC\(44/1\)325\)](#). Laboratory procedures involve heating anhydrous sodium succinate with phosphorus trisulfide under a carbon dioxide stream. The crude thiophene is condensed, steam distilled, and purified [\(43OSC\(2\)578\)](#). Industrial processes involve continuous vapor-phase techniques that use C_4 raw materials and sulfur compounds in the presence of metal oxide catalysts. For example, thiophene has been prepared in high yield from furan and hydrogen sulfide at 300–400°C [\(66GEP1228273\)](#). Other C_4 precursors include but-1-ene, butadiene, and butanol, with carbon disulfide as the sulfur source [\(73GEP2225443\)](#). These processes afford higher yields of thiophene by eliminating formation of thiophene tars, a problem generally encountered in some of the earlier methods. These latter processes are also used for the formation of 2- and 3-alkyl thiophenes.

In addition to being naturally present in coal tar and shale oil, thiophene derivatives have also been found in plants and fungi. In most cases, these compounds are derived from C_{10} or longer conjugated acetylenic precursors. Thiophene formation is presumed to arise from addition of hydrogen sulfide (or its biological equivalent) to the C—C triple bond. A multistage process is proposed since thienol ethers have also been simultaneously detected. A survey of naturally occurring thiophenes has been published by Bohlmann and Zdero [\(85HC\(44/1\)261\)](#).

Thiophene has also found widespread use in the synthesis of biologically active species [\(91HC\(44/4\)397\)](#). Since thiophene is structurally and electronically similar to benzene, thiophene analogues of biologically active benzene derivatives could possess similar activities. Additionally, the presence of a heteroatom could alter the metabolic effect and perhaps be a better therapeutic drug. Being an electron-rich aromatic system, thiophene is expected to be superior to benzene in

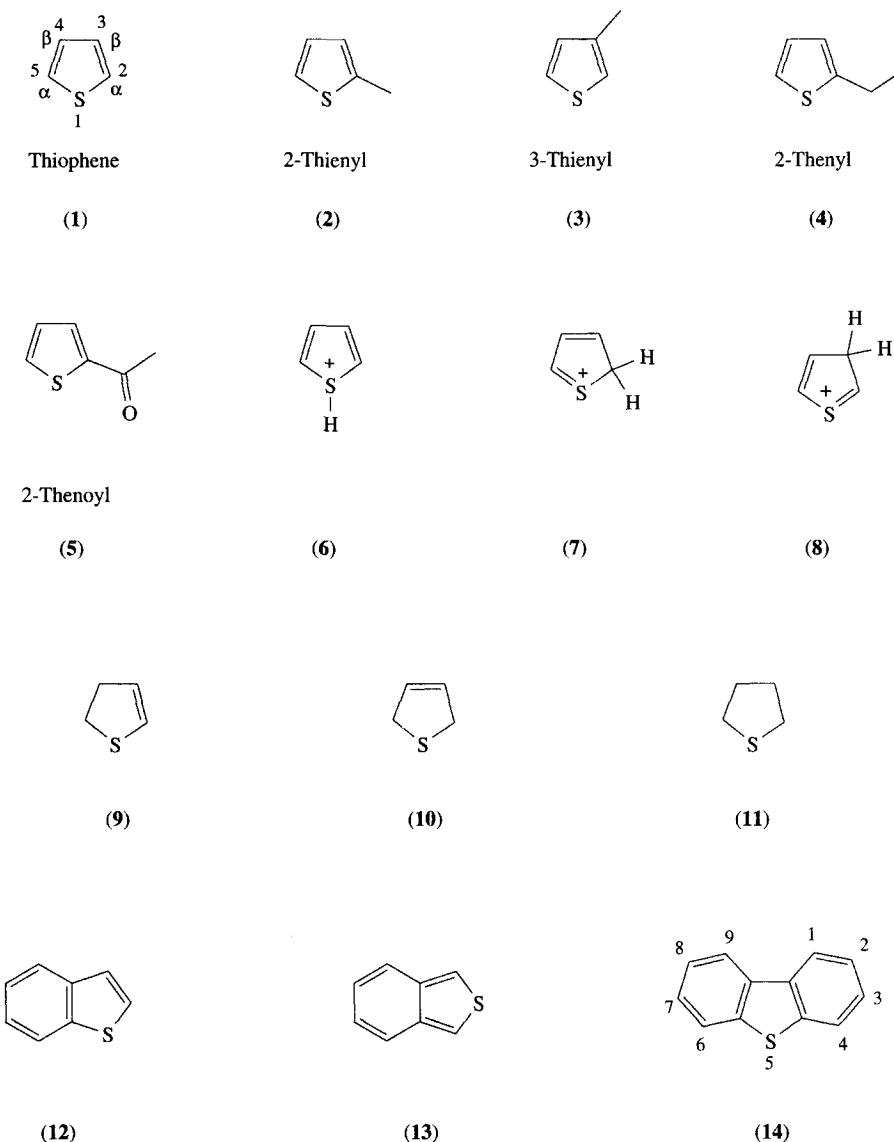


Figure 1 Thiophene and some common derivatives.

certain cases. Thus, biologically active thiophene derivatives contain thiophene either as the central ring or as part of a central fused ring system. Thiophene containing drugs have been used in the therapy of the central nervous system, metabolic, and infectious diseases and also as pharmacodynamic and agricultural agents.

Several books and reviews are available on the chemistry of thiophenes. Much of the work up to 1950 has been documented by Hartough <52HC(1), B-54MI 209-01>. Over the past three decades, Gronowitz has either authored or edited a variety of articles dealing with thiophene. Some of them have appeared in the *Advances in Heterocyclic Chemistry* series, <63AHC(1)> and supplemented periodically in *Organic Compounds of Sulfur, Selenium, and Tellurium* <B-72MI 209-01, B-75MI 209-01, B-77MI 209-01, B-79MI 209-01>, and also in a five-part series entitled *Thiophene and Its Derivatives* in the Weissberger series *The Chemistry of Heterocyclic Compounds* <85HC(44/1), 86HC(44/2), 86HC(44/3), 91HC(44/4), 94HC(44/5)>. Much of the work up to 1980 has been documented in *Comprehensive Heterocyclic Chemistry* (CHEC-I) and consequently, the work here concentrates on the chemistry of thiophene since then.

Table 1 Physical properties of thiophene **⟨94MI 209-01⟩**.

<i>Physical property</i>	<i>Value</i>	<i>Physical property</i>	<i>Value</i>
Melting point	−38.3 °C	Critical temperature	579.4 K
Boiling point	84.4 °C	Critical pressure	5.69 mPa
Flash point	−1.11 °C	Critical molar volume	219 cm ³ mol ^{−1}
Dipole moment	0.55 D	Diamagnetic susceptibility	57.2 (−χ _m × 10 ⁶)
Dielectric constant (16 °C)	2.76	Enthalpy of fusion (−39.4 °C)	−1.19 kcal mol ^{−1}
Refractive index	1.5289 ²⁰	Enthalpy of vaporization (25 °C)	8.30 kcal mol ^{−1}
Density	1.6049 ^{20/4} g cm ^{−3}	Vapor pressure (mm Hg)	Temperature (°C)
Heat capacity	123.8 J mol ^{−1} K ^{−1}	10	−10.9
Surface tension (25 °C) (50 °C)	30.68 mN m ^{−1} 27.36 mN m ^{−1}	40	+12.5
Thermal conductivity (25 °C) (50 °C) (100 °C)	0.199 W m ^{−1} K ^{−1} 0.195 W m ^{−1} K ^{−1} 0.186 W m ^{−1} K ^{−1}	100 400 760	+30.5 +64.7 +84.4

The large number of reports pertaining to the synthesis of thiophene and its derivatives corroborates the continuing intrigue and importance of these compounds in biology, chemistry, industry, and medicine **⟨88H(27)1731, 91FOR87, 91HC(44/4)397⟩**.

Amongst the derivatives of thiophene, the chemistry of thiophenium salts and S,C- and S,N-thiophenium ylids has also been reviewed **⟨89AHC(45)151⟩** as has the chemistry of the thiophene 1-oxides, 1,1-dioxides, and sesquioxides **⟨85HC(44/1)572⟩**. The chemistry of benzo[*b*]thiophenes has been reviewed by Scrowston **⟨81AHC(29)171⟩** and there is a study by Gronowitz on the isomeric dithienothiophenes **⟨94JHC641⟩**.

Interest in thiophene has also been extended to the study of oligomers of thiophene and their derivatives. Interest in this arises due to its wide range of photobiological effects **⟨91T8443, 93MI 209-01⟩** and as alternatives to inorganic materials in the synthesis of a class of organic conducting polymers **⟨B-86MI 209-01, 92JPS(A)1891⟩**. These electron-rich conjugated oligomers have π-electron systems similar to the linear *cis,trans*-polyenes. These oligomers display high electrical conductivity in the oxidized form and possess nonlinear optical properties **⟨B-86MI 209-01, B-87MI 209-01, B-91MI 209-01⟩**. Polythiophene is attractive in that it is stable in air and when some of the hydrogens are substituted by alkyl or phenyl groups, it is soluble in most organic solvents **⟨86SM169⟩**. The interesting behavior of this class of conducting polymers has attracted many theorists and experimentalists to investigate and understand their electronic properties. Results of *ab initio* studies on some of these thiophene oligomers will be discussed briefly in the next section (see Section 2.09.2)

2.09.2 THEORETICAL METHODS

2.09.2.1 General

Molecular orbital (MO) calculations have been used to obtain properties of molecules, ions, and radicals, some of which include bond distances, bond angles, heats of formation, ionization energies and dipole moments. Early methods such as *Hückel Molecular-Orbital* (HMO) calculations **⟨B-87MI 209-02⟩** treated the σ and π electrons separately. The advent of powerful computers and the development of software packages has enabled MO calculations to be carried out by including all electrons in a molecule. These calculations are termed *ab initio* which actually means “from first principles” **⟨B-85MI 209-01, B-86MI 209-02⟩**. Initial interest in the *ab initio* study stemmed from its ability to include the sulfur *d*-orbitals in its calculations and determine to what extent these orbitals played a role in the reactivity and property of sulfur heterocycles. As we shall see later, not all calculations are significantly affected by the inclusion of the *d*-orbitals.

Cheaper and quicker methods involve semiempirical calculations. The CNDO method was first used by Pople *et al.* in 1965 **⟨65JCP(43)S129, 65JCP(43)S136⟩**. Dewar is credited with the development of the modified intermediate neglect of differential overlap (MINDO/3) method **⟨75JA1285⟩**; the modified neglect of diatomic overlap (MNDO) method **⟨77JA4899⟩** and the Austin model 1 (AM1) **⟨85JA3902⟩**. Since then, there have been many modifications of the above semiempirical methods.

Results from initial studies found in the literature have been covered in CHEC-1. In addition, an excellent review by Henriksson-Enflo **⟨85HC(44/1)215⟩** has also covered literature up to 1981; the reader is encouraged to consult them for complete details on prior work.

2.09.2.2 The Role of *d*-Orbitals on Sulfur

Initial MO calculations on thiophenes assumed that only the $3p_z$ -atomic orbital of sulfur contributed to the π -electron MO wave function $\langle 35JA2086 \rangle$ and thus treated it similar to its iso- π -electronic counterparts pyrrole and furan. The fact that thiophene is more aromatic than either of these two led Schomaker and Pauling $\langle 39JA1769 \rangle$ to believe that *d*-orbitals could participate in the hybridization. Bielefeld and Fitts later calculated the total energy of thiophene by employing a basis set in the LCAO approximation which included the $3d_{\pi}$ and $4d_{\pi}$ functions on sulfur $\langle 66JA4804 \rangle$ and compared the results with two other LCAO MO approximations. The first considered only the $2p_z$ orbitals on the carbon atom and the second included the $3d_{xy}$ and $3d_{yz}$ atomic orbitals on the sulfur atom. The Pariser–Parr–Pople (PPP) calculations indicate that the $3d_{\pi}$ -orbital participates to only a small extent. High level *ab initio* $\langle 70CC319, 72TCA171 \rangle$ calculations later showed that in actuality, the effect of the $3d$ -orbitals was negligible. The difference in the total energies calculated by these methods was attributed to the selection of the basis set which seems to be more important than the inclusion of $3d$ -orbitals.

Although the population of the $3d$ -orbital is very small, its inclusion in the *ab initio* calculation causes noticeable changes in the populations of the atoms, especially on the adjacent carbon atoms. Gelius *et al.* $\langle 72TCA171 \rangle$ showed the population of $3d$ -orbitals on sulfur to be 0.143 electrons in the $3d_{\sigma}$ -orbital and 0.038 in the $3d_{\pi}$ -orbital which are much smaller than the value of 0.24 and 0.138 electrons obtained by Clark from CNDO calculations $\langle 68T2663 \rangle$. A comparison of the populations on sulfur and on the adjacent carbon atoms is shown in Table 2.

Table 2 Atomic populations on sulfur and adjacent carbon atoms in thiophene.

Method	Basis on sulfur	Population in 3d on S		Population in 2p on C_{α}		Ref.
		$3d_{\sigma}$	$3d_{\pi}$	$2p_{\sigma}$	$2p_{\pi}$	
PPP	$3p_z, 3d_{xz}, 3d_{yz}$		0.050			66JA4804
CNDO	$3s, 3p, 3d$	0.24	0.14	1.96	1.06	68T2663
<i>Ab initio</i>	Double ζ			2.135	1.109	72TCA171
	Double ζ, H_{2p}			2.076	1.105	72TCA171
	Double $\zeta, 3d$	0.143	0.038	1.976	1.085	72TCA171
	Double $\zeta, 3d, H_{2p}$	0.143	0.037	1.184	1.080	72TCA171

Depending upon the basis set, the gross charges on sulfur and on the other atoms vary to a much greater extent than the population. When no polarization function is included in the basis set, the charge on sulfur is found to be +0.482 $\langle 72TCA171 \rangle$. This is reduced to +0.016 when the $3d$ -orbitals on sulfur are included and to +0.001 when the $2p$ -orbitals on hydrogen and the $3d$ -orbitals on sulfur are included. This decrease is larger than the corresponding $3d$ -population. The effect of the $3d$ function is to increase the populations in the sulfur $3s$ - and $3p$ -orbitals; thus it acts as a polarization function rather than as a valence orbital. This is in contrast to compounds where sulfur is bonded to more electronegative atoms such as in SO_4^{2-} and SF_6 $\langle 71TCA368, 71TCA590 \rangle$ where the $3d$ -level is stabilized and available for additional bonding. Table 3 compares the charges on the various atoms in thiophene as obtained from various calculations with basis sets that do, and do not, include the sulfur $3d$ -orbitals.

Total dipole moments depend on contributions from: (i) net atomic charge densities; (ii) atomic $s-p$ polarizations obtained from mixing s - and p -orbitals on each atom; and (iii) atomic $p-d$ polarizations obtained from the sulfur $3p$ - and $3d$ -orbitals. Thus quantum chemical methods such as INDO which do not include *d*-orbitals in their approximations would not compare favorably with experimental values obtained for compounds containing sulfur. Inclusion of the $3d$ -orbitals in the basis set usually leads to a lowering of the dipole moment. For example, *ab initio* calculations employing a double zeta basis set on sulfur, gives a dipole moment of 0.96 D which is lowered to 0.62 D when the basis set includes $3d$ -orbitals on sulfur and $2p$ -orbitals on hydrogen $\langle 72TCA171 \rangle$ which is much closer to the experimental value of 0.55 D $\langle 53JCS1622 \rangle$. Dipole moments calculated by various methods are discussed in more detail in Section 2.09.2.5.

2.09.2.3 Total Energies

The stability of a molecule is usually determined by its total energy from which one can determine heats of formation, resonance energies, and localization energies. In most cases, *ab initio* methods

Table 3 Gross charges on the different atoms in thiophene as calculated by various methods.

Method	Basis on sulfur	Gross charges on the atoms					Ref.
		S	C _α	C _β	H _α	H _β	
PPP	3p _z	0.21	-0.06	0.04			66JA4804
	3p _z , 3d _{xz} , 3d _{yz}	0.16	-0.09	0.01			66JA4804
CNDO	3s, 3p	0.13	-0.05	-0.07	0.03	0.03	68T2663
	3s, 3p, 3d	-0.04	-0.06	-0.02	0.05	0.03	68T2663
Ab initio	Double ζ	0.48	-0.57	-0.18	0.27	0.24	72TCA171
	Double ζ , H _{2p}	0.49	-0.44	-0.06	0.15	0.11	72TCA171
	Double ζ , 3d	0.02	-0.25	-0.24	0.25	0.23	72TCA171
	Double ζ , 3d, H _{2p}	0.00	-0.11	-0.12	0.12	0.10	72TCA171
	Minimal	0.14	-0.24	-0.17	0.17	0.26	72TL4165
	Minimal, 3d	0.04	-0.17	-0.16	0.16	0.15	72TL4165
Ab initio	Minimal, 3d, 3s	0.03	-0.17	-0.17	0.16	0.15	72TL4165

have been used to determine the total energy of thiophene. It is imperative that all electrons be considered in the calculations, hence theories involving only π -electrons (HMO, PPP) or all-valence electrons (EHT, CNDO, INDO, etc.) cannot generally be employed. However, as shown by Dewar and co-workers (67JA3089, 69JCP(50)1262, 75JA1285), some of these can be parameterized to give good energy values.

As discussed previously in Section 2.09.2.2, inclusion of the 3d-orbitals in the basis set fails to show any significant difference in the total energy. Clark (68T2663) obtained only a 1.77% energy lowering by including the 3d-orbitals in his calculations and 2.02% when the 4s- and 4p-orbitals were also included. Clark and Armstrong (70CC319) obtained an energy decrease of 74 kcal mol⁻¹ when the 3d-functions on sulfur were included in the basis set. By contrast, Gelius *et al.* (72TCA171) obtained an energy decrease of 18.8 kcal mol⁻¹ when they included the 3d-functions on sulfur and 14.4 kcal mol⁻¹ when the 2p-functions on hydrogen were included. The two functions were found to be independent of each other. The total energy calculated by Gelius *et al.* was lower than that by Clark and Armstrong due to the fact that a larger set of contracted Gaussians were used in the former case. Thus here the basis set is more important than is the inclusion (or exclusion) of the 3d-function of sulfur.

A comparison of the total energy of thiophene obtained by various methods is given in Table 4. We see from the Table that CNDO calculations which use only the all valence electrons give higher energy values (less negative) than the *ab initio* methods which includes all electrons in its approximations. The total energy calculated by employing the spin-coupled approach is lower in energy than that obtained from SCF calculations by 37.5 kcal mol⁻¹ (0.06 a.u.) (89JCS(P2)263), a trend also observed with pyrrole and furan with energy lowerings of 39.4–43.7 kcal mol⁻¹.

Calculations at the STO-3G level on the protonation of thiophene and chlorothiophenes show energy lowerings of 232–250 kcal mol⁻¹ (84BCJ1312). The calculations show that a chlorine atom at the β -position (**16**) lowers the energy to a greater extent than at the α -position (**15**) while protonation at the α -position (**7**), lowers the energy 11.7 kcal more than at the β -position (**8**), consistent with previous study (83BCJ2208) where only α -protonated products have been observed. Thus protonation of 2-chloro-, 2,3-dichloro- and 2,5-dichlorothiophene occurs at the 5-position only. With two chloro substituents, the 2,4-derivative is the most stable one, whilst amongst the cations, the 2-H,3,5-dichlorothiophenium cation (**17**) is the most stable one.

Quantum chemical investigations have also been carried out on the 1,2-proton shift in protonated five-membered heterocycles (84CHE966). As the proton travels round the ring, the intermediates are either at the local minima or in a transition state and consequently, the change in energy can be calculated. Calculations for thiophene by the SCF–MO–LCAO method in the MINDO/3 approximation and nonempirically in the OST-3GF* basis both indicated protonation at the α -position to be more favorable, in line with results observed above.

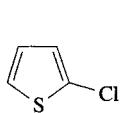
2.09.2.4 Charge Distribution

In Section 2.09.2.2, it was reported that, although inclusion of the sulfur 3d-orbitals in the calculations showed negligible changes in the 3d_σ and 3d_π populations on the sulfur atom, the gross charges on all atoms showed large variations. Table 5 lists the variations in charges on sulfur and

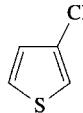
Table 4 Total energy of thiophene obtained via various methods.

Method	Basis on sulfur	Total energy (a.u.) ^a	Ref.
CNDO	3s, 3p	-507.148	68T2663
CNDO	3s, 3p, 3d	-516.149	68T2663
CNDO	3s, 3p, 3d, 4s, 4p	-517.338	68T2663
<i>Ab initio</i>	Minimal	-550.417	70CC319
	Minimal, 3d	-550.535	70CC319
<i>Ab initio</i>	Double ζ	-550.923	72TCA171
	Double ζ , H ₂ p	-550.946	72TCA171
	Double ζ , 3d	-550.976	72TCA171
	Double ζ , 3d, H ₂ p	-550.999	72TCA171
<i>Ab initio</i>	Minimal	-550.075	72TL4165
	Minimal, 3d	-550.144	72TL4165
<i>Ab initio</i>	Minimal, STO-3G	-545.087	85JCS(P2)97
<i>Ab initio</i>	Minimal, STO-3G	-545.092	77G55, 79JA311
<i>Ab initio</i>	Minimal, STO-3G	-545.092	84BCJ1312
<i>Ab initio</i>	Split valence, 4-31G	-550.599	80JCC348
<i>Ab initio</i>	4-31G + d	-550.662	82JA1375
<i>Ab initio</i>	Spin-coupled	-546.497	89JCS(P2)263
<i>Ab initio</i>	SCF	-546.437	89JCS(P2)263
<i>Ab initio</i>	SCF	-551.064	82MP649
<i>Ab initio</i>	HF	-551.077	76JES179
<i>Ab initio</i>	3-21G	-548.473	89JST(186)101
	3-21G*	-548.515	89JST(186)101
<i>Ab initio</i>	TZVP-SCF	-551.361	92ZN(A)203
	TZVP-Cl	-551.922	92ZN(A)203

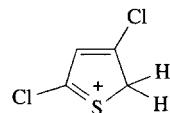
^a1 a.u. = 2625 kJ mol⁻¹ = 627 kcal mol⁻¹.



(15)



(16)



(17)

on the carbon atoms obtained when the 3d-orbitals were, and were not, included in the calculations. From the Table we see large variations in the charges on the atoms from one calculation to another and even within the same methods themselves. For example, by HMO calculations, the charge on sulfur varies from 0.12 to 0.75 while in the PPP method, the charge varies from 0.09 to 0.36, and between 0.0 to 0.49 by *ab initio* methods.

Table 5 Variation in gross charges on sulfur and on carbon atoms in thiophene as calculated by various methods.

Method	Variation in gross charges			Ref.
	S	C _α	C _β	
HMO	0.12 to 0.75	0.02 to -1.13	0.07 to -0.22	35JA2086, 58JA5543 52BCJ179 61JCP(34)389
PPP	0.09 to 0.36	-0.02 to -0.13	0 to -0.07	63T157, 70ACS23 65CJC1569, 70TCA49
CNDO	0.13 to -0.05	-0.05 to -0.06	-0.01 to -0.07	68T2663
CNDO/2	-0.06	-0.005	0.038	89CHE874
MNDO	0.10	-0.06 to -0.15	-0.004 to -0.09	86IJQ1599, 89CHE874
<i>Ab initio</i>	0 to 0.49	-0.07 to -0.57	-0.05 to -0.24	72TCA(27)171, 76JES179, 72TL4165, 79JA311, 77G55, 80JCC348

For the *ab initio* methods even a change in the basis set causes large changes in the atomic charges although, if a large basis set is used, charges calculated with $\langle 72TCA171 \rangle$ and without $\langle 76JES179 \rangle$ d-orbitals are about the same. There is, however, a trend that is observed in almost all cases. Most

calculations show the sulfur atom to bear a positive charge and the carbons to bear a negative charge with the α -carbon atom to be a bit more negative.

Calculations using the CNDO method gave a positive value for the sulfur atom (0.136) when the d -orbitals of sulfur (method I) were not included in the calculations <68T2663>. When the basis set included the sulfur $3d$ -orbitals (method II) the value calculated was -0.0358 , and -0.0514 when the $4s$ - and $4p$ -orbitals were also included (method III). Calculations via method I show the sulfur atom to be a σ electron acceptor and π electron donor. Since the latter effect is greater, the net charge is positive. The σ inductive effect is felt on the adjacent carbon atoms rendering them σ electron deficient while the C_β carbon atoms are relatively unaffected and thus approximately neutral with respect to the σ electrons. Inclusion of the d -orbitals in the calculations (method II) leads to a net negative charge due to the drift of the σ and π electrons towards the sulfur atom. The σ charge mainly results from the $3p_x$, $3p_y$, and $3d_{xy}$ orbitals with smaller contributions from $3d_{x^2-y^2}$ and $3d_z^2$ implying that the d -orbitals are at least as important in σ bonding as in π bonding. Further changes in the orbital populations due to the inclusion of the $4s$ - and $4p$ -orbitals (method III) are very small.

Charges on five-membered heterocycles calculated using the MNDO approximation are generally greater than those by CNDO/2 <89CHE874>. For *N*-methylpyrrole, the charge on the nitrogen atom differs by a factor of 5–6 while in thiophene, the two methods differ not only in value but also in sign. By comparison, CNDO calculations without the $3d$ -orbitals affords a positive value. Similarly, the charge on the β -carbon atom calculated by the CNDO/2 is found to be $+0.038$, contrary to the other methods where the charges are negative.

2.09.2.5 Dipole Moments

The experimental value of the total dipole moment as measured in the gas phase is found to be 0.550 ± 0.040 D <53JCS1622>. In sulfur-containing compounds, the $p-d$ polarization also contributes to the total dipole moment value. Thus depending on the method employed, a large variation is expected for thiophene (see Table 6).

Table 6 Dipole moments of thiophene obtained from various calculations.

Method	Basis on sulfur	Dipole moment (D)	Ref.
Experimental		0.55	53JCS1622
HMO		2.50	52BCJ179
PPP		0.50	63T157
CNDO	$2p$	-0.18	66JA4804
	$2p, 3p, 3d$	0.68	66JA4804
	$2p, 3p, 3d, 4p$	0.72	66JA4804
	$3d$	0.63	87CHE454
	$3s, 3p$	0.84	68T2663
	$3s, 3p, 3d$	2.26	68T2663
	$3s, 3p, 3d, 4s, 4p$	1.84	68T2663
CNDO/S	$3s, 3p, 3d$	1.23	85CPB3077
CNDO/2	$3s, 3p, 3d$	0.42	83JST(94)115
CINDO/SHIFT/UV	$3s, 3p$	1.94	83JST(94)115
	$3s, 3p, 3d$	1.78	83JST(94)115
	$3s, 3p, 3d, C_{3d}$	1.24	83JST(94)115
INDO/S		2.71	83JST(94)115
MNDO		0.90	83MI 209-01
		0.90	86IJQ1599
MINDO/3		2.22	80IJQ797
MP2	$6-31G(+sd+sp)$	0.45	92JPC(96)7301
<i>Ab initio</i>	Double ζ	0.96	72TCA171
	Double ζ, H_{2p}	0.97	72TCA171
	Double $\zeta, 3d$	0.61	72TCA171
	Double $\zeta, 3d, H_{2p}$	0.62	72TCA171
	HF	0.65	76JES179
	Split valence, 4-31G	0.38	80JCC348
	Minimal	-0.29	82MP649
	Minimal, $3d, H_{2p}$	0.07	82MP649
	Minimal, $3d, H_{2p}, C_{3d}$	-0.07	82MP649
	$3-21G$	1.34	89JST(186)101
	$3-21G^*$	0.75	89JST(186)101
	SCF/6-31G(+sd+sp)	0.91	92JPC(96)7301

The fact that dipole moments are generally overestimated at the Hartree–Fock level is shown by the relatively high value of 1.34 D obtained by employing the 3–21G basis set $\langle 89\text{JST}(186)101 \rangle$. When the *d* polarization function on sulfur is included (the 3–21G* basis set), the value of the dipole moment drops to 0.75 D. *Ab initio* calculations that are closest to the experimental value are those obtained by Gelius *et al.* $\langle 72\text{TCA}171 \rangle$ (0.61 D) and von Niessen *et al.* $\langle 76\text{JES}179 \rangle$ (0.65 D). The slight overestimation in the latter case is expected when wave functions calculated with a double ξ basis set do not use polarization functions. Amongst the semiempirical methods, calculations by the PPP method $\langle 63\text{T}157, 87\text{CHE}454 \rangle$ are generally in good agreement with the experimental value.

The HMO method $\langle 52\text{BCJ}179 \rangle$ and MINDO/3 $\langle 80\text{IJQ}797 \rangle$ calculations gave very high dipole moments. For the MINDO/3 method, when the *d*-orbitals are neglected, the large polarization term causes an overestimation of the total dipole moment. Inclusion of the 3*d*-orbitals in the basis set should show improvement in the value. A similar overestimation is also observed in the MNDO method for thiophene and for a variety of other sulfur compounds which arises due to the non-inclusion of the 3*d* atomic orbitals $\langle 83\text{MI} 209-01, 86\text{IJQ}1599 \rangle$.

CNDO calculations gave the best values when the *d*-orbitals were excluded from the basis set $\langle 68\text{T}2663 \rangle$. The dipole moment of 2.26 D obtained when the sulfur *d*-orbitals are included is lowered to 1.84 D when the 4s and 4*p* are also included and to 0.895 D when only the 3s and 3*p* are taken into account. The larger values calculated by the PPP method $\langle 66\text{JA}4804 \rangle$ when the sulfur 3*d*- or the 4*p*-orbitals are included is not surprising, since inclusion of the sulfur 3*d*-orbitals in the calculations leads to a drift of the σ and π electrons towards the sulfur atom (see Section 2.09.2.4). As a result, μ_{π} becomes smaller in magnitude and less negative making the net dipole moment more positive. For the CNDO method, inclusion of the sulfur 3*d*-orbital changes the contribution from the charge density from –1.153 D to +0.582 D. Although the *p*-*d* polarization factor is negative, it is still not large enough to offset the change and hence the large value of 2.26 D in this case. When the *d*-orbitals are excluded from the basis set $\langle 66\text{JA}4804 \rangle$, a negative value is obtained indicating the dipole is directed away from the heteroatom.

A comparison of results from INDO/S and CNDO/2 calculations $\langle 83\text{JST}(94)115 \rangle$ show that the value concerning the charge densities are nearly equal in both cases and in good agreement with the experimental value. For thiophene, contributions from the *s*-*p* and *p*-*d* polarizations are opposite in sign and much higher than the charge density. However, since the INDO/S approximation does not include the sulfur *d*-orbitals, there is no contribution from the *p*-*d* polarization function and thus the net dipole moment calculated is much larger than the 0.412 D obtained from CNDO/2. From CINDO/SHIFT/UV (the spectroscopic version of CNDO/2) calculations, the results obtained are generally high, due to the large difference in the two polarization contributions. The dipole moment calculated from charge densities alone (0.40 D) is in good agreement with the experimental value. Inclusion of *d*-orbitals on both sulfur and carbon reduces the dipole moment from 1.935 D to 1.236 D, but this is still much higher than that obtained by experimental or by some of the other methods. However, one must realize that the CINDO/SHIFT/UV method is mainly parameterized for spectroscopic properties such as electron transitions.

With the diffusely polarized 6–31G(+*sd*+*sp*) basis set, a better correlation is obtained with MP2 values than with SCF values $\langle 92\text{JPC}7301 \rangle$. With this basis set, the MP2 level tends to overestimate the experimental value for oxygen but underestimates sulfur and selenium. The SCF overestimates in all cases.

Brouckère *et al.* $\langle 82\text{MP}649 \rangle$ have obtained satisfactory results for the dipole moments of furan, pyrrole, and dihydrothiophene from *ab initio* SCF calculations. For thiophene, the value differs considerably. With no polarization function, or when an extra *d*-function on sulfur is included, negative values are obtained. The SCF calculated dipole moment is sensitive to the basis set used. For example, in this case, the dipole moment as calculated without the *d*-function on carbon was found to be +0.066 D while that using a smaller basis set and no carbon *d*-function gave a value of 0.62 D $\langle 72\text{TCA}171 \rangle$, which is in close proximity to the experimental value. Reasonable results can be obtained as long as the basis set is not too large.

2.09.2.6 Orbital Energies-Ionization Potentials

Orbital energies have generally been used for predicting and assigning ionization potentials. As a general rule of thumb, the orbital energy can be (according to Koopmans' theorem $\langle 33\text{MI} 209-01 \rangle$) assumed to be the negative of the ionization potential, i.e., $\varepsilon = -\text{IP}$. The photoelectron spectrum

of thiophene has been studied by Eland <69IJM471> and by Derrick *et al.* <71IJM(6)177> and x-ray electron spectroscopic studies by Gelius *et al.* <72TCA171>. The assignments by Derrick *et al.* were made based on experimental data, comparison of spectra with similar compounds and on extended Hückel and *ab initio* calculations but the order has been questioned. The assignments of the first seven bands made by Derrick *et al.* <71IJM(6)177> were of the order 1a₂(π), 2b₁(π), 1b₁(π), 6a₁, 4b₂, 5a₁, 3b₂. *Ab initio* calculations <72TCA171, 76JES179> are generally in good agreement with the experimental values as are semiempirical, although the latter could also be due to the choice of parameters selected. A selection of recent references and some key earlier references dealing with the application of semiempirical and *ab initio* methods for the calculations of ionization potentials and electron spectra is given in Table 7.

Table 7 References to various semiempirical and *ab initio* calculations of ionization potential for thiophene and its benzo derivatives.

Method	Thiophene	Benzothiophene	Dibenzothiophene
Experimental	69IJM471, 79CRV77, 71IJM(6)177, 82JCS(P2)539	56JCS3438, 69IJM471	56JCS3438, 73JCS(F2)1155
ETH	71IJM(6)177		
PPP	66JA4804		
CNDO	68T2663, 76JCP(64)3021, 74TCA(33)19, 83JST(105)375		
CNDO/S	74TCA19, 85CPB3077, 83ACH97, 86IZV2251		
INDO/S	83JST(105)375	83JST(105)375	83JST(105)375
MNDO	83JCC84, 86IJQ1599, 85JCS(P2)97		
<i>Ab initio</i>	69BCJ933, 72TCA171, 76JES179, 85JCS(P2)97, 70CC319, 75JCS(P2)974, 83JST(105)375, 89JST(186)101	83JST(105)375	83JST(105)375

In most cases, the assignments of the first two orbitals are unambiguous. The band at 12 eV initially assigned by Derrick *et al.* to be the 2b₁(π) band was later shown to arise from σ orbitals. *Ab initio* calculations <69BCJ933, 75JCS(P2)974, 76JES179>, while supporting the existence of the σ orbitals, generally differ on the amount of σ orbitals present between the π_1 and π_2 orbitals. Thus while for Gelius *et al.* the order was 1a₂(π) < 2b₁(π) < 6a₁(n) < 4b₂ < 1b₁(π), calculations by von Niessen *et al.* <76JES179> indicated only the 6a₁ orbital to lie between the two b₁(π) orbitals. Subsequent experiments observed the He^{II}/He^I changes in the photoelectron spectrum, and were able to reassign the band at 12.5 eV to that from the 1b₁(π) orbital <82JCS(P2)539>. Based on the results observed here, the ordering is assigned as 1a₂(π), 2b₁(π), 6a₁(n), 1b₁(π), 4b₂, 5a₁, 3b₂ which is in agreement with that of von Niessen *et al.* <76JES179>. *Ab initio* calculations obtained by employing the STO-3G basis set tend to underestimate the first few ionization potentials.

CNDO calculations show that the MO energies are not affected by the inclusion of the *d*-orbitals <83JST(105)375>. A modified version of the CNDO/S method used to interpret the UPS spectra of pyrrole, furan, and thiophene show there to be only one σ level which is strongly localized on the sulfur atom and is thus an *n*-type <83ACH97>. Calculations were obtained by three methods; the first excluded the *d*-orbitals, the second included the sulfur *d*-orbitals, while the third included both the sulfur and carbon *d*-orbitals. The values are in good agreement and the assignments the same in all three cases indicating that the *d*-orbitals on sulfur do not affect the orbital energies to any significant extent as they do some of the other molecular properties; a trend also observed by Poirier *et al.* <89JST(186)101>. A small decrease in the ionization energy observed in going from the 3-21G to 3-21G* basis set indicates the negligible effect of the *d*-orbitals in ionization potential calculations in contrast to some of the other electronic properties.

MINDO/3 calculations <80IJQ797> compare relatively well with the experimental values and correlate better than those obtained by Hartree-Fock *ab initio* calculations <76JES179>. MINDO/3 does tend to underestimate the binding energy of upper level σ orbitals, but the other ionization potentials are calculated to within 0.5 eV of the experimental values and from *ab initio* calculations obtained via the many-body approach. The CNDO/S and INDO/S calculations give results for the low binding energy region but tend to overestimate the high binding region. For the CNDO/2 and INDO methods, the eigenvalues need to be corrected when used for photoelectron calculations.

2.09.2.7 Excitation Energy–UV Spectra

Quantum chemical calculations on the electronic spectrum of compounds are generally carried out by separate calculations on the ground state and on each excited state. Most of the initial calculations on thiophene have been carried out by the PPP method, although calculations by CNDO and INDO have also been done. Results obtained prior to 1981 are discussed in detail in the review by Henriksson-Enflo $\langle 85HC(44/1)215 \rangle$.

In most of the earlier calculations, the d -orbitals on sulfur were omitted. Although the values differ due to the various approximations and parameters employed, most results assign the weak peak at ca. 5.33 eV to the in-plane polarized $\pi \rightarrow \pi^*$ transition and the band at 5.62 eV to the out-of-plane $\pi \rightarrow \pi^*$ transition. The strong peak observed at 6.6 eV in the experimental spectrum is assumed to consist of two transitions, one of which is in-plane and the other, an out-of-plane transition. Low lying triplets of A_1 and B_1 symmetries have also been found in the calculations.

Inclusion of the sulfur 3d-orbital helps in lowering the 1A_1 and 1B_1 transitions of the second band from 7.1 and 7.3 eV to 6.9 and 6.6 eV, respectively, $\langle 66JA4804 \rangle$ which is closer to the experimentally calculated value to 6.6 eV $\langle 85HC(44/1)215 \rangle$. However, in both PPP $\langle 66JA4804 \rangle$ and in the CNDO $\langle 74TCA19 \rangle$ methods, the presence of the d -orbitals in the calculations leads to changes in the ordering of the assignments and thus do not agree any more with the experimentally observed polarizations. PPP calculations for the first band give values of 5.7 and 5.2 eV for the singlet 1A_1 and 1B_1 transitions. The difference in the two drops to 0.1 eV when both the 3d- and 4p-orbitals on sulfur are added to the basis set, but the assignments are reversed. When only the 3d-orbital is included, assignments are the same but the energies drop to 5.0 and 4.9 eV, respectively. With the CNDO method $\langle 74TCA19 \rangle$, from calculations obtained without the d -orbitals, the transition with the lowest energy (ca. 5.4 eV) was assigned to the 1B_2 transition, while calculations that included the d -orbital of sulfur assigned the value at 5.0 eV to an 1A_1 transition.

PPP calculations also show four triplet states for thiophene. When only the 3p-orbital is employed in the basis set, the assignments are 3.3, 4.0, 5.4, and 6.0 eV which correspond to the 3B_1 , 3A_1 , 3A_1 , and 3B_1 transitions, respectively. When the $3d_{xy}$ and $3d_{yz}$ orbitals are included, the four transitions are calculated to be at 3.2, 3.1, 5.5, and 5.7 eV, respectively. Inclusion of the 4p_{*z*} orbital alters the values to 4.0, 4.0, 5.5, and 5.8 eV. The two lowest energies are extremely close to the experimental values of 3.90 and 3.96 eV obtained by excitation measurements $\langle 52MI\ 209-01 \rangle$.

The CINDO/S/SHIFT/UV method $\langle 83JST(94)115 \rangle$ which is the spectroscopic version of the CNDO/2 method, has been used to investigate the function of d -orbitals. Inclusion of the sulfur 3d-orbitals and sulfur and carbon d -orbitals in the calculations does not affect the lower energy transitions but tends to lower the higher energy transition. The pattern observed from the CNDO/S calculations with and without the d -orbitals are similar to those obtained elsewhere $\langle 83ACH97 \rangle$. When the d -orbitals are excluded from the calculations, the energies of the first three $\pi \rightarrow \pi^*$ transitions were found to be comparable to those calculated by the INDO/S and CINDO/S/SHIFT/UV methods $\langle 83JST(94)115 \rangle$. However, in the latter case, the fourth absorption band is calculated to be about 0.5 eV lower in energy than the experimental value. Transition energies of heterocyclic compounds containing the second-row elements which are calculated by the CNDO/S method show better correlation with experimental values when the *spd* basis set is employed than with those that exclude the d -orbitals $\langle 85CPB3077 \rangle$.

Amongst the methods investigated, the results obtained by the CNDO/S $\langle 85CPB3077 \rangle$ and INDO/S $\langle 83JST(94)115 \rangle$ methods coincide the best with experimental values. CNDO/S/SHIFT/UV calculations afford good interpretation of the optical spectrum for thiophene and its benzo analogues. The calculations also show that the d -orbital contributions are negligible since the low energy transitions mainly arise from the *p*-atomic orbitals.

Interest in the application of heterocyclic oligomers in various fields has resulted in computational chemistry playing a major role in predicting whether particular oligomers could possess the required properties or not. The PPP model with configuration interaction (PPP-CI) has been used to predict the long wavelength excitation energies, that is, for estimating band gaps (E_g) for several planar oligomers including those of thiophene and benzo[*c*]thiophene $\langle 87MM2023 \rangle$. There is good correlation between the calculated values and experimental data, although they are slightly overestimated. This is encouraging since it enables prediction of E_g for polymeric cases of hypothetical infinite chain length. Although the PPP-CI method has limitations, it is suitable for calculating π -symmetry electron transitions for conjugated systems, it is readily available and provides an inexpensive first approximation for experimentalists interested in the design and synthesis of polymers possessing certain properties.

2.09.2.8 Vibrational Frequencies

The vibrational spectrum of a compound is usually calculated by harmonic force field calculations <B-55MI 209-01>. For thiophene, frequencies obtained from these calculations <69ACS3139, 69ACS3407, 69JSP(31)451> are in closer proximity than those by MINDO <77JA1685> and vary from experimental frequencies by less than 20 cm⁻¹ (see Table 8).

Table 8 Experimental and theoretical vibrational frequencies (cm⁻¹) of thiophene.

Assignment	Exptl <65SA689>	Force field <69ACS3139>	MINDO <77JA1685>	MP2 <88JPC1739>
A ₁ C—H str	3126	3127	3561	3328
C—H str	3098	3104	3501	3302
C=C, C—C, ring str	1409	1427	1677	1471
C=C str, CCH bend	1360	1364	1348	1420
CCH bend in-plane	1083	1072	1058	1111
CCH bend C—C str	1036	1030	988	1079
C—S str	839	844	778	885
Ring def. in-plane	608	642	460	628
A ₂ C—H wag out-of-plane	898	893	802	822
C—H wag out-of-plane	683	698	712	596
Ring def. out-of-plane	565	565	435	516
B ₁ C—H str	3125	3129	3558	3325
C—H str	3086	3089	3490	3287
C=C, ring str	1504	1532	1729	1542
CCH bend in-plane	1256	1254	1100	1296
CCH bend in-plane	1085	1069	970	1114
C—S str	872	857	774	909
Ring def. in-plane	763	745	605	780
B ₂ C—H wag out-of-plane	867	865	795	768
C—H wag out-of-plane	712	712	699	680
Ring def. out-of-plane	452	450	315	447

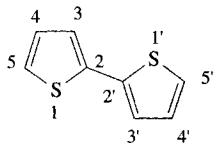
Assignment	SCF <69ISM3491>	SCF <92JST(259)181>	ACPF <92JST(259)181>	QCFF/PI+CISD <94JCP(100)2571>
A ₁ C—H str	3125	3130	3135	
C—H str	3092	3099	3095	
C=C, C—C, ring str	1421	1422	1415	1420
C=C str, CCH bend	1359	1356	1361	1352
CCH bend in-plane	1077	1077	1088	1089
CCH bend C—C str	1023	1027	1032	1006
C—S str	829	833	837	825
Ring def. in-plane	605	604	603	556
A ₂ C—H wag out-of-plane	908	901	878	1092
C—H wag out-of-plane	703	697	726	846
Ring def. out-of-plane	550	575	564	491
B ₁ C—H str	3123	3126	3132	
C—H str	3078	3085	3083	
C=C, ring str	1504	1504	1499	1536
CCH bend in-plane	1262	1262	1251	1310
CCH bend in-plane	1076	1074	1084	1061
C—S str	870	865	872	936
Ring def. in-plane	757	761	753	677
B ₂ C—H wag out-of-plane	877	878	873	1086
C—H wag out-of-plane	687	692	696	728
Ring def. out-of-plane	452	446	451	398

Harmonic vibrational frequencies have also been calculated by *ab initio* methods at the MP2 level with a double ζ basis set with one set of polarization functions (DZP) <88JPC1739>. Although the correlation is better than with those from MINDO calculations, the results are not nearly as good as those from force field calculations. For the high-frequency in-plane stretches, the theoretical values are about 6.5% higher. At the other end of the spectrum, the difference is smaller which is partly due to the anharmonicity of these modes. At the MP2 level the out-of-plane vibrations for both A₂ and B₂ symmetry are lower than the experimental frequencies obtained by gas- and liquid-

phase IR spectra and liquid Raman spectra <65SA689>. This is attributed to the fact that the prediction of harmonic frequencies for bending modes are lower than the experimental fundamentals for aromatic systems. Flexible basis sets which include polarization functions could circumvent this problem.

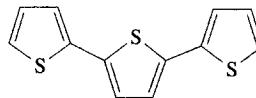
Systematic *ab initio* studies were carried out with two basis sets on the vibrational spectra of thiophene and its oligomers <92JST(259)181>. The first basis set was applied at the SCF level and the second at the averaged couple pair functional (ACPF) level. For thiophene, the latter showed an excellent agreement with the experimental values <65SA689, 66JSP(19)188> with deviations of up to 10 cm^{-1} for the in-plane frequencies (see Table 8).

The computed harmonic force fields for thiophene and its oligomers have been scaled as well. The same SCF scaling factors that were used for the thiophene, were used for 2,2'-bithienyl (**18**) and its oligomers <92JST(259)181>. For bithienyl, the frequencies of the three conformers, for example *syn*, *anti-gauche*, and *anti*, have also been calculated and compared with the solid-state Raman and IR frequencies <90SM299, 91JCP(94)4637>. Previous vibrational frequency calculations have also been studied at the SCF level by Cui *et al.* <91SM3491> but only the minimal basis set (STO-3G) employed. The differences in frequency between the *anti* and the *anti-gauche* conformers are less than 5 cm^{-1} in most cases <92JST(259)181> which is not unexpected since there is only a small energy difference between these two conformations. The difference between the *anti-gauche* and *syn* form is much greater. Although the calculations do not correlate extremely well, the agreement is acceptable. The scaling factors afford a good description of the vibrational spectrum and consequently have been used to determine the vibrational spectra of the antiplanar form of terthiophene (**19**) and poly-thiophene.



2,2'-Bithienyl

(**18**)



(**19**)

Negri and Zgierski <94JPC(100)2571> have employed semiempirical calculations involving the quantum consistent force field/ π electron configuration international singles diffraction (QCFF/PI + CISD) method and *ab initio* calculations using the complete active space self-consistent field (CASSCF) and HF/6-31G* methods. At higher frequencies, the in-plane modes calculated by the semiempirical method agree quite well with the experimental values. At lower frequencies, the discrepancies are larger. This is not unexpected since the C—C—C angle bending is usually not well described by QCFF/PI + CISD for five-membered rings <91CPL(179)131, 93JCP(99)3721>. Large differences are also observed for the out-of-plane C—C—H bending modes for A_2 and B_1 symmetries.

The QCFF/PI + CISD force field method has also been used to calculate vibrational frequencies of the in-plane modes for the deuteriated isotopomers of thiophene. The results compare relatively well with experimental values. Reliable results here have enabled application of this method to obtain vibrational frequencies for thiophene oligomers <94JPC(100)2571>. Vibrational frequencies for the bi-, ter-, and tetra-oligomers have been calculated by QCFF/PI + CISD, HF/3-21G*, and MP2/3-21G methods. Other theoretical studies on the vibrational dynamics of polythiophenes can be found in the following references <91JCP(94)957, 91JCP(94)965, 91JCP(95)4783>.

2.09.2.9 Bond Lengths and Angles

The optimized geometry of thiophene, its derivatives, iso- π -electronic heterocyclic partners, and other Group 16 containing heteroatoms has been calculated by both semiempirical and theoretical methods. Some of the calculations are discussed here and the results summarized in Tables 9 and 10.

Overall there is reasonably good agreement between the calculated bond lengths and the experimental results obtained by microwave spectroscopy <61JSP(7)58>. In most cases, the difference between the experimental and calculated bond lengths are less than 0.04 Å and the angles are within

Table 9 Bond lengths (in Å) of thiophene as calculated by various methods^a.

Method	C—S	C(2)=C(3)	C(3)—C(4)	Ref.
Experimental	1.714	1.370	1.423	61JSP(7)58
MP2	1.713(-1)	1.385(+15)	1.423(0)	88JPC1739
QCFF/PI + CISD	1.711(-3)	1.378(+8)	1.453(+30)	94JCP(100)2571
3-21G*	1.722(+8)	1.348(-22)	1.438(+15)	86PAC75
SCF/3-21G*	1.723(+9)	1.347(-23)	1.437(+14)	88JA4204
3-21G*	1.723(+9)	1.347(-23)	1.438(+15)	89JST(186)101
6-31G*	1.726(+12)	1.345(-25)	1.437(+14)	86PAC75
HF/6-31G*	1.726(+12)	1.345(-25)	1.437(+14)	94JCP(100)2571
4-31G + d	1.726(+12)	1.348(-22)	1.432(+9)	82JA1375
MM2	1.726(+12)	1.346(-24)	1.457(+34)	85TL2403
CI-SD(basis I)	1.728(+14)	1.363(-7)	1.434(+11)	92JST(259)181
SCF(basis I)	1.729(+15)	1.350(-20)	1.437(+14)	92JST(259)181
TZVP	1.729(+15)	1.344(-26)	1.435(+12)	92ZN(A)203
SCF(basis II)	1.732(+18)	1.356(-14)	1.435(+12)	92JST(259)181
STO-3G	1.732(+18)	1.335(-35)	1.454(+31)	84BCJ1312
STO-3G	1.732(+18)	1.335(-35)	1.454(+31)	86JCP(84)4228
STO-3G*	1.733(+19)	1.323(-47)	1.484(+61)	88JST(163)173
CASSF/3-21G*	1.734(+20)	1.361(-9)	1.445(+22)	94JCP(100)2571
MNDO	1.693(-21)	1.367(-3)	1.454(+31)	85JCS(P2)97
MNDO	1.692(-22)	1.368(-2)	1.456(+33)	89CHE874
MNDO	1.692(-22)	1.368(-2)	1.457(+34)	86JCP(84)4228
MNDO	1.692(-22)	1.368(-2)	1.458(+35)	86IJQ1599
ACPF(basis II)	1.745(+31)	1.378(+8)	1.442(+19)	92JST(259)181
ACPF(basis I)	1.753(+39)	1.360(-10)	1.433(+10)	92JST(259)181
MINDO/3	1.757(+43)	1.346(-24)	1.462(+39)	80IJQ797
3-21G	1.797(+83)	1.335(-35)	1.448(+25)	89JST(186)101

^aValue in parenthesis corresponds to difference between experimental and theoretical value $\times 10^{-2}$.

Table 10 Bond angles (in °) of thiophene calculated by various methods.

Method	C-S-C	S-C-C	C-C-C	Ref.
Experimental	92.17	111.47	112.45	61JSP(7)58
3-21G	89.2	111.7	119.3	89JST(186)101
MM2	90.3	113.2		85TL2403
STO-3G	90.4	112.7	112.1	84BCJ1312
ACPF(Basis I)	90.5	111.9	112.9	92JST(259)181
TZVP	91.1			92ZN(A)203
4-31G + d	91.2	111.8	112.6	82JA1375
SCF(Basis I)	91.2	111.9	112.5	92JST(259)181
ACPF(Basis II)	91.2	111.9	112.5	92JST(259)181
CASSF/3-21G*	91.2	112.1	112.3	94JCP(100)2571
HF/631G*	91.4	111.8	112.5	94JCP(100)2571
SCF(Basis II)	91.3	111.8	112.6	92JST(259)181
SCF/3-21G*	91.4	111.9	113.4	88JA4204
3-21G*	91.4	111.9	122.2	89JST(186)101
CI-SD(Basis I)	91.5	111.9	112.4	92JST(259)181
MP2	92.3	111.6	112.2	88JPC1739
MNDO	93.1	112.0	111.4	86IJQ1599
MNDO	93.2	111.9	111.5	89CHE874
QCFF/PI + CISD	93.8	110.8	112.3	94JCP(100)2571
MINDO/3	94.3	108.4	114.5	80IJQ797

3°. In almost all cases, the lengths of the C—S and the C—C bonds are overestimated while that of the C=C bond is underestimated. Thus the C—S—C angles calculated by these methods are usually smaller than the experimental values while the X—C(1)—C(2) angles are generally larger than the experimentally determined values but the difference is usually less than 1°.

MNDO calculations do not tend to follow this trend (83MI 209-01, 85JCS(P2)97, 86IJQ1599, 89CHE874). While there is excellent agreement for the C=C bond (difference of less than 0.003 Å), these calculations also tend to underestimate the C—S bond due to the noninclusion of the 3d atomic orbitals which result in smaller sulfur atomic orbitals and hence shorter C—S bonds. Consequently, the C—S—C angles obtained from MNDO calculations are about 1° larger than experimental.

Although MINDO/3 calculations $\langle 80\text{IJQ}797 \rangle$ follow the trend observed by the other methods, and all calculated bond lengths are within 0.04 Å of the experimental value, the differences here are usually higher than most of the other methods. The larger difference in the bond lengths also leads to larger discrepancies in the bond angles which differ from experimental values by 2–3°. MINDO/3 studies on other five-membered heterocycles correctly predict the C—X bond length to be in the order thiophene > pyrrole > furan, and the order of the C—X—C bond angle to be pyrrole > furan > thiophene.

Amongst the *ab initio* methods, the best correlation between theoretical and experimental values are those obtained by the MP2 method $\langle 88\text{JPC}1739 \rangle$. The double zeta valence with one set of polarization function (DZP) basis predicts the bond lengths to within 0.016 Å and the angles to less than 0.7°. This is a tremendous improvement over other *ab initio* calculations especially those with the 3–21G basis set where the C—S bond is overestimated by 0.08 Å due to the absence of *d*-orbitals on sulfur in the 3–21G basis set $\langle 89\text{JST}(186)101 \rangle$. Inclusion of the *d*-orbitals in the basis set (3–21G*) reduces the C—S bond by about 0.07 Å. A similar shortening is also observed for C—S single and double bonds in other acyclic sulfur compounds $\langle 88\text{JA}4204, 89\text{JST}(186)101 \rangle$. Although there is a large difference in the C—X bond for thiophene, the difference between the 3–21G and 3–21G* calculations decreases in going from sulfur to tellurium and thus a better correlation results between the two methods. The reason for this is that, unlike the sulfur 3–21G basis set, the selenium and tellurium 3–21G basis sets already contain *d*-orbitals which are occupied and hence the extra *d*-function is not a polarization function but merely a supplement to the basis set. Similarly, the C—S—C bond angle as calculated with the 3–21G basis set is smaller than the experimental value by about 3° and is reduced to less than 1° when the *d*-orbitals are included. The opposite trend is observed from STO–3G $\langle 84\text{BCJ}1312 \rangle$ and STO–3G* $\langle 88\text{JST}(163)173 \rangle$ calculations where the bond lengths calculated without the inclusion of the sulfur *d*-orbitals (STO–3G) are better.

Ab initio calculations of ^{33}S nuclear quadrupole coupling constants have been carried out on a variety of sulfur compounds using a TZVP basis set $\langle 92\text{ZN(A)}203 \rangle$. The equilibrium geometric parameters calculated by this method follows the trend of the other *ab initio* methods and the values are within the acceptable limits.

Molecular mechanics is known to be a reliable and quick method for determining structures, energies, and properties of a variety of compounds. Calculations involving the MM2 force field method, has usually been limited to conjugated hydrocarbons $\langle 84\text{TL}2297 \rangle$. This approach has now been extended to compounds containing nitrogen, oxygen, and sulfur atoms $\langle 85\text{TL}2403 \rangle$. The bond lengths follow the pattern of *ab initio* calculations where the C—S bond length is overestimated. Agreement is good between the experimental and calculated bond lengths and angles for thiophene, as well as for some of the other heterocyclic systems tested.

The properties of oligomers of thiophene at the ground and excited states have been investigated by semiempirical and *ab initio* methods. Semiempirical calculations for the ground state of thiophene involve the QCFF/PI + CISD method $\langle 94\text{JCP}(100)2571 \rangle$, while *ab initio* calculations are carried out at the Hartree–Fock/6–31G* and the CASSF/3–21G* levels $\langle 94\text{JCP}(100)2571 \rangle$ and also at the SCF and the ACPF levels, with (basis set I) and without (basis set II) the sulfur 3*d*-orbitals $\langle 92\text{JST}(259)181 \rangle$.

The molecular geometry of thiophene obtained by the QCFF/PI + CISD method is in good agreement with experimental and with the other *ab initio* methods. Upon excitation to the $^1\text{B}_2$ state, this method is able to predict geometry changes but tends to underestimate the angle changes; a problem previously observed in the calculations for cyclopentadiene $\langle 93\text{JCP}(99)3721 \rangle$. Incidentally, while *ab initio* methods predict an elongation of the C—S bond for both the $^1\text{B}_2$ and $^2\text{A}_1$ excited states, the semiempirical method predicts a shortening for the latter state. Other than that, results from the QCFF/PI + CISD method for the $^2\text{A}_1$ excited state agree well with those from CASSF/3–21G*.

The optimized structures of the *syn*, *anti*, and *anti-gauche* conformers of 2,2'-bithienyl calculated at the SCF level do not deviate too much from that of the monomer $\langle 92\text{JST}(259)181 \rangle$. The bond lengths of the *anti* and the *anti-gauche* conformers differ from each other by less than 0.002 Å while the angles differ by only 0.2°. The intermolecular C(2)—C(2') bond length is only 0.03 Å longer than the ring C(3)—C(4) bond. HF/3–21G* calculations $\langle 94\text{JCP}(100)2571 \rangle$ for the *anti*-planar conformer agree extremely well with the experimental values $\langle 58\text{ACS}1671 \rangle$. The MP2/3–21G calculations, in general, tend to overestimate the C—X bond in five-membered rings. This is especially pronounced here, where the C—S bonds are overestimated by 0.1 Å. Addition of *d*-orbitals on sulfur should shorten the calculated bond lengths and lead to better approximations.

Optimized planar geometries of the all-*anti* terthiophene and tetrathiophene have also been determined by SCF $\langle 92\text{JST}(259)181 \rangle$ and by QCFF/PI + CISD and HF/3–21G* $\langle 94\text{JCP}(100)2571 \rangle$ methods. No significant changes are observed upon the oligomerization of thiophene except that

the inter ring C—C bond lengths tend to decrease as the chain length increases, in line with that observed for oligomers of pyrrole and in linear polyenes.

For chlorinated thiophenes, the C_{β} —Cl and the C_{β} —H bonds calculated at the STO-3G level are longer than the C_{α} —Cl and C_{α} —H bonds [\(84BCJ1312\)](#). The interior angles of the carbon atoms bearing the chlorine substituents are also larger than the corresponding angles in thiophene. The S—C—C angle in 2-chlorothiophene (**15**) is 113.8° vs. 111.47° in thiophene, while the C—C—C angle in 3-chlorothiophene (**16**) is 113.7° vs. 112.45° in thiophene. For the *2H*-thiophenium cation (**7**), the C(3)—C(4) and C(5)—S bonds are shorter than in thiophene while all others are longer. Deprotonation of thiophene also leads to an increase in the length of the bond linking the deprotonated carbon atom with the adjacent atoms albeit by a smaller amount than the 0.08 – 0.18 Å increase observed during protonation. MNDO calculations [\(89CHE874\)](#) predict that deprotonation at C(2) leads to an increase in the C—S bond by 0.013 Å and in the C(2)—C(3) bond by 0.011 Å as compared to the neutral molecules. In general, increases between 0.02 – 0.04 Å were obtained for the other five-membered heterocyclic compounds as well as their benzo analogues.

2.09.2.10 Other Molecular Properties

The effect of the inclusion of the $3d$ -orbitals of sulfur in semiempirical and *ab initio* calculations has been reported. One of the factors affected by the inclusion of the $3d$ -orbitals is the dipole moment. *Ab initio* calculations generally show a decrease when the $3d$ -orbitals are included. This change is caused by a reduction of the atomic charges resulting in almost nonpolar bonds. Quadrupole moments behave similarly under these conditions [\(72TCA171\)](#). Due to the enhanced electron density around the sulfur atom, the expectation value $(Z_2)_{\text{cm}}$ is lowered (assuming the y and z axes are in the molecular plane and that the z axis bisects the C—S—C angle). The greatest effect is observed in the value of Q_{zz} which increases from 0.8×10^{-26} to 1.3×10^{-26} esu cm². Calculations performed by the one-particle approximation gave a value of 1.2×10^{-26} esu cm² [\(76JES179\)](#).

Other *ab initio* calculations of one-electron observables [\(82MP649\)](#) also show smaller changes in the quadrupole moment as compared to the dipole moment. As before, Q_{zz} is closest to the experimental value when the basis set includes one extra d -function on sulfur. The quadrupole moments Q_{xx} , Q_{yy} , and Q_{zz} in this case, are between those calculated without any polarization function and those calculated without the d -function on carbon. With the 6-31G(+*sd*+*sp*) basis set [\(92JPC7301\)](#), the MP2 and SCF values do not compare as favorably as results predicted by Gelius *et al.* although relatively large experimental errors makes it difficult to make accurate comparisons [\(72TCA171\)](#).

Contrary to the effect observed for the quadrupole moments, the effect of the $3d$ -orbitals on the diamagnetic susceptibility tensor is negligible [\(72TCA171, 82MP649\)](#). There is good agreement between the experimental values and theoretical calculations [\(76JES179\)](#).

Gelius *et al.* [\(72TCA171\)](#) have also carried out MO–SCF–LCAO calculations for the quadrupole coupling constants for ^{33}S in thiophene, but were unable to compare the results with any experimental data at that time. However, since similar calculations for the quadrupole coupling constants for ^{33}S in SO₂ were in good agreement with experimental data, they were confident that the results obtained for thiophene were acceptable.

Ab initio calculations of the ^{33}S nuclear quadrupole coupling constants (NQCC) have been carried out using the TZVP basis set [\(92ZN\(A\)203\)](#). For bivalent sulfur compounds, there is a large reduction in the π -NQCC when one goes from the acyclic dimethyl sulfide to the aromatic thiophene. As before, there is no MW data available to compare the results, but the results obtained here are in good agreement with those obtained above by Gelius *et al.* [\(72TCA171\)](#). In most cases, the calculated electric field gradients correlate well with the experimental NQCC, including the ^{33}S atomic quadrupole moment, implying good predictability with the TZVP basis set.

2.09.2.11 Miscellaneous

Didehydroheteroarenes (or heteroarynes) and tetradehydroheteroarenes are generated by removal of one and two pairs of vicinal hydrogen atoms respectively from the parent heterocycle. While the chemistry of benzene and of the heteroarynes have been summarized in several reviews, much less is known about the tetradehydroheteroarenes. Theoretical calculations involving the didehydroheteroarenes have been mainly semiempirical in nature [\(64TL1577, 69JA2590, 77CC539, 84JA5256\)](#).

The earliest report on a systematic *ab initio* study on these systems was by Radom *et al.* in 1986 (86PAC75). Amongst the five-membered didehydroheteroarenes, the didehydrothiophenes have been studied the most. These exist either as the 2,3- (**20**) or the 3,4-didehydrothiophene (**21**) isomer. *Ab initio* calculations at the CASSCF/3-21G level show (**20**) to be 0.23 kcal mol⁻¹ lower in energy than (**21**). Bond lengths calculated by the above method for the two isomers as well as for tetrahydrothiophene (**22**) are listed in Table 11. In all cases, the C—S bond is longer than in thiophene. Although the 3,4-didehydro isomers of furan and thiophene show similar behavior, there is a substantial difference in the 2,3-didehydro isomers of the two. For furan, the C(3)—C(4) bond is predicted to be quite long (ca. 1.516 Å) while in 2,3-didehydrothiophene (**20**), it is 1.424 Å, which is quite similar to that found in thiophene. Calculations on (**22**) show it to be a stable molecule, unlike tetrahydrofuran where calculations predict spontaneous rupture of the C(3)—C(4) bond.

Table 11 Predicted bond lengths (in Å) for di- and tetrahydrothiophenes.

Thiophene	C ₂ S	C ₃ S	C ₂ C ₃	C ₄ C ₅	C ₃ C ₄
Thiophene ^a	1.714	1.714	1.370	1.370	1.423
2,3-Didehydro	1.743	1.780	1.235	1.355	1.424
3,4-Didehydro	1.771	1.771	1.342	1.342	1.259
Tetrahydro	1.786	1.786	1.220	1.220	1.491

^aExperimental values (61JSP(7)58).



(20)

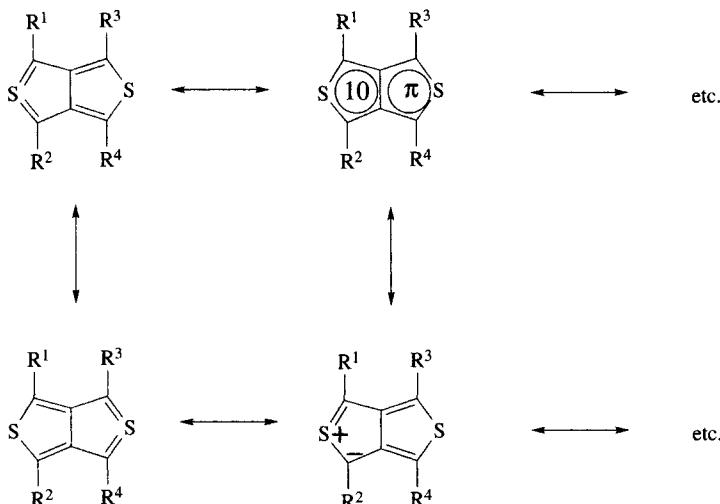


(21)



(22)

The thieno[3,4-*c*]thiophene system is an intriguing 10 π-electron system consisting of two fused thiophene units. This nonclassical thiophene can exist in many isomeric forms (see Scheme 1) and is thus of synthetic and theoretical interest. The parent compound (*R* = H) is unstable and only a few derivatives have been synthesized. Information regarding the theoretical and synthetic aspects of this system can be found in (83JA1705, 83JA1979, 87BCJ1981, 88JA1793, 94JOC2223) and the interested reader is encouraged to refer to them.



Scheme 1

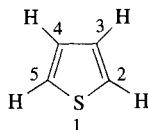
Semiempirical and *ab initio* calculations have also been carried out to determine aromatic energies of thiophene and other heterocycles. This will be discussed later in the section on aromaticity.

2.09.3 EXPERIMENTAL STRUCTURAL METHODS

2.09.3.1 Molecular Structure

Highly accurate molecular geometries for five-membered heterocycles have been obtained by microwave spectroscopy. Bak *et al.* (56JCP(25)892, 60ACS1865, 61JSP(7)58) have studied the microwave spectra of thiophene, deuteriothiophene, and ¹³C-labeled thiophene. The molecular structure has also been determined by electron diffraction (70AX(B)1010) and the geometry as obtained by these two methods is listed in Table 12. The results from MW spectroscopy described here (61JSP(7)58) are an improvement over earlier results (56JCP(25)892). The C—C distances here are closer to the benzenoid C—C bond length. Within limits of error, the C(2)—C(3) bond length and the C(3)—C(4) bond length are symmetrically displaced with respect to the benzene C—C bond. The measured C—S bond is almost midway between a pure single and a pure double bond; its double-bond character is estimated to be 40%. Results from electron diffraction compare reasonably well with MW spectral analysis except for the C—H bond lengths which are somewhat smaller than that determined from MW spectroscopy.

Table 12 Bond lengths and angles for thiophene from MW spectroscopy^a and electron diffraction^b.



Bond	MW spectroscopy	Electron diffraction
length (nm)		
C—S	1.714 ± 0.0014	1.717 ± 0.004
C=C	1.370 ± 0.0017	1.368 ± 0.004
C—C	1.423 ± 0.0023	1.424 ± 0.002
C(2)—H	1.078 ± 0.0015	1.071 ± 0.015
C(3)—H	1.081 ± 0.0014	1.071 ± 0.015
angle (°)		
C(5)—S—C(2)	92.1 ± 0.1	91.9 ± 0.3
S—C(2)—C(3)	111.5 ± 0.2	111.9 ± 0.3
C(2)—C(3)—C(4)	112.5 ± 0.2	
S—C(2)—H	119.8 ± 0.8	121 ± 3
C(3)—C(4)—H	124.25 ± 0.1	120 ± 6

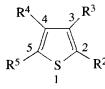
^a(61JSP(7)58). ^b(70AX(B)1010).

The molecular structure of thiophene has also been determined by liquid crystal LC NMR spectroscopy (84MP779, 88MCLC267) as well as electron diffraction (ED) and rotational spectroscopy. All three methods have their limitations and thus are generally used for only simple models. The fact that each method complements the other was made use of in a determination of the *r_a* structure of thiophene by a combined analysis of the three methods (88JST(178)227). The ED data is useful for determining the absolute size and positions of the heavy atoms. It is however unable to properly locate the hydrogen atom. As a result, the C—H bond distance appears too large. Furthermore, the C—C and C=C bond lengths and the C—S—C bond angle do not agree well with results from other methods.

From LC NMR coupling constants, the location of the hydrogen atoms can be determined. However, since this method does not give information about the absolute size, a few structural parameters are fixed. By combining the two methods, the deviations from MW spectroscopy are smaller (61JSP(7)58) and this is further improved by addition of rotational spectroscopy data.

A search of the Cambridge Crystallographic Database (updated in 1993 ca. 120000 entries) for thiophene not fused to another ring yielded 546 hits. While it is impossible to list all, a few compounds will be discussed here and their geometries are summarized in Table 13.

Although the molecular structure of thiophene has been actively investigated (61JSP(7)58, 70AX(B)1010, 84MP779, 88JST(178)227, 88MCLC267, 88JA4204), there have not been many reports on that of the methyl derivatives. The molecular structure of 2,5-dimethylthiophene has been determined by gas electron diffraction (GED) and the results compared with *ab initio* calculations carried out

Table 13 Molecular geometries of various substituted thiophenes.

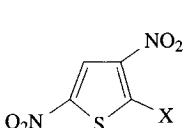
R^2	R^3	R^4	R^5	r_{12}	r_{23}	r_{34}	r_{45}	r_{15}	θ_{215}	θ_{123}	θ_{234}	θ_{345}	θ_{451}	Ref.
Me	H	H	Me	1.736	1.372	1.438	1.372	1.736	92.6	110.7	113.0	113.0	110.7	93JST(301)107
H	Bu ^t	Bu ^t	H	1.78	1.39	1.66	1.39	1.78	90.0	117.0	108.0	108.0	117.0	80CC922
Bu ^t	Bu ^t	Bu ^t	Bu ^t	1.720	1.388	1.499	1.387	1.720						92TL5947
4-NO ₂ C ₆ H ₄	Ph	Ph	4-NO ₂ C ₆ H ₄	1.724	1.381	1.429	1.381	1.724	93.0	110.7	112.8	112.8	110.7	86AX(C)363
CN	CN	CN	CN	1.69	1.40	1.40	1.34	1.71	89.1	113.7	110.8	111.8	114.3	68AX(B)725
Cl	NO ₂	H	NO ₂	1.71	1.37	1.41	1.36	1.71	90.4	111.7	113.9	109.8	114.2	88JHC177
SO ₂ Ph	NO ₂	H	NO ₂	1.706	1.366	1.403	1.342	1.709	89.9	111.1	114.7	109.0	115.4	88JHC177
NH ₂	CO ₂ Et	Ph	H	1.725	1.396	1.452	1.353	1.733	91.2	112.0	111.5	111.9	113.3	91AX(C)1748
CO ₂ H	H	H	H	1.693	1.362	1.414	1.363	1.701	92.0	111.8	112.4	111.9	111.8	62AX913
CO ₂ H	H	H	H	1.693	1.362	1.41	1.363	1.701	92.0	111.8	112.4	111.9	111.8	62AX737
CO ₂ H	H	H	H	1.707	1.369	1.414	1.350	1.695	91.6	111.5	112.0	112.3	112.5	89M1 209-01
COCH ₃	OH	H	H	1.730	1.381	1.431	1.351	1.710	91.4	111.4	111.9	112.4	113.0	69ACS2031
COCH ₃	H	H	Br	1.72	1.37	1.44	1.34	1.72	91	112	112	111	114	70RTC(89)392
CO ₂ H	COCH ₃	H	H	1.718	1.406	1.433	1.376	1.717	93.1	110.3	112.6	112.3	111.8	72BSB319
COCH ₃	CO ₂ H	H	H	1.723	1.381	1.397	1.343	1.699	91.8	110.8	111.5	114.3	111.5	72BSB319
H	CO ₂ H	COCH ₃	H	1.693	1.346	1.454	1.356	1.698	91.7	111.9	113.1	109.3	113.9	72BSB319

at the 3–21G* level $\langle 93\text{JST}(301)107 \rangle$. For the equilibrium state, GED results show one of the C—H bonds of the methyl substituent to be *cis* with respect to the S—C bond of thiophene, contradicting STO–3G* results which indicate one of the bonds to be *trans*. This contradiction is considered to arise due to the deficiency in the basis set. However, the STO–3G* calculations parallel that of the STO–3G calculations on 2-methylthiophene $\langle 79\text{JA}311 \rangle$. A GED study of 2-methylthiophene should be able to determine the stable configuration of this. The C(2)—Me distance is smaller than a normal C—C single bond and quite close to the C—C bond length in nonconjugated alkanes. The C—S bond length here is larger than in thiophene as is also the C—S—C angle. In general, the STO–3G* calculations reproduce most of the experimental differences between 2,5-dimethylthiophene and thiophene.

The presence of bulky groups adjacent to each other leads to variations from normal trends due to steric interaction. This is more so in six-membered rings than in five-membered heterocycles. For example, x-ray results of 3,4-di-*t*-butylthiophene indicate that the ring is almost planar $\langle 80\text{CC}922 \rangle$. However, results do show appreciable internal strain in the molecule. The C(3)—C(4) bond length is 1.667 Å as compared to 1.423 Å in thiophene. The two substituents are also pushed away from each other, the C(3)—C(4)—Bu^t angle being 133° as compared to about 124° in other cases.

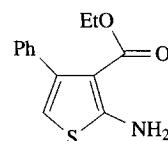
The x-ray structure of tetra-*t*-butylthiophene has also been determined $\langle 92\text{TL}5947 \rangle$. The ring is not planar any more, the torsional angle being 16.2°. The torsional angle between the 3- and 4-groups is 44° while that between the 2- and 3-substituents is 26.8°. The C—Bu^t bonds lengths here are also longer (ca. 1.567 Å) as compared to 1.49 Å in 3,4-di-*t*-butylthiophene $\langle 80\text{CC}922 \rangle$. The twisting between the *t*-butyl groups and in the ring releases most of the strain and thus the ring bond lengths are smaller than the di-*t*-butyl derivative and hence closer to thiophene. In tetra-*t*-butyl-1,1-dioxide, the ring becomes nonaromatic and bond alternation is much more pronounced. Although the C=C bond length decreases, all other bond lengths increase as does the torsional angle between the *t*-butyl groups at the 3- and 4-position $\langle 92\text{TL}5947 \rangle$.

X-ray analysis show the phenyl rings in 2,5-bis(4-nitrophenyl)-3,4-diphenylthiophene are twisted –72.0° from the thiophene plane, while the angle between the nitrophenyl rings and thiophene is 26.6° $\langle 86\text{AX(C)}363 \rangle$. In 2,4-dinitrohalobenzenes, the nitro groups are rotated with respect to the benzene rings. In five-membered ring compounds, the distance between adjacent substituents is larger which tends to reduce the interaction between the halo and the nitro group. In 2-chloro-3,5-dinitrothiophene (**23**), the thiophene ring is almost planar $\langle 88\text{JHC}177 \rangle$. The 5-nitro substituent is rotated by 1° which increases to 8.3° when the chloride atom is substituted by a phenylsulfonyl moiety (**24**). This relatively small deviation is common for 4-unsubstituted 5-nitrothiophenes $\langle 79\text{CHE}1201 \rangle$. The dihedral angle for 3-nitrophenyl is higher with it being 17.5° for (**23**) and 21.0° for (**24**) as compared to 40° in benzene. The strain is further released by a deformation which causes the C(3)—C(2)—X angle to increase to 129.9° and 132.2°, respectively.



(23) X = Cl

(24) X = SO2Ph



(25)

In ethyl 2-amino-4-phenylthiophene-3-carboxylate (**25**), steric repulsion between the ethoxy group and the phenyl ring is reduced by the phenyl ring being twisted out of the plane by an angle of 70.2°. The phenyl ring is also pushed away as is seen by the larger C(3)—C(4)—Ph angle $\langle 91\text{AX(C)}1748 \rangle$.

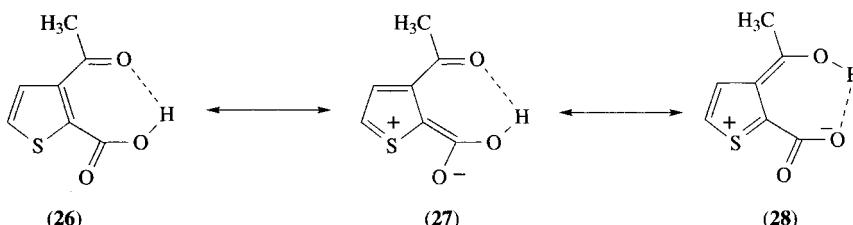
Initial determination of the molecular structure of 2-thiophenecarboxylic acid was not accurate due to poor resolution in the projections $\langle 58\text{G}229 \rangle$. Subsequent refinements were in good agreement with each other (see Table 13) $\langle 62\text{AX}737, 62\text{AX}913 \rangle$. Although the molecule loses its symmetry due to the substituent at the 2-position, the S—C bond lengths are approximately equal as are the two C=C bonds. The molecule is practically planar except for the sulfur atom which lies about 0.03 Å out of the plane. The carboxyl group is pulled towards the heteroatom making the S—C(2)—COOH angle smaller than the C(3)—C(2)—COOH angle.

A reinvestigation on 2-thiophenecarboxylic acid $\langle 89\text{MI} 209-01 \rangle$ confirms previous reports and also determines the dihedral angle between thiophene and the carboxyl group to be 1.49°. Furthermore,

the C=O bond length here is determined to be 1.235 Å which is longer than the 1.201 Å previously reported <62AX737>. 2-Thiophenecarboxylic acid is intermolecularly linked via hydrogen bonding and the pair forms a centrosymmetrical dimer.

The crystal structure of 2-acetyl-3-hydroxythiophene has been investigated in order to determine the amount of hydrogen bonding in the solid phase <69ACS2031>. The x-ray structure showed the carbonyl oxygen to be *cis* with respect to the sulfur atom. Thus the two oxygen atoms within the molecule are too far apart (4.27 Å) to bond intramolecularly. The distance between the hydroxyl group in one molecule and the carbonyl oxygen in another is much closer (2.64 Å) and thus capable of hydrogen bonding. The carbonyl oxygen in the first molecule is similarly bonded to a hydroxyl group of a third molecule; thus a chain is formed.

3-Dimensional x-ray analysis has been used to determine the x-ray structure of the three *ortho*-acetylthiophenecarboxylic acids <72BSB319>. In all cases the carbonyl groups are in the same plane as the ring. For 3-acetyl-2-thiophenecarboxylic acid (**26**) the bond length of the C(2)=C(3) bond is 1.406 Å which is 0.036 Å longer than the corresponding bond in thiophene. The O—H bond length here is determined to be 1.52 Å while the distance between the acetyl oxygen and the carboxylic hydrogen is 1.06 Å, implying strong intramolecular hydrogen bonding. In fact, its positioning hints at a possible enol character. This is not surprising since the molecule could also exist in two other tautomeric forms (**27**) and (**28**) (Scheme 2).

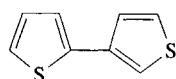


Scheme 2

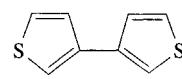
In 2-acetyl-3-thiophenecarboxylic acid, the C(2)=C(3) bond is shorter than in the previous case but the carboxylic group is angled further away from the acetyl group. This is seen in the O—H bond lengths where the bond length of the carboxylic O—H is 1.26 Å while that between the acetyl oxygen and the carboxylic hydrogen is 1.37 Å indicating less hydrogen bonding here and thus less influence from the resonance structure analogous to (**28**).

Tetrachlorothiophene-1,1-dioxide is nonplanar, with the sulfur atom being displaced from the plane by 0.087 Å. The ring is also deformed as is seen by the difference in the two S—C and C=C bond lengths. Due to lack of conjugation between the SO₂ group and the double bonds, there is noticeable bond alternation here with the C=C bond length being ca. 1.33 Å while the C(3)—C(4) bond length is 1.476 Å. The four C—Cl bond length are all different and range from 1.682 to 1.696 Å <93AX(C)1197>.

Interest in the chemistry of polythiophenes has stemmed from their potential as organic conducting polymers <B-86MI 209-01>. Theoretical studies (see Section 2.09.2) have been carried out on these compounds to predict their properties, stabilities, etc. The simplest polythiophene is bithienyl, which could exist in the isomeric forms 2,2'-(**18**), 2,3'-(**29**), or 3,3'-(**30**). Furthermore, the molecules can rotate round the intermolecular C—C bond and thus each isomer can possess various conformations. Initial studies indicated that, in the solid phase, the molecules are planar and have the *anti* conformation <68AX(B)467>. In the gas phase the two molecules are twisted around the central bond by approximately 34° <58ACSC1671>. The molecule is slightly distorted with the C(2)—C(3)—C(4) angle being about 9° smaller than the C(3)—C(4)—C(5) angle. For 2,3'-bithienyl (**29**), the conformation could not be obtained due to the disorder in the crystals. Similarly, from the x-ray of 3,3'-bithienyl (**30**), it was not possible to determine if the *anti* conformation holds for all the molecules. The C—S bond lengths in bithienyl do not differ much from that in thiophene and consequently, the thiienyl substituent does not alter the geometry of thiophene to any extent.



(29)



(30)

X-ray studies on the structure of 3,3'-dimethoxy-2,2'-bithienyl show the molecule to lie on a crystallographic center of symmetry and the two rings to be in the *anti* form $\langle 88AX(B)509 \rangle$. Comparison of the experimental results with *ab initio* calculations show extremely good agreement. Although x-ray shows the molecule to be planar, MNDO calculations indicate it to be 17 kcal mol⁻¹ more stable when the two rings are at 90° to each other $\langle 77JA4899 \rangle$. A similar result was also observed for 3,3'-dihydroxy-2,2'-bithienyl where the nonplanar forms were found to be more stable. However, *ab initio* calculations show that in the nonhydrogen-bonded conformation, the planar form is more stable. Since the hydrogen atom of the hydroxyl group in the nonbonded case points in the same direction as the methyl group in the methoxy case, one can assume that the x-ray structures are correct and that MNDO calculations are not accurate in this case.

In 4,4'-dimethoxy-2,2'-bithienyl, molecules in different halves of the unit cell have different geometries. For cases not involving H atoms, the differences in bond lengths and angles are up to 0.014 Å and 0.8°, respectively, while for H-related parameters the differences are up to 0.1 Å and 4–5° $\langle 89JST(196)171 \rangle$.

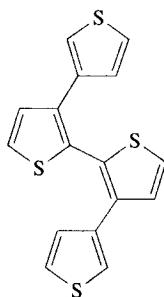
Contrary to 2-bromothiophene where the S—C(2) bond is longer than the S—C(5) bond $\langle 70AX(B)1010 \rangle$, the x-ray analysis of 5,5'-dibromo-2,2'-bithienyl shows the S—C bonds to be of equal length (within experimental error) $\langle 88AX(C)562 \rangle$. The C—S—C angles in the monomer and dimer are approximately the same as are the S—C(2)—C(3) and the S—C(5)—C(4) angles. The major difference is between the C(2)—C(3)—C(4) and C(3)—C(4)—C(5) angles with the latter being smaller by about 2.5°. This occurs since both a thiényl substituent as well as a 2-bromo substituent cause the C(2)—C(3)—C(4) angle to be 9° to 5° smaller than the C(3)—C(4)—C(5) angle. The small difference here is due to the fact that the substituents are on opposite sides and thus tend to cancel each other.

While the 5,5'-dibromo derivative is planar in the solid phase $\langle 88AX(C)562 \rangle$, the 5,5'-dinitro derivative exhibits a small dihedral angle of 3.3° $\langle 80MI\ 209-01 \rangle$ while in 3,5,5'-tribromo-2,2'-bithienyl it is 4.6° $\langle 88AX(C)1800 \rangle$. In the monosubstituted ring, the C(2)=C(3) bond length is 0.08 Å longer than the C(4)=C(5) bond length, while in the disubstituted ring, they are the same. The C(2)—C(3)—C(4) and the C(3)—C(4)—C(5) bond angles are the same in the monobromo substituted ring while in the other ring the latter is smaller by 6.3°.

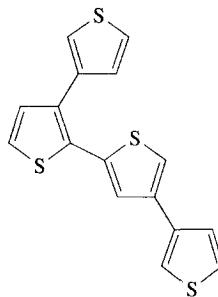
In 5-dimethylamino-5'-nitro-2,2'-bithienyl the dihedral angles between the two rings is 3.7°, between the dimethylamino group and the ring 4.5°, and between the nitro group and the ring 2.1° $\langle 93AG(E)719 \rangle$. The presence of donor–acceptor substituents in the molecule and planarity leads to extended conjugation within the molecule as seen by the distinct equalization of the C—C bond lengths. Thus all the C—C ring bond lengths are between 1.36 and 1.40 Å.

Although 3,3'-bithienyls are planar $\langle 68AX(B)467 \rangle$ substituents at the 2,2';4,4'-positions lead to restricted rotation and as a result, these compounds are not planar $\langle 75CS205 \rangle$.

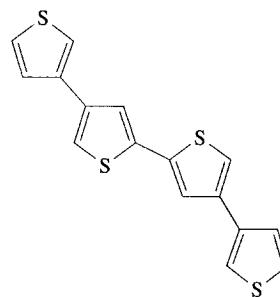
Unlike the 2,2'-bithienyls, 3,3';2',2";3",3"-tetrathiophene (**31**) is not planar with the angles between the 3,3'-rings being 20° while that between the 2',2"-rings is 110° $\langle 88H(27)1391 \rangle$. In the plane of the terminal thiophene rings, two orientations of sulfur were observed in a ratio of 2:1 indicating the presence of two other isomers (**32**) and (**33**).



(31)



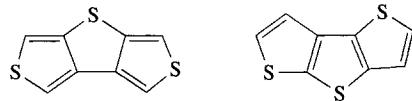
(32)



(33)

In addition to polythiophenes, fused thiophenes also possess interesting optical and electronic properties. The x-ray structure of dithieno[3,4-*b*;3',4'-*d*]thiophene (**34**) shows each thiophene ring to be practically planar, the maximum displacement being 0.006 Å $\langle 88AX(C)545 \rangle$. The dihedral angles between the central ring and the two outer rings are 1.2° and 2.4°. The C—S bond lengths for the central ring are about 0.05 Å longer than those of the outer rings. This difference is less so in the fused thiophene (**35**) $\langle 83JCP(87)2317 \rangle$. In both cases, the differences in the C—C bond lengths

for the central rings are much smaller than for the other rings indicating a different bond order in the central ring and thus enhanced aromaticity.

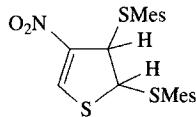


(34)

(35)

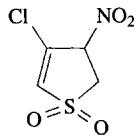
The x-ray crystallographic search for dihydrothiophenes revealed 42 hits. In most of the compounds, the thiophene ring was fused to a cyclic compound. X-ray studies of some dihydrothiophene-1,1-dioxides are also available. In most cases, the x-ray studies were used to determine the configurations of the substituents at the 2,3-position (i.e., *cis* or *trans*).

2-Mesylthio-4-nitrothiophene is synthesized from 3,4-dinitrothiophene via a 2,3-dihydro intermediate <85JCS(P2)1291>. The regiospecificity here is opposite to that in other heterocycles. The intermediate is of interest to assess the stereochemistry of the above reaction. The x-ray structure of *trans*-2,3-bis(mesylthio)-4-nitro-2,3-dihydrothiophene (36) shows the molecule to be puckered, the torsion angles being between -28° and $+23^\circ$. The conformation is thought of to be a half-chair with a pseudo twofold axis through C(5) and the center of the C(2)—C(3) bond; a conformation also observed in other 2,3-disubstituted 2,3-dihydrothiophenes <80JCS(P2)1764>, as well as in *spiro*-2,3-dihydrothiophene <81CB1074>. The nitro group is planar with the C(3)—C(4)—C(5)—S plane of the molecule with the C(5)—H being bent away from the nitro group to allow for hydrogen bonding with the oxygen atom. The S—C(2) bond length (1.824 Å) is much longer than the S—C(5) bond length (1.710 Å), while the shorter bond length of C(3)—C(4) as compared to C(2)—C(3) arises due to conjugation between the nitro group and the thiophene sulfur atom.



(36)

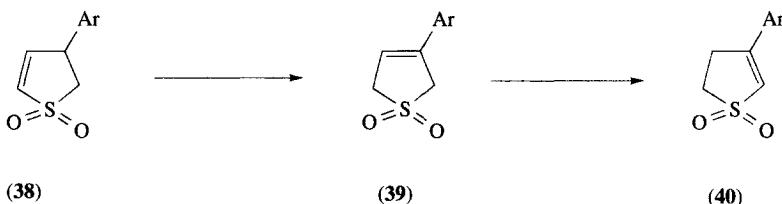
The x-ray structure of 3-chloro-4-nitro-4,5-dihydrothiophene-1,1-dioxide (37) indicates the molecule to be planar within 0.03 Å, with the nitro group being twisted at an angle of 88.9° <84JGU1058>. The two S—C bond lengths are different; the difference depending on the substituents on C(3) and C(4). The S—O bond lengths as well as the C=C bond length here are smaller than those found in the 3-aryl derivative (40) <80T1667>. The C—Cl bond here is 0.03 Å shorter than a comparable vinyl chloride bond and occurs due to the interaction of the unshared electron pair of the halogen with the unoccupied 3d-orbitals of the sulfur atom through the C(2)=C(3) bond.



(37)

4-Aryl-4,5-dihydrothiophene-1,1-dioxides (38) undergo base-catalyzed isomerization to 3-aryl-2,5- (39) and 3-aryl-4,5-dihydrothiophene-1,1-dioxide (40) (Scheme 3). Although 2,5-dihydrothiophene-1,1-dioxide is more stable than its 4,5-isomer, the presence of a substituent at the β position, shifts the equilibrium to the right <80T1667>.

In (38), the two rings are twisted at an angle of 35° , while in (40) they are planar. The sulfur atom is at the apex of a distorted tetrahedron in both cases. The C—S bonds in (40) are shorter than in (38) due to the extended conjugation between the aryl group and the C=C in (40). This conjugation also explains the bond length of 1.42 Å for the C—C bond between the two rings which is considerably shorter than a normal C—C single bond. Although there is not a great deal of difference between the geometries of the two molecules, the biggest difference lies in the orientation of the phenyl group with respect to the five-membered ring.



Scheme 3

For the fully saturated heterocycle tetrahydrothiophene, 344 hits were obtained. Many of these references involved the structure of tetrahydrothiophene with metal complexes and also as perhydrobenzothiophenes. The variation is too great and thus will not be discussed here.

A comparison of the molecular geometries of some of the simple derivatives of benzo[*b*]thiophene is listed in Table 14. In benzo[*b*]thiophene, both rings are planar. Introduction of a substituent on the thiophene ring usually causes the two rings to be inclined to each other at about 1.0° (74AX(B)2058, 84AX(A)C277). The average C—S bond length is longer than in thiophene with the S—C(2) bond being the longer of the two. The C=C bonds in the five-membered ring which is fused to the benzene ring is longer by 0.044 Å. The C(2)=C(3) bond found here is also shorter than that in thiophene.

In ethyl 3-amino-5-nitrobenzo[*b*]thiophene-2-carboxylate, the two rings are inclined at 2.18° to each other (91MI 209-01). In the ester functionality, the carbonyl oxygen is *cis* to the sulfur atom and the NH bond lengths of the amino group indicate one hydrogen to be intramolecularly bonded to the oxygen of the OEt group and the other to be intermolecularly bonded to the carbonyl oxygen.

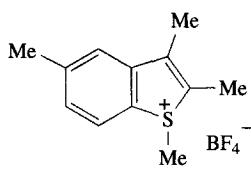
The x-ray structure of 3-acetoxybenzo[*b*]thiophene-2-carbaldehyde (42) which is formed by the acylotropic rearrangement of (41) has been determined (85JOU784) and is discussed in the section on tautomerism.



(41)

(42)

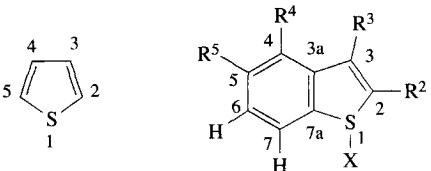
For benzo[*b*]thiophene-1,1-dioxide, its 2-bromo, and 2,3-dimethyl derivatives (87AX(C)2421) as well as for the 2- and 3-methyl analogues (88AX(C)498), the bond lengths and angles are approximately similar to their unoxidized precursors, the largest difference being in the C(2)=C(3) bond which is much smaller in the dioxide. As before, the two rings are tilted towards each other at about 1° . The geometries are also in good agreement with 1,2,3,5-tetramethylbenzo[*b*]thiophenium tetrafluoroborate (43) (81JCS(P2)266). The bonds about the sulfur atom are pyramidal in nature with the methyl group being out of the plane of the molecule. In comparison to benzo[*b*]thiophene derivatives (see Table 14), the salt has longer C—S and C(3)—C(3a) bonds but a shorter C(2)=C(3) bond indicating more bond alternation here due to the lack of delocalization.



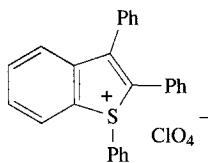
(43)

In the thienyl salt (44) (93T5055), the Ph—S⁺ bond length is shorter than that for Me—S⁺ indicating it to be a relatively stable molecule. As in the other salts, the bonds around sulfur are arranged pyramidally.

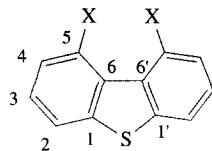
A search for x-ray studies on dibenzothiophenes reveal 32 hits from the crystallographic database.

Table 14 Molecular geometries from x-ray studies of some benzo[*b*]thiophene derivatives.

X	R ²	R ³	R ⁴	R ⁵	r ₁₂	r ₂₃	r _{33a}	r _{3a7a}	r _{17a}	θ _{217a}	θ ₁₂₃	θ _{233a}	θ _{33a7a}	θ _{3a7a1}	Ref.
Thiophene															
-	Me	H	H	H	1.714	1.370	1.423	1.370	1.714	92.1	111.5	112.5	111.5	92.1	61JSP(7)58
-	Me	Me	H	Br	1.772	1.382	1.485	1.386	1.741	92.4	111.7	111.4	113.3	111.3	85AX(C)929
-	Cl	Cl	H	H	1.754	1.355	1.446	1.399	1.741	91.7	112.4	112.4	112.9	110.7	74AX(B)2058
-	H	H	Ph(CH ₂) ₂	NO	1.758	1.341	1.418	1.398	1.765	90.0	112.0	115.1	111.1	111.7	86AX(C)696
-	CO ₂ Et	NH ₂	H	NO ₂	1.712	1.326	1.417	1.397	1.696	91.5	113.4	112.2	112.0	110.9	82AX(B)685
-	CHO	OCOMe	H	H	1.749	1.376	1.447	1.404	1.724	91.3	112.9	111.4	112.5	111.9	91MI 209-01
Compound 41															
O ₂	H	H	H	H	1.739	1.365	1.419	1.409	1.736	90.9	111.7	114.8	110.0	112.6	85JOU784
O ₂	Me	H	H	H	1.755	1.483	1.464	1.392	1.750	91.2	112.1	109.6	112.8	114.3	85JOU784
O ₂	H	Me	H	H	1.757	1.323	1.467	1.391	1.579	93.0	110.7	114.8	112.3	109.3	87AX(C)2421
O ₂	Me	H	H	H	1.771	1.319	1.472	1.388	1.751	92.7	109.4	115.6	112.5	108.7	88AX(C)498
O ₂	H	Me	H	H	1.746	1.321	1.480	1.395	1.765	93.1	111.7	113.8	112.6	108.8	88AX(C)498
O ₂	Me	Me	H	H	1.766	1.335	1.480	1.401	1.757	94.1	110.2	114.2	113.2	108.3	87AX(C)2421
O ₂	Br	H	H	H	1.770	1.320	1.458	1.383	1.770	92.2	111.3	113.8	113.8	108.8	87AX(C)2421
Me	Me	Me	H	Me	1.779	1.340	1.468	1.389	1.768	92.2	111.0	113.2	113.6	109.2	81JCS(P2)266
Ph	Ph	Ph	H	H	1.790	1.346	1.471	1.400	1.762	92.1	111.1	113.4	113.2	109.9	93T5055



The x-ray structure of dibenzothiophene (**45**) was first determined by Schaffrin and Trotter *<70JCS(A)1561>*. Although each of the rings are planar, the molecule is slightly bow shaped with the dihedral angles between the planes being 0.4° and 1.2° . As for benzo[*b*]thiophene, the C—S bond length at 1.740 \AA is longer than in thiophene as are the C(1)—C(6) and C(1')—C(6') bond lengths. The x-ray structure of dibenzothiophene-1,1-dioxide *<68AX(B)981>* is quite similar to dibenzothiophene.



Octafluorodibenzothiophene would be expected to be distorted due to the larger size of the fluoro atom. Although the fluoro substituents at C(5) and C(5') are closer than the sum of the accepted van der Waals radii, there is very little change in the molecular geometry *<88PS(35)67>*. The C—S—C angle is only slightly smaller than in dibenzothiophene (89.8° vs. 91.5°) and the C(5)—C(6)—C(6') angle increases to 131.5° due to the larger fluorine atoms. There is a slight relief in strain since the two fluorine atoms are displaced by -0.011 \AA and $+0.011\text{ \AA}$ from the plane of the molecule.

1,9-bis(Dimethylamino)dibenzothiophene (**46**; $\text{X} = \text{NMe}_2$) belongs to a group of compounds known as proton sponges. X-ray structure analysis shows excessive steric strain in this molecule as a result of bulky groups in the 5,5'-positions *<88TL1905>*. As a result, the torsion amounts to 21.3° and the C(5) and C(5') atoms deviate from the mean plane by 0.33 and 3.0 \AA . This causes the nitrogen atoms to be 28.6 \AA apart. Protonation causes a relief in the strain. The torsion angle is reduced to 7.7° as is the N···N distance due to the formation of the N···H···N bond which is almost linear (ca. 175°).

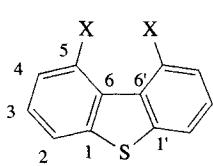
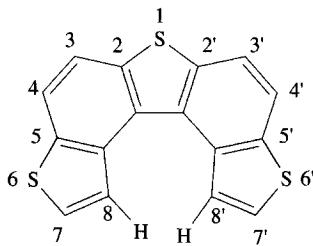
With arylthio groups at the 5,5'-positions (**47**; $\text{X} = \text{SAr}$), the central ring is distorted due to the steric repulsion of the substituents *<92H(33)101>*, the distance between the sulfur atoms being 3.012 \AA . The aryl substituents are *anti* and are close to the dibenzothiophene ring.

Although the x-ray structures of carbohelicenes have been extensively studied, those of the heterohelicenes have received less attention. The x-ray structure of trithia[5]heterohelicene (**48**) *<84AX(C)1039>* shows the terminal thiophene rings to be planar but possess a dihedral angle of 36.6° with each other. The three other rings are somewhat twisted, the dihedral angles between the central thiophene and the adjacent benzene rings being 7.9° while that between the benzene ring and the terminal rings is 10.6° . The atoms H(8) and H(8'), H(8) and C(8') are closer than the sum of the van der Waals radii and consequently H(8) and H(8') are displaced out of the plane of the thiophene ring. The S(6)—C(7) bond length is close to the value observed in thiophene while the S(6)—C(5) and S(1)—C(2) bond lengths are longer and closer to those found in dibenzothiophene *<70AX(B)1010>*. The packing mode of the heterohelicene (**48**) is quite different from that found in carbohelicenes.

2.09.3.2 Molecular Spectroscopy

2.09.3.2.1 Proton NMR spectroscopy

Spectroscopy is an important tool for the structure elucidation of compounds. Modern methods enable determination of conformation, aromaticity, mechanism, and other physical properties. A

(47) $X = \text{SAr}$ 

(48)

systematic investigation of mono- and di-substituted thiophenes was carried out by Hoffman and Gronowitz *60AK501, 60AK563* which was later followed by a review of the ^1H NMR spectroscopy of thiophene by Gronowitz *63AHC(1)1*. Since then, other reviews on the spectroscopy of thiophene compounds have appeared, including ones being in CHEC-I *84CHEC-I(4)1, 84CHEC-I(4)713* and in the Weissberger series *The Chemistry of Heterocyclic Compounds* *86HC(44/2)135, 91HC(44/4)1*.

The ^1H NMR spectrum of thiophene (in CDCl_3) consists of two multiplets at 7.18 ppm and 6.99 ppm, the one at lower field being assigned to the α -hydrogens *65SA85*. In thiophene, as in other five-membered heterocycles, the H-2 and H-3 protons are about 1 ppm, downfield as compared to their 4,5-dihydro derivatives indicating the presence of an aromatic ring current. The chemical shifts and coupling constants for thiophene in CDCl_3 and acetone- d_6 are listed in Table 15. The vicinal proton couplings here are much smaller than in benzene due to the greater separation of the hydrogen atoms in five-membered rings than in six-membered rings. Similarly, smaller coupling constants are also observed for pyrrole and furan. The chemical shifts of the protons in thiophene are solvent dependent *86BCJ1650*; the H-2 proton resonates at 6.89 ppm and 7.16 ppm in benzene- d_6 and in cyclohexane *65BCJ1041, 74JOM(77)49* and at 7.46 ppm in acetone- d_6 *68ICA12*.

Table 15 Proton NMR spectral data for thiophene^a.

	CDCl_3	CDCl_3	CDCl_3	CDCl_3	Acetone- d_6
H-2	7.20	7.18	7.34	7.35	7.46
H-3	6.96	6.99	7.12	7.14	7.14
$J_{2,3}$	4.8	4.90	4.95	5.0	4.6
$J_{2,4}$	1.0	1.04	1.05	0.9	1.1
$J_{2,5}$	2.8	2.84	2.85	3.0	3.6
$J_{3,4}$	3.5	3.50	3.50	4.1	2.8
Ref.	60AK563	65SA85	83BCJ2463	68ICA12	68ICA12

^aChemical shifts in ppm, coupling constants in Hz.

The presence of a methyl or an alkyl substituent at the 2-position shifts the other protons upfield by 0.2–0.4 ppm. A similar effect is also observed with electron-donating substituents viz. OMe, OBu^t, and NH₂ *60AK539*. Substituents at the 3-position also cause the protons to shift upfield. With electron-donating substituents, the H-2 hydrogens are found more upfield than the H-4 hydrogens. For example, in 3-aminothiophene, the H-2 proton appears at 5.95 ppm while the H-4 hydrogen is found at 6.43 ppm. Electron-withdrawing substituents at the C-2 position cause substantial downfield shifts of the H-3 and H-5 protons while the H-4 proton chemical shift is hardly affected. For 3-substituents, the H-2 and H-4 protons are shifted downfield.

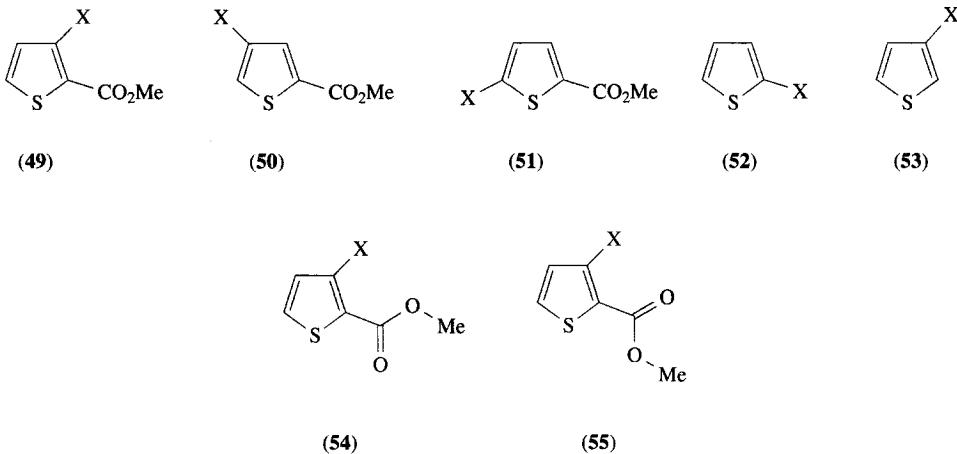
For mono- and di-substituted derivatives, the coupling constants for most compounds were as follows: $J_{2,3}$ (or $J_{4,5}$) 4.9–5.8 Hz, $J_{2,4}$ (or $J_{3,5}$) 1.2–1.7 Hz, $J_{2,5}$ 3.2–3.6 Hz, $J_{3,4}$ 3.4–4.3 Hz *60AK501, 60AK563*. For thiophenes containing only alkyl substituents the coupling constants are relatively close to those found in the parent molecule with values being typically about 4.9, 1.3, 2.7, and 3.3 Hz, respectively *74JOM(77)49, 86HC(44/2)135*. In the presence of strongly electropositive or electronegative substituents, values outside this range are observed; a $J_{3,4}$ of 6.0 Hz is observed for 2-amino-5-nitrothiophene *81JHC851*.

The chemical shifts and coupling constants of a large number of mono-, di-, and tri-substituted thiophene derivatives have been reported *86HC(44/2)135*.

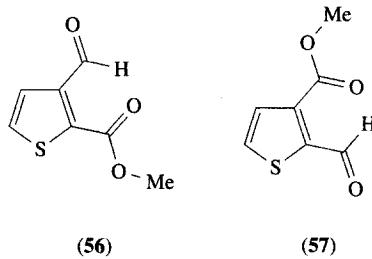
In benzo[b]thiophene, the H-2 and H-3 protons resonate at 7.33 ppm and 7.22 ppm *66BCJ2316*.

which is slightly downfield from that observed for thiophene, while for benzo[c]thiophene, the H-1, H-3 protons appear at 7.63 ppm (76JCS(P2)81).

The ^1H NMR spectra of methyl 3-, 4-, and 5-substituted 2-thiophenecarboxylates (**49–51**) has also been obtained to compare their substituent effects with those of 2- and 3-substituted thiophenes (**52**) and (**53**) <83BCJ2463>. In most cases, a good correlation is observed in the chemical shifts of the protons in (**49–51**) and the corresponding compounds (**52**) and (**53**) with the exception of the chemical shifts of H-5 in (**49**) and H-5 in (**53**) or H-3 in (**51**). Although the calculated chemical shifts in (**50**) and (**51**) are in good agreement with experimental values, those of (**49**) show large deviations since the carbonyl group can exist in the S,O-*cis* (**54**) or S,O-*trans* (**55**) orientation due to the presence of a substituent at the 3-position. This is seen in the IR spectrum of these compounds where two carbonyl stretching bands are observed. The coupling constants in compounds (**49–51**) vary linearly with the electronegativities of the substituents.



In methyl 3-formyl-2-thiophenecarboxylate (**56**), the aldehyde proton is observed 0.5–0.6 ppm further downfield than in 2-thiophenecarbaldehyde *<63AK265>*. This is attributed to the conformation of the ester carbonyl group which is capable of hydrogen bonding with the aldehyde proton and also due to the anisotropy effect of the ester carbonyl group *<83BCJ2463>*. For methyl 2-formyl-3-thiophenecarboxylate, the aldehyde proton is found at 10.62 ppm implying the conformation depicted in structure (**57**).



In thiophene-1,1-dioxide, the ring is no longer aromatic (see Section 2.09.3.1). Chemical shifts and coupling constants indicate the molecule to possess reasonable diene character <84ZN(B)915>. The ^1H NMR spectrum in CDCl_3 shows the α - and β -protons at 6.64 and 6.38 ppm, respectively; which is about 0.7 ppm upfield from the corresponding resonances in thiophene. In benzene- d_6 these protons resonate 1 ppm further upfield. Similarly, the H-2 and H-3 protons in 4,5-dihydrothiophene resonate at 6.06 ppm and 5.48 ppm while that of the corresponding dioxide are found at 6.66 and 6.81 ppm, respectively.

2.09.3.2.2 *Carbon-13 NMR spectroscopy*

Carbon-13 NMR studies of thiophenes have been carried out since the 1960s (65JA5333, 68JA3543, 70JPC2765), and extensive investigations carried out later (75CS76, 86HC(44/2)135, 91HC(44/4)1). The ^{13}C NMR spectrum of thiophene (in acetone- d_6) shows the C-2 and C-3 carbons at 125.6 and 127.3

ppm, respectively <65JA5333, 75CS76>. The signal of the C-2 position is more upfield than the C-3, contrary to the ^1H NMR spectrum where the H-3 proton is more upfield. The larger value of the ^{13}C -H coupling constants for the 2-position as compared to the 3-position (185 Hz vs. 168 Hz) is helpful in the structure elucidation of trisubstituted derivatives. The long range ^{13}C -H coupling constants are also distinctive and vary from 3–10 Hz which again is helpful in structure identification.

The ^{13}C NMR chemical shifts of some substituted thiophenes along with their shifts (relative to thiophene) are listed in Table 16. In most cases, a substituent causes a downfield shift of the carbon except for bromo, iodo, and cyano substituents. Electron-withdrawing substituents generally cause downfield shifts of all the other carbon atoms. Highly electronegative substituents or electron-donating groups cause the largest downfield shift on the ipso carbon atom but the adjacent carbons are upfield as compared to thiophene. For substituents at the 2-position, the C-4 carbon resonances are the least affected, while for 3-substituted thiophenes, the C-4 and C-5 resonances do not change much.

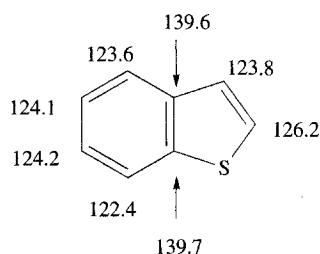
Table 16 Carbon-13 NMR chemical shifts (ppm) of some substituted thiophenes^{a,b}.

Substituent	C_2	C_3	C_4	C_5
H	125.6	127.3	127.3	125.6
2-Me	139.8(+14.2)	125.9(−1.4)	127.3(0)	123.7(−1.9)
2-F	166.5(+40.9)	108.0(−19.3)	124.7(−2.6)	114.9(−10.7)
2-Cl	129.7(+4.1)	127.4(+0.1)	129.6(+2.3)	125.3(−0.3)
2-NO ₂	151.2(+25.6)	129.9(+2.6)	128.7(+1.4)	134.2(+8.6)
2-OMe	167.4(+41.8)	104.2(−23.1)	125.5(−1.8)	112.4(−13.2)
2-Ph ^c	143.5(+17.9)	123.9(−3.4)	126.5(−0.8)	122.2(−3.4)
3-Me	121.3(−4.3)	138.2(+10.9)	130.1(+2.8)	126.1(+0.5)
3-F	104.2(−21.4)	159.2(+31.9)	117.8(−9.5)	126.4(+0.8)
3-Cl	120.9(−4.7)	125.7(−1.6)	128.1(+0.8)	127.5(+1.9)
3-NO ₂	129.2(+3.6)	149.7(+22.4)	123.1(−4.2)	128.9(+3.3)
3-OMe	97.3(−28.3)	159.8(+32.5)	119.9(−7.4)	125.6(0)
3-Ph ^c	120.1(−5.5)	142.3(+15.0)	126.2(−1.1)	126.2(+0.6)
2,5-di-Me ^d	137.4(+11.8)	125.3(−2.0)	125.3(−2.0)	137.4(+11.8)

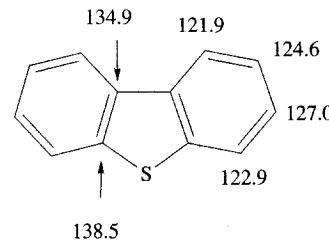
^aValue in parenthesis corresponds to shifts relative to thiophene. ^b<75CS76>.

^c<65JA5333>.

Although the C-2 carbon atom in thiophene is upfield with respect to the C-3 carbon, it is 2.4 ppm downfield to the C-3 carbon atom in benzo[*b*]thiophene <79OMR(12)647>. The ^{13}C chemical shifts for benzo[*b*]thiophene (**58**) <76OMR(8)252> and dibenzothiophene (**59**) are given below.



(58)



(59)

Carbon-13 NMR spectroscopy has also been used to determine acidity measurements of heterocyclic compounds <83CC620, 85CJC3505>. The heterocycle in question is treated with the lithium salt of an amine which is less acidic by about 4 pK units. At equilibrium, the concentration of the four species in Equation (1) is measured by ^{13}C NMR.



The equilibrium constant $K = K_1/K_2$ and thus $\Delta pK = -\log K = pK_1 - pK_2$. Based on these experiments, the proton acidity pK_1 of thiophene is determined to be 33.0, while that of benzo[*b*]thiophene is 32.4. Previously, the proton acidity of thiophene determined in cyclohexylamine was found to be 38.2 <73JA6273> indicating that these values are solvent sensitive.

The molecular r_{α} structure of thiophene dissolved in liquid crystals Merck ZLI 1167 and Phase IV has been determined through the use of ^1H — ^{13}C satellite NMR spectra $\langle 83\text{OMR}(21)143 \rangle$. An analysis of the substituent effect on ^{13}C and ^{17}O NMR chemical shifts of 5-substituted 2-acetyl-thiophenes has been studied by linear free energy relationships $\langle 93\text{ACS}160 \rangle$. The substituent–ring–probe interactions here are larger than those found in similar benzene derivatives. The data also confirms the fact that the acetyl group conjugates with the heteroaromatic ring (see also 2.09.3.1 and 2.09.4.2).

2.09.3.2.3 Sulfur-33 NMR spectroscopy

The relatively low abundance of ^{33}S (0.74%), the nuclear spin of 3/2 and the low sensitivity (2.3×10^{-3}) as compared to hydrogen, make ^{33}S NMR spectra difficult to study. The ^{33}S NMR spectrum of thiophene was initially studied as a solution in carbon disulfide $\langle 70\text{MI} 209-01 \rangle$ and its chemical shift relative to carbon disulfide was determined to be -220 ± 6 while those of 2- and 3-methylthiophene were -178 ± 9 and -197 ± 26 , respectively.

The ^{33}S chemical shift of neat thiophene (relative to aqueous caesium sulfate) was found to be -119 ppm, while that of its saturated analogue tetrahydrothiophene was -354 ppm $\langle 85\text{JCS}(F2)63 \rangle$. For tetrahydrothiophene-1,1-dioxide (sulfolane) the solvent choice and dilution is important. The ^{33}S chemical shift of neat sulfolane is 36.7 ppm and shifts upfield when the solution is diluted. A shift of 6.5 ppm is observed when the solvent system is changed from water to dioxane and the line widths for 5 mol dm $^{-3}$ solutions of sulfolane in acetone and in water are 16 and 60 Hz, respectively.

The ^{33}S quadrupole coupling constants in thiophene and tetrahydrothiophene have been determined by ^{13}C and ^{33}S relaxation time measurements $\langle 86\text{ACS}(A)218 \rangle$.

2.09.3.2.4 Mass spectroscopy

The 4.4% contribution of the ^{34}S isotope to the M + 2 peak and invariably to a (fragment + 2) peak is a good indication of a sulfur-containing compound. Thiophene, along with the other five-membered heterocycles in its group show similar ring fragmentation patterns; the first step being cleavage of the C—S bond (Figure 2). From there, it can proceed by three different pathways to afford three principal peaks: C_5H_3^+ (m/z 39) (60), $\text{HC}\equiv\text{S}^+$ (m/z 45) (61), and $\text{C}_2\text{H}_2\text{S}^+$ (m/z 58) (62).

For thiophene, its molecular ion is the base peak. Although the mass spectrum of thiophene was studied as early as in the 1950s, $\langle 59\text{CCC}1602 \rangle$, it was only recently that the detailed structures of the fragments were determined. The spectra of ^2H - and ^{13}C -labeled thiophenes show that considerable hydrogen and carbon scrambling occurs on electron impact $\langle 69\text{OMS}(2)241, 72\text{AJC}1221, 91\text{HC}(44/4)1 \rangle$.

The fragment ions (60) and (61) are formed from a common precursor, while formation of (62) is presumed to arise from two pathways depending on the beam energy. Initial fragmentation of the C(3)—C(4) bond with concomitant ring closure and loss of alkyne affords (62). It is also possible that initial cleavage of the C(2)—C(3) bond is followed by cleavage of the C(4)—C(5) bond which eliminates alkyne and forms (62) $\langle 84\text{CHEC-I}(4)713 \rangle$. Furthermore, it is this ion which has the maximum intensity contrary to pyrrole and furan where (60) is the most intense peak $\langle 84\text{CHEC-I}(4)1 \rangle$.

A quantum chemical interpretation of the MS fragmentation of organic molecules has been investigated. The interpretation is based on the premise that bond cleavage caused by electron impact is related to their self-consistent π -electron orders $\langle 87\text{CHE}512 \rangle$. The pattern of the spectrum is determined by rearrangements of the intermediate cation radicals or cations. Cyclizations occur via the long-range bond orders which to a certain degree are a measure of its aromaticity. Based on the bond orders, the weakest bond is the C(3)—C(4) bond and hence should fragment first and to a much greater extent than the S—C or the C(2)—C(3) bond. This then forms the divinyl sulfide radical cation (63) which cyclizes to (64) and then eliminates acetylene to form (62) (Figure 3). On the other hand, it is also possible that the bicyclic intermediate (65) is formed first which could fragment to form (66) and/or (64) both of which lose acetylene to form (62). Theoretical calculations predict (62) to be the major fragment in thiophene while predicting (60) to be larger in the case of furan and pyrrole, in line with that observed experimentally.

For 2- and 3-alkyl thiophenes, the base peak at m/z 97 is assigned to the $\text{C}_5\text{H}_5\text{S}^+$ ion which arises from the β -cleavage of the alkyl substituent (Figure 4) and the thiopyrylium structure (67) is proposed. The thiopyrylium cation (67) is the base peak for long chain alkyl groups at the 2-

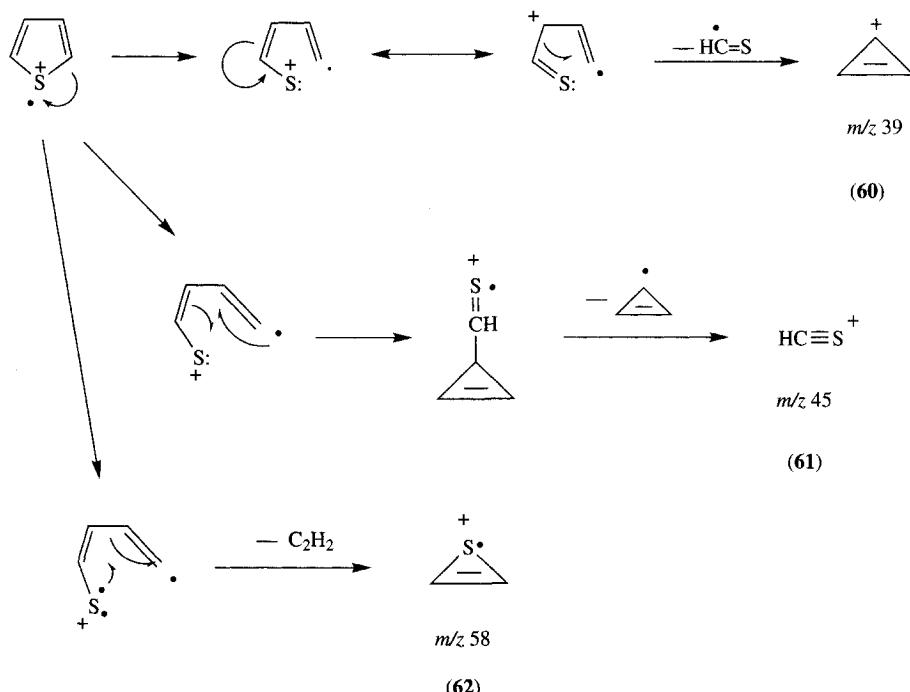


Figure 2 Fragmentation pattern in thiophene.

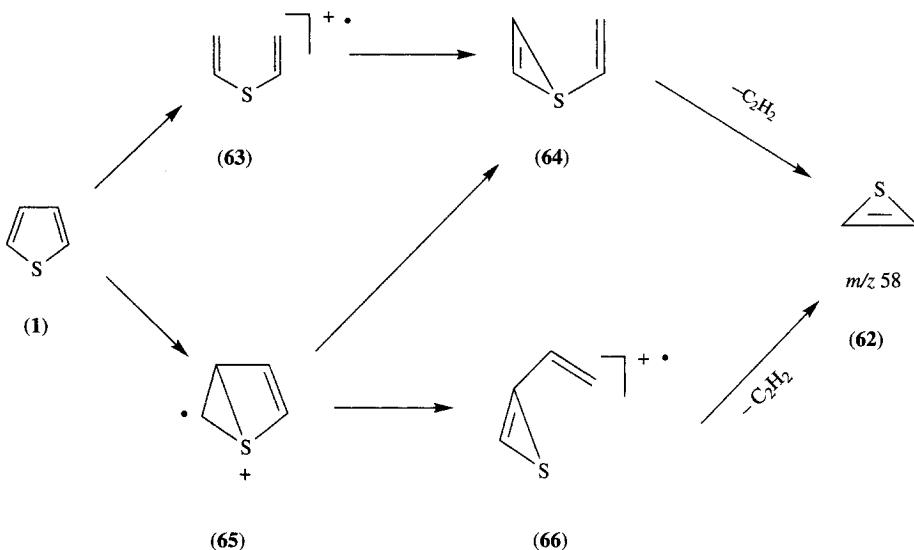


Figure 3 Fragmentation pattern based on bond orders.

position. If another such group is present at the 5-position, the molecular ion is found to be the base peak *<B-67MI 209-01, 76JCED380>*.

In the collision-activated dissociation MS of thiophenic ions, the ions formed due to the loss of the SH^{\cdot} radical are prominent in polythiophenes but not in the case of alkylthiophenes *<82ANC574>*. The ions are generated under positive chemical ionization conditions.

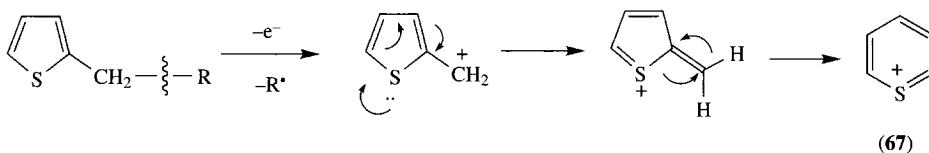
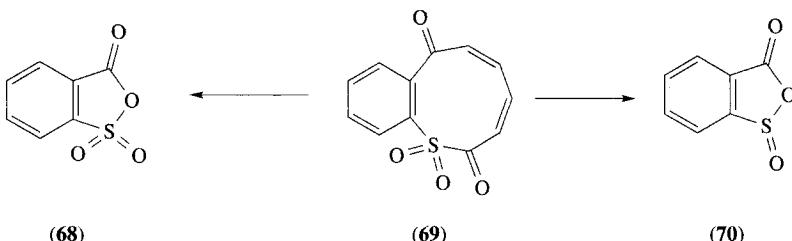


Figure 4 Fragmentation pattern for 2-alkylthiophenes.

Dibenzothiophene undergoes surface-catalyzed oxidation when subjected to negative chemical ionization (NCI) with oxygen [\(93MI 209-02\)](#). In the mass spectrum, the m/z ion at 184 initially attributed to $M^{-\bullet}$, is now shown to be the anion of 2-sulfonylbenzoic acid cyclic anhydride (**68**). Formation of (**68**) is presumed to arise by initial oxidation of dibenzothiophene to the sulfone (m/z 216) followed by oxidation of the angular carbon atoms to form the bicyclic intermediate (**69**) (m/z 248). Further attack by oxygen cleaves the ring to form (**68**) or (**70**) (Scheme 4). The mechanism has been proposed on the basis of further studies on the NCI(O_2) MS of dibenzothiophene-5-oxide, -5,5-dioxide, and also of various alkylidibenzothiophenes where similar patterns were observed.



Scheme 4

2.09.3.2.5 Ultraviolet spectroscopy

The ultraviolet spectrum of thiophene and its derivatives has been extensively investigated [\(72JCS\(F\)2009, 78JCP\(69\)5077, 81BCJ1511, 82JCS\(P2\)761, 86HC\(44/3\)1, 91HC\(44/4\)1\)](#). In the gas phase, the UV spectrum consist of three bands originating at 240, 207, and 188 nm, respectively. Initial reports [\(41PRS201\)](#) claimed only one transition between 200–240 nm while Milazzo described three transitions [\(48G835\)](#).

High resolution and temperature dependance measurements were recorded for the lowest energy UV transition (230–250 nm) of thiophene. Based on these results, the first system of the UV spectrum is assigned to the $\psi_4 \leftarrow \psi_3$ (B_2) transition [\(82JCS\(P2\)761\)](#). The results were confirmed by comparisons of the UPS and UV spectral properties of the Group 16 five-membered heterocycles. A vibrational progression in the 965 cm^{-1} frequency mode is found to dominate. The absorption spectra between 225 nm and 246 nm has also been studied at elevated temperatures [\(85SA\(A\)1413\)](#). At 296 K, 13 features are observed between 227.6 nm and 242.7 nm. At 573 K there is almost no vibrational structure in the system, while near 773 K the vibration structure is lost.

Based on the correlation of electron transitions and ionization potentials, the transition at 207 nm was assigned as the $A_1 \leftarrow A_1$ ($\pi_4^* \leftarrow \pi_2$) valence transition [\(86JST\(140\)253\)](#). The spectra of halothiophenes has been recorded between 200–225 nm. The band system observed in this region in the vapor phase, is absent in solution spectra and are assigned to Rydberg transitions.

The electronic absorption spectra of 2,2'-bithienyl and its derivatives have also been investigated [\(85BCJ2126\)](#) and the transitions in the spectra of 5- and 5,5'-substituted 2,2'-bithienyl compounds assigned to intramolecular charge transfer, locally excited transitions, and $n \rightarrow \sigma^*$ transitions. The MOs of 2,2'-bithienyl are built up of two thiophene molecules and excited states arise from mutual interaction of these excited states. This interaction is maximum when the molecule is planar. Distortion causes the spectrum of bithienyls to approach that of thiophene. In thiophene, a singlet $\pi \rightarrow \pi^*$ transition is observed at 235 nm as well as a shoulder at about 268 nm. By comparison, the spectrum of 2,2'-bithienyl shows three well defined regions, none of which corresponds to thiophene, indicating the molecule to be coplanar, rigid, or semirigid. The three transitions are all $\pi \rightarrow \pi^*$ and the broadness of the lowest energy band indicates that, in solution, a number of almost planar

conformations exist, all of which are of comparable energy. The coplanar configuration could be either *cis* or *trans*, with the latter having a smaller dipole moment. The spectrum displays a very small shift with solvent polarity, implying that the molecule possesses low polarity and thus the *trans* conformation. Solid state studies show the molecule to favor the planar-*trans* orientation $\langle 68AX(B)467 \rangle$ while gas phase and solution studies indicate it to be twisted 34–85° from the *cis* form $\langle 85BCJ2126 \rangle$.

2,2'-Bithienyl with alkyl or chloro substituents shows similar patterns. The presence of formyl or acetyl groups at the 5- and 5,5'-positions causes a significant shift for the lowest energy transition due to the perturbation caused by the carbonyl group which is shifted in polar solvents. Theoretical calculations indicate that 5-formyl-2,2'-bithienyl is roughly planar and interaction between thiophenecarbaldehyde and thiophene is predominant.

2.09.3.2.6 Infrared spectroscopy

The IR spectra of five-membered heterocycles has been extensively surveyed. For thiophenes, this was first done by Gronowitz in the early 1960s $\langle 63AHC(1)1 \rangle$ and has been reviewed again $\langle 91HC(44/4)1 \rangle$. The literature is also rich with theoretical calculations on the vibrational frequencies of thiophene and on its oligomers (see 2.09.2.8).

The 21 fundamental vibrations of thiophene are composed of eight vibrations of A_1 symmetry, seven of B_1 symmetry, and three each of A_2 and B_2 . The assignments of all 21 vibrations have been documented by Rico *et al.* as early as 1965 $\langle 65SA689 \rangle$ and are listed in Table 8. Based on these frequencies, harmonic force constants, and mean amplitudes of vibration have been developed $\langle 69ACS3139, 69ACS3407 \rangle$.

The complete vapor phase assignment including IR vapor, Raman vapor, and liquid spectra, have been determined to obtain a complete set of vibrational frequencies in the vapor and liquid states of thiophene $\langle 94SA(A)765 \rangle$. The results confirm the assignments made earlier by Rico *et al.* $\langle 65SA689 \rangle$ and, for several of the fundamental modes, the vapor frequency has now been measured or improved.

Due to the presence of the larger sulfur atom and correspondingly longer C—S distance, the *a* and *b* axial moments-of-inertia are not similar. Thus, in the IR vapor spectrum, the *A*-type bands now exhibit a clearer and more intense central Q-branch. Nine of the twelve possible combinations of the A_1 transition are identified by Q-branches in the Raman vapor spectrum. Nineteen new transitions have been observed here which were not previously reported by Rico *et al.*

For the B_1 species, the C—H stretching mode at 3125 cm^{-1} is unobserved here. It is possible that it is obscured by ν_1 for observation in either IR or Raman spectra. In the liquid Raman spectrum, the fundamental at 1085 cm^{-1} is also not observed, being completely hidden by the A_1 band ν_5 . The A_2 and B_2 fundamentals exhibit $3\text{--}5\text{ cm}^{-1}$ positive shifts from the vapor to liquid states for the C—H wag groups and $\approx 1\text{ cm}^{-1}$ for the nonplanar ring modes.

The far IR absorption spectrum of thiophene in the liquid and plastic phase has been studied over the region $10\text{--}200\text{ cm}^{-1}$ $\langle 81SA(A)977 \rangle$. The frequencies indicate the presence of librational motions of the molecule in potential wells and are highly hindered.

The temperature dependence on the IR absorption and Raman scattering bandwidths of some fundamental modes of A_1 , B_1 , and B_2 symmetries of thiophene has been investigated in the region $400\text{--}1600\text{ cm}^{-1}$ $\langle 81CPH251 \rangle$. The spectroscopic study was carried out in the liquid phase which requires simultaneous investigation of the bands. Results show that the IR and anisotropic Raman bandwidths increase with increasing temperature and more so in the latter case. The rotational diffusion coefficients obtained from the bandwidths indicate that the rotational and vibrational relaxation phenomena occur simultaneously. The IR and isotropic and anisotropic Raman band profiles of the A_1 symmetry mode have also been studied in the liquid phase $\langle 81CPH265 \rangle$.

The near-IR-visible vibrational spectra of thiophene compounds is dominated by two distinct anharmonic aryl C—H stretching overtones $\langle 91JPC7659 \rangle$. At particular levels of C—H stretch excitation, the overtone pattern is disturbed leading to a broadening and a loss of vibrational structure at $\Delta\nu_{\text{CH}} = 4$, while being retained at $\Delta\nu_{\text{CH}} = 3$ and 5 $\langle 93JPC809 \rangle$. The sensitivity of the spectral patterns to small changes in the C—H stretching frequency arises due to isolated nonlinear resonances present in these regions.

The spectrum of the out-of-plane band of thiophene centered at 712 cm^{-1} has been measured in Doppler-limited resolution with a diode-laser spectrometer and with a high-resolution FT spectrometer $\langle 93ZN(A)1193 \rangle$. The band at 712 cm^{-1} which is the ν_{19} band $\langle 65SA689 \rangle$, is of symmetry B_1 .

Here, the heavy atoms of the ring displace vertically to the molecular plane. This moment involves a variation of the dipole moment in this direction and thus displays a *c*-type transition. The planarity defects in the centrifugal distortion are very small. In the excited state, the inertial defects in the v_{19} band are found to be large and negative.

For 2- and 3-substituted thiophenes, the three C—H ring stretching bands are observed in the region 1350–1550 cm^{−1}, the intensities of which depend on the type of substitution <70SA(A)1651>. In addition to this, up to two bands corresponding to in-plane C—H deformations are observed in the region 1030–1085 cm^{−1}. Furthermore, the absorption pattern in the region 750–900 cm^{−1} is different for 2- and 3-substituted derivatives making it easy to identify the substitution pattern. Similarly, 2,5-dialkylthiophenes display a strong absorption at ca. 800 cm^{−1} <64CB3263>.

The IR and Raman spectra of thiophene, 2,2'-bithienyl and of the cycloalkane end-capped oligothiophenes has been studied and the results compared with theoretical calculations at the *ab initio* SCF level <93JST(298)65>. The scaled theoretical and experimental vibrational frequencies and theoretical IR and Raman intensities as well as their assignments for the above compounds have been discussed.

2.09.3.2.7 Photoelectron spectroscopy

The photoelectron spectra (PES) of thiophenes has been well studied <69IJM471, 70T4505, 71IJM(6)177, 76JES179, 79CPL(61)355>. The UV PES of thiophene (using He^I (21 eV) photon excitation) was first measured up to 18 eV by Eland <69IJM471>, and later up to 25 eV by Derrick *et al.* using He^{II} (40 eV) photon excitation <71IJM(6)177>. Theoretical studies have been carried out to assist in assigning the ionization energies to the appropriate occupied molecular orbitals and this has been discussed in Section 2.09.2.6.

Of the three lowest ionization potentials, the band at 8.87 eV has been assigned to the 1a₂(π_3) orbital, while that at 9.49 eV is due to the 2b₁(π_2) orbital <71IJM(6)177>. Both these orbitals are found to be weakly C—C bonding. The intensive band at 12.1 eV assigned earlier to be the π_2 band was later shown to arise from σ orbitals and is now assigned as the 6a₁ orbital. The Penning spectrum <80JES235> correctly assigns the band at 12.5 eV to be the 1b₁(π) orbital.

The He^I and He^{II} PES of thiophene was later rerecorded up to 15 eV <82JCS(P2)539>. Based on their observations and from previous theoretical calculations (see Section 2.09.2.6), the seven band systems (with their ionization energies (eV) in parenthesis) are assigned as: 1a₂(π) (8.85), 2b₁(π) (9.49), 6a₁(n) (12.00), 1b₁(π) (12.46), 4b₂ (13.11), 5a₁ (13.80), 3b₂ (14.23) which is similar to the *ab initio* results of von Niessen *et al.* <76JES179>.

Ionization energies of thiophene derivatives with electron releasing substituents at the 2-position cause an increase in the separation between the π_2 and π_3 orbitals. This arises due to a greater destabilizing effect on the energy of the π_3 orbital than on the π_2 orbital. Electron withdrawing substituents at the 2-position increase the ionization energies of both orbitals <76JCS(P2)276>.

The He^I_x line PES has also been determined for a variety of thiophene-fused troponones <84BCJ856>. The PES of the thiophenotroponones are quite similar to the corresponding benzotroponone analogues. This resemblance for the first band system is due to the fact that the initial ionizations are related to the molecular orbitals that are mainly localized in the troponone ring rather than the benzene or heterocyclic ring. Since the electronegativities of sulfur and carbon are approximately the same, replacement of a CH=CH bond by sulfur does not alter the IP to a noticeable extent.

Photoelectron spectroscopy is an efficient tool for the gas phase characterization of various elusive compounds <89CSR317>. It has also been used to investigate the products formed on flash vacuum pyrolysis of alkylthio derivatives of Meldrum's acid <91JOC3445>. The PES of the thiophen-3(2H)-ones formed were similar to authentic samples from which it is apparent that no keto-enol tautomerism occurred in the gas phase and that only the keto tautomers are formed in the gas phase.

The ionization potentials of benzo[*b*]thiophene <69IJM471> and dibenzothiophene <73JCS(F2)1155> have also been determined and the assignments compared with various theoretical calculations <83JST(105)375>.

The x-ray photoelectron spectrum (XPS) of thiophene has been measured in the vapor phase using Mg-K_α x-ray excitation <71MI 209-01>. The x-ray spectra complement PES since x-ray transmissions are controlled by selection rules and thus enables the valence MO structure to be studied. Initial studies of x-ray emission from vapor phase thiophene have been limited to the S—L_{II,III} <76JCP(64)3021> and to the S-K_β measurement <74MI 209-01>. The high resolution sulfur K_β emission

and S-K absorption spectra of vapor phase thiophene have been measured *⟨86JCP(84)4228⟩*. The data has been compared with MNDO MO calculated intensities and the sulfur 1s binding energy determined to be 2477.6 eV.

2.09.4 THERMODYNAMICS

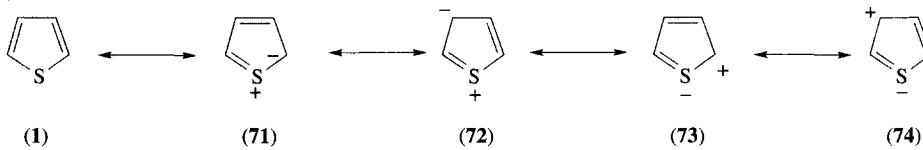
2.09.4.1 Aromaticity

The fact that aromatic compounds *⟨B-71MI 209-02, B-89MI 209-02⟩* differ from unsaturated aliphatic compounds was recognized as early as the nineteenth century. However, chemists are still unable to agree on a suitable definition of aromatic character *⟨68MI 209-01⟩*. Qualitatively, the concept of aromaticity is quite clear *⟨74AHC(17)255, B-85MI 209-02⟩*. A compound is considered aromatic if it:

- (i) is a cyclic compound with a large resonance energy, i.e., its stability is increased when compared to its classical localized structure;
- (ii) possesses an aromatic sextet which arises due to the presence of a closed loop of electrons;
- (iii) follows the Hückel rule which states that a ring system with $(4n + 2)\pi$ electrons is aromatic while one with $(4n)\pi$ electrons is not;
- (iv) is capable of sustaining an induced ring current;
- (v) has a lack of marked bond length alternation; and
- (vi) displays enhanced thermo stability.

Most aromatic compounds possess the aromatic sextet and are generally six-membered rings. However, these sextets are also found in five-membered rings, when the ring is made up of a pair of double bonds and the fifth atom possesses an unshared pair of electrons. The five *p*-orbitals overlap to form three bonding and two antibonding orbitals. Pyrrole, furan, and thiophene are some of the heterocycles that fall under this category.

Although it is easy to establish that naphthalene is less aromatic than two benzene rings or that benzo[*c*]thiophene is less aromatic than benzo[*b*]thiophene, it is more difficult in other cases. Thus a quantitative scale of aromaticity is needed. Attempts have been made in a few reviews to introduce methods and concepts where by it is possible to justify an aromaticity scale to determine and thus view aromaticity as a quantitative concept *⟨74AHC(17)255, 80IZV3, 85CHE717, 91H(32)127⟩*. Important criteria for heterocycles include its hybridization, electronegativity, and stereochemistry. For thiophene, the matter is further complicated by the fact whether the 3*d*-orbital of sulfur also participates in bond formation. If so, then the two resonance structures (73) and (74) in Scheme 5 should also be considered in determining the degree of aromaticity. However, as was previously determined (see Section 2.09.2.3), calculations have shown that for the ground state, the energy of thiophene is not affected by the inclusion of the 3*d*-orbitals.



Scheme 5

In order to determine a quantitative measurement of aromaticity, one must be capable of obtaining:

- (i) experimental methods that measure the energy or any particular parameter of the compound and compare it with a classical compound that does not possess the cyclic conjugation;
- (ii) experimental methods that have investigated geometries and magnetic properties of aromatic compounds and compare these with nonaromatic compounds; and
- (iii) MO calculations dealing with the above.

Although there is a large amount of data available, it is still difficult to construct an accurate aromaticity scale for the following reasons:

- (i) experimental results for any specific parameter are generally not available for a full series of compounds;
- (ii) errors in experimental measurements obtained from various sources;
- (iii) the precise definition of the nonaromatic or classical model that should be used to compare the aromatic compound with; and

(iv) doubt as to choice of proper parameters to be used for theoretical MO and semiempirical methods and especially for heteroatoms possessing *d*-orbitals such as sulfur.

Early methods for the determination of aromaticity involved resonance energies which were determined from heats of hydrogenation and combustion (B-75MI 209-02). Although the results by these two methods are quite similar for benzene, their application to heterocycles are more difficult. Combustion of heterocycles leads to oxyacids which can then attack the materials used for combustion or due to poisoning of the catalyst in the hydrogenation method. Variations arise from inconsistencies in the thermochemical data for the localized models, as well as selection of the model itself. For example, the stabilization energy of benzene is calculated to be 36 kcal mol⁻¹ when the localized model is assumed to be cyclohexane and 48.7 kcal mol⁻¹ from ethylene (B-75MI 209-02). The large variations in the resonance energies of thiophene obtained from various studies is depicted in Table 17. Although the values vary, the order of aromaticity generally observed is benzene > thiophene > pyrrole > furan.

Table 17 Resonance energies (kcal mol⁻¹) calculated from heats of combustion.

Ref.	Benzene	Thiophene	Ref.	Benzene	Thiophene
33JCP(1)606	37.0	31.0	B-55MI 209-02	36.0	28.7
49CB358	35.9	29.1	B-55MI 209-02	36.4	27.7
50JA4278	36.0	31.0	B-62MI 209-01		17.1 ^a
51CB916	36.0	24.1	B-75MI 209-02	36.0 ^a	17.1 ^a
63T1175	22.0	16.0			

^aFrom heats of hydrogenation.

Molecular orbital calculations have also been employed for the comparison of aromatic resonance energies. Although the Hückel rule is generally used as a distinction for aromaticity, difficulties arise in its application for large annulenes and so is not usually used as an index for the classification of aromaticity (B-69MI 209-01). The Dewar resonance energy (DRE) assumes the localized structure to be a conjugated polyene and is determined as $DRE = \Delta H_f - \Delta H_{f(loc)}$ (67MI 209-02). For heterocyclic compounds, a modified version of the resonance energy calculation (DRE') is used where the resonance energy is calculated from the AM1 heats of formation (70JA1453).

The Hess-Schaad resonance energy (HSRE) is another MO-based method used to determine aromaticity and is based on the difference between the energy of the HMO π -system and the energy of the empirically isolated π -bond (71JA305, 73JA3907, 75T295). In order to obtain the energies of the localized sulfur precursor, the π -bond energies are evaluated from conjugated acyclic polyenes containing a sulfur atom. This is done in an additive fashion from the empirical bond energies of the respective C—C bonds and carbon–heteroatom bonds. In this manner, the resonance energies of a variety of cyclic and bicyclic thiophenes, thiaannulenes, thienothiophenes, and other fused thiophene derivatives have been determined (73JA3907).

The resonance energy for thiophene as calculated by Dewar is found to be 6.5 kcal mol⁻¹ and shows a decrease in aromaticity in the order benzene > thiophene > pyrrole > furan. This is in agreement with other criteria such as chemical reactivity, etc. The HSRE is found to be 4.5 kcal mol⁻¹ and the order is benzene > pyrrole > thiophene > furan. Furthermore, the resonance energies obtained by this method are generally much lower than those by Dewar. Obviously, the parameters are defined much more clearly in the Dewar system.

Heats of formation calculated by the AM1 method can be used to determine aromatic energies of heterocycles (89H(28)1135). The aromatic energy of an aromatic molecule is defined as minus the difference between its energy and that of its analogue in which one of the bonds in the ring is replaced by a localized bond. A positive value implies stabilization. This is quite easily done if the ring contains an even number of atoms, but not necessarily so for odd-numbered rings.

The heteroaromatic analogues are more complicated due to the effects of ring strain and the problems in finding suitable nonaromatic precursors. Since AM1 calculations are generally not very accurate for these compounds the aromatic energies are calculated using experimental values for the heats of formation. Thiophene can be considered to be formed from divinyl sulfide. However, since the heats of formation of divinyl sulfide is not available, it is estimated from the heats of formation of diethyl sulfide (B-86MI 209-03). Assuming the heat of hydrogenation of divinyl sulfide is similar to divinyl ether, the heat of formation for classical (strain-free) thiophene is calculated to be 43.9 kcal mol⁻¹. With the observed ΔH_f for thiophene being measured at 27.5 kcal mol⁻¹, this gives the estimated value of the aromatic energy of thiophene to be 16.4 kcal mol⁻¹. By comparison,

the aromatic energies of pyrrole and furan are estimated to be 22.5 and 12.1 kcal mol⁻¹, respectively, indicating pyrrole to be more aromatic than thiophene.

Another quantitative index of aromaticity is the measure of the delocalization stabilization. Here the stability of the parent molecule is compared to the isolated classical bonds obtained by the bond separation reaction or the superhomodesmic reaction (88JA4204). In the latter case, the prototypes contain larger fragments of the parent heterocycle. The energy differences (ΔE) and the zero-point enthalpy differences (ΔH^0) for these reactions have been calculated using the 3-21G* Hartree-Fock energies. The bond separation reaction and the superhomodesmic reaction for thiophene and for the Group 16 five-membered heterocycles in general is depicted in Figure 5.

Bond separation reaction



Superhomodesmic reaction



Figure 5 Aromaticity as determined by bond separation and superhomodesmic reactions.

For thiophene, the energy differences by the bond separation and the superhomodesmic reactions are 30.21 and 10.07 kcal mol⁻¹, respectively, while the zero-point enthalpy differences are 32.54 and 9.80 kcal mol⁻¹, respectively. In general, the values for the energy differences by the superhomodesmic reaction are much lower than those obtained by the bond separation method. This is due to the fact that in the former case, there is a much smaller change in the molecular and electronic structures since the predecessor is made up of much larger fragments of the parent molecule. For the Group 16 five-membered rings, results from the superhomodesmic reaction predict thiophene and selenophene to be more stabilized than furan.

Ab initio SCF-MO studies on the aromaticity of some five-membered heterocycles have mostly been performed at the STO-3G level, while for sulfur, the STO-3G* level is also included (88JST(163)173). Three approaches were studied; the first uses a quantitative perturbation molecular orbital (PMO) approach and is known as the PMO method, the second is based on the computation of the π -orbital energies and is called the orbital energy method, while the total energy method, which as its name suggests, deals with the total energy approach. Optimized geometries are calculated for the compounds of interest at the levels indicated above and the values used to determine the π delocalization energies.

The PMO method tends to fail when the perturbation becomes large as in cases where bonding π interactions are studied. Hence PMO estimates of the π delocalization energy tend to be inaccurate to a certain degree. It however affords an estimation of the energy effect associated with every π -orbital interaction. On the other hand, the orbital energy method does not highlight specific energy effects associated with the various orbital interactions but does provide accurate values of the overall π delocalization energy. The two methods thus compliment each other quite well and hence are generally used together.

In the total energy method, the π delocalization energies are calculated as the difference between the total energy of the composite system (E_T) and the total energy of the system in absence of all π interactions ($E_0^0 T$). The PMO method and the total energy method both show thiophene to be more stabilizing than their acyclic counterparts. The same holds true for the other five-membered rings pyrrole and furan. For cyclopentadiene, the values indicate it to be destabilizing and more so than

its acyclic analogue. For thiophene, the results obtained using the STO-3G* values parallel that of the experimental resonance energies viz. benzene > thiophene > pyrrole > furan.

The total energy method, however, does not afford satisfactory results for thiophene. STO-3G values show thiophene and pyrrole to be destabilizing by this method. Here, the presence of a C—X bond indicates the importance of the inductive effect, and hence the π delocalization energy is small. If one considers the difference $\Delta(E_T - E^0_T)$ between the cyclic and the acyclic species, the energy effects associated with the heterocycles become stabilizing and the trend follows that observed from experimental values. Thus, while the π delocalization energy from the total energy method ($E_T - E^0_T$) affords a value of 2.62 kcal mol⁻¹, $\Delta(E_T - E^0_T)$ gives a value of -8.36 kcal mol⁻¹.

For heterocyclic systems, the interaction between the butadiene fragment and the heteroatom moiety deals with a four-electron destabilization interaction ($n_x - \phi_1$) involving the occupied orbital ϕ_1 of butadiene and the n_x orbital (which corresponds to a lone pair *p*-orbital) of the heteroatom, and a two electron stabilizing interaction ($n_x - \phi_3$) where ϕ_3 is the empty orbital of the butadiene fragment (Figure 6). In all cases, the stabilizing effect is larger than the destabilizing interaction and hence the overall result is stabilization. The destabilization interaction becomes much less in thiophene due to the longer C—S bond which results in a reduction in the overlap and a larger delocalization energy than in pyrrole or furan. The experimental trend is followed when the STO-3G* basis set is employed since the energy of the sulfur lone-pair orbital is lowered in going from the STO-3G to the STO-3G* basis set. The *d*-orbitals as such do not directly affect the π delocalization energies but reduce the energy gap between the ϕ_3 orbital of the butadiene fragment and the n_x orbital of sulfur, making the $n_x - \phi_3$ interaction for sulfur more stabilizing.

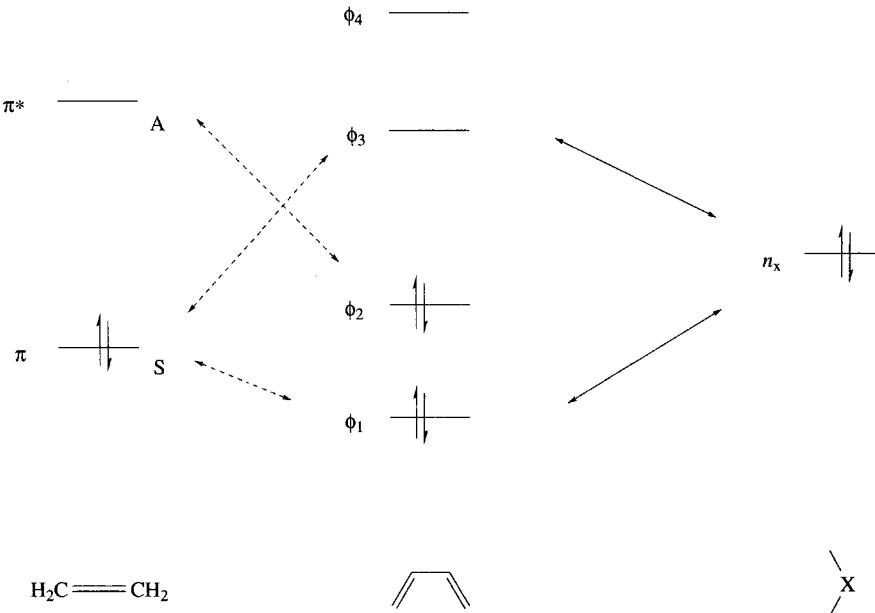


Figure 6 Interaction between the butadiene fragment and heteroatom moiety or ethylene fragment.

Benzene possesses a much larger π delocalization energy than the three heterocycles discussed here, due to the additional stabilizing interaction involving the ϕ_2 orbital of the butadiene fragment and the π^* orbital of the ethylene fragment, which is not possible in heterocycles. Since the energy difference between the two orbitals is quite small, this interaction is strongly stabilizing. The other two interactions are similar to those found for the heterocycles and hence this additional $\phi_2 - \pi^*$ interaction leads to a larger aromaticity of benzene.

A quantitative aspect of aromaticity can also be determined by nonenergetic methods. One criterion is the mesomeric dipole moment (μ_m) which is calculated as the difference between the dipole moments of the heterocycle and its fully saturated analogue (B-71MI 209-02). However, since the direction of the dipole moment in pyrrole is opposite to that of some of the other five-membered heterocycles, an unusually large value of μ_m for pyrrole causes this measure to be less reliable than some of the other quantitative concepts.

Ring geometry is another yardstick used to measure aromaticity. Here the ratio of the C(2)—C(3) to C(3)—C(4) bond length affords a quick estimate of ring aromaticity. This bond alternation

method is not too accurate since it does not account for the different sizes of the heteroatom, nor their electronegativity. A more reliable index is $\Sigma\Delta N$ which is the sum of the differences in bond orders of the three nonequivalent bonds (74JCS(P2)332). The bond order (N) of a bond in a molecule can be readily calculated from its bond length (R) using the relationship $N = aR^{-2} + b$ where a and b are constants obtained from the dependence of the bond order on bond length for selected standard compounds (47JCP(15)305). Although one can now compare aromaticities, it does not allow for comparison between different ring sizes. This problem was circumvented by Pozharskii (85CHE717) who developed a new index ΔN which is the average of the fluctuations of all the ring bonds including the single bonds.

The Julg aromaticity index (A_1) (67TCA249) is based on taking the mean square deviations of the C—C bond lengths as a measure of aromaticity, and is calculated by the formula shown in Equation (2).

$$A_1 = 1 - \frac{225}{n} \sum_{(rs)} \left(1 - \frac{d_{rs}}{d'} \right)^2 \quad (2)$$

where n = number of π -electrons

d_{rs} = bond length

$d' = \frac{1}{n} \sum_{(rs)} d_{rs}$ i.e., the average bond length.

Since all bonds in benzene are equal in length, the bond alternation ratio and the Julg aromaticity index for benzene is one. The Julg index has been modified to account for resistance to circulation of the π -electrons which is a major factor in electronegative heteroatoms (B-71MI 209-03). This correction factor A_2 is given by Equation (3).

$$A_2 = \prod_{(ij)} \left[1 - \left(\frac{\Delta q_{ij}}{d_{ij}} \right)^2 \right] \quad (3)$$

In Equation (3) Δq_{ij} is the difference in the π -charge on neighboring atoms, and d_{ij} the interatomic distance.

Based on this, the new Julg index $A = A_1 A_2$. This index however, has a few setbacks, the main one being the difficulty in evaluating the π -charges for molecules with heavy heteroatoms. The aromaticity indices of thiophene and benzene as determined by geometric criteria are shown in Table 18.

Table 18 Aromaticity indices from geometric criteria.

Criteria	Benzene	Thiophene	Ref.
μ_m	0	1.38	72JA8854
Bond alternation	1	0.963	61JSP(7)58
$\Sigma\Delta N$	0	0.90	74JCS(P2)332
ΔN	0	0.27	85CHE717
A_1	1	0.93	74JCS(P2)332
A	1	0.67	B-71MI 209-03
I_x	100	66	85T1409/86T89
I_A	100	81.5	92T335
RE	45.8	43	92T335

The character of a chemical bond is associated to its vibrational frequency. Bonds with low force constants possess high vibrational frequencies and small amplitudes of vibration and are rigid, while those with large mean amplitudes are the most reactive. Ionic and polar bonds fall into this latter category. The fundamental frequencies of a molecule can be obtained from vibrational spectra. From this, it is possible to calculate the force field which in turn, is used to obtain the mean amplitudes of vibration for the individual bonds in a molecule. This process has been studied in the Group 16 five-membered heterocycles (85MI 209-03).

The symmetric and asymmetric C—X stretching frequency decreases as one goes down the column from oxygen to tellurium while the interatomic distances increase. This implies a decrease in the force constants and a corresponding increase of the mean amplitudes of vibration. The C—O bond is thus more rigid than the C—Te bond. The force constants for the C=C is found to increase in

the order thiophene < selenophene < tellurophene < furan, a trend also observed in the symmetric stretching frequency of the double bonds implying greater localization of the double bond and thus a decrease in aromaticity. Thus thiophene is shown to be more aromatic than furan. Similar comparisons with the C—C bond in benzene show these heterocycles to be less aromatic than benzene.

If ring substitution should occur via a loose vibration, i.e., a C—H bond with a low force, it might be possible to predict the order of reactivity. However, for these heterocycles, the C—H force constants and mean amplitudes of vibration are approximately equal, making it difficult to compare reactivity. On the other hand, the potential energy distribution shows a vibrational coupling between the C_{α} —H and C_{β} —H, the degree of coupling being furan < selenophene ~ tellurophene < thiophene, which is the opposite of the reactivity order in electrophilic substitution (73JCS(P2)2097). Thus, it is possible to determine the order of aromaticity for a variety of heterocycles from the calculated force constants and mean amplitudes of vibration.

An alternate approach to aromaticity involves a relationship between bond order and ring current applicable to monocyclic, polycyclic, nonplanar, and nonbenzenoid rings (83JOC1344). The semiempirical MO method SINDO1 is used to perform the calculations. Aromatic compounds tend to reduce the alternation in bond length between a single and double bond as would be otherwise found in a classical, nonresonating structure. This is complicated when a heteroatom is introduced in the molecule since it is not easy to determine how much bond alternation has been reduced. By utilizing only bond orders, one can overcome this problem. Since the magnitude of the ring current is determined by the weakest link in the ring, the bond with the lowest bond order is the weakest link. Since these are not π -electron bond orders, this method is not limited to planar systems. The advantage here is that the results do not depend on parametrization, nor is there a need for comparison with a fictitious model.

The concept of bond orders for aromaticity has also been exploited by Bird (85T1409, 86T89, 87T4725) and is based on a statistical evaluation of the deviations in peripheral bond orders, which are readily obtainable from bond lengths. Thus aromaticity indices for a variety of five-membered (I_5), six-membered (I_6) and benzo-fused five-membered ($I_{6.5}$), and six-membered ($I_{6.6}$) systems have been determined using the relationship (Equation (4)).

$$\text{Aromaticity index } (I_x) = 100 \left(1 - \frac{V}{V_K} \right)$$

where coefficient of variation $V = \frac{100}{\bar{N}} \sqrt{\frac{\sum (N - \bar{N})^2}{n}}$

(4)

\bar{N} = arithmetic mean of the various bond orders (N), and
 n = number of bonds.

The nondelocalized Kekulé form V_K depends on the ring system. Thus $V_K = 35$ for five-membered and for fused five- and six-membered rings, and 33.3 for six-membered rings. Since benzene is a fully delocalized system, V has the value zero and I_6 for benzene is 100. Similarly, the aromaticity index (I_5) for thiophene is 66 while those for pyrrole and furan are 59 and 43, respectively. Quantitatively, these values agree with that predicted from their chemical behavior.

Although the indices are capable of comparing the degree of aromaticities, they are sensitive to ring type. Thus it is not possible to compare the aromaticity of a five-membered vs a six-membered or a benzo-fused heterocycle. Subsequent work by Katritzky *et al.* (89JA7) established good correlation between the aromaticity indices and resonance energies. This relationship is used by Bird to define a unified aromaticity index which compares the Hückel molecular orbital delocalization energies of the parent five-, six-membered and benzo-fused carbocycles (92T335). Benzene is still the standard and has an I_6 value of 100. The other ring sizes follow the relationship $I_A = I_6 = 1.235 \times I_5 = 1.34 \times I_{6.6} = 2.085 \times I_{5.6}$ (see Table 18). There is an excellent relationship between this index and the aromaticity parameter which is determined by the dilution shift method (74JCS(P2)332).

It is also possible to determine the relationship between I_A and resonance energy. Resonance energies have been calculated by employing a Laidler bond energy scheme (B-70MI 209-02). Bond energies used for C—C were $-4.62 \text{ kcal mol}^{-1}$, for C=C, $37.90 \text{ kcal mol}^{-1}$, and for C—S, $5.29 \text{ kcal mol}^{-1}$. The resonance energy of thiophene is then 43.0 kcal (Table 18), while that for benzo[*b*]thiophene is calculated to be 69.8 kcal (92T335). By comparison, the values for benzene and naphthalene are 45.8 and 80.3 kcal, respectively. The order of aromaticity is found to be benzene > thiophene > pyrrole > furan which is in agreement with many of the other systems. The

resonance energies calculated by this method are related to the unified aromaticity index by the equation $RE = 0.531 \times I_A$ making it possible to rank the aromaticity of any heterocycle as long as the ring bond lengths are available for estimation of their resonance energies.

π -Electron contributions to the diamagnetic susceptibility (χ^1) have also been used as an index to measure aromaticity $\langle 87\text{CHE}454 \rangle$. These are calculated relative to benzene and depend on the measure of the induced ring current. Thus it is possible to construct a scale of aromatic character for five-, six-membered, and fused heterocycles. Based on this method, the diamagnetic susceptibility of thiophene (relative to benzene) is found to be 0.664.

The aromaticity of thiophene has also been measured by NMR ring currents. However, various results have been obtained by different workers. Thus the aromaticity determined by Elvidge $\langle 65\text{CC}160 \rangle$ is calculated to be 75%, while that by DeJongh and Wynberg $\langle 65\text{T}515 \rangle$ was estimated to be 77%. On the other hand, calculations by Abraham *et al.* $\langle 65\text{CC}43 \rangle$ gave a value of 100%; a similar value was also obtained for furan. Obviously this is not an accurate concept for aromaticity. The main problem arises in obtaining the appropriate model compounds and making the right corrections. Another spectroscopic based aromaticity concept is the difference in the chemical shifts of the α - and β -protons $\langle 65\text{SA}85 \rangle$. The smaller the difference, the greater the aromaticity. According to this criteria, the order for aromaticity is benzene > thiophene > pyrrole > furan.

The observation that the shifts of nuclear protons due to the introduction of a methyl group depends on the aromaticity of a ring has led to the development of another aromaticity index (B) $\langle 74\text{JCS(P2)}332 \rangle$. A quantitative relationship of this index is shown in Equation (5). Interestingly, while some aromaticity parameters determine pyrrole to be slightly more aromatic than thiophene, this method shows pyrrole to be even less aromatic than furan.

$$B = 1 / \left| \sum_j [(\Delta\delta_2)_j - (\Delta\delta_2)] \right| \quad (5)$$

In Equation (5) $\Delta\delta_2$ is the difference in the ring proton chemical shifts of the 2-methyl derivative and of the parent heterocycle, and i and j refer to the nonequivalent protons (3-H, 4-H, and 5-H).

The dilution shift parameter ($\Delta\delta_1 V_m$) is another spectroscopic parameter used to determine aromaticity, where $\Delta\delta_1$ is the difference between the chemical shifts of aromatic protons in a pure liquid and in an infinitely dilute solution in a nonpolar solvent, and V_m the molar volume of the compound $\langle 74\text{JCS(P2)}332 \rangle$. Based on this concept, the aromaticity of a compound is defined as $A = \Delta\delta_1 V_m^{2/3}$ $\langle 72\text{BSF}1022 \rangle$. The values correlate well with the Pauling resonance energies $\langle 33\text{JCP(1)}606 \rangle$ and enables estimates of resonance energies of heterocycles which could not have otherwise been obtained.

The solvent shift parameter (S) is the difference in the chemical shift of the protons of a mixture of acetonitrile and cyclohexane in cyclohexane as the solvent and in the aromatic compound as the solvent $\langle 71\text{JA}556 \rangle$. The premise behind this concept is that the positive end of the acetonitrile dipole locates on top of the aromatic ring where the π -electron density and diamagnetic shielding is high. The chemical shifts thus depend on the degree of aromaticity; the greater the aromaticity, the greater the anisotropy effect and the larger the S value. A scale relative to benzene is thus created. While most normal alkenes are zero, benzene has a value of 1.0 and thiophene is calculated to be 0.745.

The diamagnetic molar susceptibility (χ_m) also depends on ring current and can be measured relatively easily. The difference between this value and that obtained for a classical localized model affords the diamagnetic susceptibility exaltation (Λ) $\langle \text{B-71MI } 209-04 \rangle$. A comparison of the aromaticity indices of thiophene and benzene by magnetic criteria are displayed in Table 19. In all cases, the order of aromaticity as determined by these magnetic criteria follow the sequence benzene > thiophene > pyrrole > furan.

Carbon-13 NMR studies have also been used as a quantitative measure of electron deficiency and excessiveness $\langle 82\text{OMR}(19)192 \rangle$. The difference in the chemical shifts observed between a given unsubstituted carbon atom and its substituted counterpart, varies significantly for different aromatic compounds. The presence of an electron-withdrawing substituent X will cause a larger chemical shift at the substituted carbon if the ring is electron rich. If the ring is electron deficient, the extent of deshielding will be less since there is a counter effect here. Based on this, the ratio ${}^{13}\rho$ is defined by Equation (6).

$${}^{13}\rho = \left[\frac{\delta(\text{ppm})(\text{het}-X) - \delta(\text{ppm})(\text{het}-H)}{\delta(\text{ppm})(\text{benzene}-X) - \delta(\text{ppm})(\text{benzene}-H)} \right] \quad (6)$$

For π -deficient systems, this ratio is < 1 , while for π -excessive, it is > 1 . As a result it is possible

Table 19 Aromaticity indices of benzene and thiophene based on magnetic criteria.

Method	Benzene	Thiophene	Ref.
χ^1	1	0.664	87CHE454
$\delta_a - \delta_b$	0	0.19	65SA85
Dilution shifts	13.93	11.56	74JCS(P2)332
Solvent shifts	1	0.745	71JA556
B	5.0	3.85	74JCS(P2)332
Λ^a	13.7	13.0	B-71MI 209-04

^aIn units of $-4\pi 10^{-12} \text{ m}^3 \text{ mol}^{-1}$.

to obtain a quantitative measure of the π -excessiveness or deficiency and thus the degree of aromaticity. Based on this, the aromaticity indices for 2- and 3-substituted thiophenes were calculated to be 1.35 as compared to 1.14 and 1.31 for the corresponding furan derivatives, indicating thiophene to be more aromatic than furan.

The absolute hardness of a chemical species has been shown to be a good measure of aromaticity <88TL4843>. As a first approximation, it can be assumed to be equal to half the difference between the ionization potential and its electron affinity <83JA7512>. Alternatively, if the Hartree-Fock or the Hückel model is used, the absolute hardness can also be represented as half the HOMO-LUMO energy gap <86PNA(83)8440>.

Zhou and Parr have introduced the concept of relative hardness (η_r) and topological resonance energy per π electron (TREPE) <89JA7371>. Within the Hückel theory, η_r is the difference between the absolute hardness of the molecule and the absolute hardness of its hypothetical acyclic analog. Consequently, the absolute and the relative hardness have been obtained for a variety of benzenoid and heteroconjugated hydrocarbons and compared with either the resonance energy, the resonance energy per π electron (REPE), or the TREPE. In almost all cases, there is good correlation between the hardness and energies. According to the hardness concept, thiophene is shown to be aromatic and follows the trend observed by TREPE and REPE.

Katritzky *et al.* <89JA7> have developed a principal component analysis (PCA) system to determine aromaticity. Various characteristics consisting of geometrical, energetic, and magnetic data for a series of compounds are assembled and subjected to PCA. Values for the characteristics of individual compounds recalculated from the scores were found to exhibit good agreement with those used in the treatment. Scores can then be estimated to predict values of characteristics for other compounds where there is limited data available.

The PCA method transforms a given set of principal components that are uncorrelated to each other. The principal component model is described by Equation (7).

$$x_{ik} = \bar{x}_{ik} + \sum_{(a=1)}^A t_{ia} p_{ak} + e_{ik} \quad (7)$$

where

\bar{x}_{ik} = mean scaled value of the experimental quantities

t_{ia} = scores i = chemical compound under study

p_{ak} = loadings k = variable (experimental measure)

e_{ik} = residuals a = principal component

The geometrical properties selected are the Bird's aromaticity indices which are calculated from experimental bond lengths (I_x) <85T1409, 86T89> and also from AM1 calculated ring geometries (I_x') <90JPR(332)853>, the Julg index which is based on the concept of ring current <83JOC1344> and the Pozharskii index (ΔN) <85CHE717>. Energetical properties considered are the DRE <70JA1453>, HSRE <73JA3907, 75T295>, the difference in the experimental heats of aromatization (ΔH_A) <69JA6321>, the experimental heats of formation (ΔH_f) <83JCC84>, and the calculated values ($\Delta H_{f(MNDO)}$) <83MI 209-01> or ($\Delta H_{f(AM1)}$) <90JPR(332)853>. Magnetic criteria include the diamagnetic susceptibility exaltation (Λ) <74AHC(17)255>, and an aromaticity index I_1 based on the anisotropic polarizability of the molecule <84JGU1427>. For heterocycles containing a nitrogen atom, the ^{15}N chemical shifts were also included.

From the PCA model, a SIMCA modeling and classification method is applied <B-86MI 209-04>. The partial least squares method (PLS) is then used to predict the values of each of the variables

used in the PC analysis and thus assess the self-consistency of the model. To confirm the predictive power or reliability of a characteristic, a data point x_{ik} is successively omitted and a PC analysis performed with the remaining set of data. The new value for the data omitted is recalculated using the new scores and new values of the loadings. The closer the recalculated value to the input value, the greater the reliability and the predictive power of the model. Principal component scores t_1 , t_2 , and t_3 are calculated for each compound as are the residual standard deviations. By plotting a three-dimensional graph of the scores t_1 , t_2 , and t_3 it is possible to separate the compounds into groups. From the first principal component scores t_1 , it is possible to distinguish five-membered rings from six-membered and also oxygen containing heterocycles from those containing sulfur and nitrogen. The second principal component scores t_2 , depend mainly on the number of heteroatoms in the molecule irrespective of whether they are five- or six-membered. The t_3 scores depend on the heteroatom present in five-membered rings.

For benzene, the t_1 , t_2 , and t_3 scores are all positive. Heterocycles with two or more nitrogens are found in the region with t_1 positive and t_2 negative. Pyrrole, furan, and thiophene all show t_1 as negative and t_2 as positive. For those containing no oxygen and more than one heteroatom, t_3 is negative. Oxygen containing heterocycles, e.g., furan, oxazole and isooxazole all show a positive score for t_3 .

For thiophene, the principal component scores t_1 , t_2 , and t_3 as obtained from the principal component analysis model and with nine characteristics are -1.643 , 0.731 , and -2.433 , respectively $\langle 89JA7 \rangle$. With 11 characteristics, the values change to -0.918 , 2.444 , and -1.737 , respectively $\langle 90JPR(332)853 \rangle$. Although the values differ, the scores of the compound obtained in both papers show a good correlation implying a reliable quantitative concept. The multiple correlation coefficient is a good measure as to the reliability of the parameters. The closer the recalculated values are to the input values, the more reliable the model and the characteristic employed. Most of the characteristics displayed high correlation coefficients (>0.8). However, for the five-membered heterocycles, the $\Delta H_{f(AM1)}$ are less well predicted by this treatment since the heats of formation are overestimated by the AM1 method.

The principal component analysis model has also been employed for the comparison of aromaticity for benzo-fused five- and six-membered heterocycles $\langle 90JPR(332)870 \rangle$. The loadings for the bicyclic compounds show a close correlation to those of the corresponding monocyclic heterocycles. The data for the characteristics and the scores for thiophene and for benzo[*b*]thiophene (along with benzene and naphthalene) are listed in Table 20.

Table 20 Characteristic data and scores for thiophene,^a benzene,^a benzo[*b*]thiophene,^b and naphthalene.^b

Property	Thiophene	Benzene	Benzo[<i>b</i>]thiophene	Naphthalene
Bird's aromaticity index (I_x^c)	66.0	100.0	57.0	77.3
Bird's aromaticity index (I'_x^d)	67.7	100.0	76.1	76.9
Jug's aromaticity index (RC)	1.53	1.77	1.52	1.65
Pozharskii's index (ΔN)	0.25	0	0.18	0.18
Dewar resonance energy (DRE) ^e	1.08	3.77	2.48	3.36
Dewar resonance energy (DRE) ^f	0.96	3.84	1.18	3.35
Hess-Schaad resonance energy (HSRE) ^g	0.032	0.065	0.044	0.055
Heat of formation (ΔH_f^h)	27.6	19.8	40.0	36.1
Heat of formation ($\Delta H_{f(AM1)}^i$)	40.1	22.0	53.9	40.8
Molar diamagnetic susceptibility (χ_m^j)	57.4	54.8	93.3	91.9
Diamagnetic susceptibility exaltation (Λ^j)	17.8	17.9	34.9	36.2
Score t_1	-0.92	3.20	1.30	3.57
Score t_2	2.44	3.20	-2.04	-1.12
Score t_3	-1.74	1.18	0.39	8.80

^a $\langle 90JPR(332)853 \rangle$. ^b $\langle 90JPR(332)870 \rangle$. ^cFrom experimental bond lengths. ^dFrom AM1 ring geometries. ^eFrom experimental heats of formation (kcal mol⁻¹). ^fFrom AM1 heats of formation (kcal mol⁻¹). ^gIn units of β . ^hkcal mol⁻¹. ⁱAM1 heats of formation. ^j($\times 10^{-6}$).

From Table 20, we see a change in sign for the t_2 score of naphthalene as compared to benzene. This arises due to a change in sign of the loading value p_2 which is allowed in a principal component analysis system where the relevant information is associated with the magnitude rather than the absolute value. Replacement of a $\text{CH}=\text{CH}$ in naphthalene by sulfur reduces t_1 by a reasonable amount and even more so when it is replaced by nitrogen or oxygen. The magnitude of t_1 increases when a benzo ring is attached to thiophene but t_2 generally becomes smaller. Although this latter

effect is small in going from thiophene to benzothiophene, it is much more pronounced in others such as benzene, pyrazole, and triazole.

Most of the characteristics are predicted quite well. In general, the multiple correlation coefficient of the values recalculated by the PLS method for five- and six-membered heterocycles are much higher than for the benzo-fused analogues. This indicates smaller deviations in the recalculated values for the former cases. For thiophene, the largest deviations (using the PLS method) were observed in the recalculated values of HSRE, and the diamagnetic susceptibility exaltation. For benzo[*b*]thiophene, there is negligible deviation for the recalculated value of I'_{χ} , but a large deviation for the I_{χ} recalculated value. The other geometric characteristics are predicted quite well. Amongst the energy characteristics, the recalculated DRE and HSRE values show a good correlation coefficient but a much larger deviation for the AM1 calculated energy (DRE'). The recalculated values of χ_m for benzothiophene and for other sulfur containing bicyclics are lower, while oxygen containing compounds have higher recalculated values.

Although the data for the two series of compounds <90JPR(332)853, 90JPR(332)870> are completely different, there is a significant relationship between the loadings and the scores for both series which indicates good reliability for this aromaticity concept.

Energy-based criteria for aromaticity have, in general, not correlated well with experimentally obtained data and that from chemical reactivity. This lack of correlation is especially pronounced in heteroaromatic compounds. Kollmar <79JA4832> employed a “reference” molecule, localized the π -orbitals and calculated the energy of the optimized molecule with localized double bonds. Although satisfactory results were obtained for benzene and naphthalene, the method is not so reliable for heterocycles <90IJQ843>. This is circumvented by localizing only the lowest π -orbital rather than the entire π -bonding system <86ZN(A)49>. The aromatic criteria of five-membered heterocycles obtained by this modification correlates well with chemical reactivity, thermodynamic data and the Bird's aromaticity index. This has been further modified by localizing only the lowest π -orbital and subtracting the eigenvalues calculated for the lowest delocalized π molecular orbital <90IJQ843>. $\Delta\epsilon_{\pi L}$ (NLMO) is thus defined as: $\Delta\epsilon_{\pi L}$ (NLMO) = ϵ_{π} (MO) - ϵ_{π} (NLMO) where ϵ_{π} (MO) = eigenvalues of the lowest π delocalized MO, and ϵ_{π} (NLMO) = eigenvalues of the lowest π natural localized MO.

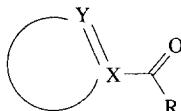
The localization procedure developed by Boys <60MI 209-01> was also used and $\Delta\epsilon_{\pi L}$ (Boys) was calculated as above. Values calculated by both methods correlate well with experimental aromaticity criteria although the Boys method provides better correlation. The order of aromaticity as shown by these calculations is thiophene > pyrrole > furan which is not always the case by some of the other methods.

2.09.4.2 Conformational Analysis

Organic carbonyl compounds in which the carbonyl group is not part of a cyclic structure possess interesting conformational properties depending on the system. For example, the carbonyl group —C(O)R attached to an atom X in a ring, gives rise to two scenarios:

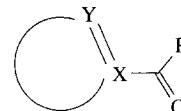
(i) if X is in an sp^2 -hybridization state as in an aromatic or heterocyclic system (**75**), it can exist as either the Y,O-cis (**75a**) or Y,O-trans (**75b**) conformer in the ground state. The transition state would be where the C=O bond is perpendicular to the plane of the ring;

(ii) if X is an sp^3 -hybridized atom, a threefold barrier exists which depends on the ring conformation.



Y,O-cis

(75a)



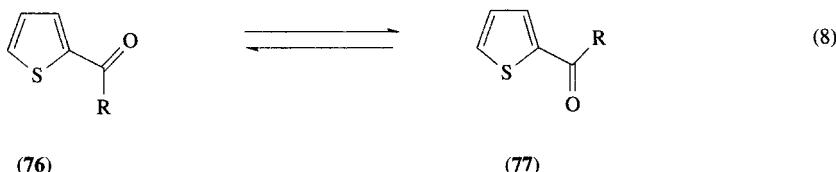
Y,O-trans

(75b)

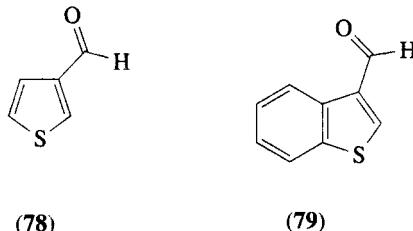
The rotational isomerism in carbonyl-containing compounds of five-membered heterocycles has been well reviewed <77JCS(P2)1601, 81RCR336, 84KGS579, 87AHC(41)75>. The energy of rotation around two sp^3 -hybridized C—C bonds is about 2.9 kcal mol⁻¹, while that for two sp^2 -hybridized C=C

bonds (*cis-trans* isomerism) is about 5–7 kcal mol⁻¹. In carbonyl containing heterocyclic compounds, the extent of π -conjugation between the carbonyl group and the ring is the main factor in determining the energy of rotation. For thiophene derivatives, this could be of the order of 10.7–12 kcal mol⁻¹.

2-Formylthiophene or thiophene-2-carbaldehyde can exist either as the S,O-*trans* (76) or S,O-*cis* (77) conformer (Equation (8)). Initial results from microwave spectroscopy indicated the compound to exist as the *trans* isomer in the gas phase (65ZN(A)1323). This was later found to be wrong and the *cis* conformer was shown to be the major isomer (76CA(84)58451). The predominance of this conformation has been supported by experimental and calculated dipole moments (74JGU1291, 75JCS(P2)744), from Kerr constants (75JCS(P2)744) and by other methods (87AHC(41)75) including theoretical calculations (71JGU374, 73T2545, 75JOU1968, 79JA311). The energy barrier for the *trans-cis* isomerization was determined to be 10 kcal mol⁻¹ as determined by ultrasonic pulse techniques (69JCS(A)713). It has been shown that the molecule is planar and that >90% of the molecule exists in the S,O-*cis* orientation (85JCS(P2)1839). The same holds true for the corresponding benzo[*b*]thiophene derivative (83JCS(P2)911). Compound S,O-*cis*-thiophene-2-carbaldehyde (77) is also more polar than the *trans* form (79JA311) and is thus even more preferred in polar solvents. With the exception of furan-2-carbaldehyde, the conformations are quite rigid for most of the other five-membered heterocycles.



CNDO/2 (74JOU848) and *ab initio* calculations (79JA311) show the S,O-*trans* form of 3-formyl derivatives (78) to be slightly more stable. NMR studies show a large preference for the S,O-*trans* form of benzo[*b*]thiophene-3-carbaldehyde (79).



Steric interactions exist between the formyl group and the adjacent hydrogen atom. For thiophene-3-carbaldehyde (78), there are two adjacent hydrogen atoms while for the 2-formyl derivatives there is only one. Thus in the ground state, the latter displays greater stabilization than the former (84JCS(P2)819).

The presence of a substituent at the adjacent position tends to alter the conformation due to hydrogen bonding, steric and electrostatic effects. Thus a C(3) substituent in thiophene-2-carbaldehyde (77) increases the stability of the S,O-*cis* form. For the 3-formyl derivative, a —TeMe substituent at the C(2) or C(4) position leads to a predominance of the *cis* conformer (80JST(67)251).

For 2,5-diformyl derivatives, the 2-*cis*,5-*cis* form predominates although 20–30% of the *cis,trans* form is also detected (72JCS(P2)755). There is however less than 1% of the *trans,trans* conformer. For thiophene-2,3-dicarbaldehyde, the *cis,cis* form is preferred over the *trans,trans* by a factor of 2 : 1 (71TL145).

Theoretical calculations (79JA311) show the *cis* form of thiophene-2-carbaldehyde (77) to be more stable by 0.71 kcal mol⁻¹, while for substituents other than carbonyl groups, e.g., 2-hydroxy- and 2-methyl-thiophene, the S,H-*trans* orientation is more stable by 2.2 and 0.88 kcal mol⁻¹, respectively. The opposite holds true for the 3-substituted derivatives where calculations show the *cis* form to be more stable. The *cis* conformer is preferred in both 2- and 3-vinylthiophene.

In ketones, the coplanarity between the ketone group —C(O)R and the heterocycle depends strongly on steric interactions. For 2-acetylthiophene, the S,O-*cis* form (77; R = Me) is preferred and the molecule is practically planar (81RCR336). Low temperature ¹³C NMR confirms the predominance (>95%) of the S,O-*cis* form (85JCS(P2)1839), while at room temperature, lanthanide-

induced shift (LIS) NMR shows it to be about 85% in the case of the methyl derivative, and 75% for the isopropyl case (77; R = Prⁱ). A similar result is also observed by LIS NMR studies for 2-acetylbenzo[*b*]thiophene (83JCS(P2)911).

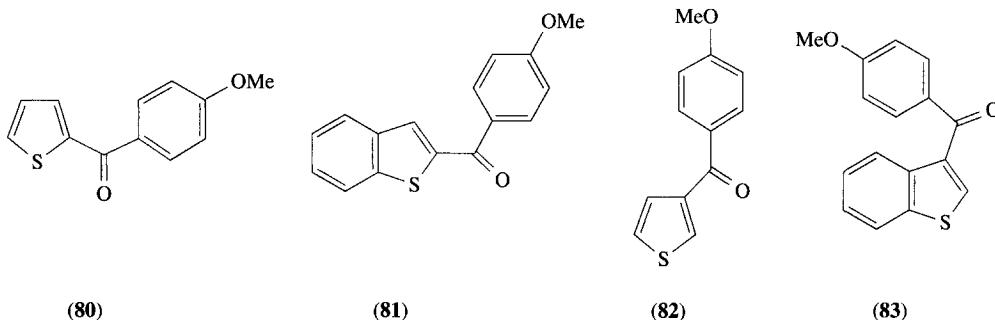
As in the 3-formyl derivatives, both conformers are observed in 3-acetylthiophene, the ratio of S,O-*trans* to S,O-*cis* being roughly 3:2 (76OMR(8)525). Furthermore, the presence of an alkyl group reduces the energy barrier for *cis-trans* isomerization for 2- and 3-keto substituents as compared to their formyl analogues (85JCS(P2)1839).

For aryl derivatives, the phenyl ring is too large to be planar with the heterocycle. Since the carbonyl group conjugates better with the heterocycle rather than with a phenyl group, it is the latter which is twisted out of the plane [\(78JCS\(P2\)1232\)](#). However, it has been difficult to accurately verify the actual conformation by NMR, UV, and dipole moments. It is possible that both the carbonyl group as well as the phenyl ring are twisted to a certain degree, although the angle in the first case is practically zero. For thiophene, the S,O-*cis* orientation is preferred and the phenyl ring is twisted by 55–67°, which increases to about 90° when *ortho* substituents are present on the phenyl ring [\(81JMC865, 81RCR336\)](#). In 3-benzoylthiophene, equilibrium mixtures of the S,O-*cis* and S,O-*trans* forms exist. As before, the phenyl ring is twisted to a large degree.

Theoretical calculations of the total molecular energy show that both rings in 2-benzoylthiophene are twisted relative to the carbonyl plane. They also confirm experimental data which shows that the phenyl ring is twisted to a larger extent and that the S,O-*cis* form is more stable. *Ab initio* calculated charge densities on sulfur (+0.273) and on oxygen (-0.223) indicated the possibility of an interaction between the two atoms and thus a preference for the *cis* conformer. For 3-benzoylthiophene, the two rings are rotated almost equally.

Conformational studies were carried out on the 2- and 3-*p*-anisoyl derivatives of thiophene and benzo[*b*]thiophene by x-ray and LIS NMR analysis <87JCS(P2)1851>. The 4-methoxy substituent was selected since a substituent at the 4-position is not expected to significantly alter the conformational preference of the two rings but it helps provide simple spectra.

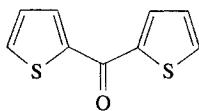
X-ray studies show the 2-aryl derivatives (**80**) and (**81**) to favor the S,O-*cis* orientation and the 3-aryl compounds (**82**) and (**83**) to adopt the S,O-*trans* form. In (**82**) and (**83**), the C(2)—C(3)—C(O) angle is approximately equal to the C(4)—C(3)—C(O) angle while for the 2-aryl case (**80**) and (**81**) the S—C(2)—C(O) angle is much smaller than the C(3)—C(2)—C(O) angle. In general, the heterocyclic moiety has more coplanar character for the 2-substituted compounds than the 3-substituted compounds. For the 2-aryl case, the S···O distance is smaller than the sum of the van der Waals radii, probably due to interactions between the two atoms. Packing energy calculations show that for (**80**)–(**82**), the nonbonded energy is increased by rotating the heterocycle and reaches a maximum after 80° and 260° rotations and a minimum at 180°. For (**83**) the values are high over the region 10–350°.



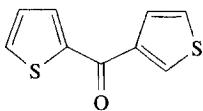
NMR studies indicate a low field shift (ca. 0.6 ppm) on 3-*H* for (**80**) and (**81**) and on 2-*H* for (**82**) and (**83**) which indicated preferred S,O-*cis* and S,O-*trans* conformations, respectively for the two classes. The ^1H NMR spectrum of (**80**) and (**81**) in CDCl_3 shows the presence of both conformers with the S,O-*cis* form being preferred. For (**82**) the S,O-*trans* form is slightly preferred but in (**83**), only the S,O-*trans* form is observed.

In biphenyl ketone the two heterocycles are twisted in a conrotatory fashion from each other by about 40° with respect to the carbonyl group (72CR(C)1112) with the S,O-*cis* conformer prevailing for both rings. X-ray analysis of 2,2'-(84), 2,3'-(85), and 3,3'-(86) biphenyl ketone show (85) and (86) to be disordered. In all cases, the preferred conformation between the carbonyl group and the thiophene moiety is the same as that observed for the formyl and acetyl derivatives (89JCS(P2)1741). *Ab initio* calculations at the 3-21G* level show that for (84), the S,O-*cis*,S,O-*cis* orientation is

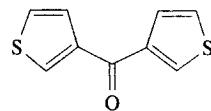
found in greater than 70%; in good agreement with that observed from LIS NMR measurements. Furthermore, the twist of the rings obtained from both methods is also in close agreement.



(84)



(85)



(86)

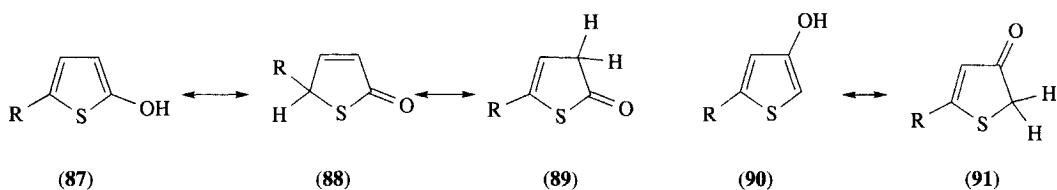
Theoretical calculations and LIS NMR measurements on (85) indicate the S,O-*cis* orientation for the 2-thienyl fragment while the 3-thienyl ring adopts both forms. In the solid state, the 3-S,O-*trans* form is observed with both rings being twisted from the carbonyl plane. In (86), the *trans* conformer is predicted to be more stable, in agreement with LIS NMR results.

2.09.4.3 Tautomerism

The presence of a hydroxy-, thio-, or amino-substituent in five-membered heterocycles, leads to various tautomeric forms. In most cases, one of the tautomeric forms is not aromatic and the degree to which the tautomeric form exists depends on the loss in resonance energy. Thus, compounds which are less aromatic would be more prone to tautomerize than the more aromatic ones.

2.09.4.3.1 Compounds with a hydroxy group

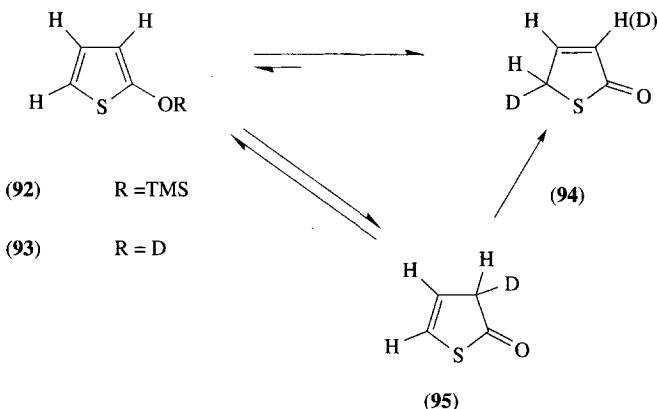
Hydroxythiophenes are very unstable, air- and acid-sensitive compounds <B-76MI 209-01>. 2-Hydroxythiophenes are generally found in the tautomeric forms (87)–(89), while the 3-hydroxy isomer can exist in either the hydroxy form (90) or the keto form (91). Depending on the nature of the substituents and the solvent system, either of the tautomeric forms (90) or (91) can be the predominant one. Although some of these systems could exist as mixtures or exclusively in the keto form, we shall generically refer to them as hydroxythiophenes for simplicity.



(i) 2-Hydroxythiophenes

For the 2-hydroxythiophenes, the equilibrium is almost completely in the keto form. Furthermore, the conjugated isomer 2(5*H*)-thiophenone (88) is generally more stable and formed to a larger extent than (89). The greater thermodynamic stability of (88) is due to the conjugation between the keto group and the double bond, while in (89), the stability exists only by hyperconjugation between the double bond and the substituent (if any) in the 5-position. In the parent molecule where there is no substituent, only (88) is detected.

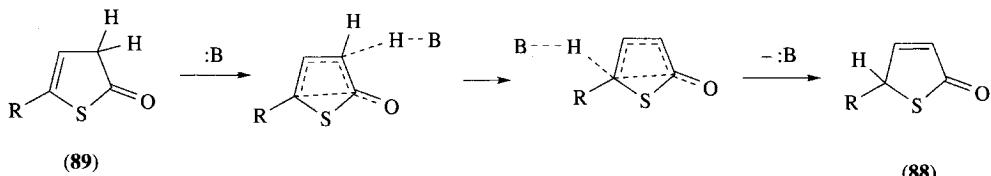
Hydrolysis of 2-[(trimethylsilyl)oxy]thiophene (**92**) in DMSO-*d*₆/D₂O to (**93**) occurs readily at 32°C (89JA5346). However, it is unstable and isomerizes rapidly (ca. 10 min) to a 2:1 mixture of the 5-deutero (**94**) and the 3-deutero (**95**) keto derivatives (Scheme 6). The latter is unstable and converts to 5-deutero-3-thiolen-2-one (**94**) within an hour.



Scheme 6

In general, the 2(*5H*)-thiophenones (**88**) have higher dipole moments than the 2(*3H*)-thiophenones (**89**). Thus the equilibrium shifts to the former with increasing polarity of the solvent (68AK461). With a phenyl group at the 5-position, only 5-phenyl-2(*5H*)-thiophenone (**88**; R = Ph) is formed as evidenced by the NMR spectrum in CCl₄ (64AK211). However, in methanol, the hydroxy compound (**87**; R = Ph) has also been detected in amounts of 25–30%. For substituents at the 3- and 4-position, the 2(*5H*)-thiophenone form predominates since, in addition to the keto group, the substituent can also conjugate with the double bond (62ACST89).

The base-catalyzed rearrangement of 5-alkyl-2(*3H*)-thiophenone (**89**) to the corresponding 2(*5H*)-form (**88**) is first order in substrate and also in base. The tautomerism proceeds through a two-stage mechanism depicted in Scheme 7. For R = Me, tautomer (**88**) is more stable than (**89**) by 2.8 kcal mol⁻¹ with an activation energy barrier of 21.5 kcal mol⁻¹ (68MI 209-02, 86HC(44/3)1). Evidence for the two-step mechanism has been verified by hydrogen–deuterium exchange studies at the 3-position (68AK247).



Scheme 7

In most cases, the keto form (**88**) and/or (**89**) predominates. Spectroscopic evidence of the hydroxy form has been detected when there is a carbonyl substituent in the adjacent position. This conformation is stabilized by intramolecular chelation (67T871).

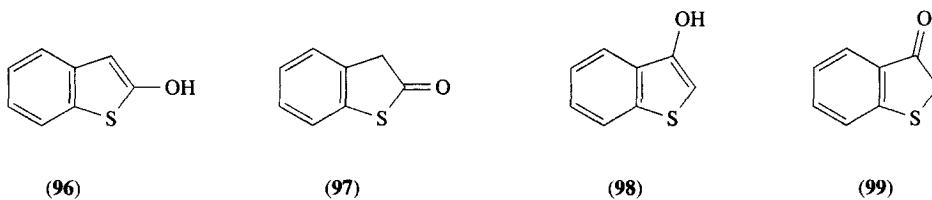
In the ¹H NMR spectrum of (**88**), the coupling constant between the hydrogen atoms at the 3- and 4-position are larger (ca. 6.1 Hz) than those found in thiophene (64AK211). Carbonyl substituents at the 3-position which generally cause the equilibrium to shift exclusively to the hydroxy form, show unusually large (>6.0 Hz) *J*_{4,5} coupling constants (67T871). Chemical shifts and coupling constants of a variety of hydroxythiophenes have been tabulated elsewhere (82S1056, 86HC(44/3)1) and will not be discussed here.

The carbonyl absorption in 2(*5H*)-thiophenones (**88**) is found in the region 1670–1695 cm⁻¹, while that in the 2(*3H*)-thiophenones is found between 1730–1750 cm⁻¹ (63AK239). The former derivatives also display a strong band between 805 cm⁻¹ and 970 cm⁻¹ while the nonconjugated keto forms (**89**) have a strong band between 970 cm⁻¹ and 985 cm⁻¹. The appearance of a band in only one region is usually a good indication of the exclusiveness of that tautomeric form (64AK211).

The UV spectra of hydroxythiophenes has been summarized recently by Gronowitz and Hörnfeldt (86HC(44/3)1). In general, the 2(5H)-thiophenones display a band around 220 nm in the UV spectra which shifts to higher wavelength when substituents at the 3- and 4-position (including hydroxy groups) are introduced. The second band at 265 nm is generally unaffected by the introduction of substituents (63AK(21)239).

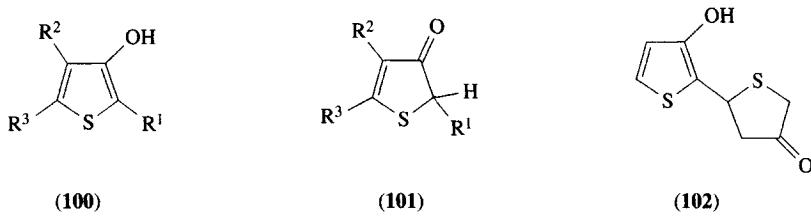
(ii) 2-Hydroxybenzo[b]thiophenes

In the solid form and in solution, only the keto form (97) exists [\(70AHC\(11\)296\)](#). The hydroxy form (96) was detected by ^1H NMR spectroscopy when its trimethylsilyl precursor was hydrolyzed ($\text{CD}_3\text{COCD}_3/\text{D}_2\text{O}/\text{DCl}$). At -25°C , the signal at 6.45 ppm which is assigned to the alkenic proton at the 3-position disappears within 15 min and is replaced by a broad singlet at 4.2 ppm, indicating rapid conversion to the keto form (97) [\(89JA5346\)](#).



(iii) 3-Hydroxythiophenes

Spectral evidence for 3-hydroxythiophenes show them to exist as mixtures of both forms (**100**) and (**101**) *<56JCS4985, 57JCS4620>*. Recent synthesis of 3-hydroxythiophene shows the keto form (**101**) to predominate by a factor of 2.9 *<86TL3275, 89JA5346>*. It is, however, unstable and tends to dimerize to the bithienyl (**102**) *<90CC375>*. 3-Hydroxythiophene was prepared from the trimethylsilyl derivative and was sufficiently stable to obtain its NMR in a variety of solvents *<89JA5346>*. In most cases, 100% of the enol form was detected. In CCl₄, both tautomers were observed, contrary to an earlier report where only the keto form was observed *<86TL5155>*. Although ketonization of 3-hydroxyfuran in water or DMSO affords over 99% of the keto form at equilibrium, substantial amounts of 3-hydroxythiophene can be detected at equilibrium *<87PAC1577>*.



The 2-methyl derivative is reasonably stable and exists mainly in the hydroxy form (**100**; R¹ = Me), while there is nearly a 1 : 1 ratio for the 2-*t*-butyl derivative <65ACS1249>. For 2,5-dialkyl substituted compounds the keto form (**101**) is generally favored over the hydroxy form by a ratio of 2 : 1 <76CS126>. In solution, the keto–enol equilibrium is established very rapidly, the equilibrium ratio varying from 1.04 to 8, depending on the solvent used. The high percentage of the hydroxy form in thiophene and benzothiophene in contrast to the predominance of the keto form in pyrrole and furan systems is attributed to the higher aromaticity of thiophene <74AHC(17)255>, and thus a larger energy barrier required to break the aromatic sextet <76CS126>.

Initial reports of carboxy substituents on 3-hydroxythiophenes indicated that the compounds all existed in the hydroxy form (65T3331, 67T871, 68CJC2255, 71T3839), irrespective of the position of the substituent. However, reports have indicated the existence of tautomeric mixtures of both forms (70JCS2409).

NMR data of substituted 3-hydroxythiophenes indicate that in cases where the hydroxy group is nonchelated (e.g., with alkyl substituents), the hydroxyl proton resonates between 5.6 and 6.7 ppm.

〈65ACS1249〉 while intramolecularly chelated hydroxylic protons are observed at about 9.5 ppm 〈65T3331〉. The NMR spectra of 2-cyano- (**100**; R¹ = CN) and 2-phenyl-3-hydroxythiophene (**100**; R¹ = Ph) show the hydroxylic protons at 8.8 and 5.5 ppm, respectively, indicating the former is intramolecularly chelated 〈71T3853〉. The strong absorption between 3130 cm⁻¹ and 3180 cm⁻¹ in the IR spectrum, which does not change with concentration, further indicates the presence of chelation in the cyano derivative.

In the IR spectra of 3-hydroxy derivatives, in addition to the carbonyl band between 1655–1680 cm⁻¹, an O—H stretching band (not observed in the case of the 2-hydroxy derivatives) is also observed between 3300 cm⁻¹ and 3600 cm⁻¹ 〈76CS126〉.

(iv) 3-Hydroxybenzo[*b*]thiophenes

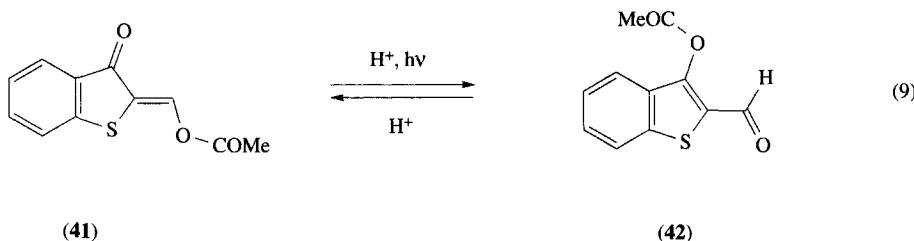
As in the case of 3-hydroxythiophenes, the benzo analogue is also unstable. There have been conflicting reports as to whether the hydroxy tautomer (**98**) or the keto form (**99**) is more stable. IR evidence indicates that in the solid state, it exists in the keto form 〈58JCS1217〉. However, Buu-Hoi *et al.* 〈65BSF2658〉 report the ¹H NMR spectrum of the compound (in CDCl₃/CF₃CO₂H) which displays five aromatic protons and no aliphatic signals for the protons at the 2-position of the keto form. They thus assumed presence of only the enol form (**98**). Spectra run later in CCl₄ and CDCl₃ showed >95% of the keto form 〈74CS184〉. This conflicting observation is attributed to the slow equilibrium of the two tautomers 〈69T2807, 84CHEC-I(4)34〉. The half-life for the conversion of the enol form (**98**) to the keto form (**99**) is found to be 3 min at pH 2.3 and at 20°C.

Synthesis has indicated isolation of the keto form in the solid state 〈74CS(6)184, 87PAC1577, 89JA5346〉. A strong carbonyl absorption is observed at 1690 cm⁻¹ and the absence of a band between 3000 cm⁻¹ and 4000 cm⁻¹ indicates the absence of a hydroxy group. The ¹H NMR spectrum run in DMSO-*d*₆ also implies the exclusive existence of the keto form, but it is gradually converted to the enol form (**98**). The rate of conversion depends on the amount of water present in the solvent. In CDCl₃, only the keto form is observed which remains unchanged over time. Hydrolysis of the trimethylsilyloxy derivative of 3-hydroxybenzo[*b*]thiophene generates the hydroxy compound (**98**) exclusively 〈86TL3275〉. However, this is not stable and slowly tautomerizes to a mixture containing 40% of the keto form (**99**) 〈89JA5346〉.

The effect of solvent on the equilibrium constants has been studied for the 3-hydroxy derivatives of five-membered heterocyclics and their benzo-fused derivatives 〈86TL3275, 89JA5346〉. The enols are much more stable in hydrogen bonding solvents than in aprotic solvents. Thus while (**98**) is barely detected in C₆D₆, CCl₄, or CDCl₃, it is predominant in C₅D₅N and DMSO-*d*₆. All enols (including those of furan and pyrrole) show spontaneous or water-catalyzed ketonization. For acid-catalyzed ketonization, the 3-hydroxy monocyclic compounds tautomerize 10 to 10³ times faster than their benzo analogs, presumably via a mesomeric effect due to the lone pair on the heteroatom. This is greatest in the case of the nitrogen heterocycles. During base-catalysis, ketonization of 3-hydroxybenzo[*b*]thiophene (**98**) and 3-hydroxybenzo[*b*]furan occur 100 times faster than in 3-hydroxyindole.

The rate of ketonization of the hydroxythiophenes and benzothiophenes in acetonitrile–water (9 : 1) is as follows: 2-hydroxybenzo[*b*]thiophene > 2,5-dihydroxythiophene > 2-hydroxythiophene > 3-hydroxybenzo[*b*]thiophene > 3-hydroxythiophene. 3-Hydroxythiophene does not ketonize readily in the above solvent system, but in 1 : 1 acetonitrile–water, it ketonizes 6.5 times slower than 2-hydroxythiophene 〈87PAC1577〉.

The acetyl derivative of 3-hydroxybenzo[*b*]thiophene-2-carbaldehyde exists in the keto form 2-acetoxyethylenebenzo[*b*]thiophen-3(2*H*)-one (**41**) which is stable in hydrocarbon solvents up to 100°C 〈85JOU784〉. In the presence of acids it undergoes rearrangement to the carbaldehyde (**42**) (Equation (9)). Equilibrium is reached within 2 h at 25°C. The IR spectrum of (**41**) displays two strong bands at 1685 and 1770 cm⁻¹ due to the ring carbonyl and the ester group, respectively. At equilibrium, bands at 1660 cm⁻¹ and 1765 cm⁻¹ are detected which are assigned to the aldehyde and hydroxyacetyl groups in (**42**). In the ¹H NMR spectrum, the intensity of the methine proton at 8.85 ppm is reduced and a new signal at 9.95 ppm appears, which corresponds to the aldehyde proton in (**42**). Compound (**41**) exists in the *Z* form as shown by the ¹H NMR spectrum where the signal for the methine proton is downfield at 8.85 ppm which can only arise when the methine proton is in the descreening zone of the carbonyl group.

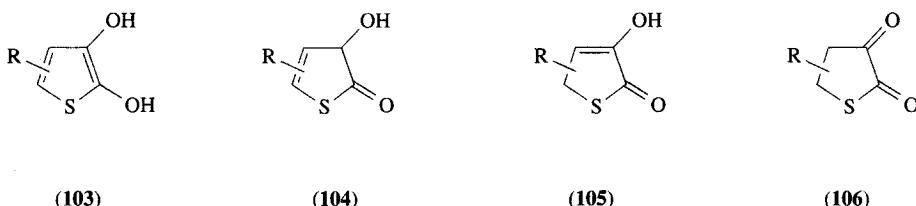


The structures of the two compounds were also confirmed by x-ray spectroscopy. For (41), a weak intramolecular hydrogen bond is observed between the methine proton and the oxygen atom of the acetyl group ($O \cdots H = 2.35 \text{ \AA}$) indicating the latter to be in the S-*trans* position relative to the exocyclic C=C bond. The molecule is almost planar with the largest deviation being 1.324 \AA . In the rearranged molecule (42), the acetyl group is turned from the plane by an angle of 87.7° since this is the least sterically hindered conformation. The O—COMe bond is stronger in (42) than in (41) as shown by the smaller bond length in (42). Since (42) exists in the Z conformation, it is not aligned correctly for the acylotropic rearrangement. It is possible however, that in acid medium, the first step is formation of an *H* complex or an ion pair which permits isomerization from the Z conformer to the E conformer which then undergoes acylotropic rearrangement. A similar type of behavior has also been reported for 2-*N*-acylaminomethylene derivatives (85JOU784).

2.09.4.3.2 Compounds with more than one hydroxy group

(i) 2,3-Dihydroxythiophenes

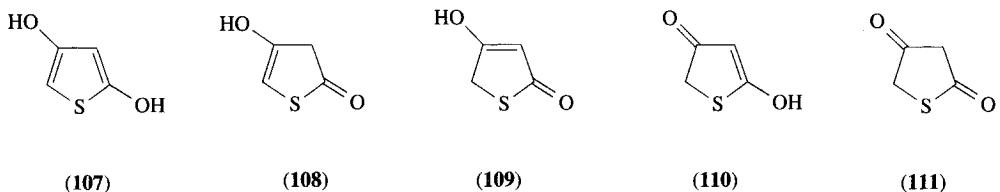
In general, 2,3-dihydroxythiophenes can possess four tautomeric forms (**103**)–(**106**). Spectroscopic evidence shows the hydroxyketo form (**105**) to predominate (71T3839). The presence of a doublet at 3.87 ppm and integrating for two protons indicates that none of the other forms exist. The hydroxyl proton is observed at 6.40 ppm indicating no intramolecular chelation with the oxo group. In the IR spectra, peaks at 1680 cm^{-1} and 1645 cm^{-1} correspond to the C=O and C=C bonds, while the broad band at 3320 cm^{-1} implies a hydroxy stretching of an enol group.



Initial reports of 2,3-dihydroxy-5-ethoxycarbonylthiophene (**103**; R = 5-CO₂Et) indicated it to exist in the tautomeric form (**104**) <65T3331>. Comparison of the IR spectrum with those of related compounds assigns the band at 1470 cm⁻¹ to an unconjugated ester function implying that the correct structure is (**105**; R = 5-CO₂Et) <71T3839>. In most cases the 3-hydroxy-2-keto form observed parallels that in the furan series, the only exception being the 4-bromo compound which strangely enough exists as the diketo tautomer (**106**; R = 4-Br).

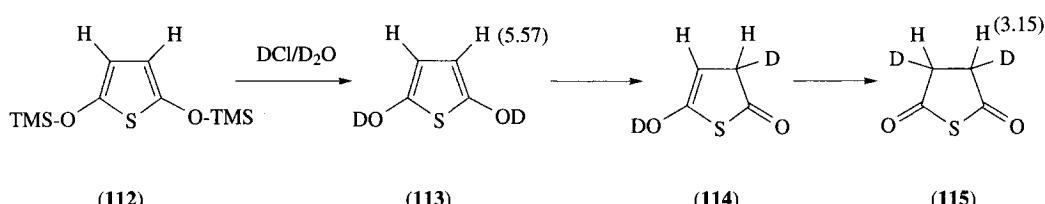
(ii) *2,4-Dihydroxythiophenes*

2,4-Dihydroxythiophenes can exist in any of the five tautomeric forms (**107**)–(**111**). In most cases, the 4-hydroxy-2-keto form (**109**) predominates. The NMR spectra of these compounds usually display a doublet at 4.0 ppm and a triplet at 5.4 ppm with a long range coupling of $J = 0.9$ Hz (71T3839).



(iii) 2,5-Dihydroxythiophenes

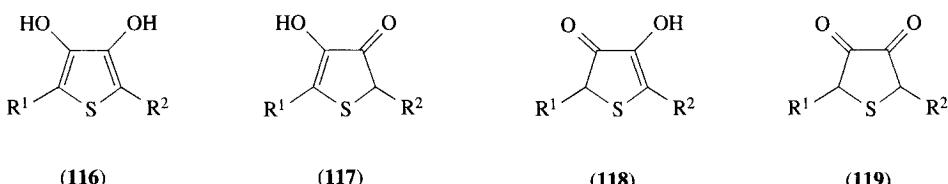
The 2,5-dihydroxythiophenes are only found in the dioxo form <63T1867, 68ACS1056, 71T3839>. By careful hydrolysis of 2,5-bis(trimethylsilyloxy)thiophene (112), it is possible to generate the *O*-deuteriated-dihydroxy compound (113) as confirmed by the singlet at 5.57 ppm in the ¹H NMR spectrum of the compound <89JOC1211>. Disappearance of this signal with concomitant appearance of a signal at 3.15 ppm indicates formation of the diketo tautomer (115). This conversion is complete within an hour. During a similar hydrolysis <87PAC1577>, the mono- and dihydroxy intermediates were detected but not (114) indicating that the tautomerism from (114) to the diketo form (115) occurs rapidly (Scheme 8).



Scheme 8

(iv) 3,4-Dihydroxythiophenes

Mono- and disubstituted-3,4-dihydroxythiophenes can potentially exist in four tautomeric forms (116)–(119). For unsubstituted and for most disubstituted derivatives, the hydroxyketo form (117) or (118) is observed. In monosubstituted products ($R^1 \neq H, R^2 = H$), (117) is the only one observed <71T3839>. These compounds also follow a trend similar to that found in the furan series with the exception of the parent compound 3,4-dihydroxyfuran which exists in the dioxo form <60JA3219>. The only thiophene derivative not to follow the trend is the 2,5-diethoxycarbonyl substituted compound which exists in the dihydroxy form (116; $R^1, R^2 = CO_2Et$).

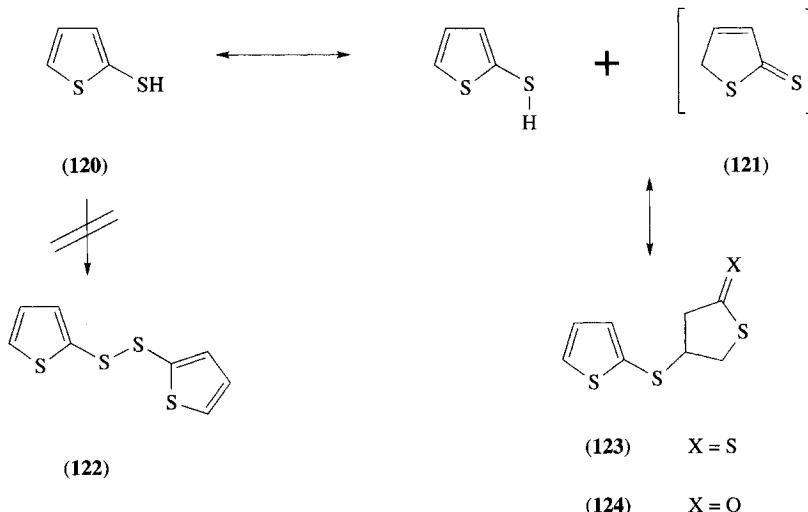


The ¹H NMR spectra of these compounds generally show the hydroxyl proton at about 5.9 ppm. The presence of a carboethoxy group in the molecule, shifts the hydroxyl proton downfield to about 9.0 ppm due to intramolecular hydrogen bonding. The IR spectra are similar to those of the 2,3-dihydroxythiophenes. The UV spectra of 3,4-dihydroxythiophene displays a shoulder at 335 nm <71T3839>. The introduction of a methyl substituent at the 2- and/or 5-position gives rise to two bands at 255 nm and 343 nm.

2.09.4.3.3 Compounds with a thiol group

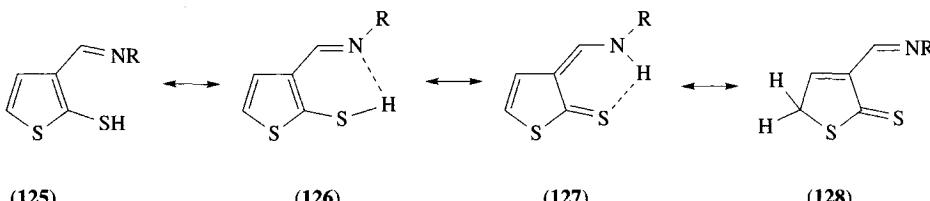
Unlike the hydroxy derivatives, no tautomerism tends to exist in the simple 2- and 3-thiophenethiols <77ACS(B)198>. Similarly, 3-thiolbenzo[b]thiophene exists in the 3-thiol form

〈70JCS(C)2431〉. 2-Thiophenethiol (**120**) is not stable and slowly solidifies on standing. Although one would expect the disulfide (**122**) to form due to air oxidation, it is the dimer (**123**) which is actually formed. It is possible that there is a slow tautomerism to the mercapto form (**121**) which is then susceptible to Michael addition by (**120**) to yield the dimer (**123**) which can be converted back to (**120**) 〈89JOC3223〉. The possibility of (**121**) forming was corroborated by the fact that Michael addition of (**120**) with 2-hydroxythiophene (which exists exclusively in the keto form (**88**)), afforded the dimer (**124**) (Scheme 9).



Scheme 9

The presence of a proton acceptor site external to the ring such as an aldimine group at the 3-position, leads to the possibility of four tautomeric forms (**125**)–(**128**) (Scheme 10). The ^1H NMR and IR spectra of these compounds indicate that in the solid state, as well as in solution, the compound exists as (**127**). At higher temperatures, the equilibrium shifts to the left forming (**126**). The nature of the hydrogen bonding depends on the substituent at nitrogen. The chemical shift for the hydrogen atom is in the region 12–14 ppm 〈70CHE1232〉. A similar behavior is also observed in the corresponding benzo[*b*]thiophene analogs 〈74JPR(316)970〉.



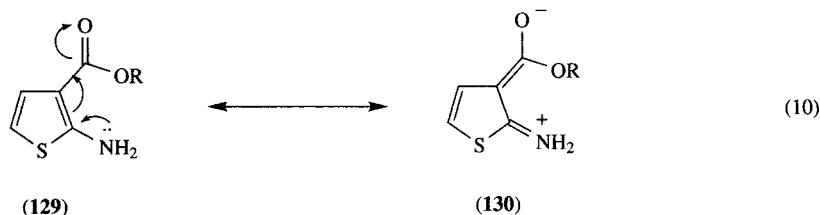
Scheme 10

2.09.4.3.4 Compounds with an amino group

Tautomerism of amino-substituted systems in five-membered rings has previously been reviewed 〈63AHC(2)1, B-76MI 209-01〉. However, literature since 1980 has been sparse with respect to tautomeric interest in these compounds. This is not surprising since as in the case for the thiol derivatives, 2- and 3-amino derivatives of thiophene and benzo[*b*]thiophene generally exist in the amino form 〈65JOC4074, 71T5873, 73JHC1067〉. MO calculations on simple aminothiophenes show them to exist in the aromatic amino form rather than in the nonaromatic imino tautomeric form 〈81MI 209-01〉. The 2- and 3-aminothiophenes are generally unstable in air. They are much more stable as salts or as their *N*-acyl derivatives and are also more stable in solution than in the neat liquid state.

Proton NMR studies on 2- and 3-thiophenamine 〈61AK515, 77S255, 82RTC205〉 as well as their substituted derivatives all indicate the exclusive existence of the imino form. The only case where

an imino form does exist in the presence of an electron-withdrawing substituent in the *ortho* position (**129**). Thus, due to the push–pull effect, the imino form (**130**) can be generated (Equation (10)).



Amongst the diamines, the electron-rich 3,4-diaminothiophene (**131**) exists in the amino form <83BSF153>, while the 2,3-diamino derivative exists in the amino-imino form (**132**) <75ZC100>. In the hydroxyamino compounds, it is usually the hydroxy system that tautomerizes to the keto form rather than the amino function to the imino one (see compounds (**133**) and (**134**)) <78JOC3539, 81JCS(P1)1078>.

