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THE CHEMISTRY OF THIOPHENE 1-OXIDES

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An exhaustive literature survey has been made of the chemistry of thiophene 1-oxides (thiophene *S*-oxides). Syntheses, structures, and reactions of thiophene 1-oxides are described to understand the present status of this chemistry. The chemistry of selenophene 1-oxides is also described briefly.

Keywords: Selenophene *Se*-oxides; selenoxides; sulfoxides; thiophene *S*-oxides

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1. INTRODUCTION

Thiophene 1,1-dioxides (thiophene *S,S*-dioxides) are compounds of much importance both from synthetic and mechanistic points of view, and their chemistry has an important role in the field of heterocyclic and heteroatom chemistry. They act either as a 2π or 4π component, undergoing a range of cycloadditions with 2π, 4π, and 6π components thermally or photochemically in addition to 1,3-dipolar cycloadditions. They also react with nucleophiles, often providing synthetically important ring-opening reactions. Many reactions on the sulfur or oxygen atom are also known.

In contrast, apparently, the chemistry of thiophene 1-oxides (thiophene *S*-oxides) has never attracted extensive attention. We therefore felt that their chemistry should be much more explored both from synthetic and mechanistic points of view. Keeping this in mind, we have made an exhaustive literature survey of these compounds to have a good grasp of the present status of their chemistry. Syntheses, structures, and reactions of thiophene 1-oxides are summarized here. The literature was searched to 1994 by means of *Chemical Abstracts*, although more recent reports have also been included to the extent possible.

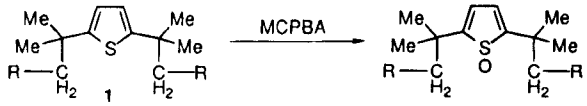
2. SYNTHESES

Thiophene 1-oxides are more reactive and thermally labile species than the corresponding thiophene 1,1-dioxides. This property makes the preparation of thiophene 1-oxides difficult. Particularly, monocyclic thiophene 1-oxides are highly reactive species unless stabilized kinetically by steric protection or thermodynamically by mesomeric effects. Fusion of benzene ring(s) to the thiophene ring makes the corresponding compounds more stable, and thus a large number of benzo[*b*]thiophene 1-oxides and dibenzothiophene 5-oxides have been synthesized.

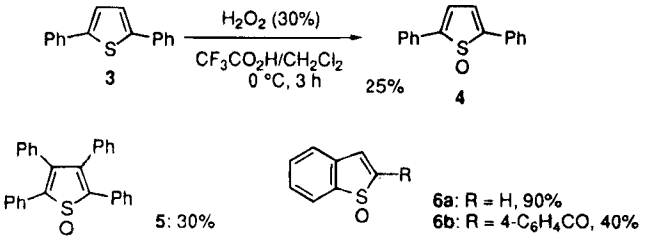
2.1. Oxidation of Thiophenes

Apparently, oxidation of thiophenes provides the most straightforward way to the corresponding thiophene 1-oxides. However, the oxidation is usually difficult to stop at the thiophene 1-oxide stage and usually produces the corresponding thiophene 1,1-dioxides. In addition, Diels-Alder

type dimerization of the resulting 1-oxide intermediates may take place. Thus, the first synthesis of isolable monocyclic thiophene 1-oxides took place by *m*-chloroperbenzoic acid (MCPBA) oxidation of 2,5-di-*tert*-butyl- and 2,5-di-*tert*-octylthiophenes **1**, which afforded the kinetically stabilized thiophene 1-oxides **2**, though in low yields.[1]

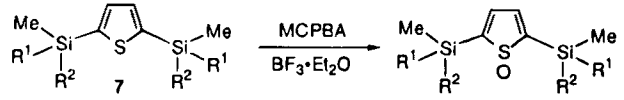


Very recently, 2,5-diphenylthiophene 1-oxide **4** was prepared in an isolated yield of 25% by oxidation of 2,5-diphenylthiophene **3** with H_2O_2 in CF_3CO_2H-CH_2Cl_2 (1:2).[2] For this synthesis, reaction conditions (time, temperature, and amounts of H_2O_2) are very important for obtaining **4** in a selective manner. This method is also applicable to the preparation of the 1-oxides **5** and **6a,b** of tetraphenylthiophene, benzo[*b*]thiophene, and 2-(4-chlorobenzoyl)benzo[*b*]thiophene.



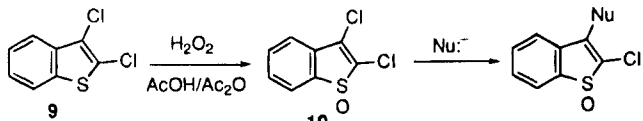
Another method, developed very recently, involves the oxidation of thiophenes with MCPBA in the presence of BF_3·Et_2O.[3] Thus, oxidation of 2,5-bis(trimethylsilyl)thiophene and related thiophenes **7** with MCPBA afforded the corresponding 1-oxides **8** in moderate yields. In this synthesis, BF_3·Et_2O may play a role not only in preventing further oxidation of the resulting 1-oxides **8** but also in increasing the reactivity of MCPBA.

Although the parent benzo[*b*]thiophene 1-oxide **6a** is stable only in dilute solution at room temperature,[2] its 2- or 3-substituted derivatives are more



8a: $R^1 = R^2 = Me$
8b: $R^1 = Me$, $R^2 = Ph$
8c: $R^1 = R^2 = Ph$

stable, and thus, oxidation of 2,3-dichlorobenzo[*b*]thiophene **9** with H_2O_2 in a mixture of acetic acid and acetic anhydride gave the corresponding 1-oxide **10** in 56% yield as a stable crystalline compound.[4] The 1-oxide **10** is susceptible to nucleophilic substition at the 3-position to give the 1-oxides **11a-c** on reactions with sodium methoxide, sodium ethoxide, and piperidine, respectively.

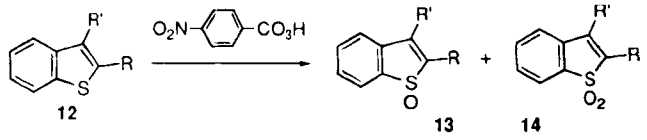


11a: Nu = OMe (46%)
11b: Nu = OEt (42%)
11c: Nu = NC_5H_{10} (15%)

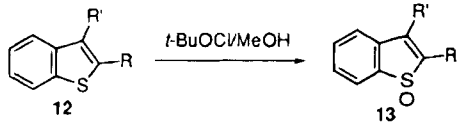
The oxidation of a series of monosubstituted benzo[*b*]thiophenes with *p*-nitroperbenzoic acid (PNPBA) and *tert*-butyl hypochlorite has been investigated.[5-7] Oxidation of benzo[*b*]thiophenes **12** with PNPBA gave a mixture of the corresponding 1-oxides **13** and 1,1-dioxides **14**. On the other hand, oxidation with the latter reagent affords the 1-oxides and/or the chlorinated 1-oxides, depending on the reaction conditions and the structure of the starting thiophenes, since it serves not only as an oxidant but also as a chlorinating reagent. Thus, in oxidation of **12b** in methanol, the chlorinated 1-oxide was produced, whereas, as exemplified by oxidation of **12a** and **12b**, oxidation in *t*-BuOH gave a mixture of 1-oxides and the chlorinated 1-oxides. Mechanistic pathways to the chlorinated products were investigated in some detail.[6,7]

Treatment of the thienoquinoline **18** with Cl_2 in buffered chloroform solution also afforded the chlorinated 1-oxide **19** along with other products.[8]

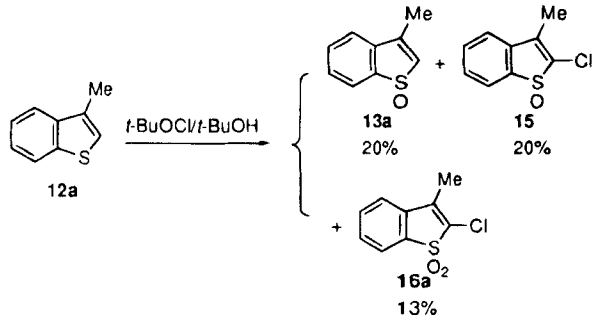
Dibenzothiophene 5-oxide **21** is a stable crystalline compound and easily prepared in generally good yields by oxidation of dibenzothiophene **20** with

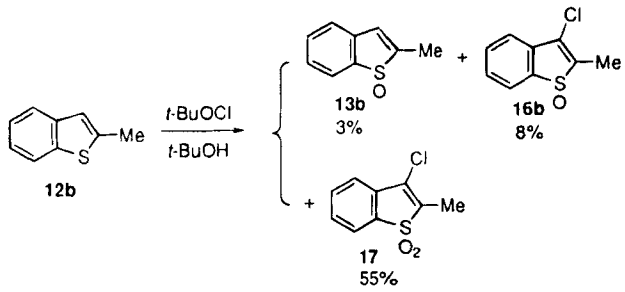


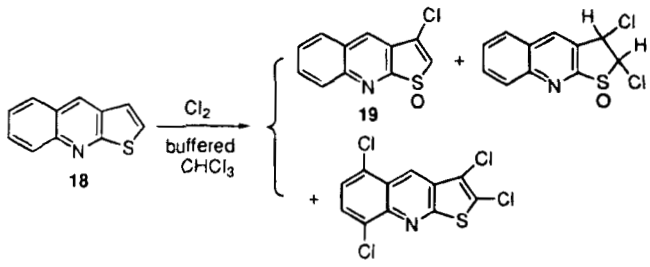
	13	14
a: R = H, R' = Me	70%	8%
b: R = Me, R' = H	40%	40%
c: R = H, R' = Br	40%	30%
d: R = Br, R' = H	30%	20%
e: R = H, R' = Cl	20%	32%
f: R = Cl, R' = H	36%	20%



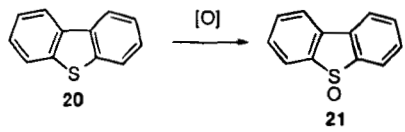
a: R = H, R' = Me: 60%
b: R = Me, R' = H → R = Me, R' = Cl: 25%
c: R = H, R' = Br: 80%
e:R = H, R' = Cl: 70%

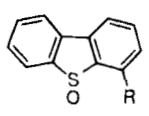


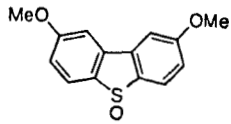


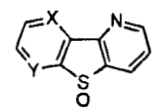


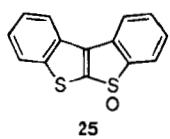
a wide variety of oxidants. Reagents or reagent systems used for this conversion involve H_2O_2 in acetic acid,[9] $H_2O_2/TiCl_3$,[10] H_2O_2/Mo (VI) complexes,[11] H_2O_2-urea/phthalic anhydride,[12] Cl_2/H_2O,[13,14] $PhI(OAc)_2$,[14,15] $PhI(OCOCF_3)_2$,[16] $^nBu_4NIO_4$/metalloporphyrins,[17] *N*-chloro-nylon-6,6,[18] cesium fluoroxysulfate,[19] *N*-sulfonyloxaziridine derivatives,[20] ceric ammonium nitrate,[21] ceric ammonium nitrate/$NaBrO_3$,[22] xenon difluoride,[23] ozone,[24] active oxygen species,[25] and electrochemical oxidation.[26] The oxides of dibenzothiophene derivatives and related compounds, **22a**,[9] **22b**,[27] **23**,[26] **24**,[28] **25**,[29] and **26**,[30] have also been prepared by oxidation methods.

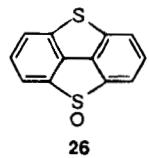






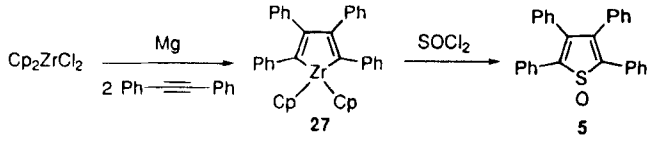




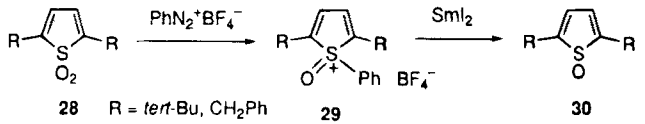


2.2. Miscellaneous Methods

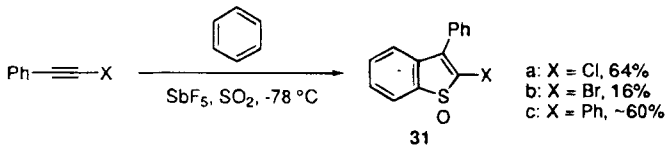
The zirconium metallacycle **27**, which is obtainable by reduction of Cp_2ZrCl_2 (Cp = η-C_5H_5) with BuLi in the presence of diphenylacetylene, reacts with $SOCl_2$ to give tetraphenylthiophene 1-oxide **5** in 52%[31,32] and 59%[33] yield. The generality of this synthesis should be investigated since it would provide a convenient way to monocyclic thiophene 1-oxides.



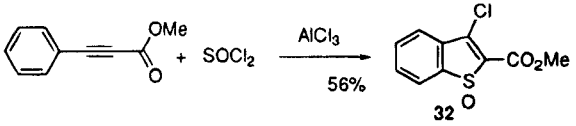
Treatment of thiophene 1,1-dioxides **28** with benzenediazonium tetrafluoroborate and reduction of the resulting sulfonium salts **29** with SmI_2 lead to the 1-oxides **30** though in low overall yields.[34]



1-Halo-2-phenylacetylenes and diphenylacetylene yield the thiophene 1-oxides **31** along with sulfinic acid derivatives, when treated with SbF_5 and benzene in liquid SO_2.[35] Though limited, this provides a facile route to benzo[*b*]thiophene 1-oxides.

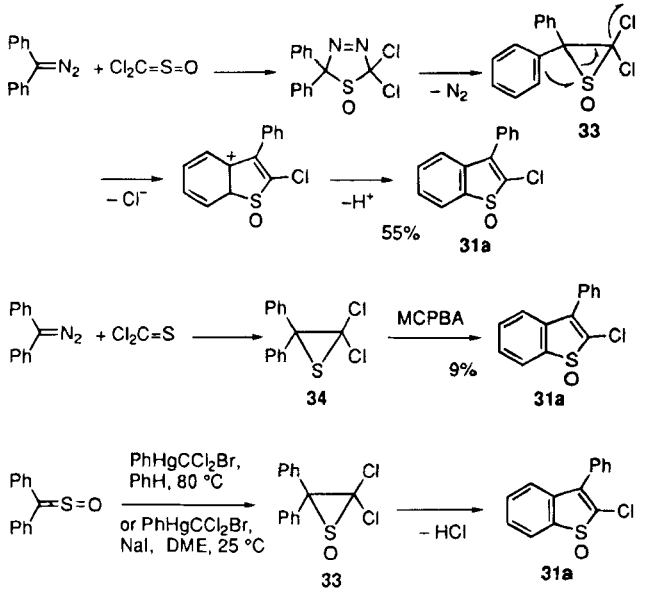


The $AlCl_3$-catalyzed reaction of methyl phenylpropiolate with thionyl chloride gave the benzo[*b*]thiophene 1-oxide **32** in 56% yield.[36] This reaction has been applied to the preparation of a number of benzo[*b*]thiophene 1-oxides.



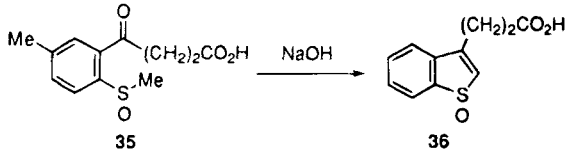
32

The reaction of diphenyldiazomethane with dichlorosulfine affords the benzo[*b*]thiophene 1-oxide **31a** in 55% yield. Several diarydiazomethanes also reacted with dichlorosulfine in a similar manner to give benzo[*b*]thiophene 1-oxide derivatives. The proposed mechanism involves a 1,3-dipolar cycloaddition followed by loss of N_2 to give the episulfoxide intermediate **33**, which then rearranges to **31a** via an electrophilic aromatic substitution.[37] Thus, the episulfide **34**, produced by reaction of diphenyldiazomethane with thiophosgene, also produces **31a** on oxidation with MCPBA via **33**, though in 9% yield. In harmony with the above mechanism, addition of dichlorocarbene to diphenylsufine also affords **31a** via **33** though in low yields.[38]



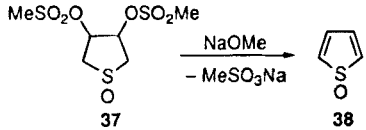
33 34 31a

Intramolecular condensation of **35** has been claimed to give the benzothiophene 1-oxide **36**.[39]

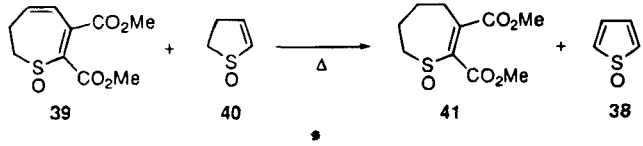


35 36

Although the formation of the parent thiophene 1-oxide **38** in dilute solution by elimination of methanesulfonic acid from **37** was claimed in 1965,[40] there is some doubt as to the true formation of this species; the reported UV data of **38** are not in harmony with those of **2a**.[1] Although it was also claimed that disproportionation between **39** and **40** afforded **41** and **38**, no evidence was given for the formation of **38**.[41]

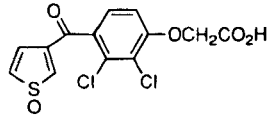


37 38



39 40 41 38

A recent study provided the first evidence for the formation of thiophene 1-oxides such as **6a** and **42** as reactive metabolites of thiophene-containing compounds.[42]



42

Transient formation of thiophene 1-oxides will also be discussed in the section of reactions of thiophene 1-oxides, in connection with their chemical trapping.

3. STRUCTURES

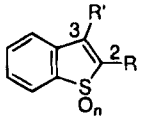
Until now, few data are available on the ^1H and ^{13}C NMR spectra of monocyclic thiophene 1-oxides. The C_3 proton of **2a** appears at δ 6.08; the corresponding signals of the thiophene **1a** and its 1,1-dioxide appear at δ 6.46 and 6.16, respectively.[1] The C_3 protons of **4**,[2] **8a**, **8b**, and **8c**[3] are observed at δ 6.94, 6.82, 6.71, and 6.76, respectively. The ring carbon signals of **8a** appear at δ 137.9 and 161.5.[3]

The ^{13}C NMR spectra of a series of benzo[*b*]thiophenes and the corresponding 1-oxides and 1,1-dioxides have been determined.[43] Table 1 summarizes the chemical shift values of the C_2 and C_3 carbons of these compounds. Based on these data, the authors reached the conclusion that the double bond C_2–C_3 in the 1,1-dioxides is more ethylenic in character than in either the 1-oxides or the thiophenes.

The ^{13}C NMR assignments of all carbons of dibenzothiophene and its 5-oxide have been carried out using deuterated derivatives and lanthanide shift reagents, and the chemical shifts and coupling constants have been discussed as a function of the nature of the central ring.[44]

The strong S-O stretching absorptions of the monocyclic 1-oxides **2a**[1], **4**[2], **5**[33], **8a**, **8b**, and **8c**[3] appear at 1050, 1050, 1045, 1048, 1046, and 1058 cm^{-1}, respectively, a normal range for sulfoxides, and those of a series of benzo[*b*]thiophenes were observed in the range of 1010–1080 cm^{-1}

TABLE 1 Chemical Shift Values (δ) of Benzo[*b*]thiophenes and the Corresponding 1-Oxides and 1,1-Dioxides



	n = 0		*n* = 1		*n* = 2	
	C_2	C_3	C_2	C_3	C_2	C_3
R = Me, R = H	140.7	121.7	150.6	128.7	140.4	125.8
R = Cl, R′ = H	124.5	122.9	143.5	129.9	129.7	126.5
R = Br, R′ = H	115.4	126.5	131.5	134.3	122.7	130.9
R = Ph, R′ = H	144.3	119.4	152.3	126.4	142.6	123.6
R = H, R′ = Me	121.8	131.9	132.1	145.2	125.8	142.9
R = H, R′ = Cl	120.6	121.1	132.4	139.2	125.9	140.1
R = H, R′ = Br	123.4	107.7	135.4	128.4	129.9	129.6
R = H, ′ = Ph	122.8	137.9	132.6	148.4	125.7	145.9
R = R, ′ = Me	133.6	127.0	143.7	136.5	134.1	133.9
R = R′ = Cl	119.7	126.1	131.1	134.1		

depending on the substituent on C_2 and C_3.[5] ThMe S-O stretching frequencies of the thiophene oxides **38**, **6a**, and **21** and of related sulfoxides have been calculated at the RHF/6–31 G (d,p) level.[45]

The only reliable UV-vis spectra of monocyclic 1-oxides are those of the 1-oxide **2a**, with two absorptions at 251 (ε 1500) and 323 nm (1950) in octane and 245 (ε 1200) and 319 nm (2300) in MeOH.[1] A range of 2- and/or 3-substituted benzo[*b*]thiophene 1-oxides also show two absorptions in the ranges of 222–236 and 320–336 nm,[5,6,36,37] whereas the parent benzo[*b*]thiophene 1-oxide **6a** has been reported to show an absorption at 320 nm (ε 2700).[7]

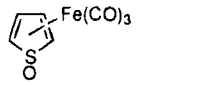
In the mass spectra, the most intense peak appears at *m/z* M-16, which results from loss of the oxygen atom of the sulfoxide moiety from the molecular ion.[5,19,23] The mechanism of this fragmentation is unknown.

An ESR study of dibenzothiophene **20** and its 5-oxide **21** and 5,5′-dioxide in a glassy solution has been reported.[46,47] The spectroscopic singlet and triplet energies of **21** have been determined as 85 and 61 kcal/mol, respectively, from the fluorescence and phosphorescence spectra at 77 K in ether/isopentane/ethanol, and the triplet EPR of **21** was also determined at 15 K in THF.[48]

The photoelectronic spectra of a series of benzo[*b*]thiophene 1-oxides and 1,1-dioxides have been recorded and the ionization potentials determined in connection with the understanding of the mechanism of 1,3-dipolar cycloadditions of these compounds.[49]

The ESCA spectra of iron tricarbonyl complexes such as **42** and **43** have been reported, assigned, and interpreted in the light of simple bond theories.[50] However, the synthetic method for **42** seemingly still remains unpublished.

An X-ray single crystal structure analysis has been carried out for the monocyclic thiophene 1-oxides **4**[2] and **5**.[33] Although, for **5**, a precise determination of the ring conformation and of the S-O and S-C distances was not possible because of structural disorder, good crystallographic data were obtained for **4**. The sulfur atom exhibits pyramidalization and lies outside the plane formed by the four thiophene carbon atoms by 0.278 Å, while



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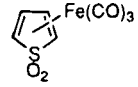

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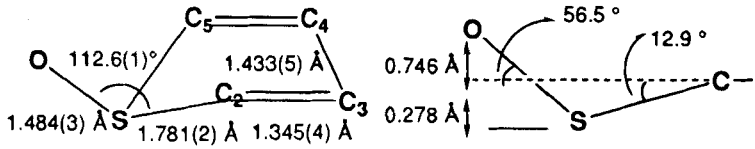


FIGURE 1 The Structure of 2,5-Diphenylthiophene 1-Oxide **4**

the oxygen atom lies outside this plane in the opposite direction by 0.746 Å. These data, as well as the main bond length and angle data given in Fig. 1, are globally in good agreement with those predicted from MNDO semi-empirical[51] and *ab initio*[52] calculations. The pyramidal configuration of the sulfur atom of **4** makes it unlikely to be aromatic. However, since the deviation from planarity is small, the sulfur and oxygen atoms being only slightly displaced out of the plane renders the possibility that some π-delocalization may still occur. This structure of dibenzothiophene 5-oxide **21** has also been determined by X-ray diffraction.[51] Selected bond angle and bond length data of **21** are given in Fig. 2. Figs. 3 and 4 contain the optimized geometries for the parent thiophene 1-oxide determined by MNDO[51] and *ab initio*[52] calculations. These calculation results are globally in good agreement with the experimental results for the thiophene oxides **4**, **5**, and **21**.

As described above, X-ray diffraction studies[2,33,51] have revealed the pyramidal configuration of the sulfoxide moiety in **4**, **5**, and **21** in the crystalline state. Also in solution, the sulfur atom of **2b** exists in a pyramidal configuration. Thus, in the ^{1}H NMR spectrum of **2b** at −10 °C, the geminal methylene protons in the side chain are magnetically non-equivalent because of the anisotropy of the sulfoxide functionality, which in turn

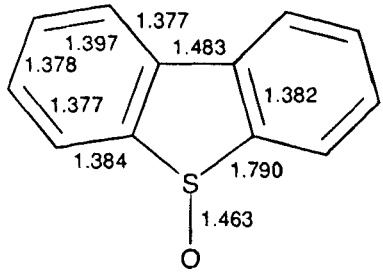


FIGURE 2 Bond Length (Å) Data of Dibenzothiophene 5-Oxide **21**

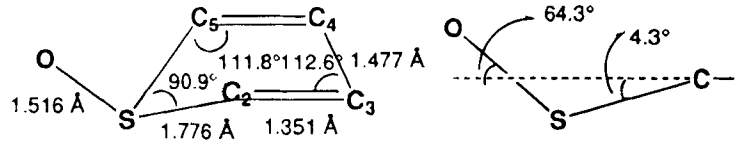


FIGURE 3 The MNDO Optimized Geometry of the Parent Thiophene 1-Oxide

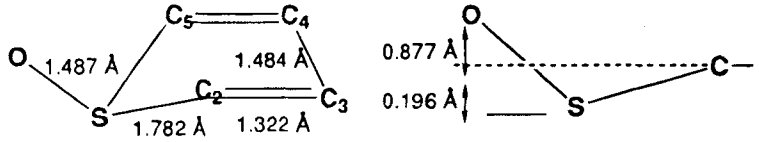
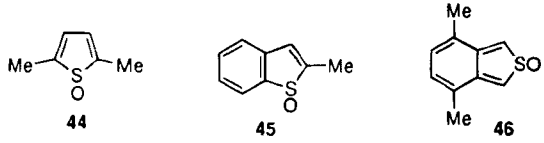


FIGURE 4 Geometries of Thiophene 1-Oxide Obtained using the STO-3G* Basis Set

reveals that the sulfur atom is pyramidal.[1] The free energy of activation of $\Delta G^{\neq}_{26}$, obtained from the coalescence temperature (26 °C), is 14.8 kcal/mol. The lowering of the inversion barrier (by ca. 20 kcal/mol) compared to those of common sulfoxides might be ascribed to the delocalization energy of the planar thiophene 1-oxide in the transition state.

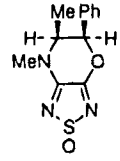
The barriers to pyramidal inversion for the 1-oxides **44**, **45**, and **46**, obtained by CNDO/2 semi-empirical calculations, are 13.3, 19.4, and 2.2 kcal/mol, respectively.[53]



44 **45** **46**

From a rate study of the epimerization of **47** in CD_3CN at 120 °C, the standard free energy of activation for the inversion at the sulfur was determined to be $\Delta G^{\neq}_{120}$ = 33 kcal/mol. This barrier is about the same as that of diaryl sulfoxides (36 kcal/mol) and much higher than that of thiophene 1-oxide **2b** (14.8 kcal/mol).[54] In the same paper, the calculated barriers of inversion of **2b** and **47** were reported to be 19.6 and 31.9 kcal/mol, respectively.

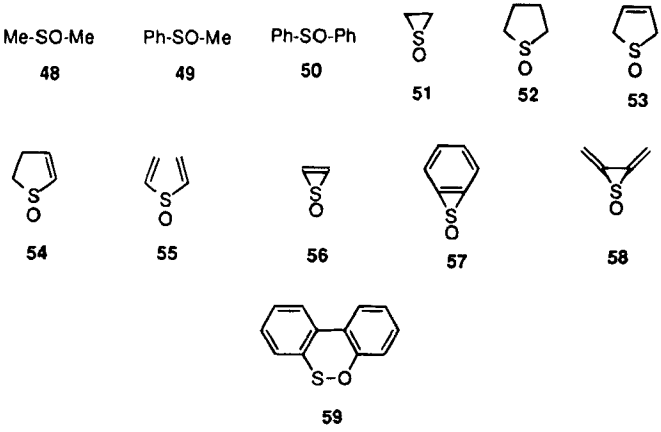
Very recently, an *ab initio* computational study on the effects of conjugation and aromaticity on sulfoxide bonds has been reported.[45] In this study the sulfoxides **38**, **6a**, **21**, and **48-58** were employed as model com-



47

pounds. The S-O bond dissociation energy of sulfoxides in which the sulfur atom is included in a formally aromatic ring (*e.g.*, **38**) was found to be decreased by as much as 25 kcal/mol, compared to DMSO. A complementary effect was observed for sulfoxides in which the sulfur atom is included in a formally antiaromatic ring (e.g., thiirene oxide **56**), in which the S-O bond energies are increased by as much as 15 kcal/mol. Both effects are attenuated by benzoannulation (*e.g.*, **6a** and **57**). An examination of the calculated geometries and isodesmic reactions with pure hydrocarbons led to the conclusion that the observed effects are due to a severe disruption of the (anti) aromaticity of the sulfur-containing ring upon oxidation. The cyclic sulfoxides (*e.g.*, **38** and **56**) appear to be neither significantly aromatic nor antiaromatic by energetic considerations. No significant S-O bond strength effect was observed for simple conjugation. The inversion energies of the sulfoxides **38**, **6a**, **21**, **48** (DMSO), **51**, **56**, and **57**, have also been calculated to be 11.2, 23.9, 32.3, 50.4, 76.6, 31.8, and 98.6 kcal/mol, respectively.

Interestingly, MNDO-PM 3 calculations showed that compound **59** is more stable than its isomer **21** by 8.6 kcal/mol. The same study showed that protonation to **21** would occur on the oxygen atom rather than on the sulfur atom.[55]



48 **49** **50** **51** **52** **53**

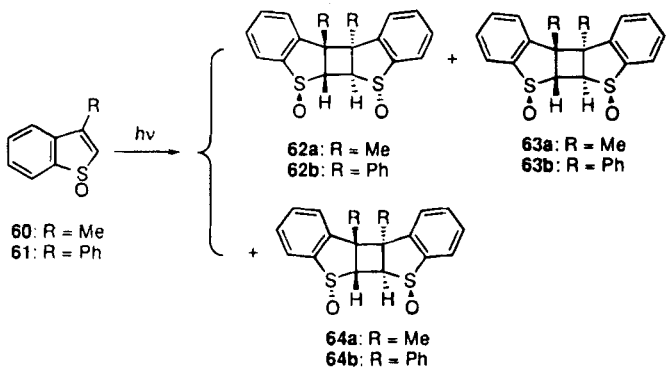
54 **55** **56** **57** **58**

59

4. REACTIONS

4.1. Photodimerization

The photochemical behavior of various benzo[*b*]thiophene 1-oxides (3-methyl, 3-phenyl, 2-methyl, 2-phenyl, 2,3-dimethyl, 2-chloro, 2-bromo, 3-chloro, and 3-bromo derivatives) has been studied in benzene as solvent.[56,57] The bromo and chloro derivatives gave no identifiable products. The 3-methyl- and 3-phenyl derivatives, **60** and **61**, gave three head-to-head anti photodimers, **63a-c** and **64a-c**, which differ only by the stereochemistry of the S-O bond. The kinetics of the photodimerization of the 3-methyl derivative **60** was studied as a function of the concentration of substrate, triplet quencher, and triplet sensitizer. A monomeric excited triplet was proposed as the precursor to the observed products. Meanwhile, the 2-methyl derivative led to a photoreduction which gave 2-methylbenzo[*b*]thiophene, probably through an excited triplet. The 2-phenyl derivative gave a mixture of the photodimer (head-to-head) and 2-phenylbenzo[*b*]thiophene. The behavior of these thiophene 1-oxides is different from that of the corresponding 1,1-dioxides, which led to a mixture of head-to-head and head-to-tail dimers for the 2-substituted compounds and the head-to-head dimer for the 3-substituted ones.



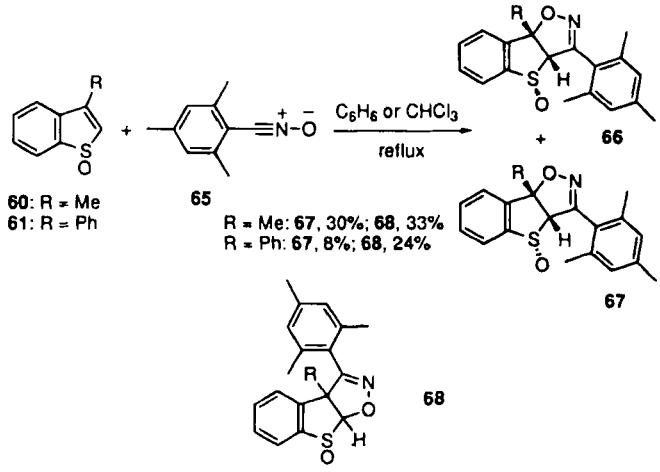
For **60**: direct irradiation (313 nm); total yield of **62a-64a**, 50%
Ph_2CO-sensitized irradiation (366 nm); total yield of **62a-64a**, 80%

For **61**: Ph_2CO-sensitized irradiation (366 nm); total yield of **62b-64b**, 40%

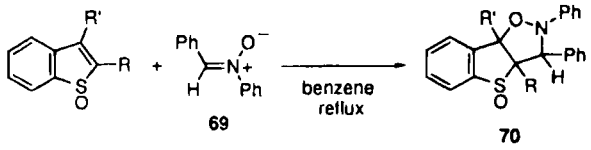
4.2. 1,3-Dipolar Cycloaddition

A series of benzo[*b*]thiophene 1-oxides including **60** and **61** undergo 1,3-dipolar cycloaddition with mesitonitrile oxide **65**.[49,58] These compounds

are much more reactive toward **65** than the original thiophenes and show reactivities comparable with those of the corresponding 1,1-dioxides. Among the two possible regioisomers, only one regioisomer, **66** and **67** is formed; no regioisomers **68** were obtained. No stereoselectivity was observed, however, giving both *syn* and *anti* adducts **66** and **67**. The major factor that governs the regioselectivity would be the HOMO (dipolarophile)-LUMO (dipole) interaction.



Benzo[*b*]thiophene 1-oxides also undergo 1,3-dipolar cycloaddition with *N*,α-diphenyl nitrone **69** to give the adducts **70**.[59] The stereochemical course of this reaction has been investigated in detail.

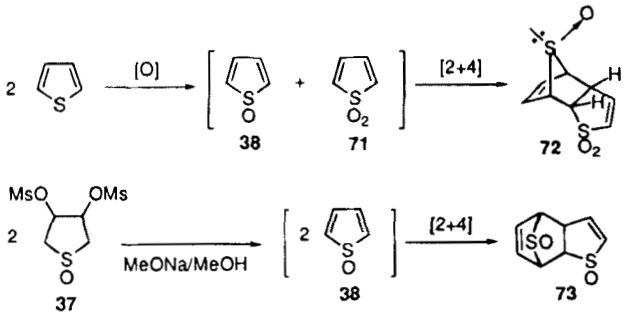


4.3. [2 + 4] Cycloaddition

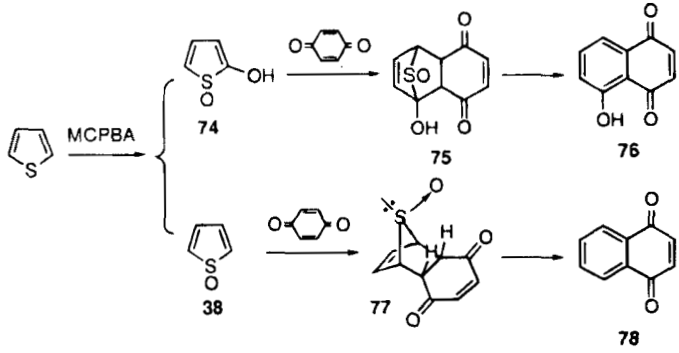
Thiophene 1-oxides are more reactive as diene than the corresponding 1,1-dioxides.

Upon oxidation, thiophene undergoes a Diels-Alder dimerization to give the thiophene sesquioxide **72**[60-63] whose structure and streochemistry

have been assigned on the basis of the NMR spectra.[64] Treatment of the mesylate **37** with MeONa in MeOH at room temperature affords a 15% yield of a compound with the molecular formula of $(C_4H_4SO)_2$ to which the structure **73** has been assigned.[40] It is produced by a Diels-Alder dimerization of **38**.

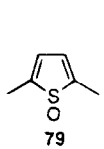


The oxidation of thiophene with two equivalents of MCPBA in the presence of benzoquinone at 0 °C in CH_2Cl_2 gives juglone **76** and naphthoquinone **78** in 21 and 7% yields, respectively.[65] Compounds **76** and **78** would be formed as depicted below. The Diels-Alder adduct **77** was isolated in 21% yield, when the oxidation was carried out in $CHCl_3$, although the adduct **75** has never been isolated. Later, the stereochemistry of **77** was unambiguously determined by X-ray single crystal structure analysis.[66] The mechanism for the formation of **74** is not clear. The thiophene 1-oxide intermediate **38** was also captured by 1,4-naphthoquinone to give anthraquinone,

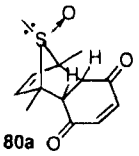


though it was not captured by phenylacetylene, ethyl propiolate, and acrylonitrile. Oxidation of 2-methyl-, 3-methyl-, and 2,5-dimethylthiophene in the presence of benzoquinone also gives the corresponding adducts in 24, 18, and 33% yield, respectively, although 2-methoxycarbonyl-, 2,4-diphenyl-, and 2-phenylthiophene failed to give the adducts.

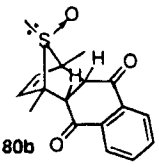
In connection with the π-facial diastereoselectivity encountered in Diels-Alder reactions, where the addends possess two different faces, a series of dienophiles have been allowed to react with 2,5-dimethylthiophene 1-oxide **79**, generated *in situ* by MCPBA oxidation. Benzoquinone, 1,4-naphthoquinone, tetracyanoethylene, *N*-phenylmaleimide (NPM), and 2-chloroacrylonitrile react with **79** to give the adducts **80a-d** in 10–30% yield.[66] In all cases, the *syn* adducts (with respect to the sulfoxide oxygen) were formed exclusively, revealing that the dienophiles added to the *syn* oxygen face. Phenylacetylene, methyl vinyl ketone, dimethyl maleate, and 2,3-dimethylmaleic anhydride failed to give the adducts. Dimethyl acetylenedicarboxylate (DMAD) gave dimethyl 3,6-dimethylphthalate directly by loss of SO from the adduct. An AM1 calculational study on the Diels-Alder reaction of maleic anhydride to C_5-substituted pentamethylcyclopentadienes and **79** was carried out to ascertain the factors controlling the π-facial selectivities and relative reactivities.[67]



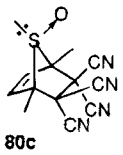
79



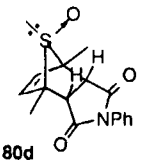
80a



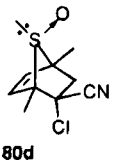
80b



80c



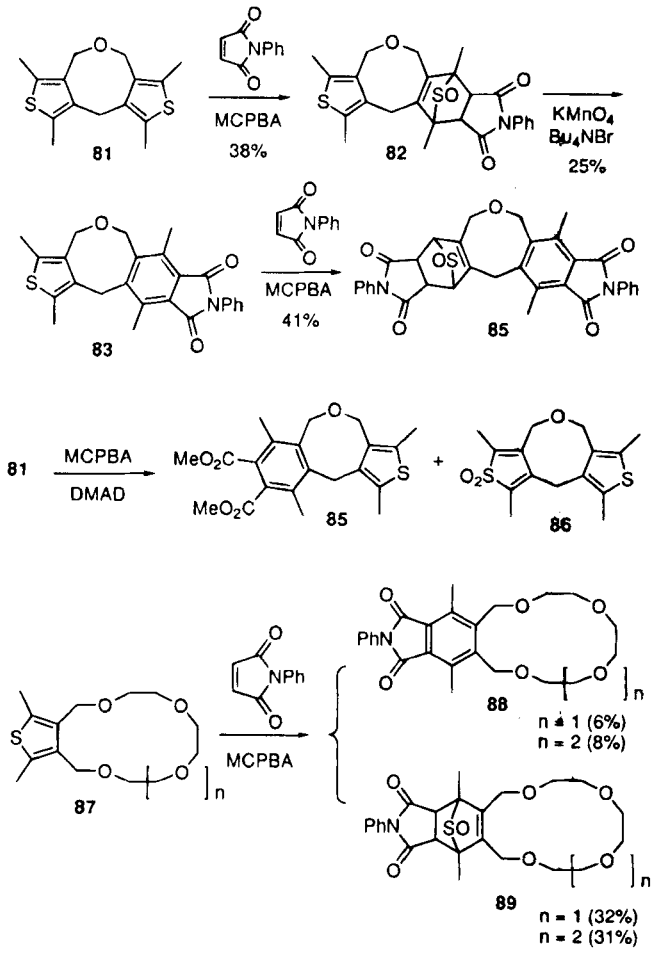
80d



80d

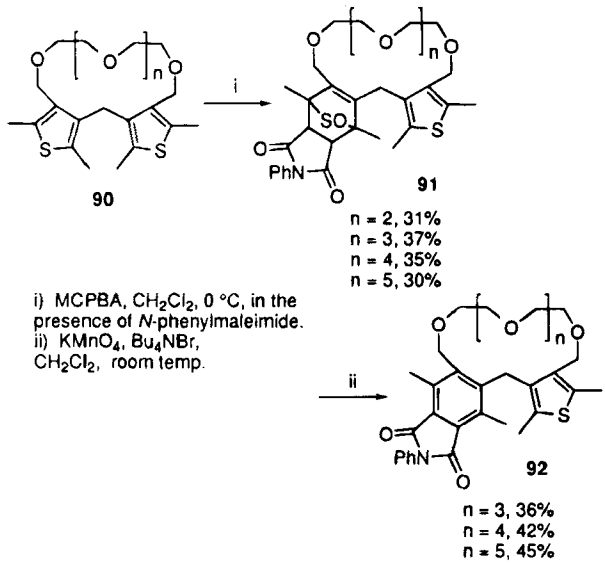
Cycloadditions of thiophene 1-oxide intermediates have been utilized the conversion of thiopheno crown ethers to phthalimido crown ethers.[68] Oxidation of **81** with MCPBA in the presence of *N*-phenylmaleimide (NPM) affords the sulfoxy bridged compound **82**, which is oxidatively converted to **83**. Oxidation of **83** in the presence of NPM gives **84**. The oxida-

tion carried out in the presence of DMAD directly provides **85** because SO is oxidatively eliminated from the sulfoxy bridged adduct under the reaction conditions. In a similar way, the thiopheno crown ethers **87** have been converted to **88** and **89**, and **90** to **92** via **91**.



4.4. Reactions on the Sulfur or Oxygen Atom

As a natural consequence, further oxidation of thiophene 1-oxides affords the corresponding 1,1-dioxides.

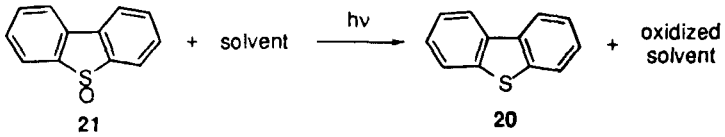


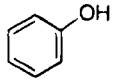
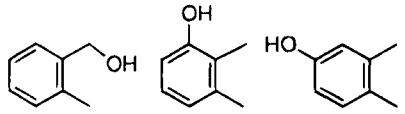
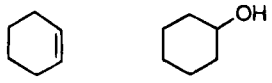
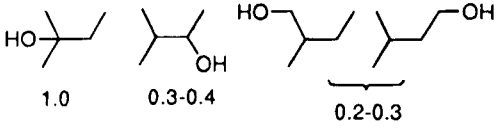
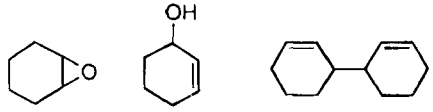
The S-O bond dissociation energy of thiophene 1-oxide **38** is decreased by as much as 25 kcal/mol, compared to DMSO.[45] Therefore, reduction to the corresponding thiophenes, which results in the recovery of aromaticity, is expected to take place easily. Until now such reductions have only been reported for benzo[*b*]thiophene 1-oxides and dibenzothiophene 5-oxides. Dibenzothiophene 5-oxide **21** is reduced to dibenzothiophene **20** in good yields by iodide ion (acid-catalyzed),[69] elemental sulfur,[70] $SnCl_2$/HCl,[71,72] sodium bis(2-methoxyethoxy)aluminum hydride,[73] $NaBH_4$ (catalyzed by *meso*-tetraphenylporphinatoiron: TPPFe(III)Cl-catalyzed),[74,75] 1-benzyl-1,4-dihydronicotinamide (catalyzed by TPPFe(III)Cl).[74,75] 2-Methyl-, 3-methyl-, 2,3-dimethyl-, 2-phenyl-, 3-phenylbenzo[*b*]thiophene are reduced quantitatively to the corresponding benzo[*b*]thiophenes over presulfided $CoO\text{-}MoO_3/Al_2O_3$ hydrodesulfurization catalyst.[76] Reaction of **21** with $POCl_3$ and $SOCl_2$ gave **20** and chlorinated **20**.[77] Catalytic hydrodesulfurization of benzo[*b*]thiophene 1-oxides and **21** over $CoO\text{-}MoO_3/Al_2O_3$ catalyst has also been reported.[78,79] Desulfurization of **21** with Ni-containing reducing agents produces biphenyl.[80]

Dibenzothiophene 5-oxide **21** is also photochemically reduced to **20**.[81] The authors suggest that the reduction proceeds by way of a dimer of **21**, which decomposes to two molecules of **20** and a molecule of singlet oxygen ($^1O_2$). The evidence for the generation of $^1O_2$ was the isolation of 2-cyclo-

hexenol upon photolysis in the presence of cyclohexene, followed by reduction with NaI. However, it is now recognized that cyclohexene is not an efficient quencher of $^1O_2$. Recent investigators found that $^1O_2$ is not formed to any detectable extent and that the reduction step is unnecessary for the formation of 2-cyclohexanol.[82] It was now found that the efficient oxenoid functionalization of a variety of hydrocarbons takes place as a result of photolysis of **21**. No discussion of the mechanism was given in this preliminary report. The oxidation products of hydrocarbon solvents (substrates) on photolysis of **21** are shown in Table 2.

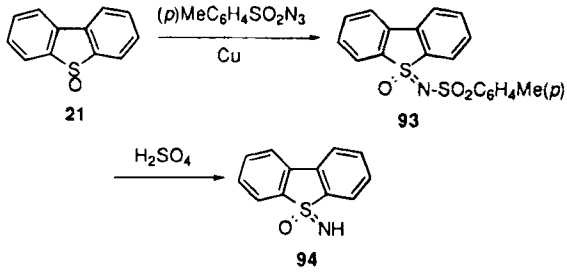
TABLE 2 Oxidation Products Observed on Photolysis of **21**



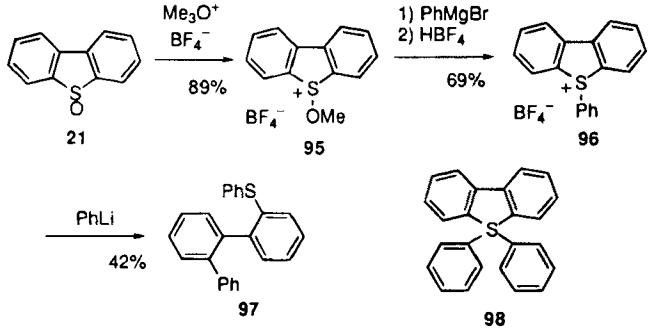
Solvent (Substrate)	*Total Yield*	*Product and Product Ratio*
	0.60–0.65	
	0.55–0.60	 1.0 0.15-0.17 0.15-0.17
	0.95–1.00	 1.0 1.9-2.2
	0.40–0.45	 1.0 0.3-0.4 0.2-0.3
	0.65–0.70	 1.0-1.4 1.0 0.2-0.3

[a] Total yield is expressed as fractions of the yield of **20**.

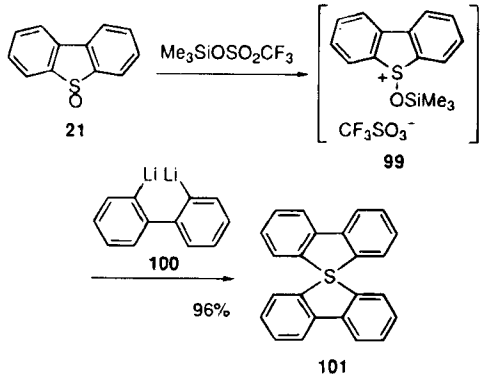
Copper-catalyzed reaction of *p*-toluenesulfonyl azide with **21** in methanol affords the *N*-tosylsulfoximide **93** in 62% yield, which, on hydrolysis, is converted to the sulfoximide **94** in 85% yield.[83]



Methylation of **21** with trimethyloxonium tetrafluoroborate gave the sulfonium salt **95**, which was then converted to another sulfonium salt **96** by reaction with PhMgBr, followed by treatment with tetrafluoroboric acid. The reaction of **96** with PhLi failed to give the expected sulfurane **98**, but gave the biphenyl derivative **97** which resulted from ligand coupling of **98**.[84] Similar results were obtained with dibenzothiophene 5-oxide carring a methoxy substituent on the benzene ring.[85]

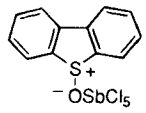


Recently, the preparation of a stable sulfurane with four C-S bonds was achieved starting from **21**.[86] Trimethylsilylation of **21** followed by reaction of the resulting sulfonium salt **99** with 2,2′-dilithiobiphenyl **100** afforded the sulfurane **101** as orange crystals, mp. 114-118 °C (dec.), in 96% yield. The structure of **101** was established by spectroscopic means and X-ray diffraction.[86]



21 99 100 101

Treatment of **21** and related compounds with $SbCl_5$ gives stable 1:1 complexes such as **102**.[87]



102

Sulfoxides are known to undergo concurrent oxygen exchange and racemization reactions with various reagents. An oxygen exchange reaction of **21** with dinitrogen tetraoxide has been reported.[88]

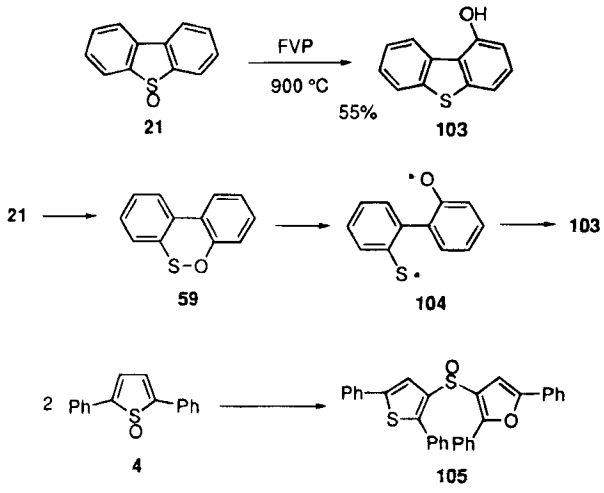
Flash vacuum pyrolysis of **21** affords 1-hydroxydibenzothiophene **103** as the major product.[89] A mechanism involving ring expansion and intramolecular radical substitution of the intermediate **104** has been presented. As already described, a calculational study predicted that **59** is more stable than **21** by 8.6 kcal/mol.[55]

During the preparation of 2,5-diphenylthiophene 1-oxide **4** formation of **105** was observed at the expense of **4** at the later reaction stage.[2] The mechanism of its formation is not clear.

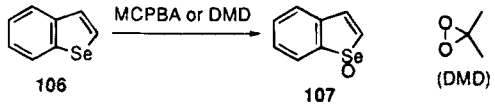
5. SELENOPHENE 1-OXIDES

Until now, only benzo and dibenzo derivatives have been synthesized.

Benzo[*b*]selenophene 1-oxide **107** has been prepared by oxidation of benzo[*b*]selenophene **106** with MCPBA[90] and dimethyldioxirane

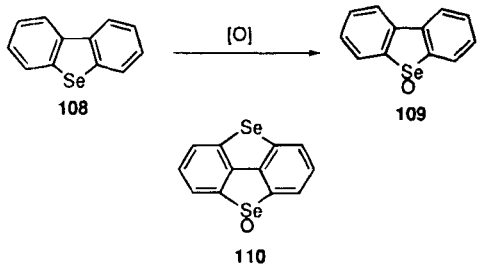


(DMD)[91] in 50–60% and 88% yield, respectively. Compound **107** is a thermally rather labile crystalline compound and decomposes above 76 °C, but is more stable than the corresponding thiophene 1-oxide **6a** which is only stable in dilute solution. The ^{77}Se NMR signal of **107** appears at δ 943. In the IR spectrum, the Se-O stretching absorption appears at 780 cm^{-1}. It is soluble in aqueous NaOH probably because the hydrate of **107** behaves as proton acid. It is easily reduced to **106** by treatment with aqueous $NaHSO_3$.

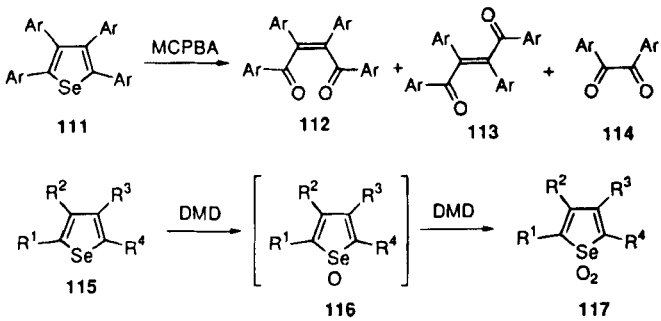


Dibenzoselenophene 5-oxide **109** has been prepared by peracid[92] and electrochemical[93] oxidation of dibenzoselenophene **108**. The dibenzo derivative **110** has also been prepared by MCPBA oxidation of the corresponding selenophene derivative.[30]

The authors' group has investigated the oxidation of tetraarylselenophenes **111** with MCPBA and some other oxidizing agents.[90] These oxidations failed to give selenophene 1-oxides or 1,1-dioxides, but gave selenium-free products such as **112-114** which result from ring opening of



the selenophenes. After much effort, this group has found that the oxidation of a variety of selenophenes **115** with DMD affords the corresponding 1,1-dioxides **117** in good yields. However, the corresponding selenophene 1-oxides **116** could not be isolated in pure form because of their labile nature.



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