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The Latest Advances in Chemistry of Thiophene 1-Oxides and Selenophene 1-Oxides

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THE LATEST ADVANCES IN CHEMISTRY OF THIOPHENE 1-OXIDES AND SELENOPHENE 1-OXIDES*

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Immediately after we had reviewed the chemistry of thiophene 1-oxides in 1996 (*Sulfur Reports*, **16**), very rapid and important progress was achieved in this field. The present article provides a supplement to the above review. The chemistry of thiophene sulfilimines (1-imino-1,1-dihydrothiophenes) as well as that of selenophene 1-oxides is also reviewed.

Keywords: Thiophene 1-oxides; selenophene 1-oxides; 1-imino-1,1-dihydrothiophenes; oxidation; cycloaddition

CONTENTS

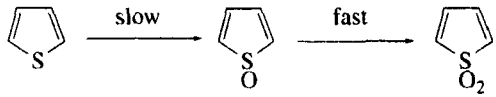
* Supplement to the review of *Sulfur Reports*, **19**, 1996.

1. INTRODUCTION

Immediately after we had written a review on the chemistry of thiophene 1-oxides in 1996,[1,2] important synthetic methods for thiophene 1-oxides were developed, thus resulting in the rapid progress of the chemistry of thiophene 1-oxides. This prompted the author to make a supplement to the above review. The chemistry of thiophene sulfilimines (1-imino-1,1-dihydrothiophenes) as well as that of selenophene 1-oxides is also reviewed. A *Chemical Abstracts* search was carried out in August, 1999. Literatures cited in the 1996 review were not included unless essentially important.

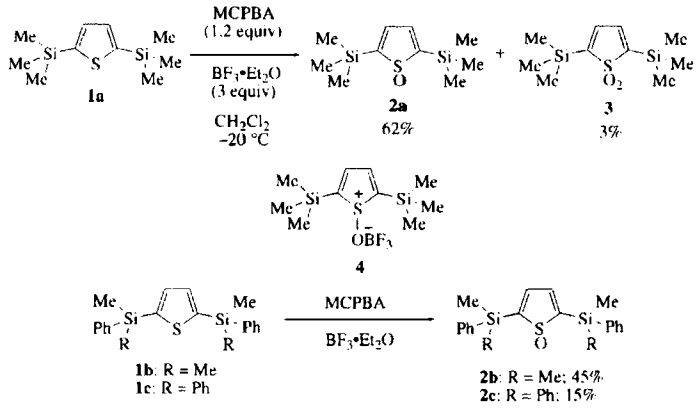
2. SYNTHESIS OF STABLE THIOPHENE 1-OXIDES

Oxidation of thiophenes to thiophene 1-oxides, a process of the virtual loss of the aromaticity of thiophenes, is much slower than oxidation of thiophene 1-oxides to thiophene 1,1-dioxides. Accordingly, it is very difficult to quench the oxidation of thiophenes at the 1-oxide stage, and this renders preparation of thiophene 1-oxides virtually impossible by oxidation of thiophenes, with one exception.[3] Recently, two methods, which overcame this difficulty, were developed.

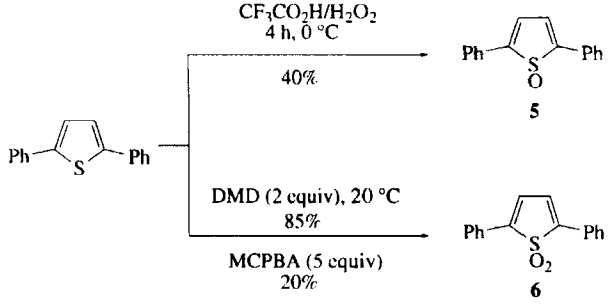


Furukawa *et al.* oxidized 2,5-bis(trimethylsilyl)thiophene (**1a**) with 1.2 equivalents of *m*-chloroperoxybenzoic acid (MCPBA) in the presence

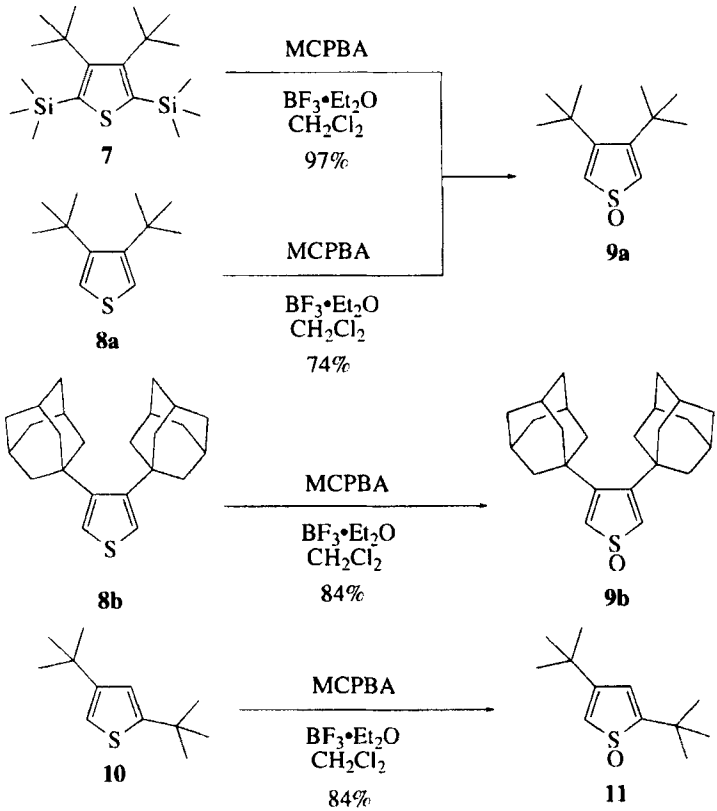
of $BF_3 \cdot Et_2O$, which furnished the thiophene 1-oxide (**2a**) in 62% yield along with a small amount of the 1,1-dioxide (**3**).[4–6] In this case, electrophilic oxidation of **2a** to **3** by MCPBA is impeded by decreased electron density on the sulfur atom due to the formation of the complex (**4**) with BF_3. Actually, **4** was isolated and its structure was determined by X-ray crystallographic analysis.[7] In similar ways, oxidation of (**1b**) and (**1c**) gave (**2b**) and (**2c**), respectively, in moderate yields.[5,6]



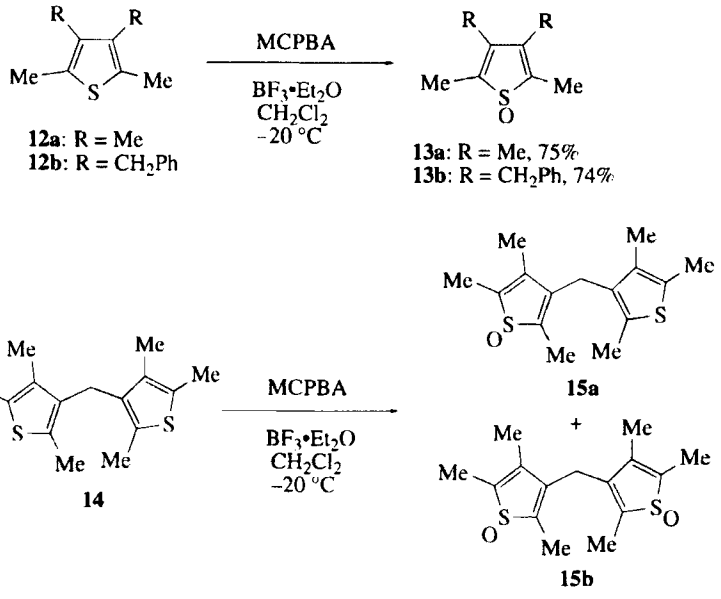
On the other hand, the group of Dansette and Mansuy developed the oxidation of thiophenes with H_2O_2 in CF_3CO_2H–CH_2Cl_2 (1 : 2).[8,9] The oxidation of 2,5-diphenylthiophene by this procedure permitted preparation of thermally unstable 2,5-diphenylthiophene 1-oxide (**5**). The oxidation of the same thiophene with dimethyldioxirane (DMD) or MCPBA afforded the 1,1-dioxide (**6**). Successful synthesis of **5** would be thus explained as a result of protonation of a strong acid, CF_3CO_2H, to the oxygen atom of **5**, which retards the oxidation of **5** to **6**.



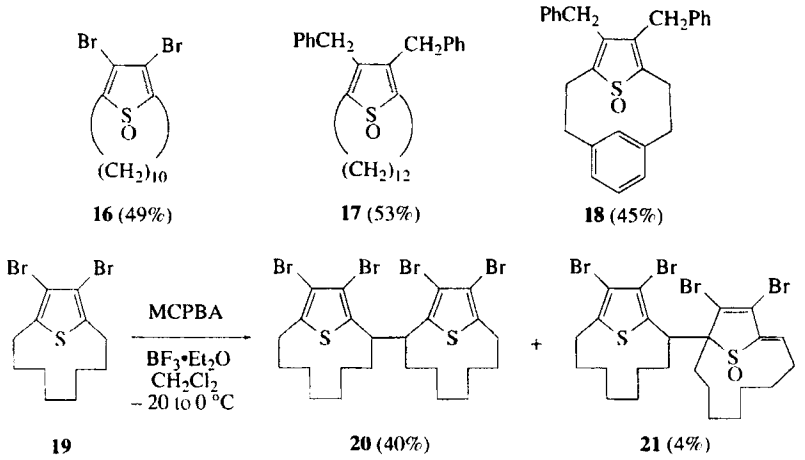
Application of the Furukawa procedure to the sterically highly congested thiophene (**7**) resulted in the formation of thiophene 1-oxide (**9a**), with unexpected concomitant desilylation, in 97% yield.[10] The 1-oxide **9a** is thermally highly stable; it was recovered in 90% yield with formation of thiophene (**8a**) in 8% yield when heated in boiling chlorobenzene for 24 h. This prompted the oxidation of the thiophene **8a** under the same conditions, which provided **9a** in 74% yield. In similar ways, thermally stable thiophene 1-oxides (**9b**) and (**11**) were synthesized in good yields.



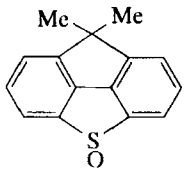
Application of the Furukawa procedure also permitted the preparation of tetrasubstituted thiophene 1-oxides (**13a**) and (**13b**) in good yields.[11,12] Oxidation of two-core thiophene (**14**) gave a mixture of 1-oxides (**15a**) and (**15b**). The yields of **15a** and **15b** depend on the number of equivalents of MCPBA used.



Oxidation of the corresponding thiophenophanes by MCPBA in the presence of $BF_3 \cdot Et_2O$ provided tetrasubstituted thiophene 1-oxides (**16**)–(**18**) in reasonable yields.[13] However, when thiophenophane (**19**) was oxidized under the same conditions, an interesting reaction took place to give compounds (**20**) and (**21**).



Thiophene oxide (**22**), whose structure was determined by X-ray crystallographic analysis, was prepared by oxidation of the corresponding thiophene.[14] The structure of **22**, determined experimentally, was compared to the structure obtained by semiempirical MO calculations (AM1). Dinaphtho derivative (**23**) was also prepared by oxidation of the corresponding thiophene with MCPBA in 85% yield.[15]



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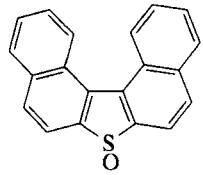

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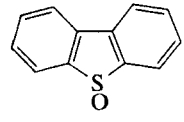

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Dibenzothiophene was used as one of substrates in a number of chemical or photochemical oxidation studies of sulfides to sulfoxides and sulfones.[16] In these reactions, dibenzothiophene 5-oxide (**24**) was the major product or the intermediate leading to the final product.

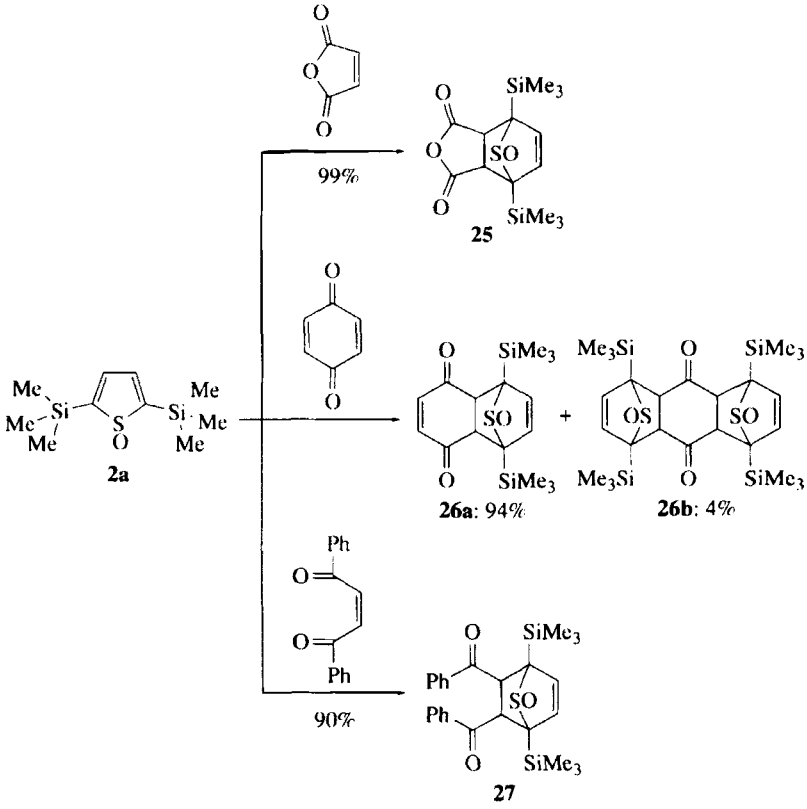
3. REACTIONS

3.1. Reactions at the Double Bonds

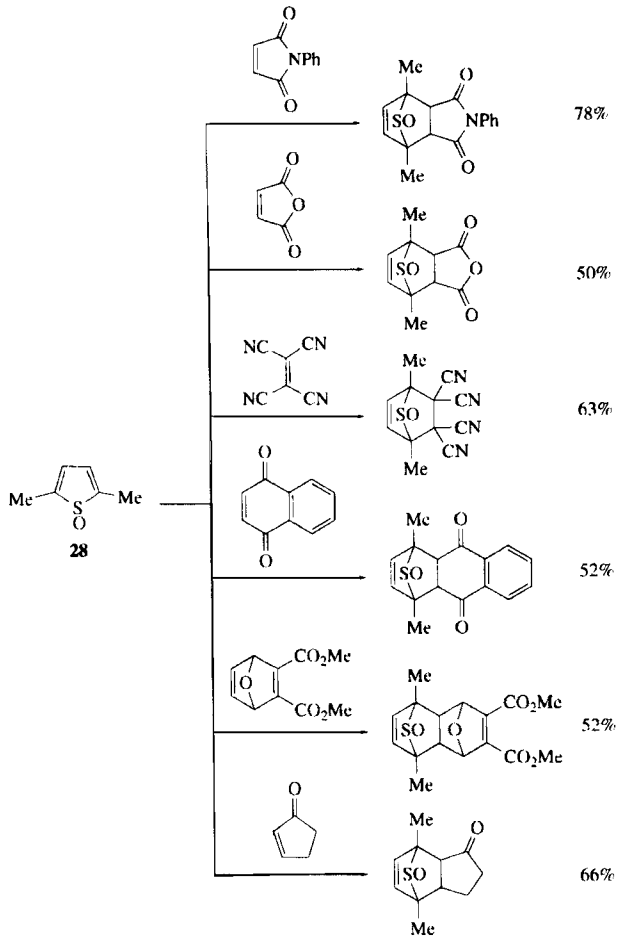
3.1.1. Cycloaddition

The 1-oxide **2a** underwent Diels–Alder reactions with maleic anhydride and *cis*-dibenzoylethylene to give adducts (**25**) and (**27**), respectively, in high yields.[6] The reaction of *p*-benzoquinone with an equivalent of **2a** gave mono-adduct (**26a**) (94%) and bis-adduct (**26b**) (4%), while the reaction with a half-equivalent of **2a** furnished **26a** (43%) and **26b** (53%). The X-ray crystallographic analyses of **25**, **26a**, and **26b** revealed that the stereochemical course of the reaction is exclusively *endo*-orientation and *syn*-direction with

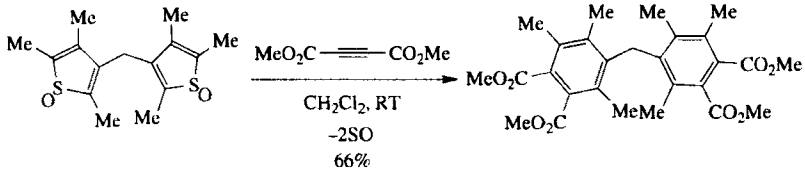
respect to the S–O bond. This stereochemistry agrees with the results obtained by RHF and MP2 MO calculations using the 6–31G(*) basis set.



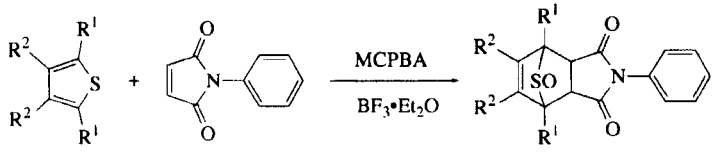
2,5-Dimethylthiophene 1-oxide (**28**) and some other thiophene 1-oxides were prepared *in situ* by the Furukawa procedure and subjected to Diels–Alder reactions with a series of dienophiles.[11,12] Typical examples with **28** are shown below. All cycloadditions gave only a single diastereoisomer as cycloadduct. The reactions showed a high π-facial selectivity, a fact that could be explained by the Cieplak-effect.



Thiophene 1-oxide **15b** furnished the bis-arene (**29**) in 66% yield, with spontaneous elimination of SO of the primary cycloadduct, on reaction with dimethyl acetylenedicarboxylate (DMAD).[12]



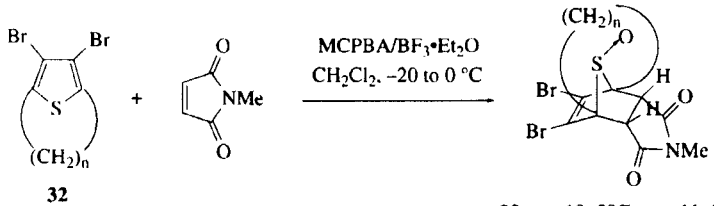
Halogenated thiophenes (**30**) were oxidized by the Furukawa procedure and the resulting 1-oxides were trapped with *N*-phenylmaleimide to provide adducts (**31**) in reasonable yields.[17]



30a: R^1 = Cl, R^2 = H
30b: R^1 = Br, R^2 = H
30c: R^1 = R^2 = Br
30d: R^1 = Me, R^2 = Br

31a: R^1 = Cl, R^2 = H; 40%
31b: R^1 = Br, R^2 = H; 42%
31c: R^1 = R^2 = Br; 45%
31d: R^1 = Me, R^2 = Br; 55%

Thiophenophanes (**32**) and (**34**) were oxidized by MCPBA/$BF_3 \cdot Et_2O$ in the presence of *N*-methylmaleimide to furnish the 1-oxide adducts (**33**) and (**35**), respectively, in good yields.[13] The same oxidation of **34** in the presence of DMAD gave a cyclophane (**36**) with spontaneous elimination of SO from the initial adduct.



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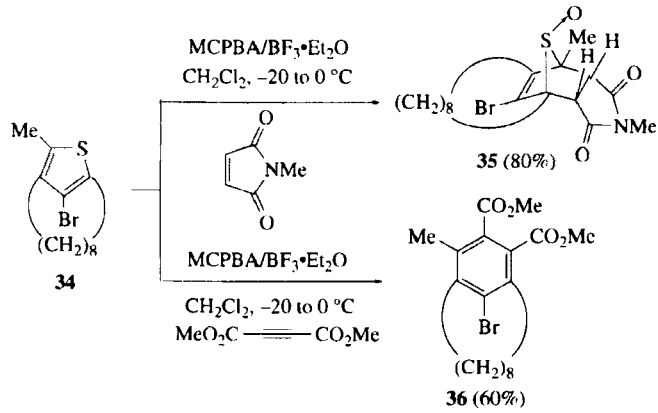
33: n = 10, 58%; n = 11, 90%; n = 14, 42%



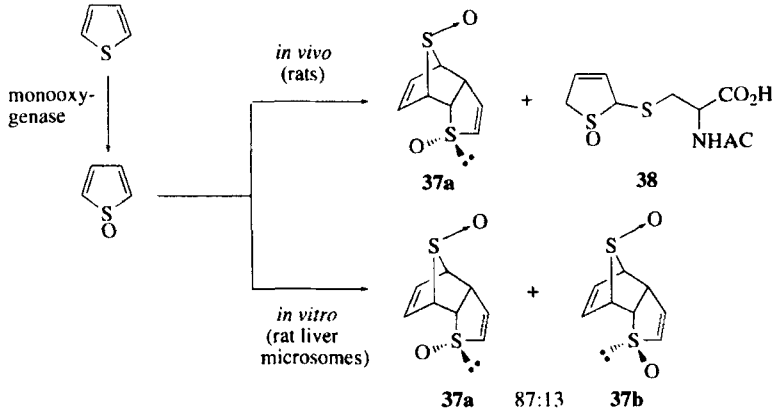
34

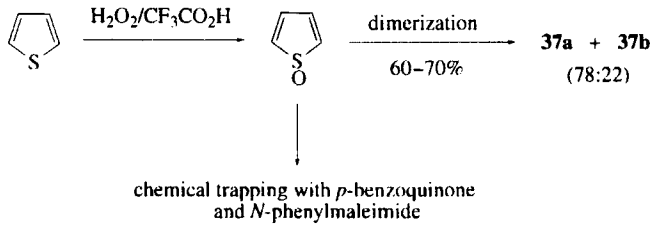
35 (80%)

36 (60%)

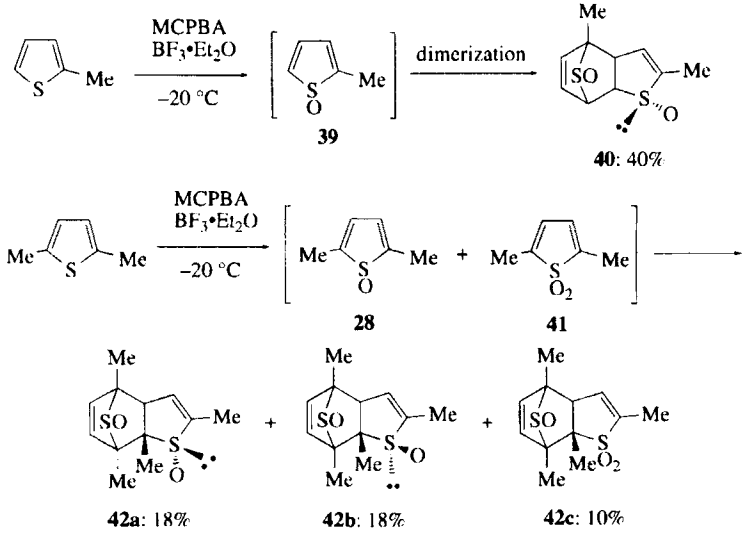
3.1.2. Self-dimerization

Direct evidence for the involvement of thiophene 1-oxide as a key intermediate in the metabolism of the parent thiophene in rats was obtained from the isolation of thiophene 1-oxide dimers both *in vitro* (isolation of the dimers **37a** and **37b** by oxidation of thiophene with rat liver microsomes) and *in vivo* (isolation of **37a** from rat urine).[18,19] *In vivo* compound (**38**), which was formed through Michael addition of glutathione to the thiophene 1-oxide, was also obtained. The structure of these dimers was established after an original preparation of identical samples by oxidation of thiophene with H_2O_2 and CF_3CO_2H. In fact, the H_2O_2/CF_3CO_2H system appeared to be the best oxidizing agent for the selective transformation of thiophene to its 1-oxide. The complete determination of the structures of **37a** and **37b** was carried out for the first time by X-ray diffraction for the former and by a sequence of chemical reactions. The reported results indicate two fates for thiophene 1-oxide *in vivo*: (i) its dimerization via a Diels–Alder reaction and (ii) its reaction with nucleophiles such as glutathione leading virtually to mercapturates. These results together with recent literature data on thiophene derivatives suggest that thiophene 1-oxides could play a central role in the metabolism and toxic effects in mammals. This situation would be different from that observed in the metabolism of other aromatic compounds, such as benzene and furan, in which arene oxides are predominant intermediates.

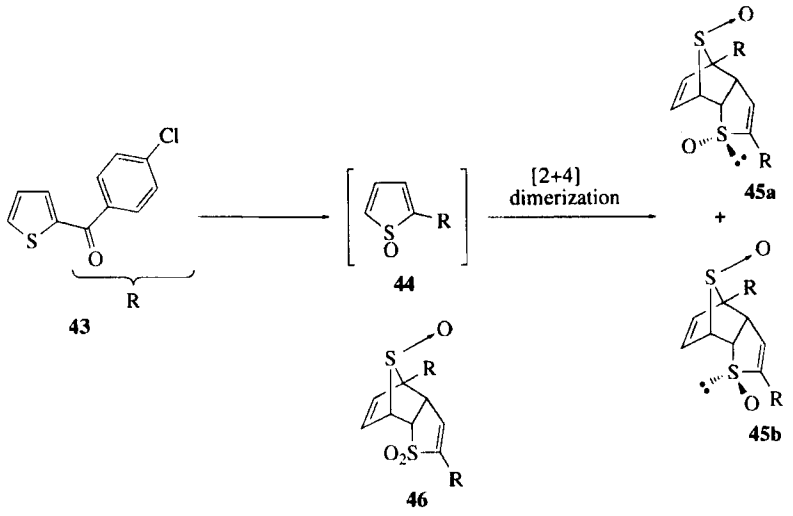




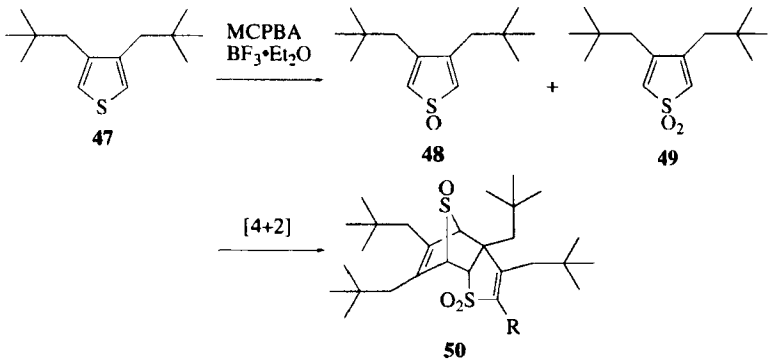
Without added dienophiles, oxidation of 2-methylthiophene by MCPBA in the presence of $BF_3 \cdot Et_2O$ gave a single dimer (**40**) as the dimerization product of 2-methylthiophene 1-oxide (**39**), whereas that of 2,5-dimethylthiophene yielded three dimers (**42a**), (**42b**), and (**42c**).[12] The adduct **42c** results from the Diels–Alder reaction of the thiophene 1-oxide **28** with 1,1-dioxide (**41**).



Oxidation of aroyl-substituted thiophene (**43**) with 0.2 equivalent of H_2O_2 in CF_3CO_2H gave the 1-oxide dimer (**45a**) in 6% yield in addition to the sesquioxide (**46**) in 4% yield, while the oxidation with an equivalent of H_2O_2 produced **46** in 19% yield.[20] On the other hand, the oxidation with 0.5 equivalent of MCPBA in the presence of $BF_3 \cdot Et_2O$ provided **45a** in 15% yield as the major dimer and a small amount of **45b** (not fully characterized) as the minor dimer, in addition to the sesquioxide **46** in 2% yield.



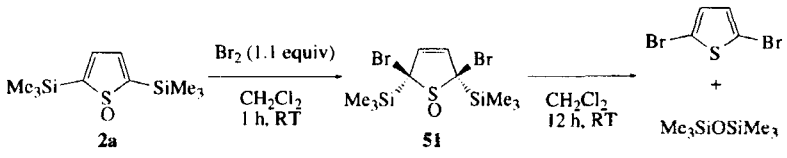
Oxidation of 3,4-dineopentylthiophene (**47**) with MCPBA (slight excess) in the presence of $Et_2O \cdot BF_3$ gave a 1 : 1 mixture of 1-oxide (**48**) and 1,1-dioxide (**49**), which underwent [4 + 2] cycloaddition, during workup, to furnish the congested adduct (**50**) in 61% yield.[21]

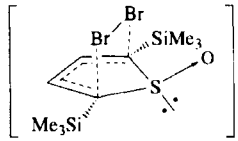


3.1.3. Cis 1,4-bromine addition

Thiophene 1-oxide **2a** underwent a stereospecific 1,4-addition of bromine to give 2,5-bis(trimethylsilyl)-2,5-*cis*-dibromodithiolene 1-oxide (**51**) quantitatively.[7] The structure of **51** was determined by X-ray diffraction analysis. Compound **51** has a C_s symmetry and the two bromine atoms are *cis* to each other and *syn* to the S–O bond. This stereospecific bromine

addition mode is identical to that of the Diels–Alder reaction of **2a** with *p*-benzoquinone.[6] The authors proposed the structure (**52**) as the intermediate leading to **51**. When **51** was allowed to stand as a CH_2Cl_2 solution at room temperature for 24 h, it decomposed to produce 2,5-dibromothiophene and bis(trimethylsilyl)ether in yields around 80%.





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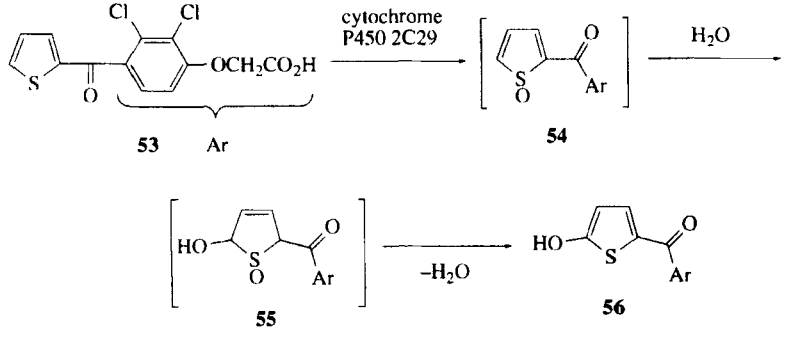
3.1.4. Michael addition

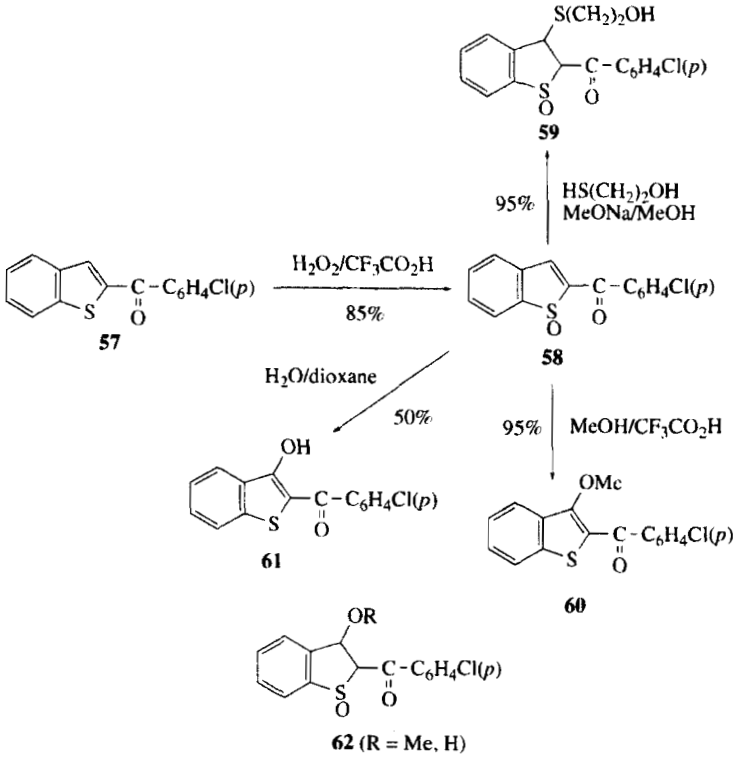
As already mentioned in Section 3.1.2, glutathione underwent a Michael addition to the parent thiophene 1-oxide *in vivo* to produce compound **38** as the final product.[18]

Tienilic acid (**53**), a diuretic drug, has been shown to act as a good substrate of cytochrome P450 2C29. Hydroxylation of **53** by P-450 2C29 took place to give 5-hydroxytienilic acid (**56**) selectively.[22–25] A mechanism, involving Michael addition of water to the initial metabolite 1-oxide (**54**) followed by Pummerer dehydration of the resulting (**55**), was proposed to this metabolism.



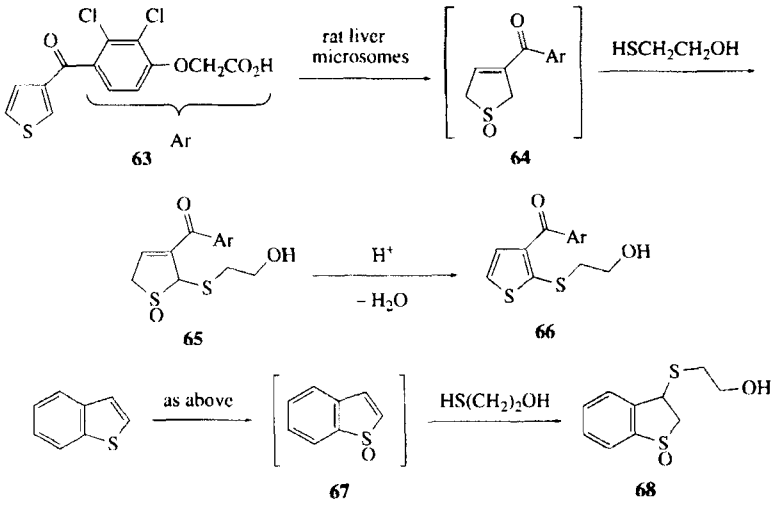
53 54 55 56

Oxidation of 2-aroyl-substituted benzo[*b*]thiophene (**57**) by H_2O_2/CF_3CO_2H was examined as a model case study of the above metabolism.[26] The oxidation provided the corresponding 1-oxide (**58**) in 85% yield. The reaction of **58** with $HS(CH_2)_2OH$ under basic conditions gave the Michael adduct (**59**) in 95% yield. On the other hand, treatment of **58** with MeOH/CF_3CO_2H and that with H_2O/dioxane provided thiophenes (**60**) and (**61**) in 95% and 50% yields, respectively, by a mechanism involving Michael adducts (**62**) and their dehydration.

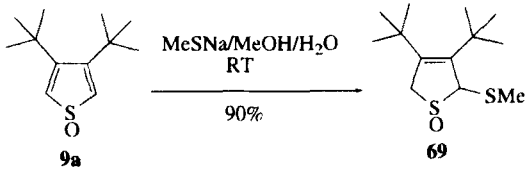


Oxidation of a tienilic acid isomer (**63**) by rat liver microsomes, in the presence of NADPH, led to metabolites most of which covalently bound to microsomal proteins (70%), and some unknown minor metabolites (30%) were also formed.[27–29] In the presence of $HS(CH_2)_2OH$, thiophene (**66**), which was produced from the initial metabolite (**64**) by a Michael addition–Pummerer dehydration

mechanism, was isolated with a dramatic decrease of the covalent bonding to proteins. Similar oxidation of benzo[*b*]thiophene yielded dihydrothiophene 1-oxide (**68**).[27,30]



Thiophene 1-oxide **9a** gave the Michael adduct (**69**) in high yield on treatment with NaSMe.[31]

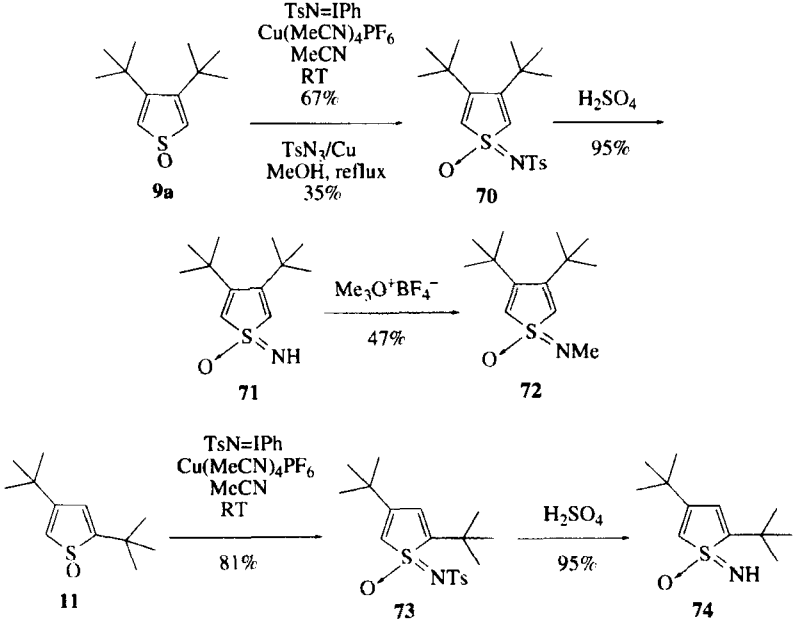


3.2. Reactions on the Sulfur Atom or Oxygen Atom

3.2.1. Conversion to thiophene sulfoximines

Treatment of the thiophene 1-oxide **9a** with TsN=IPh in the presence of $Cu(MeCN)_4PF_6$ at room temperature gave the thiophene sulfoximine (**70**) in 67% yield.[32,33] The conventional method using TsN_3 and an activated copper gave **70** in a less satisfactory yield. Hydrolysis of **70** with concentrated H_2SO_4 furnished the parent sulfoximine (**71**) in 95% yield. Methylation of **71** with $Me_3O^+BF_4^-$ provided compound (**72**). In a similar way, the parent sulfoximine (**74**)

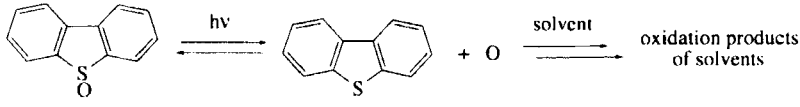
was derived from the unsymmetrically-substituted thiophene 1-oxide **11** in a good overall yield. The sulfur atom of **74** is chiral, and thus a pair of enantiomers of **74** was resolved by HPLC on a chiral column and the absolute configuration of the enantiomers was determined by X-ray crystallographic analysis.



3.2.2. *Photodeoxygenation*

A full account on the mechanism of the photodeoxygenation of dibenzothiophene 5-oxide (**24**) has appeared.[34] Photolysis of dibenzothiophene 5-oxide resulted in the formation of dibenzothiophene and oxidized solvent. Though quantum yields are low, chemical yields are quite high. Yields of the oxidized solvents can also be high. Typical products were phenol from benzene, cyclohexanol and cyclohexene from cyclohexane, and 2-cyclohexenol and cyclohexene oxide from cyclohexene. A number of experiments designed to elucidate the mechanism of the hydroxylation were carried out, including measurements of quantum yields as a function of concentration, solvent, quenchers, and excitation wavelength. These data are inconsistent with

a mechanism involving a sulfoxide dimer, which also does not properly account for the solvent oxidations. It is suggested that the active oxidizing agent may be atomic oxygen $O(^3P)$ or a closely related noncovalent complex, based on the nature of the oxidization chemistry, a comparison to known rate constants for $O(^3P)$ reactivity, and the quantum yield data.

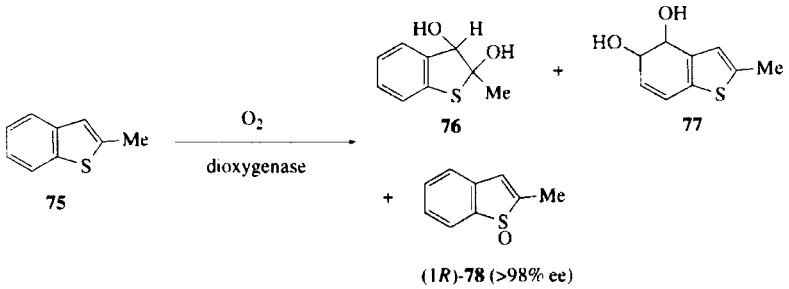


24

4. BIOLOGICAL OXIDATION OF THIOPHENES

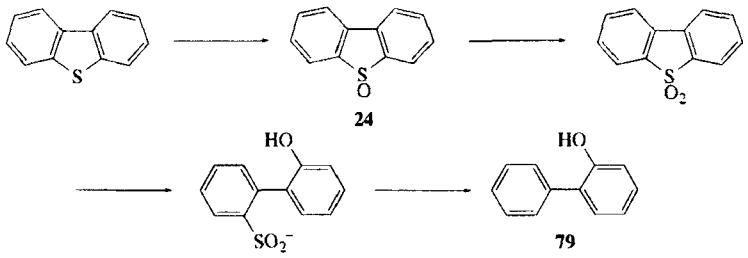
A number of papers, which are concerned with thiophene 1-oxides as metabolites of thiophenes and most of which have been already referred to, were reported by the group of Dansette and Mansuy.[18,22–25,27–29]

Substituted chiral thiophene 1-oxides and their cycloadducts of variable enantiopurity have been isolated as products of dioxygenase-catalyzed sulfoxidation of the corresponding thiophenes using intact cells of *Pseudomonas putida*.[35] Thus, addition of 2-methylbenzo[*b*]thiophene (**75**) as substrate to *P. pudia* UV4 gave the corresponding 2,3- and 4,5-dihydrodiols (**76** and **77**, 27% combined yield) as major metabolites and 2-methylbenzo[*b*]thiophene 1-oxide (**78**, 2%) as a minor metabolite. This sample of the 1-oxide **78** was found to be enantiopure (> 98% ee). Crystallographic analysis of the sample confirmed the pyramidal nature, the enantiopurity, and the (1*R*)-configuration of the sulfoxide chiral center. The kinetic studies provided the $\Delta G^{\neq}$ value of 25.1 kcal/mol for the thermal racemization of **78** at 50 °C in $CHCl_3$ solution.



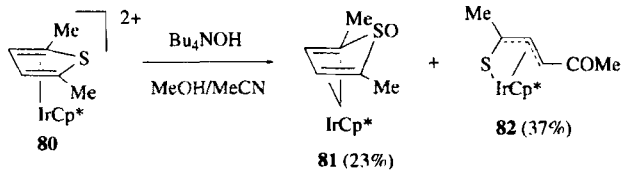
75 **76** **77** (1*R*)-**78** (>98% ee)

A large number of papers, including a review,[36] which dealt with the metabolism of dibenzothiophene and related compounds, have appeared mainly in connection with fossil fuel desulfurization and human carcinogens.[37] In a typical study, the metabolic pathway of dibenzothiophene to 2-hydroxybiphenyl (**79**) by *Rhodococcus* sp. strain IGT88 was elucidated as follows.[37j]



5. METAL COMPLEXES

It was reported that metal complex (**80**) reacted with 2 equivalents of Bu_4NOH in MeOH–MeCN to give a complex (**81**) (23%), which contains 2,5-dimethylthiophene 1-oxide as a ligand, and a complex (**82**) (37%).[38]



6. X-RAY CRYSTALLOGRAPHIC ANALYSIS

Since thiophene 1-oxides had become available in crystalline form, many X-ray crystallographic analysis studies on them have appeared.[6,8–10,35b]

Figure 1 shows a calculated molecular structure (side view) of the parent thiophene 1-oxide obtained by using the STO-3G* basis set.[39] Figures 2–4 show molecular structures of thiophene 1-oxides

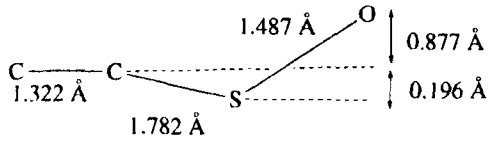


FIGURE 1 Molecular structure of the parent thiophene 1-oxide obtained using the STO-3G* basis set.

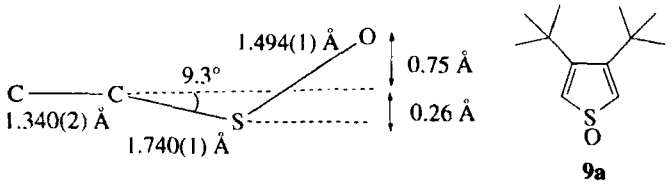


FIGURE 2 Molecular structure of 3,4-di-*t*-butylthiophene 1-oxide (**9a**) (X-ray).

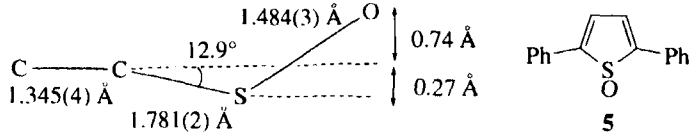


FIGURE 3 Molecular structure of 2,5-diphenylthiophene 1-oxide (**5**) (X-ray).

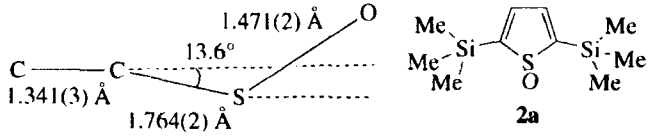


FIGURE 4 Molecular structure of 2,5-bis(trimethylsilyl)thiophene 1-oxide (**2a**) (X-ray).

9a,[10] **5**,[9] and **2a**,[6] respectively, obtained by X-ray crystallographic analyses. These are suggestive of a good agreement of theory and experiments. Thiophene rings are not planar any longer. The S–O bonds are tilted *ca.* 9–14° out of the plane composed of the four carbon atoms of the thiophene ring, the sulfur atoms thus adopting a pyramidal configuration. The C1(a)–C2(b) lengths are in the range of 1.34–1.35 Å

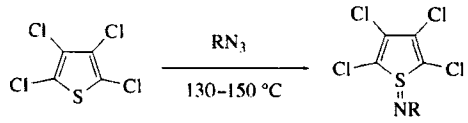
and comparable to the common carbon–carbon double bond length, revealing the occurrence of the bond alternation.

7. THEORETICAL STUDY

A semiempirical AM1 theoretical study was carried out to compare the reactivities of thiophene, thiophene 1-oxide, and thiophene 1,1-dioxide as diene for Diels–Alder reactions.[40] The results obtained were compared with experimental data when available. Generally speaking, an excellent agreement of theory and experiment was obtained. Similar calculation studies were reported by the same author.[41]

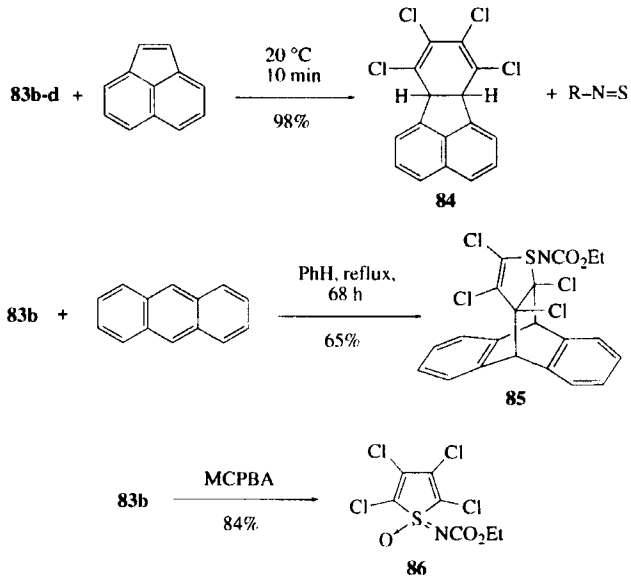
8. THIOPHENE SULFILIMINES

A 1-imino-1,1-dihydrothiophene (sulfilimine derivative of thiophene), where the oxygen atom of the thiophene 1-oxide is replaced by an imino group, is a rare class of compound. The first compounds (**83**) of this class were prepared in moderate yields by thermal decomposition of N_3CO_2Me, N_3CO_2Et, and N_3CO_2Ph and TsN_3 in tetrachlorothiophene at 130–150 °C.[42,43] However, decomposition in 2,5-di-chloro-, 2,5-dibromo-, and tetrabromothiophenes gave products arising from attack at the α-position followed by rearrangement.

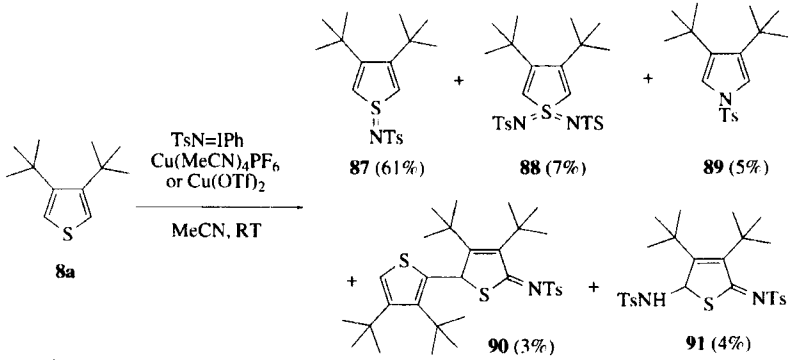


83a: R = CO_2Me, 16%
83b: R = CO_2Et, 49%
83c: R = CO_2Ph, 23%
83d: R = Ts, 24%

The highly reactive sulfilimines **83** acted as dienes toward a range of alkenes[43] in a similar fashion to tetrachlorothiophene 1,1-dioxide.[44] Thus, **83b–d** reacted with acenaphthylene at room temperature for 10 min to give the adduct (**84**) in high yields by elimination of R–N=S. They also act as dienophiles; **83b** reacted with anthracene to provide the [4 + 2] adduct (**85**) in 65% yield. Oxidation of **83b** with MCPBA afforded the sulfoximine (**86**) in 84% yield.

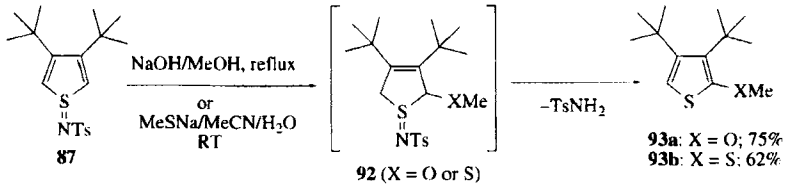


The reaction of the thiophene **8a** with TsN=IPh took place at room temperature in the presence of a copper catalyst, $Cu(MeCN)_4PF_6$ or $Cu(OTf)_2$, to produce the sulfilimine (**87**), sulfone diimine (**88**), pyrrole (**89**), and some other products.[45] When **8a** was used in excess (20 equivalents) and $Cu(MeCN)_4PF_6$ as the catalyst, **87–91** were obtained in 61%, 7%, 5%, 3%, and 4% yields, respectively.



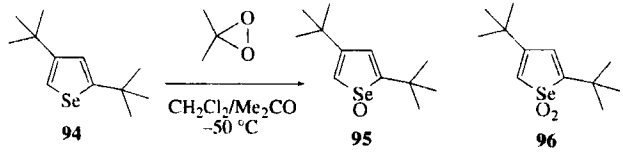
Treatment of the sulfilimine **87** with NaOH in boiling MeOH afforded an unexpected product (**93a**) in 75% yield.[31] The same reaction also took

place with MeSNa at room temperature to give (**93b**) in 62% yield. The reaction probably involves Michael addition of the nucleophiles to **87** followed by elimination of $TsNH_2$ from the resulting adducts (**92**).

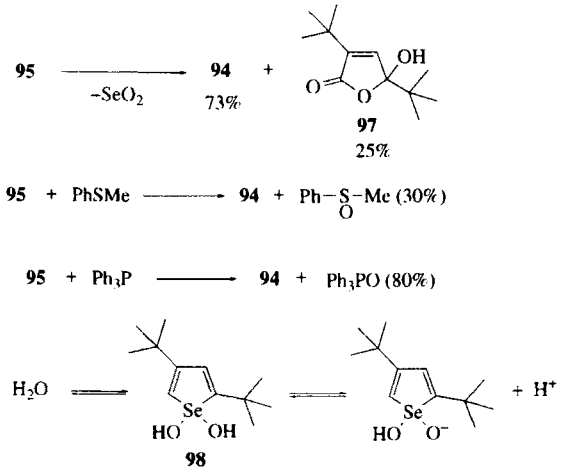


9. SELENOPHENE 1-OXIDES

Although a series of monocyclic selenophene 1,1-dioxides, which are stabilized electronically or sterically, had been prepared by oxidation of selenophenes with DMD,[46] selenophene 1-oxides, the intermediate leading to the former dioxides, remained to be isolated in pure form and characterized. 2,4-Di-*t*-butylselenophene 1,1-dioxide (**96**) is the most thermally stable of the synthetically available selenophene 1,1-dioxides because of steric protection.[46] Since this should also be true for selenophene 1-oxides, 2,4-di-*t*-butylselenophene (**94**) was chosen as the substrate of the oxidation study to obtain a selenophene 1-oxide stable enough to be isolated. Oxidation of **94** with an equimolar amount of DMD in acetone at $-50\,°C$, which was followed by removal of the solvent under vacuum below $-50\,°C$, provided, after washing of the residue with pentane, pure 2,4-di-*t*-butylselenophene 1-oxide (**95**) nearly quantitatively as colorless crystals.[47] No formation of the 1,1-dioxide **96** was observed. The 1-oxide **95** is highly hygroscopic and deliquesced on exposure to moist air. The ^1H NMR chemical shift values of **95** fall in between those of **94** and **96**. The same trend is also observed with a thiophene series.[10] The ^{77}Se NMR spectrum showed only one signal at δ 986 which is lower than chemical shift values of the common selenoxides. The IR spectrum showed the Se–O stretching vibration at 798 cm^{-1}. This assignment was supported by the Raman spectrum in which a strong band appeared at 788 cm^{-1}.

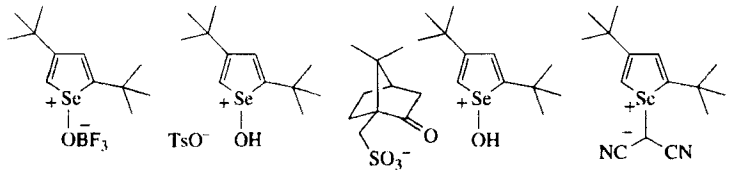


The 1-oxide **95** is far less stable than the corresponding thiophene 1-oxide **11** and selenophene 1,1-dioxide **96** and decomposed at 20 °C with half-lives of 42 and 34 min in 0.018 and 0.036 M $CDCl_3$ solutions, respectively.[47] A 0.05 M solution of **95** in CH_2Cl_2, standing at 30 °C for 0.5 h, gave **94** (73%), furanone (**97**) (25%), and SeO_2 by an unknown process; kinetics of the decomposition fitted neither first- nor second-order in **95**. As is expected from the formation of **94** and **95** functions as an oxidizing agent. Standing a 1 : 1 mixture of **95** and PhSMe in CH_2Cl_2 gave PhS(O)Me in 30% yield along with **94** (67%) and **97** (8%). Ph_3P was also oxidized by an equivalent of **95** to give Ph_3PO in 80% yield. Surprisingly, **95** is readily soluble in water, despite the presence of two hydrophobic *t*-butyl groups, to give an acidic solution (pH 6.6 for 5.7×10^{-2} M solution) (also easily soluble in MeOH). In addition, it is stabilized by water and persisted in D_2O without marked decomposition at least for 24 h at room temperature. These observations indicate that the Se–O bond is highly polarized, as supported by the foregoing deshielded ^{77}Se chemical shift value, and is solvated in water. The acidity of **95** is suggestive of the presence of an equilibrium involving the selenurane (**98**), which lies to the selenoxide side.



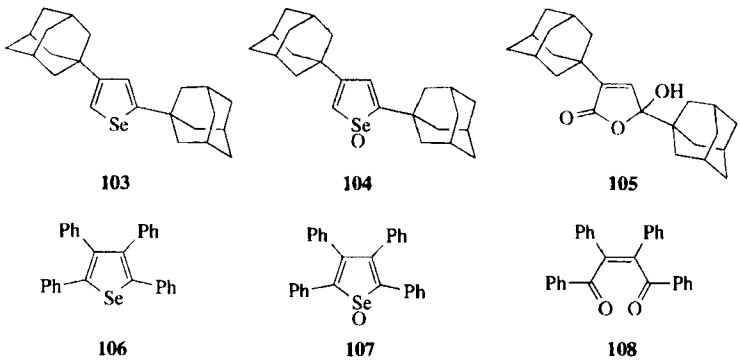
The 1-oxide **95** quantitatively forms a 1 : 1 adduct (**99**) with BF_3 when treated with $BF_3 \cdot Et_2O$ at −40 °C.[47] The 1-oxide **95** also quantitatively gave a 1 : 1 adduct (**100**) with *p*-toluenesulfonic acid at −40 °C, similar in structure to the adduct reportedly formed with dibenzyl selenoxide.

Since the selenium atom of **95** is chiral, optical resolution should be possible provided the inversion on the selenium atom and the well-known racemization process through hydration are slow. As an approach to this goal, **95** was treated with (1*S*)-(+)-10-camphorsulfonic acid. The ^{1}H NMR of the resulting 1 : 1 adduct (**101**) showed a pair of signals of equal intensities due to the α- and β-hydrogens, revealing the formation of a pair of diastereomers. This conclusion was also supported by ^{13}C- and ^{77}Se-NMR (observations of two signals at δ 957 and 959) spectra, although separation of the diastereomers was impeded by instability of the adduct. Treatment of **95** with malononitrile at −40 °C gave the selenonium ylide (**102**) quantitatively, thus providing a new route to selenophenium ylides.



99 **100** **101** **102**

Similar oxidation of 2,4-di(1-adamantyl)selenophene (**103**) and tetraphenyl-selenophene (**106**) also gave the corresponding 1-oxides (**104**) and (**107**) nearly quantitatively.[47] The 1-oxide **104**, which deliquesces on exposure to air and is slightly soluble in water, quickly decomposed at 30 °C in CH_2Cl_2 to give **103** (85%) and furanone (**105**) (12%), while **107** gave **106** (73%) and *cis*-butenedione (**108**) (25%) under the same conditions.

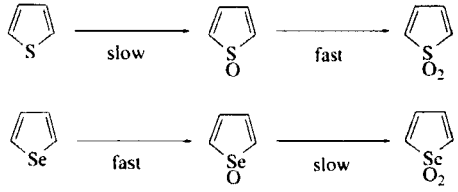


103 **104** **105**

106 **107** **108**

10. A COMMENT ON THE OXIDATION RATE OF THIOPHENES AND SELENOPHENES[48]

The difference in oxidation rates of thiophenes and selenophenes is of much importance. Oxidation of thiophenes, including the parent thiophene, is difficult to stop at the 1-oxide stage because of much faster oxidation of 1-oxides to 1,1-dioxides relative to the oxidation of thiophenes to thiophene of 1-oxides. This would be explained by the fact that thiophenes, whose aromaticity is the greatest in the five-membered, one chalcogen atom-containing heteroaromatics, resist the oxidation that results in the virtual loss of the aromaticity, but, once they are oxidized, the oxidation of 1-oxides to 1,1-dioxides takes place much easier. By contrast, the oxidation of selenophenes is easily quenched at the 1-oxide stage because of much slower oxidation of 1-oxides to 1,1-dioxides relative to the oxidation of selenophenes to selenophene 1-oxides. This might be explained partly by smaller aromaticity of selenophenes relative to thiophenes and partly by decreased electron density on the selenium atom of selenophene 1-oxides because of the highly polarized Se–O bond, which makes electrophilic oxidation slower.



REFERENCES

[1] J. Nakayama and Y. Sugihara (1996). *Sulf. Rep.*, **19**, 349.
[2] For a recent review on the chemistry of thiophene 1,1-dioxides, see J. Nakayama and Y. Sugihara (1999). *Topic. Curr. Chem.*, **205**, 131.
[3] W. L. Mock (1970). *J. Am. Chem. Soc.*, **92**, 7610.
[4] M. Higaki and N. Furukawa (1993). *Book of Abstracts, 24th Congress of Heterocyclic Chemistry*, Osaka, Japan, p. 277.
[5] N. Furukawa, S.-Z. Zhang, S. Sato and M. Higaki (1997). *Heterocycles*, **44**, 61.
[6] N. Furukawa, S.-Z. Zhang, E. Horn, O. Takahashi and S. Sato (1998). *Heterocycles*, **47**, 793.
[7] S.-Z. Zhang, S. Sato, E. Horn and N. Furukawa (1998). *Heterocycles*, **48**, 227.
[8] P. Pouzet, I. Erdelmeier, D. Ginderow, J.-P. Mornon, P. M. Dansette and D. Mansuy (1995). *J. Chem. Soc., Chem. Commun.*, 473.

[9] P. Pouzet, I. Erdelmeier, D. Ginderow, J.-P. Mornon, P. M. Dansette and D. Mansuy (1977). *J. Heterocyclic Chem.*, **34**, 1567.
[10] J. Nakayama, T. Yu, Y. Sugihara and A. Ishii (1977). *Chem. Lett.*, 499.
[11] Y.-Q. Li, M. Matsuda, T. Thiemann, T. Sawada, S. Mataka and M. Tashiro (1996). *Synlett*, 461.
[12] Y.-Q. Li, T. Thiemann, T. Sawada, S. Mataka and M. Tashiro (1997). *J. Org. Chem.*, **62**, 7926.
[13] Y.-Q. Li, T. Thiemann, K. Mimura, T. Sawada, S. Mataka and M. Tashiro (1998). *Eur. J. Org. Chem.*, 1841.
[14] T. Kimura, Y. Izumi, N. Furukawa and Y. Minoshima (1996). *Heteroatom Chem.*, **7**, 143.
[15] D. Fabbri, A. Dore, S. Gladiali, O. De Lucchi and G. Valle (1996). *Gazz. Chim. Ital.*, **126**, 11.
[16] Oxidation by $MoO_5 \cdot$ HMPT, M. Bonchio, V. Conte, M. A. De Conciliis, F. Di Furia, F. P. Ballistreri, G. A. Tomaselli and R. M. Toscano (1995). *J. Org. Chem.*, **60**, 4475; Oxidation by sulfonic peracids, R. Kluge, M. Schulz and S. Liebsch (1996). *Tetrahedron*, **52**, 5773; Oxidation by $H_2O_2/MeReO_3$, K. N. Brown and J. H. Espenson (1996). *Inorg. Chem.*, **35**, 7211; Oxidation with $NaClO_2$ catalyzed by manganese(III) acetylacetonate, M. Hirano, S. Yakabe, J. H. Clark and T. Morimoto (1996). *J. Chem. Soc., Perkin Trans. 1*, 2695; TiO_2-photocatalytic oxidation, A.-M. A. Abdel-Wahab and A. E.-A. M. Gaber (1998). *J. Photochem. Photobiol.*, **114**, 213; Photochemical desulfurization (oxidation): Y. Shiraishi, T. Hirai and I. Komasawa (1998). *Ind. Eng. Chem. Res.*, **37**, 203; Y. Shiraishi, Y. Taki, T. Hirai and I. Komasawa (1998). *J. Chem. Soc., Chem. Commun.*, 2601.
[17] T. Thiemann, M. L. Sa e Melo, A. S. C. Neves, Y.-Q. Li, S. Mataka, M. Tashiro, U. Geißler and D. Watson (1998). *J. Chem. Res. (S)*, 346.
[18] A. Treiber, P. M. Dansette, H. El Amri, J.-P. Girault, D. Ginderow, J.-P. Mornon and D. Mansuy (1997). *J. Am. Chem. Soc.*, **119**, 1565.
[19] For isolation and characterization of the parent thiophene 1,1-dioxide, see J. Nakayama, H. Nagasawa, Y. Sugihara and A. Ishii (1997). *J. Am. Chem. Soc.*, **119**, 9077; H. Nagasawa, Y. Sugihara, A. Ishii and J. Nakayama (1999). *Bull. Chem. Soc. Jpn.*, **72**, 1919.
[20] M. T. Ho, A. Treiber and P. M. Dansette (1998). *Tetrahedron Lett.*, **39**, 5049.
[21] T. Yu and J. Nakayama, unpublished results.
[22] M. P. López-Garcia, P. M. Dansette and D. Mansuy (1994). *Biochemistry*, **33**, 166.
[23] P. Jean, P. Lopez-Garcia, P. Dansette, D. Mansuy and L. Goldstein (1996). *Eur. J. Biochem.*, **241**, 797.
[24] S. Poli-Scaife, R. Attias, P. M. Dansette and D. Mansuy (1997). *Biochemistry*, **36**, 12672.
[25] C. Minoletti, S. Dijols, P. M. Dansette and D. Mansuy (1999). *Biochemistry*, **38**, 7828.
[26] P. Pouzet, I. Erdelmeier, P. M. Dansette and D. Mansuy (1998). *Tetrahedron*, **54**, 14811.
[27] D. Mansuy, P. Valadon, I. Erdelmeier, P. Lopez-Garcia, C. Amar, J.-P. Girault and P. M. Dansette (1991). *J. Am. Chem. Soc.*, **113**, 7825.
[28] P. M. Dansette, D. C. Thang, H. El Amri and D. Mansuy (1992). *Biochem. Biophys. Res. Commun.*, **186**, 1624.
[29] P. Valadon, P. M. Dansette, J.-P. Girault, C. Amar and D. Mansuy (1996). *Chem. Res. Toxicol.*, **9**, 1403.
[30] P. D. Ginderow, J.-P. Mornon, I. Erdelmeier, P. Dansette and D. Mansuy (1992). *Acta Cryst.*, **C48**, 1808.
[31] T. Otani and J. Nakayama, unpublished results.
[32] J. Nakayama, Y. Sano, Y. Sugihara and A. Ishii (1999). *Tetrahedron Lett.*, **40**, 3785.
[33] For the latest reviews on the chemistry of sulfilimines and sulfoximides, see *Sulf. Rep.*, **21**, 1999, edited by S. G. Pyne.

[34] D. D. Gregory, Z. Wang and W. S. Jenks (1997). *J. Am. Chem. Soc.*, **119**, 94; For a preliminary report, see Z. Wang and W. S. Jenks (1995). *J. Am. Chem. Soc.*, **117**, 2667.
[35] (a) D. R. Boyd, N. D. Sharma, I. N. Brannigan, S. A. Haughey, J. F. Malone, D. A. Clarke and H. Dalton (1996). *J. Chem. Soc., Chem. Commun.*, 2361; (b) D. R. Boyd, N. D. Sharma, S. A. Haughey, J. F. Malone, B. T. McMurray, G. N. Sheldrake, C. C. R. Allen and H. Dalton (1996). *J. Chem. Soc., Chem. Commun.*, 2363.
[36] B. L. McFarland, L. Beverly, D. J. Boron, W. Deever, J. A. Meyer, A. R. Johnson and R. M. Atlas (1998). *Crit. Rev. Microbiol.*, **24**, 99.
[37] (a) D. Schlenk, R. J. Bevers, A. M. Vertino and C. E. Cerniglia (1994). *Xenobiotica*, **24**, 1077; (b) T. Omori, Y. Saiki, K. Kasuga and T. Kodama (1995). *Biosci. Biotechnol. Biochem.*, **59**, 1195; (c) M. Grifoll, S. A. Selifonov and P. J. Chapman (1995). *Appl. Environ. Microbiol.*, **61**, 3490; (d) M. Ortiz-Leon, L. Velasco and R. Vazquez-Duhalt (1995). *Biochem. Biophys. Res. Commun.*, **215**, 968; (e) H. Sato and D. P. Clark (1995). *Microbios*, **83**, 145; (f) L. Bezalel, Y. Hadar, P. P. Fu, J. P. Freeman and C. E. Cerniglia (1996). *Appl. Environ. Microbiol.*, **62**, 2554; (g) S. M. Resnick and D. T. Gibson (1996). *Appl. Environ. Microbiol.*, **62**, 4073; (h) K. Okumura (1996). *Idemitsu Giho*, **39**, 530: (1996) *Chem. Abstr.*, **125**, 333 501; (i) K. A. Gray, O. S. Pogrebinsky, G. T. Mrachko, L. Xi, D. J. Monticello and C. H. Squires (1996). *Nat. Biotechnol.*, **14**, 1705; (j) C. Oldfield, O. Pogrebinsky, J. Simmonds, E. S. Olson and C. F. Kulpa (1997). *Microbiology*, **143**, 2961; (k) D. T. Seymour, A. G. Verbeek, S. E. Hrudey and P. M. Fedorak (1997). *Environ. Toxicol. Chem.*, **16**, 658; (l) K. G. Kropp, J. T. Andersson and P. M. Fedorak (1997). *Appl. Environ. Microbiol.*, **63**, 3032; (m) Z. I. Finkel'stein, B. P. Baskunov, L. N. Vavilova and L. A. Golovleva (1997). *Microbiology* (*Moscow*), **66**, 402; (n) Y. Kabe, S. Nakayama, H. Shono and K. Takahashi (1998). *Tamagawa Daigaku Nogakubu Kenkyu Hokoku*, **38**, 83: (1999) *Chem. Abstr.*, **131**, 46 896; (o) S. Gilbert, J. Morton, S. Buchanan, C. Oldfield and A. McRoberts (1998). *Microbiology*, **144**, 2545; (p) S. Frassinetti, L. Setti, A. Corti, P. Farrinelli, P. Montevecchi and G. Vallini (1998). *Can. J. Microbiol.*, **44**, 289; (q) T. MacPherson, C. W. Greer, E. Zhou, A. M. Jones, G. Wisse, P. C. K. Lau, B. Sankey, M. J. Grossman and J. Hawari (1998). *Environ. Sci. Technol.*, **32**, 421.
[38] J. Chen, Y. Su, R. A. Jacobson and R. J. Angelici (1996). *J. Organometal. Chem.*, **512**, 149; See also, A. E. Skaugest, T. B. Rauchfuss and C. L. Stern (1990). *J. Am. Chem. Soc.*, **112**, 2432; A. E. Skaugest, T. B. Rauchfuss and S. R. Willson (1992). *J. Am. Chem. Soc.*, **114**, 8521.
[39] I. Rozas (1992). *J. Phys. Org. Chem.*, **5**, 74.
[40] B. S. Jursic (1995). *J. Heterocyclic Chem.*, **32**, 1445. For a related study cited in the previous review, see N. H. Werstiuk and J. Ma (1994). *Can. J. Chem.*, **72**, 2493.
[41] B. S. Jursic (1998). *J. Mol. Struc. (Theochem.)*, **454**, 105; **459**, 215.
[42] O. Meth-Cohn and G. van Vuuren (1984). *J. Chem. Soc., Chem. Commun.*, 190.
[43] O. Meth-Cohn and G. van Vuuren (1986). *J. Chem. Soc., Perkin Trans. I*, 233.
[44] M. S. Raasch (1980). *J. Org. Chem.*, **45**, 856; **45**, 867.
[45] T. Otani, Y. Sugihara, A. Ishii and J. Nakayama (1999). *Tetrahedron Lett.*, **40**, 5549; Decomposition of TsN_3 in hot **8a** produces **89** in a low yield; J. Nakayama, Y. Sugihara, K. Terada and E. L. Clennan (1990). *Tetrahedron Lett.*, **31**, 4473.
[46] J. Nakayama, T. Matsui, Y. Sugihara, A. Ishii and S. Kumakura (1996). *Chem. Lett.*, 269; T. Matsui, J. Nakayama, N. Sato, Y. Sugihara, A. Ishii and S. Kumakura (1996). *Phos. Silic. Sulf.*, **118**, 227.
[47] T. Umezawa, Y. Sugihara, A. Ishii and J. Nakayama (1998). *J. Am. Chem. Soc.*, **120**, 12 351.
[48] J. Nakayama (2000). *Bull. Chem. Soc. Jpn.*, **73**, 1.