Lewis Acid Catalysis in the Oxidative Cycloaddition of Thiophenes[1]

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Thiophenes **1** were treated with *m*-chloroperbenzoic acid (*m*-CPBA) under BF_3·Et_2O catalysis to afford thiophene *S*-monoxides. These could be reacted *in situ* as intermediary species with a number of dienophiles to provide arenes (with alkynes as dienophiles) or 7-thiabicyclo[2.2.1]hept-2-ene 7-oxides (with alkenes as dienophiles). It was also possible to isolate thiophene *S*-monoxides in solution and to cycloadd them in a second step. In either way it could be shown that the use of BF_3·Et_2O enhances the yields of the oxidative cycloaddition of thiophenes considerably. Moreover a greater variety of dienophiles (**29a**, **29b**, **29c**) could be reacted with thiophenes than in the case of the noncatalyzed reaction. All cycloadditions catalyzed by BF_3·Et_2O give only a single diastereoisomer as cycloadduct. The reactions show a high π-facial selectivity, a fact that can be explained by the Cieplak-effect. Without added dienophiles, 2-methylthiophene (**1e**) gave a single dimer (**36**) of 2-methylthiophene *S*-monoxide, whereas 2,5-dimethylthiophene (**1a**) gave three dimers (**32a**−**c**). In the case of tetrasubstituted thiophenes, thiophene *S*-monoxides (e.g., **31b** and **31c**) could be isolated in substance.

Introduction

The Diels−Alder reaction ranks as one of the most extensively researched topics in organic chemistry. It is a very powerful tool in synthesis, as not only two new carbon bonds are formed, but also one or more stereocenters are generated. In fact, in the reaction shown below, five stereocenters are created and controlled. An impressive number of dienes and dienophiles have been studied in the Diels−Alder reaction. Nevertheless, there are still limitations in employing five-membered heterocyclic compounds as dienes in these cycloadditions. This is especially true for the use of thiophenes and its derivatives as diene-components.[2] Thiophene is known as the least reactive diene of all aromatic five-membered heterocycles. This has been explained by the presence of **3d** orbitals on sulfur which contribute to the resonance stability of the thiophene system.[3]

Where thiophenes are known to undergo the Diels−Alder reaction, there are always involved limitations as to the substrates (see below: a,b) or special reaction conditions (see below: c,d).[4] Thus it is known that cycloaddition of thiophenes can occur through one of the following: (a) the use of highly reactive dienophiles such as dicyanoacetylene or arynes;[4a,b] (b) a proper choice of substituents on the thiophene, thus enhanced electron-density in the ring system, brought about by the introduction of two methoxy groups at positions 2 and 5,[4c] increases the diene-character of the molecule as does the introduction of strain in the thiophene;[4d] (c) the use of high reaction temperatures;[4e] or (d) the use of high pressure.[4f]

Thiophenes can be oxidized by *m*-CPBA to thiophene-*S*,*S*-dioxides.[5] This reaction is known to proceed via intermediate thiophene *S*-monoxides. Owing to the absence of a lone pair of electrons on sulfur to contribute to the 6π-system of a potential aromatic system, thiophene *S*,*S*-dioxides have nonaromatic character and behave as cyclic 1,3-dienes. Diels−Alder reactions of 1,2,3,4-tetrachlorothiophene *S*,*S*-dioxide are well known with a large variety of dienophiles.[5b,c] Nevertheless, in many cases higher reaction temperatures are needed. This is especially true for the much less reactive 2,5-dimethylthiophene *S*,*S*-dioxide.

Thiophene *S*-monoxide possesses one lone pair on sulfur. However, thiophene *S*-monoxides are known to have nonaromatic character. This has been reported by W. L. Mock[6] on the basis of the interpretation of the ^1H NMR spectrum of 2,5-di-*tert*-butylthiophene *S*-monoxide[6] and the X-ray analysis of dibenzo[b,d]thiophene *S*-oxide. It could be shown that the sulfur of thiophene *S*-monoxides is in fact pyramidally configured with the

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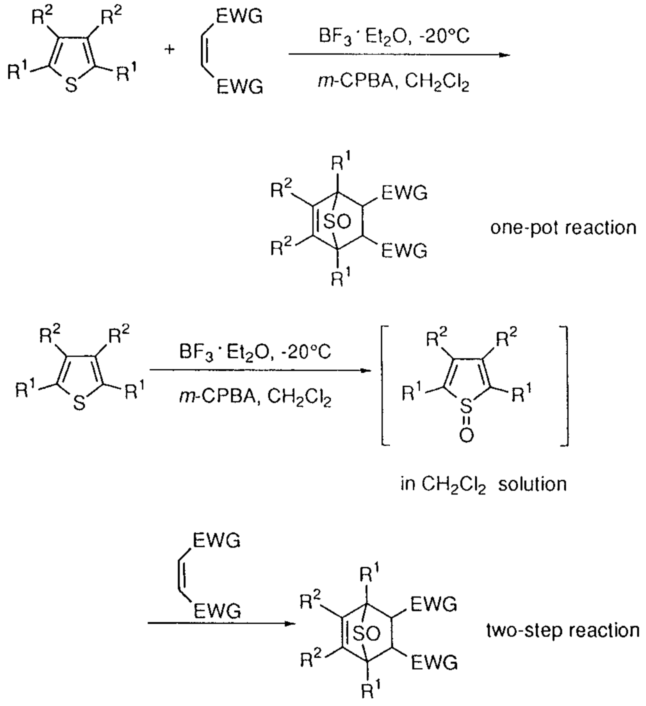
oxygen as the third ligand located off the molecular plane. Later on the structure has been found to be more general by X-ray analyses done by two groups on phenyl-substituted thiophene *S*-monoxides.[7] The geometry of the lone pair on sulfur reduces its contribution to any aromaticity of the molecule considerably. Thiophene-*S*-monoxides are very reactive molecules,[8] and, although intermediates in the oxidation of thiophenes to thiophene *S*,*S*-dioxides, they could not be isolated in such reactions until very recently. The only experimental indication of their presence in these oxidations had been the formation of dimeric cycloadducts between the intermediate sulfoxides and the sulfones[9] as byproducts. Recently,[10] however, thiophene *S*-oxides bearing two bulky substituents at ring positions 2 and 5, such as 2,5-diphenylthiophene *S*-monoxide or 2,5-bis(trimethylsilyl)thiophene *S*-oxide could be prepared in low yield under oxidative conditions from the respective thiophenes by D. Mansuy (H_2O_2-CF_3COOH)[10b] and N. Furukawa ($BF_3{\cdot}Et_2O$/*m*-CPBA).[10a] The reactivity of these 2,5-disubstituted thiophene *S*-oxides has not been reported so far. K. Torssell[11] and A. G. Fallis[12] have reported the isolation of 7-thiabicyclo[2.2.1]hept-2-ene 7-oxides as cycloadducts, when 2,5-dimethylthiophene was oxidized by *m*-CPBA in the presence of electron-poor dienophiles, such as *p*-benzoquinone and *N*-phenylmaleimide. The isolated yields of the cycloadducts, however, were low (10−30%), under the conditions used.

The authors[13] have utilized this reaction to prepare novel crown ethers[13a] and cyclophanes[13c] at room temperature from thiopheno crown ethers and thiophenophanes. Also the intramolecular cycloaddition of thiophene derivatives using this reaction has been investigated.[14] While the use of alkynes as dienophiles leads directly to arenes, thiabicyclo[2.2.1]hept-2-ene 7-oxides, formed by the oxidative cycloaddition of thiophenes with alkenes, could easily be transformed to arenes by oxidative SO-extrusion (thermolytically,[13c] photochemically,[13b] electrochemically,[15] or by using $KMnO_4$ under PTC-conditions[13a,c]) or to cyclic dienes by reaction of the primary cycloadducts with Bu_3SnH.[13b] A general drawback of the reaction has remained the poor yield and limited choice of dienophiles. In the present paper we report a modified synthetic procedure, using BF_3Et_2O as a Lewis acid catalyst in the oxidative cycloaddition of thiophenes. It will be shown that the use of $BF_3{\cdot}Et_2O$ as Lewis acid catalyst in this reaction greatly improves yields and allows for a large choice of dienophiles.

Scheme 1



Results and Discussion

Lewis acids are widely used to catalyze Diels−Alder reactions.[16,17] Many Diels−Alder reactions are accelerated by Lewis acid catalysts such as $BF_3{\cdot}Et_2O$, $AlCl_3$, $SnCl_4$, or $ZnCl_2$, and often the application of such catalysts leads to an increase of regio- and stereoselectivity as compared to uncatalyzed reactions.[16]

The reason for using a Lewis acid catalyst in the oxidative cycloaddition of thiophenes is twofold. On the one hand thiophene *S*-monoxides, formed by the oxidation of thiophenes, readily react with *m*-CPBA to form thiophene *S*,*S*-dioxides. Thiophene *S*,*S*-dioxides themselves are stable and do not cycloadd with dienophiles under these conditions (room temperature or below), and thus they are lost for the reaction for all practical purposes. If, however, the thiophene *S*-monoxide is complexed by a Lewis acid, the sulfur of the sulfoxy-moiety is less nucleophilic and is less prone to be oxidized. Thus the thiophene *S*-monoxides become more stable toward oxidation; a significant shift of the HOMO of the thiophene *S*-monoxide is not to be expected due to the poor overlap of the p-orbitals and of the lone pair of the sulfoxy-moiety with the diene unit. On the other hand a significant lowering of the LUMO of many dienophiles, such as enones, is known to occur, when a Lewis acid is used as catalyst. Here, the formation and subsequent cycloaddition of thiophene *S*-monoxides under Lewis acid catalysis were attempted in two ways (Scheme 1). In the first method, which will be designated the "one-pot"

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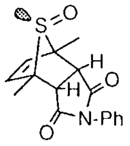

endo

3

Figure 1.

reaction, *m*-CPBA is added to a mixture of the thiophene derivative and the dienophile in the presence of the catalyst at −20 °C. In the second method, which will be called the "two-step sequence," *m*-CPBA is added to a mixture of thiophene and catalyst at −20 °C. After the reaction is over, excess *m*-CPBA, *m*-chlorobenzoic acid and catalyst are removed from the mixture; thereafter the dienophile is added to the solution of thiophene *S*-monoxide to give the cycloadduct.

In comparison to the published noncatalyzed reaction[11,12] with yields of 10−30%, the application of $BF_3 \cdot Et_2O$ as Lewis acid in the oxidation of thiophenes leads to improved yields of the cycloadducts of up to 75%. The results of the $BF_3 \cdot Et_2O$-enhanced oxidative cycloaddition of thiophenes are summarized in Table 1. The use of other Lewis acids such as $AlCl_3$ and $FeCl_3$ in this reaction was not very successful. With highly reactive dienophiles, such as *N*-phenylmaleimide (**2**), *p*-benzoquinone (**19**), naphthoquinone (**15**), and others (Table 1, entries 1−5, 10−13), which are stable under conditions of $BF_3 \cdot Et_2O$/*m*-CPBA, both the one-pot and the two-step methods can be used. For the most part the reactions are finished within 3 h at −20 °C.

When using tetracyanoethylene (TCNE) (**10**) as dienophile (entry 7) the two-step method is preferable as the separation of the excess amount of TCNE from cycloadduct **11** is exceedingly difficult. By the two-step method, the proper amount of TCNE can be added to a solution of 2,5-dimethylthiophene *S*-oxide (**31a**) in dichloromethane until the 2,5-dimethylthiophene *S*-oxide has reacted completely (TLC control).

Biscycloadduct **22** is formed from 2,5-dimethylthiophene *S*-oxide (**31a**) and *p*-benzoquinone (**19**, entry 14) in the two-step sequence. When the one-pot procedure is used, only the mono-adduct **20** forms. This agrees with the results found in the noncatalyzed reaction.[11] In the one-pot procedure a low concentration of the thiophene *S*-monoxide is maintained throughout the reaction, as the thiophene *S*-monoxide produced by the slow addition of *m*-CPBA is used up relatively quickly in the cycloaddition reaction.

As some dienophiles, such as the 1:1 furan−acetylenic ester adducts **23** and **25** (entries 15−18), are known to be sensitive[18] to acidic media in general or *m*-CPBA in particular, only poor yields of cycloadducts can be isolated in such cases, when the one-pot procedure is used (*e.g*, 5% or less of the cycloadducts **24** and **26**). This limitation of the $BF_3 \cdot Et_2O$/*m*-CPBA system can be circumvented by the use of the two-step reaction method, in which thiophene *S*-monoxide is reacted with the proper amount of dienophile under neutral conditions, and a decomposition of the dienophile is avoided. The two-step method improves the yields of **24**, **26**, **27**, and **28** up to 50%.

Halogen-substituted thiophenes are known to be less readily oxidized to the corresponding thiophene *S*,*S*-dioxides than thiophenes with alkyl-substituents. On the other hand tetrachlorothiophene *S*,*S*-dioxide is known to be a very reactive diene which reacts with various dienophiles. Under the oxidative reaction conditions presented here in the one-pot method, 2,5-dichlorothiophene and 2,5-dimethyl-3,4-dibromothiophene reacted with dienophiles such as *N*-phenylmaleimide to give cycloadducts **6** (entry 4) and **7** (entry 5) in low to moderate yields. Reaction times are longer (up to 20 h) and the needed reaction temperatures higher (0−25 °C). 2,5-Dibromothiophene and 2,3,4,5-tetrabromothiophene, however, could not be reacted with *N*-phenylmaleimide at all under the present reaction conditions. Subsequently it could be shown that these halogenated thiophenes can be reacted at even higher temperatures (50 °C) without BF_3-catalysis.[15] The halogenated thiophene *S*-monoxides are less prone to be oxidized to thiophene *S*,*S*-dioxides and undergo cycloaddition more readily, so that the cycloaddition reaction is able to compete with a further oxidation under noncatalyzed conditions.

All of the above-mentioned cycloadditions give cycloadducts as a single diastereoisomer, and the configuration of the cycloadducts **3**[19] (Figure 1), **18a** (Figure 2), and **24** (Figure 3) were determined by X-ray diffraction. All the cycloadducts are *endo*-products, the lone pair on sulfur being on the same side as the newly formed double bond of the cycloadduct. This is in accordance with other adducts formed by the oxidative cycloaddition reaction of thiophenes without Lewis-acid catalysis, where the stereochemistry of the products has been ascertained by X-ray crystal structural analyses both by A. G. Fallis[12] and by ourselves.[13a,b] The *endo*-selectivity in itself is not surprising, as the low temperature needed for the reaction should favor kinetically-controlled cycloadducts.[20] Moreover, it has been found that Lewis-acid catalysis usually increases the extent of *endo*-addition in Diels−Alder reactions.[21] Thus, oxidative cycloaddition of dimethylthiophene with **17** under Lewis acid catalysis gives only *endo*-adduct **18a**. The uncatalyzed cycloaddition of 2,5-dimethylthiophene with the related dienes 2,3-norboneno-*p*-benzoquinone (NPBQ)[22] and norbornano-*p*-benzoquinone (DNPBQ) gives the corresponding cycloadducts as a mixture of *exo*- and *endo*-adducts.[23]

The π-facial selectivity can be explained by the "Cieplak Effect",[24] an effect first proposed by Cieplak[24] to account for the directing effects of remote substituents in addition reactions to substituted cyclohexanones (Figure 4). A large number of experimental observations in Diels−Alder reactions of dienophiles with 5-substituted cyclopentadienes have shown that the dienophiles will approach *anti* to the antiperiplanar σ bond that is the better donor at 5-position of cyclopentadiene.[25] This σ-bond will best stabilize the vacant σ*-orbital of the incipient

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[18] McCulloch, A. W.; Smith, D. G.; McInnes, A. G. *Can. J. Chem.* **1974**, *52*, 1013−1018.

[19] The X-ray analysis of **3** has been performed before; see ref 12. In the case, however, **3** was formed in the uncatalyzed reaction.

[20] Although in most Diels−Alder reactions of cyclic dienes the cycloadducts are formed predominantly by *endo*-addition, there have been many reports of mixtures of *endo*/*exo*-products.

[21] This has been discussed in: (a) Houk, K. N.; Strozier, R. W. *J. Am. Chem. Soc.* **1973**, *95*, 4904−4096. (b) Alston, P. V.; Ottenbrite, R. M. *J. Org. Chem.* **1975**, *40*, 1111−1116. (c) Birney, D. M.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 4127−4133.

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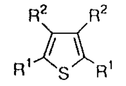
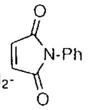
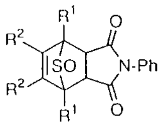
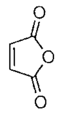
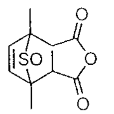
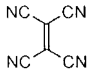
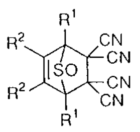
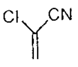
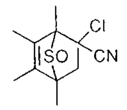
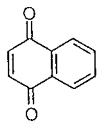
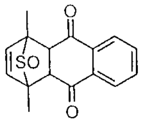
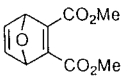
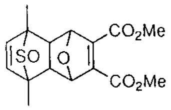
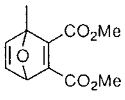
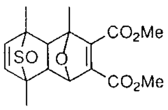
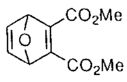
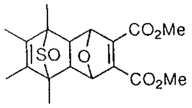
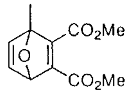
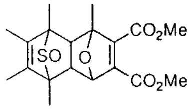
Table 1. Oxidative Diels–Alder Reaction of Thiophenes with Highly Reactive Dienophiles

entry		dienophiles	products	yield (%)	method
1	**1a**: R^1 = Me, R^2 = H	 2	 3	78	A
2	**1b**: R^1 = R^2 = Me		4	74	A
3	**1c**: R^1 = Me, R^2 = $PhCH_2$-		5	70	A
4	**1d**: R^1 =Cl, R^2 = H		6	18	A
5	**1e**: R^1 = Me, R^2 = Br		7	55	A
6	**1a**: R^1 = Me, R^2 = H	 8	 9	50	B
7	**1a**: R^1 = Me, R^2 = H	 10	 11	63	B
8	**1b**: R^1 = R^2 = Me		12	57	B
9	**1b**: R^1 = R^2 = Me	 13	 14	54	B
10	**1a**: R^1=Me, R^2=H	 15	 16	52	A
15	R^1=Me, R^2=H	 23	 24	52	B
16	R^1=Me, R^2=H	 25	 26	53	B
17	R^1=R^2=Me	 23	 27	50	B
18	R^1=R^2=Me	 25	 28	53	B

a method A: one-pot reaction; method B: two-step reaction

σ-bonds formed in the transition state. Cycloadditions to thiophene *S*-monoxides have been predicted to occur *anti* to the lone electron-pair on the sulfur, which is the better hyperconjugative donor when compared to the oxygen of the sulfoxy-moiety. The lone-pair electron orbital at the sulfur will stabilize the vacant σ*-orbitals of the developing incipient σ-bonds better than would any orbital associated with the oxygen of the sulfoxy moiety (Figure 5). This would be even more so, when the oxygen of the sulfoxy-unit is complexed by BF_3.

Adducts **18a** (as mentioned above) and **22** are the only diastereoisomers formed in the reaction of 2,5-dimethylthiophene *S*-oxide with dienophiles **17** and **19**, whereby the formation of **22** proceeds via the monoadduct **20**, which itself acts as the dienophile in the second cycloaddition. X-ray crystal structure analyses[37] show both adducts, **18a** and **24**, to be of *endo*-*trans*-*endo*-configuration. This is in agreement with results of the double-side addition of *p*-benzoquinone with cyclopentadiene, which also show the *endo*-*trans*-*endo*-configuration in the cycloadduct because of steric and electronic factors.[26] Hydrogenation of **18a** with H_2 (Pd/C) gives **18b** as the single

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(25) Macaulay, J. B.; Fallis, A. G. *J. Am. Chem. Soc.* **1990**, *112*, 1136–1144.

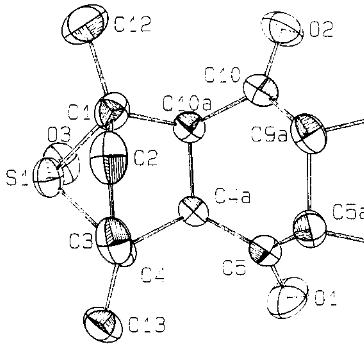
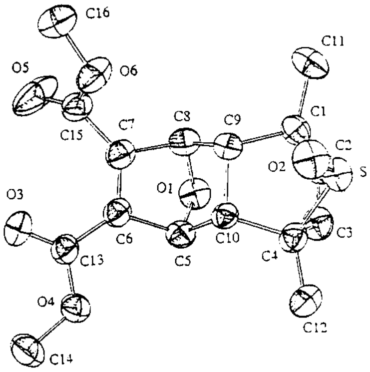
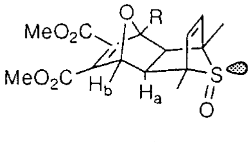


Figure 2. ORTEP structure of **18a**.





exo-endo

24

Figure 3. ORTEP structure of cycloadduct 24.

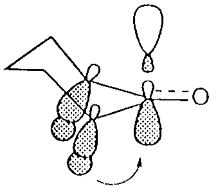


Figure 4. Cieplak effect.

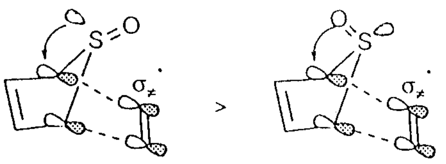
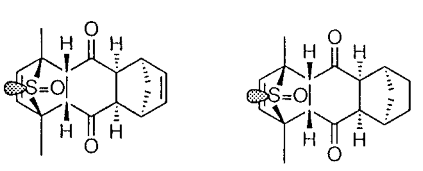


Figure 5.



anti- endo

18a

18b

Figure 6.

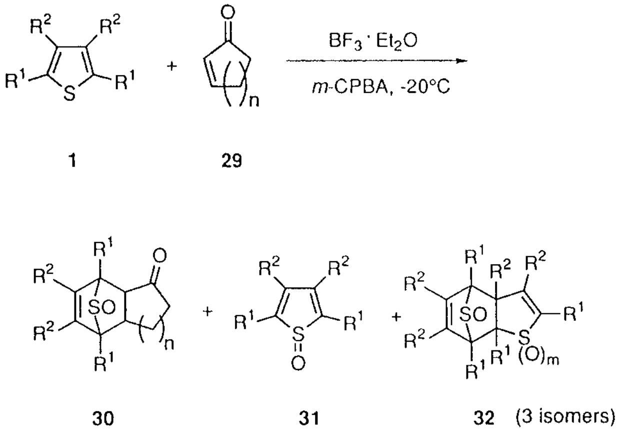
product, where the double bond of the norbornene unit is hydrogenated exclusively, and not the olefinic bond of the thiabicyclo[2.2.1]heptene oxide moiety (Figure 6).

Table 2. BF_3·Et_2O-Catalyzed Cycloaddition of Alkylthiophenes with Unreactive Dienophiles (see Scheme 2)

			products, yield (%)		
entry	thiophenes	dienophiles	**30**	**31**	**32**
1	**1a**: $R^1 = Me$, $R^2 = H$	$n = 1$ **29a**	**30a** (36)		
2	**1b**: $R^1 = R^2 = Me$	$n = 1$	**30b** (28)	**31b** (40)	
3	**1a**	$n = 2$ **29b**	**30c** (8)		(50)[a]
4	**1b**	$n = 2$	**30d** (25)	**31b** (42)	
5	**1a**	$n = 3$ **29c**			(45)[a]
6	**1b**	$n = 3$	**30e** (25)	(54)	

[a] Three isomers have been isolated.

Scheme 2



Although many stereoisomers are possible in the cycloaddition of 2,5-dimethyl- and 2,3,4,5-tetramethylthiophene *S*-oxide with dienophiles **23** and **25**, the crude NMR-spectra of cycloadducts **24**, **26**, **27**, and **28** all show only one cycloadduct formed in each reaction. The cycloaddition of the thiophenes with **23** and **25** occurs on the less substituted olefinic bond of the dienophiles. This is in contrast to the furan-analogues, which at low temperatures add to these dienophiles on the more substituted side. 2,5-Dimethylthiophene *S*-monoxide (**31a**) is much more reactive than 2,5-dimethylfuran which reacts with **23** only at temperatures of and above 100 °C. It has been reported that the bisadduct formed with 2,5-dimethylfuran shows the *exo-endo* configuration, which is kinetically favored over other configurations.[27] The X-ray analysis of the bis-adduct **24** showed it to be the *exo-endo* isomer as well. The same *exo-endo* configuration can be assumed for **26** and **28** from NMR spectra. Here the coupling constant between H_a and H_b $J_{ab} = 0$ Hz, suggesting a dihedral angle between H_a and H_b of about 90° (Figure 3).

Upon addition of BF_3·Et_2O as Lewis acid catalyst, alkylthiophenes react with mono-activated dienophiles **29a**–**c** under oxidative conditions at −20 °C, whereas the reaction does not proceed uncatalyzed. In the uncatalyzed reaction only thiophene *S*,*S*-dioxides are formed as products. The results of the oxidative cycloaddition of 2,5-dimethylthiophene (**1a**) and 2,3,4,5-tetramethylthiophene (**1b**) with less-reactive dienophiles **29** are summarized in Table 2 (Scheme 2). Here, clearly the success of the cycloaddition of alkylthiophenes with **29** can be attributed on the one hand to the reactivity enhancement of the dienophiles by the Lewis acid. On the other hand the intermediate thiophene *S*-monoxides are stabilized against further oxidation to thiophene *S*,*S*-dioxides by complexation of BF_3 on the oxygen of the

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(26) Cookson, R. C.; Hill, R. R.; Hudec, J. *J. Soc. Chem.* **1964**, 3043–3062.

(27) (a) Slee, J. D.; LeGoff, E. *J. Org. Chem.* **1970**, *35*, 3897–3901. (b) McCulloch, A. W.; Smith, D. G.; McInnes, A. G. *Can. J. Chem.* **1973**, *51*, 4125–4136.

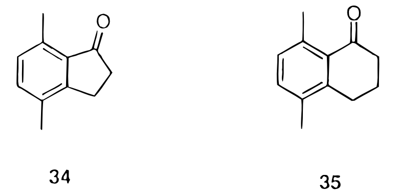


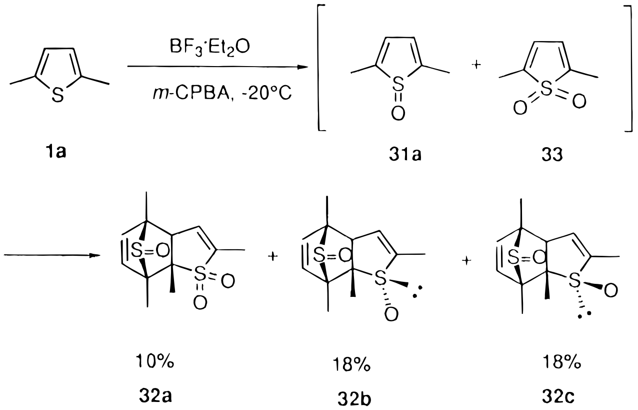
Figure 7.

sulfoxy-moiety, as mentioned above. 2,5-Dimethylthiophene in its reaction with cyclopent-2-enone (**29a**) gave cycloadduct **30a** as the only isolated product in 36% yield. In the cycloaddition of 2,5-dimethylthiophene with cyclohex-2-enone (**29b**) only 8% of the cycloadduct **30c** could be isolated along with dimers (**32**) of the intermediary produced thiophene *S*-monoxide with the thiophene *S*,*S*-dioxide in 50% yield. The ene-system in cyclohept-2-enone (**29c**) is less strained than in **29a** or **29b**; thus the reactivity of **29c** as dienophile is lower. No cycloadduct of 2,5-dimethylthiophene *S*-oxide (**31a**) with **29c** could be isolated. 2,5-Dimethylthiophene *S*-oxide dimerized under the conditions and gave only **32** as products. Clearly the dimerization of the thiophene *S*-monoxides becomes a competing factor at this point (see also below). Nevertheless, there are thiophene *S*-monoxides which do not dimerize readily. Thus the reaction of tetramethylthiophene with dienophiles **29a**−**c** gave the corresponding cycloadducts **30b**, **30d**, and **30e** and the tetramethylthiophene *S*-monoxide (**31b**). It is interesting to note that **31b** is a stable product, although thus far only thiophene *S*-monoxides had been isolated with bulky substituents at positions 2 and 5. Cycloadducts **30a** and **30c** are unstable even at low temperature and extrude their SO-bridge readily to give the indanone **34** and tetralone **35** (Figure 7).

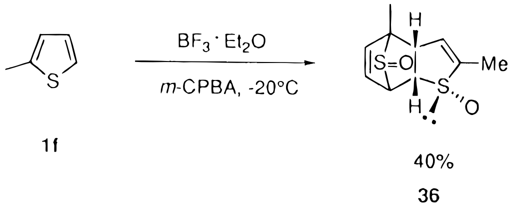
It is known that the oxidation of thiophene and substituted thiophenes leads to cycloadducts of the intermediate thiophene *S*-monoxides as byproducts (see also above). They have been named "sesquioxides".[28] The oxidation of bulkier substituted thiophenes yields virtually no sesquioxides due to steric hindrance. Usually only thiophene *S*,*S*-dioxides are produced in these cases. Only a few sesquioxides have been isolated to date and mostly in low yields; the stereochemistry of these compounds has been conjectured from IR and NMR spectra.[29]

In order to obtain more information about the dimerization of thiophene *S*-oxides, especially in view of the competition of this reaction with the cycloaddition of thiophene *S*-oxides with other dienophiles, the authors attempted a selective preparation of sesquioxides under Lewis acid catalysis. 2,5-Dimethylthiophene (**1a**) was oxidized with *m*-CPBA in the presence of $BF_3 \cdot Et_2O$ (Scheme 3). After no more 2,5-dimethylthiophene could be identified in the reaction mixture, $BF_3 \cdot Et_2O$, excess *m*-CPBA and *m*-chlorobenzoic acid were extracted from the reaction mixture. The resulting product solution in dichloromethane showed 2,5-dimethylthiophene *S*-oxide on TLC. It dimerized, however, as soon as the solvent was evaporated in vacuo, and three dimers could be isolated by careful column chromatography. ^1H, ^{13}C NMR, and mass spectra and elemental analysis showed **32a** to be a Diels−Alder adduct formed by 2,5-dimethylthiophene *S*-oxide acting as diene and 2,5-dimethylthiophene *S*,*S*-dioxide acting as dienophile. The infrared spectrum of **32a** confirmed the presence of a sulfoxide- (1079 cm^{-1}) and a sulfone-group (1146 cm^{-1}, 1284 cm^{-1}), while the IR spectra of **32b** and **32c** only showed SO stretching frequency in the range of 1000−1100 cm^{-1}. **32b** and **32c** are dimerized cycloadducts of 2,5-dimethylthiophene *S*-oxide acting as both diene and dienophile. The difference between **32b** and **32c** is the stereochemistry at one of the sulfur atoms. Meanwhile all three structures have been confirmed by X-ray structure analysis.[30] The three cycloadducts have *endo*-configuration, and the bridged sulfoxy-moiety is configurated in such a way that the lone electron pair is directed toward the newly formed double bond, in accordance to the Cieplak-effect.[24] It is also interesting to note that in the formation of **32a** thiophene *S*,*S*-dioxide plays indeed the role of the dienophile, as under the reaction conditions described, no further oxidation at sulfur can take place after the cycloaddition.

Scheme 3



Scheme 4



Under the same conditions at −20 °C, 2-methylthiophene (**1f**) gives a single dimer **36** of 2-methylthiophene *S*-oxide, stereoselectively and in 40% yield (Scheme 4). It has been known that a single sesquioxide is isolated in the uncatalyzed reaction, when **1f** is oxidized by *m*-CPBA at 0−10 °C. The structure of **36** we first have assigned on the basis of its ^1H NMR, ^{13}C NMR, $^1H-^1H$ COSY, and $^{13}C-^1H$ COSY spectra; it shows coupling patterns in the ^1H NMR similar to those described by W. J. M. van Tilborg[31] for **34**. The stereochemistry at the sulfur atoms was determined by an X-ray analysis[31] of **36** (Figure 8); it shows the two SO groups to be *anti*-configured as in cycloadduct **32b**.

Tetraalkyl substituted thiophene *S*-monoxides **31b** and **31c** could be isolated as stable compounds in 75% yield

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[28] (a) Prochazka, M. *Coll. Czech Chem. Commun.* **1965**, *30*, 1158. (b) Davies, W.; Gamble, N.; James, F. C.; Savige, W. *Chem. Ind. (London)* **1952**, 804−804. (c) Melles, J.; Backer, H. J. *Recl. Trav. Chim. Pays-Bas* **1953**, *72*, 491−496. (d) Davies, W.; James, F. C. *J. Chem. Soc.* **1954**, 15−18. (e) Okita, K.; Kambara, S. *Kogyo Kagaku Zasshi* **1956**, *59*, 547−549. *Chem. Abstr.* **1958**, *52*, 3762.

[29] Merrill, R. E.; Sherwood, G. *J. Heterocycl. Chem.* **1977**, *14*, 1251−1253.

[30] Li, Y.-Q.; Sawada, T.; Thiemann, T.; Hanss, J.; Mataka, S.; Tashiro, M. *Acta Crystallogr.*, submitted.

[31] Van Tilborg, W. J. M. *Synth. Commun.* **1976**, *6*, 583−589.

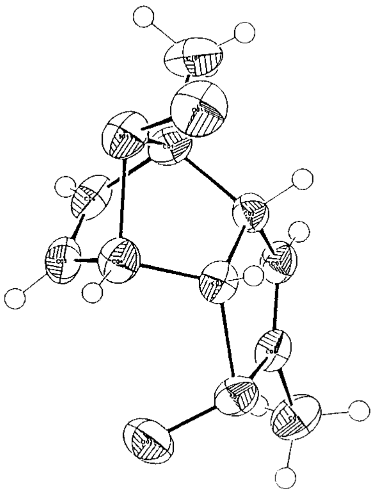
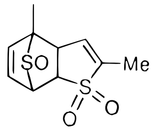


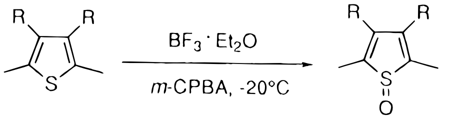
Figure 8. ORTEP structure of 36.



37 [31]

Figure 9.

Scheme 5



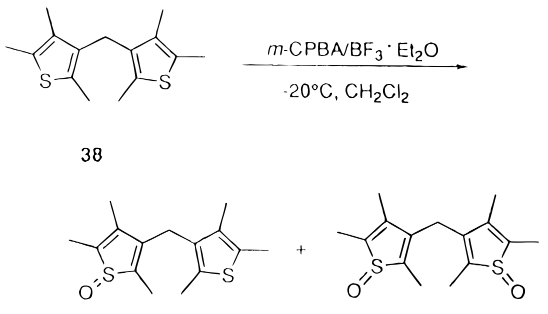
1

R = Me (**31b**), Y. 75%
R = $PhCH_2$- (**31c**), Y. 74%

(Scheme 5). They showed no tendency to dimerize immediately after workup. A formation of thiophene *S*,*S*-dioxides as byproducts could be prevented by using a 4-fold amount of $BF_3 \cdot Et_2O$ during the oxidation. Compound **31c** is rather stable in the solid state and does not change for a long time when at room temperature. **31b**, however, dimerizes slowly to give three isomers after a couple of days at room temperature. Unfortunately **31c** is more sensitive in solution, and it was difficult to get proper crystals of **31c** for X-ray analysis.

The oxidation of the two-core compound **38** gives the mono thiophene *S*-monoxide (**39**) and the bis-thiophene *S*-monoxide (**40**) (Scheme 6). The yields of **39** and **40** depend on the number of equivalents of *m*-CPBA used in the reaction. Interestingly the thiophene ring in **39** can compete with the thiophene *S*-monoxide unit for the *m*-CPBA. This clearly shows that the use of BF_3 shields the thiophene *S*-monoxide from further oxidation to thiophene *S*,*S*-dioxide. Compound **40** reacts with dimethyl acetylenedicarboxylate at room temperature to give the bisarene **41** in 60% yield (Scheme 7). As is usual in reactions with alkynes, the primary cycloadduct is unstable and extrudes SO immediately to give the aromatized products.

Scheme 6



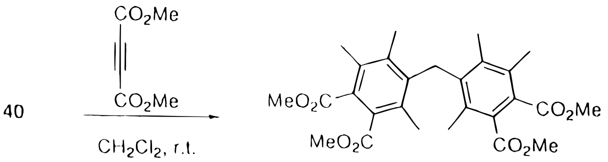
38

39

40

m-CPBA	yield (%) 39	40
1.5 equiv.	50	30
3.0 equiv.	22	68

Scheme 7



Y. 66 %

41

Conclusion

Alkylthiophenes and some halogen-substituted thiophenes cycloadd with dienophiles, when they are oxidized *in situ* by *m*-CPBA. These reactions can be catalyzed by $BF_3 \cdot Et_2O$ as Lewis acid with enhanced yields of up to 75%. The Lewis acid is thought to complex to the oxygen of the sulfoxy-moiety and to have two effects: (1) It decreases the nucleophilicity of the sulfur of the sulfoxy-moiety and thus decreases its oxidativity. (2) It increases the stereoselectivity in certain cycloadditions. Moreover, the Lewis acid catalyst increases the reactivity of certain dienophiles and thus enlarges the variety of possible dienophiles for the oxidative cycloaddition of thiophenes.

This reaction can be performed in two ways, in a one-pot reaction or a two-step synthesis. In the two-step sequence it is possible to prepare alkyl-substituted thiophene *S*-monoxides in solution by oxidation of thiophenes with *m*-CPBA under $BF_3 \cdot Et_2O$ catalysis; they can be reacted with dienophiles under neutral conditions in a second step. This prevents the decomposition of acid-labile dienophiles. The oxidative cycloaddition of thiophenes under BF_3 catalysis always gives *endo*-products with the bridge S=O group always directed to the approaching dienophile.

Oxidation of 2-methylthiophene and 2,5-dimethylthiophene under BF_3-catalysis gives dimers of the corresponding thiophene *S*-monoxides, which act as both the diene and the dienophile. When 2,3,4,5-tetramethylthiophene and 3,4-dibenzyl-2,5-dimethylthiophene are oxidized with *m*-CPBA in the presence of BF_3, the corresponding thiophene *S*-monoxides have been isolated as stable products.

Experimental Section

Melting points were determined on a Mitamurariken MELT THERMO and are uncorrected. IR spectra were recorded on a JASCO-102 spectrometer. NMR spectra were recorded at 270 MHz (proton) and at 67.9 MHz (carbon-13) with a JEOL

GSX-270 spectrometer with $SiMe_4$ as internal standard. *J*-values are given in Hz. UV spectra were measured on a Hitachi 220A spectrophotometer. Mass spectra were obtained on a JEOL JMS-O1SG-2 mass spectrometer at 70 eV using a direct-inlet system. Column chromatography was carried out on silica gel (Wako gel, C-300).

***N*-Phenyl-1,4-dimethyl-7-thiabicyclo[2.2.1]hept-5-ene-2,3-dicarboxamide 7-oxide (3). A Typical *One-Pot* Procedure for the $BF_3\cdot Et_2O$-Catalyzed Oxidative Cycloaddition of Thiophenes with Dienophiles.** To a solution of 2,5-dimethylthiophene (300 mg, 2.68 mmol) and *N*-phenylmaleimide (700 mg, 4.05 mmol) in dry CH_2Cl_2 (10 mL) was added slowly $BF_3\cdot Et_2O$ (2 mL, 16.2 mmol) under an inert atmosphere and at −20 °C. The reaction mixture was stirred for 10 min at −20 °C, and then a solution of *m*-CPBA (700 mg, 4.06 mmol) in dry CH_2Cl_2 (15 mL) was added slowly. The reaction mixture was stirred for 2 h at −20 °C. Then the suspension was poured into a mixture of concd aqueous $NaHCO_3$ solution (30 mL) and CH_2Cl_2 (50 mL) and stirred at room temperature for 20 min. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with water and brine and dried over anhydrous $MgSO_4$. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel to give **3** as colorless crystals (630 mg, 78%). **3**: mp 174−175 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ (s, 6H, 2 CH_3), 3.83 (s, 2H), 6.21 (s, 2H), 7.15 (m, 2H), 7.35 − 7.53 (m, 3H); ^{13}C NMR (67.9 MHz; $CDCl_3$) δ 14.27, 50.40, 72.56, 126.50, 128.93, 131.53, 132.56, 174.18; IR (KBr) 1774 (C=O), 1711 (C=O), 1081, 1063 cm^{-1}; MS (70 eV) *m*/*z* (%) 301 (M^+, 0.7), 253 (M^+ − SO, 85.6). Anal. Calcd for $C_{16}H_{15}NO_3S$: C, 63.77; H, 4.64; N, 5.01. Found: C, 63.77; H, 4.49; N, 5.00.

***N*-Phenyl-2,3,4,5-tetramethyl-7-thiabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide 7-Oxide (4).** **1b** (300 mg, 2.14 mmol) was reacted with $BF_3\cdot Et_2O$ (3 mL, 24.3 mmol), *m*-CPBA (480 mg, 2.78 mmol), and *N*-phenylmaleimide (130 mg, 0.7 mmol) as described for **3** to give **4** (420 mg, 74%): mp 225−226 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.75 (s, 6H, 2 CH_3), 1.80 (s, 6H, 2 CH_3), 3.75 (s, 2H), 7.10 (m, 2H), 7.35−7.55 (m, 3H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 11.88, 12.97, 50.95, 73.22, 126.36, 128.89, 129.31, 131.61, 131.75, 174.50; IR (KBr) 3074, 1773 (C=O), 1714 (C=O), 1596, 1495, 1452, 1370, 1178, 1102, 1066 cm^{-1}; MS (70 eV) *m*/*z* (%) 329 (M^+, 4.6), 281 (M^+ − SO, 17.6). Anal. Calcd for $C_{18}H_{19}NO_3S$: C, 65.57; H, 5.90; N, 4.19. Found: C, 65.65; H, 5.78; N, 4.26.

***N*-Phenyl-3,4-dibenzyl-2,6-dimethyl-7-thiabicyclo[2.2.1]-hept-5-ene-3,3-carbox-imide 7-Oxide (5).** **1c** (300 mg, 1.03 mmol) was treated with $BF_3\cdot Et_2O$ (2 mL, 16.1 mmol), *m*-CPBA (250 mg, 1.45 mmol), and *N*-phenylmaleimide (250 mg, 1.45 mmol) as described for **3** to give **5** (350 mg, 70%): mp 72−73 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.67 (s, 6H, 2 CH_3), 3.56 (d, 2H, ^2J = 16.0 Hz), 3.76 (s, 2H), 3.82 (d, 2H, ^2J = 16.0 Hz), 7.04 − 7.52 (m, 15H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 13.46, 32.72, 51.23, 73.94, 126.13, 126.77, 128.43, 128.68, 128.73, 128.95, 129.14, 131.62, 136.94, 137.05, 147.09; IR (KBr) 1700 (C=O) and 1060 cm^{-1}; MS (70 eV) *m*/*z* (%) 433 (M^+ − SO, 47.1), 342 (6.9), 193 (100). HRMS *m*/*z* $C_{30}H_{27}NO_3S$: Calcd 481.1712, Found: 481.1818. Anal. Calcd for $C_{30}H_{27}NO_3S$: C, 74.82; H, 5.65; N, 2.91. Found C, 74.82; H, 5.84; N, 2.83.

***N*-Phenyl-2,3-dibromo-1,4-dimethyl-7-thiabicyclo[2.2.1]-hept-5-ene-2,3-dicarboximide 7-Oxide (7).** **1e** (300 mg, 1.11 mmol) was transformed with $BF_3\cdot Et_2O$ (2 mL, 16.2 mmol), *m*-CPBA (480 mg, 2.78 mmol), and *N*-phenylmaleimide (250 mg, 1.45 mmol) to produce **7** (280 mg, 55%): mp 232−234 °C (from hexane/benzene); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.90 (s, 6H, 2 CH_3), 3.88 (s, 2H), 7.16 (m, 2H), 7.43 − 7.48 (m, 3H); IR (KBr) 1781 (C=O), 1715 (C=O), 1037 (w), 991 (s, S=O) cm^{-1}; MS (70 eV) *m*/*z* (%) 413, 411, 409 (M^+ − SO, 15.8). HRMS *m*/*z* $C_{16}H_{13}Br_2NO_3S$: Calcd 4060.8944; 458.8963; 456.8983. Found: 460.8949; 458.8960; 456.8980. Anal. Calcd for $C_{16}H_{13}Br_2NO_3S$: C, 41.85; H, 2.85; N, 3.05. Found: C, 41.24; H, 3.10; N, 3.82.

1,12-Dimethyl-15-thiatetracyclo[10.2.1.0^{2,11}.0^{4,9}]pentadeca-4,6,8,13-tetraene-3,10-dione 15-Oxide (16). Cycloaddition of 2,5-Dimethylthiophene to Naphthoquinone (15). **1a** (250 mg, 2.23 mmol) was reacted with $BF_3\cdot Et_2O$ (3 mL, 24.3 mmol), *m*-CPBA (580 mg, 3.36 mmol), and naphthoquinone (800 mg, 4.6 mmol) as described for **3** to give **16** (440 mg, 52%): mp 169−170 °C dec; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.75 (s, 6H, 2 CH_3), 3.83 (s, 2H), 5.88 (s, 2H), 7.73 (dd, 2H, *J* = 3.3 Hz, *J* = 5.9 Hz), 7.99 (dd, 2H, *J* = 3.3 Hz, *J* = 5.9 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 14.34, 52.74, 74.25, 126.70, 132.76, 134.46, 136.69, 194.93; IR (KBr) 1679 (C=O) and 1076 cm^{-1}; MS (70 eV) *m*/*z* (%) 238 (M^+ − SO, 28), 223 (4.2). HRMS *m*/*z* $C_{16}H_{14}O_3S$: Calcd 286.0664. Found 286.0656. Anal. Calcd for $C_{16}H_{14}O_3S$: C, 67.12; H, 4.92. Found: C, 67.04; H, 5.43.

1,12-Dimethyl-15-thiapentacyclo[10.2.1.1^{5,8}.0^{2,4}.0^{4,9}]-hexadeca-6,13-diene-3,10-dione 15-Oxide (18a). **18a**: (440 mg, 65%): mp 282−283 °C (dec, from benzene); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.23 (d, 1H, ^2J = 9.0 Hz), 1.47 (d, 1H, ^2J = 9.0 Hz), 1.54 (s, 6H, 2 CH_3), 2.96 (m, 2H), 3.26 (s, 2H), 3.36 (m, 2H), 6.18 (m, 2H), 6.24 (s, 2H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 13.69, 45.71, 47.53, 57.34, 73.76, 132.90, 137.10, 208.44; IR (KBr) 1700 (C=O), 1070, 1050, 1030 cm^{-1}; MS (70 eV) *m*/*z* (%) 302 (M^+, 32.5), 226 (M^+ − SO, 10), 210 (8.7). Anal. Calcd for $C_{17}H_{18}O_3S$: C, 67.52; H, 6.00. Found: C, 67.54; H, 6.03.

1,12-Dimethyl-15-thiapentacyclo[10.2.1.1^{5,8}.0^{2,4}.0^{4,9}]-hexadeca-13-ene-3,10-dione 15-Oxide (18b). A mixture of **18a** (120 mg, 0.40 mmol) and Pd/C (10 wt %, 10 mg) in MeOH (5 mL) was stirred under a hydrogen atmosphere. After 24 h Pd/C was filtered off and washed with MeOH. The filtrate was concentrated *in vacuo* to yield **18b** (100 mg, 83%) as colorless crystals.

18b: (100 mg, 83%): mp 185 °C (dec, from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.13−1.38 (m, 6H), 1.47 (s, 6H), 2.54 (s, 2H), 2.65 (s, 2H), 3.31 (s, 2H), 6.16 (s, 2H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 12.45, 22.71, 38.69, 52.72, 56.86, 73.24, 131.55, 207.31; IR (KBr) 1690 (C=O), 1440, 1070 cm^{-1}; MS (70 eV) *m*/*z* (%) 256 (M^+ − SO), 241. HRMS *m*/*z* $C_{17}H_{20}O_3S$: Calcd 304.1133. Found: 304.1125.

1,8-Dimethyl-11-thiatricyclo[6.2.1.0^{2,7}]undeca-4,9-diene-3,6-dione 11-Oxide (20). Cycloaddition of 2,5-Dimethylthiophene with *p*-Benzoquinone (19). **1a** (300 mg, 2.68 mmol) was treated with $BF_3\cdot Et_2O$ (2 mL, 16.2 mmol), *m*-CPBA (600 mg, 3.48 mmol), and *p*-benzoquinone (580 mg, 5.3 mmol) as described for **3** to yield **20** (370 mg, 58%): mp 152−154 °C (dec, from benzene, lit. 139 °C[11]); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.63 (s, 6H, 2 CH_3), 3.54 (s, 2H), 5.99 (s, 2H), 6.62 (s, 2H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 14.21, 51.45, 73.84, 132.88, 143.01, 196.37; MS (70 eV) *m*/*z* (%) 236 (M^+, 32.5), 188 (M^+ − SO, 77).

1,8,9,10-Tetramethyl-11-thiatricyclo[6.2.1.0^{2,7}]undeca-4,9-diene-3,6-dione 11-Oxide (21). Cycloaddition of 2,3,4,5-Tetramethylthiophene with *p*-Benzoquinone (19). **1b** (300 mg, 1.03 mmol) was reacted with $BF_3\cdot Et_2O$ (2 mL, 16.2 mmol), *m*-CPBA (550 mg, 3.2 mmol), and *p*-benzoquinone (460 mg, 4.29 mmol) as described for **3** to give **21** (370 mg, 60%): mp 175 °C (dec., from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.61 (s, 6H, 2 CH_3), 1.63 (s, 6H, 2 CH_3), 3.51 (s, 2H), 6.64 (s, 2H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 11.90, 12.79, 52.40, 74.68, 132.00, 142.50, 196.69; IR (KBr) 1676, 1072 (s), 1035 cm^{-1}; MS (70 eV) *m*/*z* (%) 264 (M^+, 4.0), 216 (M^+ − SO, 91.2). Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10. Found: C, 63.56; H, 6.28.

1,5,8,12-Tetramethyl-15,16-dithiapentacyclo-[10.2.1.^{15,8}.0^{2,11}.0^{4,9}]hexadeca-6,13-diene-3,10-dione 15,16-Dioxide (22). Synthesis of Bis-Cycloadduct of 2,5-Dimethylthiophene with *p*-Benzoquinone (19). Typical Two-Step Procedure of Oxidative Cycloaddition of Thiophenes with Dienophiles. $BF_3\cdot Et_2O$ (2 mL, 16.2 mmol) was added to a solution of 2,5-dimethylthiophene (300 mg, 2.68 mmol) in dry CH_2Cl_2 (10 mL) under an inert atmosphere and at −20 °C. The mixture was stirred for 10 min at −20 °C. Then a solution of *m*-CPBA (700 mg, 4.06 mmol) in CH_2Cl_2 (20 mL) was added dropwise, and the resulting mixture was stirred for 2 h at −20 °C. Then the suspension was poured into a mixture of concd aqueous $NaHCO_3$ solution (20 mL) and CH_2Cl_2 (50 mL) and stirred at room temperature for 20 min. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic solution was washed with water and dried over anhydrous

$MgSO_4$. The $MgSO_4$ was filtered off, and to the filtrate was added *p*-benzoquinone (100 mg, 0.9 mmol) in several portions until the 2,5-dimethylthiophene *S*-oxide reached completely (TLC control). The solvent was evaporated *in vacuo*, and the residue was chromatographed on silica gel to give a trace of **20** (10 mg, 4%) and **22** (320 mg, 50%) as colorless crystals.

22: mp 204 °C (from ether); ^{1}H-NMR (270 MHz, $CDCl_3$) δ 1.63 (s, 12H, 4 CH_3), 3.40 (s, 4H), 6.28 (s, 4H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 14.36, 58.28, 72.60, 133.30, 205.48; IR (KBr) 1703 (C=O), 1457, 1382, 1355, 1300, 1186, 1106, 1070, 1020 cm^{-1}; MS (70 eV) *m/z* (%) 416 (M^+ − SO), 268 (59.0). Anal. Calcd for $C_{18}H_{20}O_4S_2$: C, 59.32; H, 5.53. Found: C, 58.89; H, 5.69.

5,5,6,6-Tetracyano-1,4-dimethyl-7-thiabicyclo[2.2.1]hept-2-ene *S*-Oxide (11). **1a** (200 mg, 1.8 mmol) was reacted with $BF_3 \cdot Et_2O$ (2 mL, 16.2 mmol), *m*-CPBA (400 mg, 2.3 mmol), and TCNE (150 mg, 1.17 mmol) as described for **3** to yield **11** (290 mg, 63%): mp 235 °C (dec, from ether); ^{1}H NMR (270 MHz, CD_2Cl_2) δ 2.06 (s, 6H, 2 CH_3), 6.53 (s, 2H); ^{13}C NMR (67.9 MHz, CD_2Cl_2) δ 13.10, 77.00, 107.78, 110.37, 135.31; IR (KBr) 1448, 1390, 1090, 1073 cm^{-1}; MS (70 eV) *m/z* (%) 256 (M^+), 208 (M^+ − SO, 39.7), 193 (100). Anal. Calcd for $C_{12}H_8N_4OS$: C, 56.24; H, 3.15; N, 21.86. Found: C, 55.57; H, 3.30; N, 21.16. HRMS *m/z* $C_{12}H_8N_4OS$: Calcd 256.0415. Found: 256.0419.

5,5,6,6,-Tetracyano-1,2,3,4-tetramethyl-7-thiabicyclo[2.2.1]hept-2-ene *S*-Oxide (12). **1b** (300 mg, 2.14 mmol) was reacted with $BF_3 \cdot Et_2O$ (1.5 mL, 11.8 mmol), *m*-CPBA (480 mg, 2.79 mmol), and TCNE (160 mg, 1.25 mmol) as described for **3** to give **12** (350 mg, 57%): mp 258−259 °C (dec, from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.99 (s, 6H, 2 CH_3), 2.00 (s, 6H, 2 CH_3); ^{13}C NMR (67.9 MHz, CD_2Cl_2) δ 11.54, 12.67, 52.60, 78.04, 108.12, 110.31, 135.63; IR (KBr) 1453, 1391, 1117, 1078 cm^{-1}; MS (70 eV) *m/z* (%) 236 (M^+ − SO, 16.8), 221 (80.5), 194 (40.8).

5-Chloro-5-cyano-1,2,3,4-tetramethyl-7-thiabicyclo[2.2.1]hept-2-ene *S*-Oxide (14). **1b** (140 mg, 1.0 mmol) was reacted with $BF_3 \cdot Et_2O$ (0.6 mL, 4.73 mmol), *m*-CPBA (220 mg, 1.3 mmol), and 1-chloro-1-cyanoethylene (170 mg, 2.0 mmol) to give **14** (130 mg, 54%): mp 90 °C (from hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.47 (s, 3H, CH_3), 1.76 (s, 3H, CH_3), 1.83 (s, 6H, 2 CH_3), 2.42 (d, 1H, ^2J = 14.5 Hz), 3.36 (d, 1H, ^2J = 14.5 Hz); IR (KBr) 2980, 2932, 2234, 1642, 1458, 1386, 1072 cm^{-1}; MS (70 eV) *m/z* (%) 243 (M^+, 6.9), 195 (M^+ − SO, 100). Anal. Calcd for $C_{11}H_{14}NOClS$: C, 54.20; H, 5.79; N, 5.75. Found: C, 54.13; H, 5.81; N, 5.85.

Dimethyl 1,8-Dimethyl-12-oxa-11-thiatetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene-4,5-dicarboxylate 11-Oxide (24). Cycloadduct of 2,5-Dimethylthiophene with 1:1 Adduct of Furan with DMAD (23). $BF_3 \cdot Et_2O$ (2 mL, 16.2 mmol) was added to a solution of 2,5-dimethylthiophene (300 mg, 2.68 mmol) in dry CH_2Cl_2 (10 mL) under an inert atmosphere and at −20 °C. The mixture was stirred for 10 min at −20 °C. Thereafter a solution of *m*-CPBA (1.10 g, 5.90 mmol) in CH_2Cl_2 (20 mL) was added dropwise, and the resulting reaction mixture was stirred for 2 h at −20 °C. Then the suspension was poured into a mixture of a concd aqueous solution of $NaHCO_3$ (20 mL) and CH_2Cl_2 (50 mL) and stirred at room temperature for 20 min. The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (3 × 20 mL). The combined organic solution was washed with water and dried over anhydrous $MgSO_4$. $MgSO_4$ was filtered off, and to the filtrate was added dimethyl 7-oxabicyclo[2.2.1]hepta-2,5-diene-3,4-dicarboxylate (**23**) (400 mg, 3.57 mmol). The resulting reaction mixture was stirred for 1 h at ambient temperature. The solvent was evaporated *in vacuo*, and the residue was chromatographed on silica gel to yield **24** (475 mg, 52%) as colorless crystals.

24: mp 110−112 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.57 (s, 6H, 2 CH_3), 3.09 (s, 2H), 3.82 (s, 6H, 2 $COOCH_3$), 5.03 (s, 2H), 6.02 (s, 2H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 15.31, 52.89, 54.81, 70.68, 82.16, 132.00, 147.15, 162.80; IR (KBr) 1740 (C=O), 1640, 1430, 1220, 1050 cm^{-1}; MS (70 eV) *m/z* (%) 232 (M^+ − 2[$C_2H_2O_2$], 4.3), 184 (232 − SO, 16.2), 153 (69.4), 106 (100). Anal. Calcd for $C_{16}H_{18}O_6S$: C, 56.79; H, 5.36. Found: C, 56.79; H, 5.19.

Dimethyl 1,3,8-Trimethyl-12-oxa-11-thiatetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene-4,5-dicarboxylate 11-Oxide (26). **1a** (200 mg, 1.79 mmol) was reacted with $BF_3 \cdot Et_2O$ (2 mL), *m*-CPBA (400 mg, 2.32 mmol), and **25** (320 mg, 1.43 mmol) as described for **24** to produce **26** (330 mg, 53%): mp 103−105 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.56 (s, 3H, CH_3), 1.60 (s, 3H, CH_3), 1.61 (s, 3H, CH_3), 3.08 (d, 1H, ^3J = 7.6 Hz), 3.23 (d, 1H, ^3J = 7.6 Hz), 3.79 (s, 3H, $COOCH_3$), 3.83 (s, 3H, $COOCH_3$), 4.92 (1H, s), 6.03 (d, 1H, ^3J = 6.9 Hz), 6.09 (d, 1H, ^3J = 6.9 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 14.58, 15.94 (2C), 52.23 (2C), 55.87, 57.81, 69.42, 70.12, 79.35; 91.12, 130.85, 132.06, 145.14, 151.28, 162.05, 163.92; IR (KBr) 1740 (C=O), 1720 (C=O), 1630, 1430, 1050, 1010 cm^{-1}; MS (70 eV) *m/z* (%) 246 (M^+ − 2[$C_2H_2O_2$], 199 (100). Anal. Calcd for $C_{17}H_{20}O_6S$: C, 57.94; H, 5.72. Found: C, 57.76; H, 5.79.

Dimethyl 1,8,9,10-Tetramethyl-12-oxa-11-thiatetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene-4,5-dicarboxylate 11-Oxide (27). **1b** (160 mg, 1.14 mmol) was reacted with $BF_3 \cdot Et_2O$ (2 mL, 16.2 mmol), *m*-CPBA (260 mg, 1.5 mmol), and **23** (250 mg, 1.2 mmol) as described for **24** to give **27** (260 mg, 50%): mp 166−168 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.52 (s, 6H, 2 CH_3), 1.72 (s, 6H, 2 CH_3), 2.94 (s, 2H), 3.81 (s, 6H, 2 $COOCH_3$), 4.92 (s, 2H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 12.33, 13.46, 52.42, 53.78, 70.13, 81.42, 129.67, 147.00, 162.44; IR (KBr) 1720 (C=O), 1640, 1430, 1058, 990 cm^{-1}; MS (70 eV) *m/z* (%) 335 (4.3), 182 (36.1), 135 (100). Anal. Calcd for $C_{18}H_{22}O_6S$: C, 59.00; H, 6.05. Found: C, 58.64; H, 6.15.

Dimethyl 1,3,8,9,10-Pentamethyl-12-oxa-11-thiatetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene-4,5-dicarboxylate 11-Oxide (28). **1b** (160 mg, 1.14 mmol) was reacted with $BF_3 \cdot Et_2O$ (2 mL, 16.2 mmol), *m*-CPBA (260 mg, 1.5 mmol), and **25** (260 mg, 1.2 mmol) is described for **24** to give **28** (230 mg, 53%): mp 125−126 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.48 (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 1.59 (s, 3H; CH_3), 1.76 (s, 3H, CH_3), 1.84 (s, 3H, CH_3), 3.01 (d, 1H, ^3J = 7.6 Hz), 3.05 (d, 1H, ^3J = 7.6 Hz), 3.78 (s, 3H, $COOCH_3$), 3.82 (s, 3H, $COOCH_3$), 4.82 (s, 1H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 12.54, 12.60, 13.39, 14.72, 15.36, 52.33, 52.36, 55.27, 58.22, 69.38, 70.96, 79.17, 91.07, 129.34, 131.19, 145.35, 150.71, 162.12, 164.11; IR (KBr) 1710 (C=O) and 1058 cm^{-1}; MS (70 eV) *m/z* (%) 199 (9.7), 167 (17.3), 135 (100). Anal. Calcd for $C_{19}H_{24}O_6S$: C, 59.98; H, 6.36. Found: C, 59.95; H, 6.42.

1,7-Dimethyl-10-thiatricyclo[5.2.1.0^{2,6}]dec-8-en-3-one 10-Oxide (30a). $BF_3 \cdot Et_2O$-Catalyzed Cycloaddition of 2,5-Dimethylthiophene with Cyclopent-2-enone (29a). $BF_3 \cdot Et_2O$ (2 mL) was added to a solution of 2,5-dimethylthiophene (300 mg, 2.68 mmol) and cyclopent-2-enone (**29a**) (0.45 mL, 5.4 mmol) in CH_2Cl_2 (15 mL) under an inert atmosphere and at −20 °C. The reaction mixture was stirred for 10 min at −20 °C. Then a solution of *m*-CPBA (700 mg, 4.05 mmol) in dry CH_2Cl_2 (15 mL) was added slowly. The reaction mixture was stirred for another 4 h at −20 °C. Then the suspension was poured into a mixture of a concd aqueous solution of $NaHCO_3$ (30 mL) and CH_2Cl_2 (50 mL). The resulting mixture was stirred for 20 min at room temperature. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with water and brine and dried over anhydrous $MgSO_4$. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel to give **30a** (200 mg, 36%) as a colorless oil. **30a**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.53 (s, 3H, CH_3), 1.64 (s, 3H, CH_3), 1.67−2.28 (m, 4H), 3.21 (d, 1H, *J* = 9.4 Hz), 3.46 (ddd, 1H, *J* = 3.4 Hz, 9.4 Hz, 9.7 Hz), 6.08 (d, 1H, ^3J = 7.1 Hz), 6.12 (d, 1H, ^3J = 7.1 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 13.78, 14.18, 19.64, 41.53, 46.27, 57.43, 73.46, 73.64, 132.95, 133.67, 218.29; IR (neat) 1720 (C=O) and 1060 cm^{-1}; MS (70 eV) *m/z* (%) 210 (M^+, 8.4) and 164 (19.5).

1,7,8,9-Tetramethyl-10-thiatricyclo[5.2.1.0^{2,6}]dec-8-en-3-one 10-Oxide (30b). Cycloaddition of 2,3,4,5-Tetramethylthiophene with Cyclopent-2-enone (29a). 39b: (190 mg, 28%): mp 106−107 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.49 (s, 3H, CH_3), 1.59 (s, 3H, CH_3), 1.67 (s, 3H, CH_3), 1.80 (s, 3H, CH_3), 1.97−2.29 (m, 4H), 3.06 (d, ^{1}H, *J* = 9,5 Hz), 3.47 (ddd, 1H, *J* = 3.8 Hz, 9.5 Hz, 9.5 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 13.19, 13.50, 13.71, 18.94, 67.57, 72.27, 73.69, 75.87, 126.70, 127.15, 129.11, 134.93, 145.59; IR (KBr)

1729 (C═O), 1464, 1440, 1189, 1165, 1104, 1060, 959 cm^{-1}; MS (70 eV) *m/z* (%) 238 (M$^+$, 4.4), 191 (75.3), 172 (53.5), 148 (100). Anal. Calcd for $C_{13}H_{18}O_2S$: C, 65.51; H, 7.61. Found: C, 65.41; H, 7.65.

1,8-Dimethyl-11-thiatricyclo[6.2.1.0^{2,7}]undec-9-en-3-one 11-Oxide (30c). Cycloaddition of 2,5-Dimethylthiophene with Cyclohex-2-enone (29b). 30c: (90 mg, 8%): mp 80−82 °C (from ether/hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.49 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 2.08−2.60 (m, 6H), 3.24 (d, 1H, J = 3.9 Hz), 3.28 (d, 1H, J = 3.9 Hz), 5.82 (d, 1H, ^3J = 6.9 Hz), 6.20 (d, 1H, ^3J = 6.9 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 13.68, 15.29, 21.71, 23.92, 38.87, 45.45, 55.42, 71.18, 71.43, 131.12, 135.42, 212.09; IR (KBr) 1700 (C═O), 1440, 1380, 1350, 1290, 1150, 1080, 900 cm^{-1}; MS (70 eV) *m/z* (%) 224 (M$^+$, 3) and 176 (M$^+$ − SO, 100). Anal. Calcd for $C_{12}H_{16}O_2S$: C, 64.25; H, 7.19. Found: C, 64.08; H, 6.87.

1,8,9,10-Tetramethyl-11-thiatricyclo[6.2.1.0^{2,7}]undec-9-en-3-one 11-Oxide (30d). Cycloaddition of 2,3,4,5-Dimethylthiophene with Cyclohex-2-enone (29b). 30d: (170 mg, 25%): mp 132−133 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.48 (s, 3H, CH_3), 1.66 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 1.79 (s, 3H, CH_3), 1.89−2.41 (m, 6H), 3.17 (m, 1H), 3.18 (m, 1H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 12.35, 12.42, 12.62, 14.02, 21.78, 23.67, 39.01, 46.51, 55.10, 71.81, 72.04, 130.93, 134.47, 212.70; IR (KBr) 1698 (C═O), 1445, 1376, 1057, 1027, 878 cm^{-1}; MS (70 eV) *m/z* (%) 252 (M$^+$, 12.9), 203 (42.6), 161 (82.3). Anal. Calcd for $C_{14}H_{20}O_2S$: C, 66.63; H, 7.99. Found: C, 66.75; H, 8.01.

1,9,10,11-Tetramethyl-12-thiatricyclo[7.2.1.0^{2,8}]dodec-10-en-3-one 12-Oxide (30e). Cycloaddition of 2,3,4,5-Tetramethylthiophene with Cyclohept-2-enone (29c). 30e: (140 mg, 25%): mp 115−117 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.80−0.85 (m, 1H), 1.42 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.57 (m, 1H), 1.65 (s, 3H, CH_3), 1.71 (m, 1H), 1.79 (m, 1H), 1.90 (s, 3H, CH_3), 2.32 (m, 1H), 2.51 (m, 1H), 2.82 (ddd, 1H, J = 1.5 Hz, 11.5 Hz, 11.5 Hz), 3.78 (d, 1H, J = 10.0 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 12.37, 12.47 (2C), 13.34, 23.52, 25.27, 27.14, 43.65, 45.61, 60.58, 70.41, 71.66, 129.58, 133.76, 210.80; IR (KBr) 2880, 1703 (C═O), 1456, 1134, 1095, 1056 cm^{-1}; MS (70 eV) *m/z* (%) 266 (M$^+$, 3), 218 (100), 190 (16). Anal. Calcd for $C_{15}H_{22}O_2S$: C, 67.63; H, 8.32. Found: C, 67.52; H, 8.28.

BF_3-Catalyzed Oxidation of Dimethylthiophene (1a) in the Absence of Additional Dienophiles. $BF_3\cdot Et_2O$ (2.0 mL, 16.1 mmol) was added to a solution of 2,5-dimethylthiophene (400 mg, 3.57 mmol) in dry CH_2Cl_2 (10 mL) under an inert atmosphere and at −20 °C. The reaction mixture was stirred for 10 min at −20 °C. Then a solution of *m*-CPBA (900 mg, 5.20 mmol) in dry CH_2Cl_2 (20 mL) was added slowly. The reaction mixture was stirred for another 2 h at −20 °C. Then the suspension was poured into a mixture of a concd aqueous solution of $NaHCO_3$ (20 mL) and CH_2Cl_2 (50 mL). The resulting mixture was stirred for 20 min at room temperature. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with water and brine and dried over anhydrous $MgSO_4$. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel to give **32a−c.**

1,2,4,7-Tetramethyl-3,10-dithiatricyclo[5.2.1.0^{2,6}]deca-4,8-diene 3,3,10-Trioxide (32a) (49 mg, 12%): R$_f$ 0.40 (ether); mp 176−178 °C (dec, from benzene); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.57 (s, 3H, CH_3), 1.74 (s, 3H, CH_3), 1.87 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 3.65 (bs, 1H), 5.81 (d, 1H, ^3J = 6.9 Hz), 6.04 (bs, 1H), 6.25 (d, 1H, ^3J = 6.9 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 9.60, 12.36, 13.46, 15.94, 61.24, 70.62, 71.93, 73.46, 127.58, 127.84, 136.15, 142.43; IR (KBr) 1440, 1284, 1146, 1079, 1058 cm^{-1}; MS (70 eV) *m/z* (%) 224 (M$^+$ − SO, 21.7), 160 (20.1), 145 (93.4). Anal. Calcd for $C_{12}H_{16}O_3S_2$: C, 52.92; H, 5.92. Found: C, 52.86; H, 6.04.

1,2,4,7-Tetramethyl-3,10-dithiatricyclo[5.2.1.0^{2,6}]deca-4,8-diene 3,10-Dioxide (32b) (84 mg, 0.33 mmol, 18%): R$_f$ 0.30 (ether/MeOH 20:1); mp 128−130 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.52 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 1.77 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 3.78 (bs, 1H), 5.63 (d, 1H, ^3J = 6.6 Hz), 5.86 (bs, 1H), 6.27 (d, 1H, ^3J = 6.6 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 13.19, 13.50, 13.71, 18.94, 67.57, 72.27, 73.69, 75.87, 126.70, 127.15, 129.11, 134.93, 145.59; IR (KBr) 1642, 1441, 1373, 1352, 1277, 1263, 1081, 1059, 1038 cm^{-1}; MS (70 eV) *m/z* (%) 256 (M$^+$, 10.3), 208 (M$^+$ − SO, 63.4), 191 (100), 176 (50.6), 159 (41.9). Anal. Calcd for $C_{12}H_{16}O_2S_2$: C, 56.22; H, 6.29. Found: C, 56.09; H, 6.32.

1,2,4,7-Tetramethyl-3,10-dithiatricyclo[5.2.1.0^{2,6}]deca-4,8-diene 3,10-Dioxide (32c) (82 gm, 0.32 mmol, 18%): R$_f$ 0.11 (ether/MeOH 20:1); mp 159 °C (from ether); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.52 (s, 3H, CH_3), 1.69 (s, 3H, CH_3), 1.73 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 4.03 (s, 1H), 6.00 (d, 1H, ^3J = 6.9 Hz), 6.02 (s, 1H), 6.12 (d, 1H, ^3J = 6.9 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 12.89, 12.98, 13.70, 14.20, 69.29, 71.12, 72.33, 81.82, 131.07, 133.78, 133.89, 145.48; IR (KBr) 1650, 1439, 1359, 1184, 1081, 1040, 906 cm^{-1}; MS (70 eV) *m/z* (%) 256 (M$^+$, 1.3), 208 (M$^+$ − SO, 28.0), 191 (100), 176 (100), 159 (72.0). Anal. Calcd for $C_{12}H_{16}O_2S_2$: C, 56.22; H, 6.29. Found: C, 56.12; H, 6.34.

4,7-Dimethylindanone (34): mp 71−72 °C (lit. 78 °C)[32] (from hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.31 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 2.65 (t, 2H, ^3J = 5.6 Hz), 2.98 (t, 2H, ^3J = 5.6 Hz), 7.00 (d, 1H, ^3J = 7.7 Hz), 7.25 (d, 1H, ^3J = 7.7 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 17.39, 17.99, 24.28, 36.66, 126.20, 132.79, 134.19, 134.39, 135.95, 154.80, 208.46; IR (KBr) 1700 (C═O), 1580, 1490, 1440, 1380, 1320, 1240, 820 cm^{-1}; MS (70 eV) *m/z* (%) 160 (M$^+$, 100). HRMS m/z $C_{11}H_{14}O_2S$ Anal. Calcd: 210.7150. Found: 210.7170.

5,8-Dimethyltetralone (35): mp 29−30 °C (lit. 31.5 °C)[33] (from hexane); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.11 (m, 2H), 2.63 (t, 2H, ^3J = 6.3 Hz), 2.84 (t, 2H, ^3J = 6.3 Hz), 6.98 (d, 1H, ^3J = 7.8 Hz), 7.20 (d, 1H, ^3J = 7.8 Hz). Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.53; H, 8.11.

4,7-Dimethyl-3,10-dithiatricyclo[5.2.1.0^{2,6}]deca-4,8-diene 3,10-Dioxide (36). In an inert atmosphere and at −20 °C, $BF_3\cdot Et_2O$ (1.5 mL, 12.2 mmol) was added to a solution of 2-methylthiophene (300 mg, 3.06 mmol) in dry CH_2Cl_2 (10 mL). The reaction mixture was stirred for 10 min at −20 °C. Then a solution of *m*-CPBA (680 mg, 3.95 mmol) in dry CH_2Cl_2 (15 mL) was added slowly. The reaction mixture was stirred at −20 °C for another 3 h. Then the suspension was poured into a mixture of concd aqueous $NaHCO_3$ solution (20 mL) and CH_2Cl_2 (50 mL) and stirred for 20 min at ambient temperature. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with water and brine and dried over anhydrous $MgSO_4$. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel to yield **36** (140 mg, 40%) as colorless crystals. **36**: mp 148−149 °C (from benzene/hexane, dec); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.63 (s, 3H, CH_3), 2.10 (dd, 3H, J = 1.6 Hz, 2.0 Hz), 3.96 (m, 1H), 4.07 (dd, 1H, J = 4.1 Hz, 4.3 Hz), 4.82 (dd, 1H, J = 4.1 Hz, 7.9 Hz), 5.80 (d, 1H, J = 6.8 Hz), 5.82 (m, 1H), 6.37 (dd, 1H, J = 4.1 Hz, 6.8 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 13.41, 13.73, 57.23, 62.71, 62.80, 75.02, 127.51, 127.69, 130.10, 147.46. IR (KBr) 1640, 1570, 1440, 1380, 1342, 1310, 1280, 1262, 1210, 1150, 1110, 1098, 1070, 1030 cm^{-1}; MS (70 eV) *m/z* (%) 228 (M$^+$, 1.5), 180 (M$^+$ − SO, 22.8), 163 (100). Anal. Calcd for $C_{15}H_{20}O_2S_2$: C, 52.60; H, 5.30. Found: C, 52.76; H, 5.38.

2,3,4,5-Tetramethylthiophene *S*-Oxide (31b). $BF_3\cdot Et_2O$ (1.5 mL, 12.2 mmol) was added to a solution of 2,3,4,5-tetramethylthiophene (300 mg, 2.78 mmol) in dry CH_2Cl_2 (10 mL) under an inert atmosphere and at −20 °C. The reaction mixture was stirred for 10 min at −20 °C. Then a solution of *m*-CPBA (480 mg, 2.78 mmol) in dry CH_2Cl_2 (10 mL) was added slowly. The reaction mixture was stirred for another 2 h at −20 °C. Then the suspension was poured into a mixture of a concd aqueous solution of $NaHCO_3$ (20 mL) and CH_2Cl_2 (50 mL). The resulting mixture was stirred for 20 min at room temperature. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The

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combined organic phase was washed with water and brine and dried over anhydrous $MgSO_4$. After removal of the solvent *in vacuo* (bath temperature should not exceed 30 °C) the residue was flash-chromatographed on silica gel to give **31b** (250 mg, 74%) as colorless crystals. **31b**: R_f 0.30 (ether); mp 122−124 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.25 (s, 6H, 2 CH_3), 2.17 (s, 6H, 2 CH_3); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 10.22, 12.67, 137.45, 139.53; IR (KBr) 2910, 1640, 1440, 1380, 1210, 1130, 1030 cm^{-1}; MS (70 eV) *m/z* (%) 156 (M$^+$, 10.8), 141 (16.3), 123 (77.4). HRMS *m/z* $C_8H_{12}OS$: Calcd 156.0605. Found: 156.0604.

3,4-Dibenzyl-1,2-dimethylthiophene *S*-Oxide (31c). 31c: (160 mg, 74%); mp 111−112 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.25 (s, 6H, 2 CH_3), 3.47 (s, 4H), 7.03 (m, 4H), 7.21−7.27 (m, 6H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 10.60, 32.27, 127.80, 127.92, 128.84, 137.21, 138.52, 143.09; IR (KBr) 1600, 1500, 1450, 1290, 1040 cm^{-1}; MS (70 eV) *m/z* (%) 308 (M$^+$, 42.4), 277 (100), 242 (85.9), 218 (76.5). Anal. Calcd for $C_{20}H_{20}OS$: C, 77.88; H, 6.54. Found: C, 77.61; H, 6.69.

Lewis Acid Catalyzed Oxidation of Bis(2,4,5-trimethylthien-3-yl)methane (38). $BF_3{\cdot}Et_2O$ (1.5 mL, 12.2 mmol) was added to a solution of **38** (330 mg, 1.25 mmol) in dry CH_2Cl_2 (10 mL) under an inert atmosphere and at −20 °C. The reaction mixture was stirred for 10 min at −20 °C. Then a solution of *m*-CPBA (760 mg, 4.40 mmol) in dry CH_2Cl_2 (20 mL) was added slowly. The reaction mixture was stirred for another 2 h at −20 °C. Then the suspension was poured into a mixture of a concd aqueous solution of $NaHCO_3$ (20 mL) and CH_2Cl_2 (50 mL). The resulting mixture was stirred for 20 min at room temperature. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with water and brine and dried over anhydrous $MgSO_4$. After removal of the solvent *in vacuo* the residue was chromatographed on silica gel to give **39** and **40**.

Bis(2,4,5-trimethylthien-3-yl)methane *S*-Oxide (39) (180 mg, 52%): as colorless crystals; R_f 0.32 (ether); mp 117−118 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.79 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 3.48 (s, 2H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 9.96, 10.30, 12.74 (2C), 13.10, 13.42, 26.70, 129.02, 130.10, 131.89, 132.67, 137.50, 137.64, 139.82, 141.17; IR (KBr) 1640, 1580, 1440, 1370, 1150, 1020 cm^{-1}; MS (70 eV) *m/z* (%) 280 (M$^+$, 52.9), 265 (43.7). HRMS *m/z* $C_{15}H_{20}OS_2$: Calcd 280.0956. Found: 280.0975. Anal. Calcd for $C_{15}H_{20}OS_2$: C, 64.24; H, 7.19. Found: C, 63.93; H, 7.48.

Bis(2,4,5-trimethylthien-3-yl)methane *S,S′*-Dioxide (40) (110 mg, 30%): R_f 0.12 (ether/MeOH 6:1); mp 182−183 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.86 (s, 6H, 2 CH_3), 2.16 (s, 6H, 2 CH_3), 2.19 (s, 6H, 2 CH_3), 3.35 (s, 2H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 10.35, 10.60, 12.87, 26.28, 35.65, 136.26, 141.00, 142.72; IR (KBr) 1638, 1580, 1430, 1378, 1130, 1030 cm^{-1}; MS (70 eV) *m/z* (%) 296 (M$^+$, 6.0), 280 (100). HRMS *m/z* $C_{15}H_{20}O_2S_2$: Calcd 296.0905. Found: 296.0900. Anal. Calcd for $C_{15}H_{20}O_2S_2$: Calcd 60.78; H, 6.80. Found: C, 60.55; H, 7.08.

Bis[1,2-bis(methoxycarbonyl)-3,5,6-trimethylphenyl]methane (41). Dimethyl acetylenedicarboxylate (380 mg, 2.68 mmol) was added to a solution of **40** (230 mg, 0.78 mmol) in CH_2Cl_2 (15 mL) at ambient temperature. The mixture was stirred for 6 h. The solvent was evaporated *in vacuo*, and the residue was purified by column chromatography to give **41** (250 mg, 66%) as colorless crystals. **41:** mp 160 °C (from ether); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.00 (s, 6H, 2 CH_3), 2.16 (s, 6H, 2 CH_3), 2.23 (s, 6H, 2 CH_3), 3.84 (s, 6H, 2 $COOCH_3$), 3.86 (s, 6H, 2 $COOCH_3$), 4.20 (s, 2H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 17.23, 17.68, 17.93, 33.21, 52.36 (2C), 130.58, 130.82, 132.11, 132.86, 138.51, 140.77, 169.52, 169.58; IR (KBr) 1731 (C═O), 1564, 1438, 1318, 1216, 1167, 1032 cm^{-1}; MS (70 eV) *m/z* (%) 454 (45.6), 438 (100). Anal. Calcd for $C_{27}H_{32}O_8$: C, 66.93; H, 6.66. Found: C, 66.44; H, 6.65.

X-ray Crystallographic Analysis of 18a. $C_{17}H_{16}O_3S$, M = 302.40, monoclinic, space group $P2_1/n$, $a = 12.635(1)$ Å, $b = 16.936(2)$ Å, $c = 6.819(1)$ Å, $\beta = 93.62(1)°$, $V = 1456.3$ Å^3, $Z = 4$, $D_c = 1.38$ g/cm^3, monochromated Cu K$_\alpha$ radiation, $\lambda = 1.541\ 84$ Å. A colorless prism of compound **18a** (from, approximate dimensions 0.50 × 0.30 × 0.20 mm), mounted on a glass fiber in a random orientation, was used for X-ray data collection. Data were collected on an Enraf-Nonius CAD-4 diffractometer using $\omega{-}2\theta$ scan at a temperature of 23 ± 1 °C. A total of 2683 reflections were collected of which 2463 were unique. The structure was solved by direct methods (SIR 88)[34a] and refined by full-matrix least-squares calculations to give $R = 0.045$, $R_w = 0.063$ for 2149 observed independent reflections [$|F_o{}^2| > 3\sigma(F_o)^2$, $2° < \Theta < 65°$]. All non-hydrogen atoms were located in succeeding difference Fourier syntheses and anisotropically treated. Hydrogen atoms were included in the refinement but restrained to ride on the atom to which they are bonded. All calculations were performed on a MicroVAX 3100 computer using MolEN.[35]

X-ray Crystallographic Analysis of 24. $C_{16}H_{18}O_6S$, M = 338.38, monoclinic, space group $P2_{1/n}$, $a = 12.798(1)$ Å, $b = 14.012(1)$ Å, $c = 9.017(1)$ Å, β-91.18(1)°, $V = 1616.7$ Å^3, $Z = 4$, $D_c = 1.39$ g/cm^3, monochromated Cu K$_\alpha$ radiation, $\lambda = 1.541\ 84$ Å. A colorless prism of compound **24** (from ether, approximate dimensions 0.50 × 0.40 × 0.20 mm), mounted on a glass fiber in a random orientation, was used for X-ray data collection. Data were collected on an Enraf-Nonius CAD-4 diffractometer using $\omega{-}2\theta$ scan at a temperature of 23 ± 1 °C. A total of 5759 reflections were collected, of which 2757 were unique. The structure was solved by direct methods (SIR 88)[34a] and refined by full-matrix least-squares calculations to give $R = 0.045$, $R_w = 0.059$ for 1963 observed independent reflections [$|F_o{}^2| > 3\sigma(F_o)^2$, $2° < \Theta < 65°$]. All non-hydrogen atoms were located in succeeding difference Fourier syntheses and anisotropically treated. Hydrogen atoms were included in the refinement but restrained to ride on the atom to which they are bonded. All calculations were performed on a MicroVAX 3100 computer using MolEN.[35]

X-ray Crystallographic Structure of 36. $C_{12}H_{16}O_2S_2$, M = 256.34, monoclinic, space group $P2_{1/n}$, $a = 11.536(2)$ Å, $b = 8.428(1)$ Å, $c = 11.471(3)$ Å, $\beta = 109.35(2)°$, $V = 1052.3(4)$ Å^3, $Z = 4$, $D_c = 1.441$ g/cm^3, monochromated Cu K$_\alpha$ radiation, $\lambda = 1.541\ 84$ Å. A colorless prism of compound **36** (from approximate dimensions 0.30 × 0.30 × 0.27 mm), mounted on a glass fiber in a random orientation, was used for X-ray data collection. Data were collected on an Enraf-Nonius CAD-4 diffractometer using $\omega{-}2\theta$ scan at a temperature of 23 ± 1 °C. A total of 3765 reflections were collected of which 3765 were unique. The structure was solved by direct methods (SIR 92)[34b] and refined by full-matrix least-squares calculations to give $R = 0.049$, $R_w = 0.113$ for 1989 observed independent reflections [$|F_o{}^2| > 3\sigma(F_o)^2$, $2° < \Theta < 65°$]. All non-hydrogen atoms were located in succeeding difference Fourier syntheses and anisotropically treated. Hydrogen atoms were included in the refinement but restrained to ride on the atom to which they are bonded. All calculations were performed on an IBM RISC System/6000 380 computer using SHELX-93.[36]

Supporting Information Available: NMR spectra for compounds **5**, **11**, **12**, **16**, **18b**, **20**, **22**, **30a**, **31b**, **34**, and **41** (25 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any masthead page for ordering information.

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(37) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.