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THE SYNTHESIS OF AZULENES BY THE [6+4] CYCLOADDITIONS OF
6-AMINOFULVENES TO THIOPHENE-S,S-DIOXIDES

A Dissertation

Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy

in

The Department of Chemistry

by
Stephen Elliott Reiter
B.S., University of Florida, 1972
December, 1977

to Diane

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Abstract

The nucleophilic reactivity of 6-aminofulvenes suggested that these compounds might potentially undergo [6+4] cycloaddition reactions to electrophilic dienes. Thus, the reaction of 6-dimethylamino-fulvene with thiophene dioxide was investigated. This reaction was found to proceed smoothly, with spontaneous loss of sulfur dioxide and dimethylamine, to give azulene in moderate yield after simple workup. Because of this success and the likelihood that a great variety of substituted azulenes could be made in this way, the reaction has been investigated in detail.

The azulenes are of considerable practical and theoretical interest. They have been used as antioxidants in cosmetic and medicinal preparations, as a uv screen in suntan preparations, and have been studied as physiological agents for a number of skin disorders. The related hydroazulenes also show great promise as medicinal chemicals, especially as anti-tumor agents. From a theoretical viewpoint, azulenes have long intrigued chemists with their intense blue to purple colors, unusual for relatively small hydrocarbons, and the spectroscopy of azulenes has been studied extensively over the years. Because of the possible importance of these compounds if they were more generally available, the reactivity and regiochemistry of the aminofulvene-thiophene dioxide cycloaddition reaction with a variety of substituted reactants was investigated. More than thirty different azulenes have been obtained by application of this synthetic method, indicating its utility as a means of preparing azulenes. The variety of compounds

obtained illustrate the substitution patterns on azulene uniquely and unambiguously obtainable by this synthetic route.

Prior to this work, thiophene-S,S-dioxides have been prepared most commonly from the appropriate thiophene via oxidation. This is an unsatisfactory procedure, in general, since the intermediate thiophene monoxides and product thiophene dioxides are very reactive and are not usually isolable under the conditions of preparation. In this work, a general, non-oxidative, route to thiophene dioxides was developed. Cycloaddition of sulfur dioxide to dienes, bromination of the resulting 2,5-dihydrothiophene dioxides, and base promoted dehydrohalogenation of the dibromides gave a wide variety of thiophene dioxides, including 2-methyl, 3-methyl, 2-ethyl, 3-ethyl, and 3-phenylthiophene dioxides. In all, eleven thiophene dioxides were prepared and studied.

6-Aminofulvenes are readily prepared by Hafner's method, condensing sodium cyclopentadienide with alkylated amides, which are in turn obtained by reacting dimethyl sulfate or triethyl-oxonium tetrafluoroborate with the corresponding amide. Ring substitution on the fulvene is achieved by starting with substituted cyclopentadienes. Six aminofulvenes were prepared by this method, including 6-dimethylaminofulvene, 6-methyl-6-dimethylaminofulvene, 6,6-bis(dimethylamino)fulvene and 6-phenyl-6-dimethylaminofulvene.

A thorough understanding of the effect of substitution on the reactivity and regiochemistry of the cycloaddition of aminofulvenes and thiophene dioxides will make possible the application of this synthesis to the preparation of a wide range of azulenes.

A qualitative pattern of reactivity has emerged in these studies: alkyl substitution of the thiophene dioxide slows the reaction, while phenyl or chloro substitution accelerates the reaction. These trends are readily explained in terms of frontier molecular orbital interactions. Substitution of the 6-position of the aminofulvene slows the reaction, presumably due to steric inhibition of overlap of the fulvene π -system and the amine lone pair. Azulenes are still formed with a 6-methyl or 6-dimethylamino substituent, but a 6-phenyl substituent is apparently too bulky to allow the [6+4] reaction to occur.

For reactions of the unsymmetrical thiophene dioxides, two regioisomers can be formed. In most reactions studied, only one of the two possible products is obtained exclusively. The observed regiochemistry can be explained in terms of frontier molecular orbital theory. A 3-substituted aminofulvene can undergo [6+4] cycloadditions in two different orientations, leading to 1- or 2-substituted azulenes. Examples of both orientations of addition have been observed, but in general only one product is obtained from each reaction.

I. INTRODUCTION

The research described in this dissertation began with the discovery of a new type of reaction between aminofulvenes and thiophene dioxides:

This dissertation describes the results of an investigation of the scope and limitations of this reaction as a means for the synthesis of azulenes. In the introduction, the importance of azulenes is outlined, former synthetic approaches to these compounds are discussed, and the preparation and chemistry of aminofulvenes and thiophene dioxides is briefly reviewed. Finally, a theoretical discussion of fulvene chemistry, the initial impetus for this work, is included.

PART A. Azulenes

Azulenes have intrigued chemists ever since the discovery of these substances over a hundred years ago. Their intense blue to purple colors, unusual for low molecular weight hydrocarbons, were of particular interest, but it took until 1936¹ before the structure of the parent, as well as the naturally occurring azulenes, was established. The naturally occurring azulenes, such as guaiazulene and chamazulene, have substituents in the 1, 4, and 7 positions.

A number of azulenes are not naturally occurring, but are isolated upon degradation of naturally occurring sesquiterpenes. The azulenes have been studied for their anti-inflammatory properties², their anti-oxidant properties in a number of cosmetic³, lubricant⁴, and medicinal⁵ preparations, and as a uv screen⁶ in suntan preparations. A number of hydroazulenes⁷ (partially reduced and functionalized derivatives) such as those shown below, have antitumor^{8a} and hypnotic^{8b} activity.

Euparotin acetate

Lactucin

The anomalous fluorescence of azulenes (emission from S_2 but not from S_1 is observed) has been the subject of a great deal of study, including work currently underway.⁹ The azulenes are non-alternant aromatic hydrocarbons, undergoing substitution reactions with radicals, electrophiles and nucleophiles.¹⁰ The resonance energy of azulene is estimated to be about 30 kcal/mol, roughly half that of its isomer, naphthalene.

In the early part of this century, many synthetic routes to azulenes were developed, both to prove the structures of the naturally occurring azulenes, and to enable further investigations of the chemistry of these unique aromatic systems. All of these routes involve a number of steps, frequently giving a mixture of products, generally in very poor yield.

A great deal of work in recent years has added to the number of available routes to azulenes. The most versatile of these is the Ziegler-Hafner synthesis.¹² The work reported here and the complementary work by Dunn¹³ represent useful extensions of the known synthetic routes to azulenes.

The preparation and chemistry of azulenes has been extensively

reviewed through 1959^{10,11,14}. The most important synthetic routes used before 1959 and the more recent methods developed for the preparation of azulenes will be summarized here, but no attempt has been made to exhaustively review the literature.

Early routes to azulenes involved, first, the construction of the bicyclo[5.3.0]decane (perhydroazulene) skeleton, followed by subsequent dehydrogenation. The most versatile of these involved ring expansion of appropriately substituted indans by treatment with diazo compounds and heat¹⁵ or uv irradiation.¹⁶ The esters formed are hydrolyzed, and the corresponding acids then decarboxylate during dehydrogenation. More recently, diazomethane photolysis has been used to effect ring expansion.¹⁷

Ring closure of elaborated 1,2-disubstituted cyclopentanes or cycloheptanes was a second popular route to the desired bicyclo[5.3.0]decanone system.

Figure 1. Bicyclo[5.3.0]decanones from elaborated cyclopentanes and cycloheptanes

Further elaboration of the basic skeleton could be performed as needed before dehydrogenation was carried out, or appropriately substituted precursors were used.

A dehydrogenation step^{10,18} is common to all of the early azulene syntheses, and this represents one of the problems inherent in all previous preparations. The precursor hydroazulene, from which two to ten hydrogen atoms must be removed, is treated with sulfur, selenium, or palladium on carbon, and the product is removed by flash distillation at 200–300°. These conditions are often sufficiently vigorous to induce rearrangement of the azulene skeleton to the isomeric naphthalene system^{19,32}, as well as migration of substituents on the azulene system.²⁰

The problems of dehydrogenation are avoided by the Ziegler-Hafner route.¹² This preparation involves cyclization of an amino-dienylfulvene prepared by condensation of cyclopentadiene and a "Zincke's" aldehyde (1). Zincke's aldehyde is prepared by hydrolyzing

an alkylated pyridine or dihydropyran derivative, as shown below.

Figure 2. Ziegler-Hafner synthesis of azulene

A wide variety of azulenes have been obtained by application of this synthetic method. A recent modification involving condensation of sodium cyclopentadienide with pyridinium or pyriliun salts has been described by Hafner.²¹ This condensation occurs under very mild conditions, a significant improvement over the original Ziegler-Hafner preparation (which requires 200–250° to carry out the desired cyclization).

Another dehydrogenation-free azulene synthesis has been developed by Nozoe.²² α -Halotropones or tropolone methyl ethers are condensed with two moles of an active methylene compound such as ethyl cyanoacetate to give the 1,2,3-trisubstituted azulene shown below.

This azulene can be partially or completely hydrolyzed, then mono or di-decarboxylated. The amino group may be replaced by various other groups employing the well known Sandmeyer reactions. This reaction sequence is best applied to the synthesis of azulenes substituted in the 5-membered ring.

The ultimate goals of this work were to apply the aminofulvene-thiophene dioxide cycloaddition reaction to the preparation of azulenes with controlled substitution patterns, preferably possessing the naturally occurring substitution patterns. In the following paragraphs, the substitution patterns obtained by carrying out the cycloaddition work described herein will be summarized along with the earlier preparative routes to those substitution patterns.

4-Substituted Azulenes

The earliest preparation of 4-substituted azulenes involves the oxidation of tetralin, followed by aldol condensation to the desired bicyclo[5.3.0]decan-2-one system.¹ Grignard addition to this ketone followed by dehydration and dehydrogenation leads to a wide variety of 4-substituted azulenes.

Ring closure of the diacid system cyclopentane-1-carboxylic-2-valeric acid to the bicyclo[5.3.0]decan-2-one system has also been used as a means of preparing higher substituted azulenes that include a 4- or 8- substituent.²³ (See Figure 1, n=0).

4-Substituted azulenes have been prepared by the modified

Hafner route.²¹ 2-Substituted pyridines are alkylated with methyl iodide and added to a sodium cyclopentadienide solution in diglyme. The product azulene is extracted from this reaction mixture following heating for three hours at 80°.

Hafner has also described the preparation of 4-substituted azulenes from the parent azulene in two steps.²⁴ Attack by nucleophiles such as alkyl- or aryl- lithium species gives a 4-substituted dihydroazulene. Re-aromatization is affected by treatment with chloranil.

The work currently being carried out by Dunn¹³ is well suited for the preparation of 4-substituted azulenes. Reaction of 6-alkyl- or aryl- substituted fulvenes with diethylaminobutadiene gives a 4-substituted dihydroazulene that is subsequently dehydrogenated by treatment with sulfur or chloranil.

Figure 3. Preparation of 4-substituted azulenes¹³

It has been discovered in this work that reaction of the parent thiophene dioxide with 6-alkyl substituted 6-dimethylaminofulvenes produces 4-substituted azulenes in one step. These reactions will be discussed in the Results and Discussion section of this dissertation.

5-Substituted Azulenes

Ring expansion of 5-substituted indanes with diazoacetate constitutes the earliest routes to 5-substituted azulenes.²⁵ This procedure is not unambiguous, however, as a mixture of 5- and 6-substituted azulenes are obtained.

Treatment of unsubstituted indan with diazoacetate yields a mixture of hydroazulene esters that can be elaborated to alkylazulenes, the 5-isomer predominating. Numerous chromatographic²⁶, extraction²⁷, and complexation techniques²⁸ have been developed that allow isomer separation.

The related Demjanow ring-expansion method²⁹, an intramolecular version of the diazoacetate expansion described above, also gives a mixture of 5- and 6-substituted azulene precursors.

The first synthesis of pure 5-methyl azulene was carried out by the ring closure of cyclopentane-1-acetic-2-butyric acid.³⁰ The resulting bicyclo[5.3.0]-decan-3-one (see Figure 1, n=1), can be elaborated to a variety of 5-substituted azulenes.

The Ziegler-Hafner procedure can be applied to the preparation of 5-substituted azulenes beginning with 3-substituted pyridines.³¹ Treatment of the appropriate pyridine with cyanogen bromide, hydrolysis to "Zincke's" aldehyde, condensation with cyclopentadiene, and ring closure at 200-300° leads to the formation of 5-substituted azulenes (see Figure 2).

The modified Hafner procedure already mentioned has also been applied to the synthesis of 5-substituted azulenes.³² Alkylated 3-methyl pyridine is added to sodium cyclopentadienide and pyrolyzed. The synthesis is thus reduced to one step, but the overall yield is dropped considerably.

The reaction of 2-substituted thiophene dioxides with 6-dimethylaminofulvene have been discovered to give 5-substituted azulenes in the course of this work, as discussed later.

6-Substituted Azulenes

The ring expansion methods discussed earlier are not applicable to the preparation of 6-substituted azulenes. Non-uniform products are commonly obtained, especially in the attempted preparation of 5- or 6- substituted azulenes.

The earliest unambiguous preparation of 6-methylazulene involved the ring closure of cyclopentane-1,2-dipropionic acid (see Figure 1, n=2).³³ Elaboration of the resulting bicyclo[5.3.0]decan-4-one to a variety of 6-substituted azulenes is possible.

The Hafner procedure beginning with 4-methylpyridine gives 6-methylazulene in very low yield.³¹ In this case the modified, one-pot procedure already discussed provides a significant improvement over the original Hafner route.³²

An important new route to 6-substituted azulene has recently been described by Scott.³⁴ The key step of this synthesis involves copper(I) chloride catalyzed decomposition of the diazoketones derived from dihydrocinnamic acids.

The bicyclo[5.3.0]decatrienone can be elaborated to either a 6-substituted or 1,6-disubstituted azulene. This method should also be applicable to the preparation of 4- and 5-monosubstituted azulenes as well. Mixtures of disubstituted products would be expected since the intermediate ketocarbene could add in two ways to the un-

symmetrical ortho or meta substituted dihydrocinnamic acid derivatives.

In this work, it has been discovered that reaction of 3-alkyl substituted thiophene dioxides with 6-dimethylaminofulvene gives 6-substituted azulenes exclusively. 3-Aryl substituted thiophene dioxides, however, produce mixtures of 5- and 6-substituted azulenes, the 6-substituted compound predominating. These reactions and the observed regioselectivity will be discussed later in detail.

4,5-Disubstituted Azulenes

4,5-Dimethylazulene has been prepared by the diazoacetate method from 4,5-dimethylindan.³⁵ The yield of azulene for just the final three steps (ring expansion, hydrolysis, dehydrogenation) from the indan is less than one percent. In addition, the preparation of the appropriately substituted indan involves a number of steps.

The modified Hafner procedure has also been used for the preparation of 4,5-dimethylazulene.³² Condensation of 1,2,3-trimethyl pyridinium iodide with sodium cyclopentadienide followed by standard

workup gives the expected product, although the yield is again quite low.

Alder and Whittaker³⁵ have developed a novel route to 4,5-disubstituted azulenes involving an [8+2] cycloaddition reaction. Addition of dimethyl acetylenedicarboxylate to dimethylaminovinylfulvene gives dimethyl 4,5-azulenedicarboxylate in moderate yield.

Presumably this diester could be further elaborated, extending the scope of this reaction.

In the course of this work, it has been discovered that reaction of 2-substituted thiophene dioxides with 6-substituted-6-dimethylaminofulvenes gives 4,5-disubstituted azulenes in low yield. These reactions will be discussed in detail later.

4,6-Disubstituted Azulenes

4,6-Dimethylazulene has been prepared in a manner analogous to the preparation of 6-methylazulene.³⁷ Condensation of ethyl cyclopentanone-2-carboxylate with ethyl α -bromopropionate is the key step. Further elaboration is carried out as already discussed.

The modified, one pot Hafner procedure is quite successful for the preparation of 4,6-dimethylazulene.³² Addition of alkylated 2,4-dimethylpyridine to sodium cyclopentadienide as discussed earlier gives the expected azulene in better than 40% yield.

The preference for attack at the 4- and 8- position of azulene by organometallic species²⁴ should also be useful for the preparation of 4,6-disubstituted azulenes by treating a 6-substituted azulene with the appropriate organometallic.

The [6+4] cycloaddition reaction of 6-substituted fulvenes with 3-substituted aminobutadienes gives a variety of 4,6-disubstituted dihydroazulenes (see Figure 3).¹³ These are converted to the corresponding azulene by application of any of the dehydrogenation procedures mentioned earlier.

The reaction of 3-substituted thiophene dioxides with 6-substituted-6-dimethylaminofulvenes has been discovered in the course of this work to give a variety of 4,6-disubstituted azulenes. The reaction of the parent aminofulvene with 2,4-disubstituted thiophene dioxides will also give the 4,6-disubstitution pattern on the pro-

duct azulene. These reactions will be discussed in detail in the Results and Discussion section.

4,7-Disubstituted Azulenes

Diazoacetate ring expansion of 4,6-disubstituted indans represents the earliest synthesis of 4,7-disubstituted azulenes.³⁸ More recently, the Hafner procedure has been applied to the preparation of 4,7-disubstituted azulenes. Alkylation of a 2,5-disubstituted pyridine with methyl iodide, followed by low temperature addition of this complex to sodium cyclopentadienide, then heating at 80–260° for 8 minutes³⁹ to 3 hours³² produces 4,7-disubstituted azulenes in low yield on workup.

Elaboration of appropriately substituted cycloheptanones has been applied to the preparation of the bicyclo[5.3.0]decane system. The polyphosphoric acid catalyzed intramolecular acylation of lactones⁴⁰ has been used in addition to the Dieckmann condensation discussed earlier (see Figure 1). The preparation of the 1,4,7-trisubstituted azulene, guaiazulene, illustrates the application of this method.

The reaction of 2,5-dimethylthiophene dioxide with 6-dimethylaminofulvene has been discovered to give 4,7-dimethylazulene, as discussed later. This reaction may prove to be of general application for the preparation of 4,7-disubstituted azulenes.

5,6-Disubstituted Azulenes

Very few examples of 5,6-disubstituted azulenes exist in the literature. 5,6-Dimethylazulene was first reported in 1966. It was prepared by the modified Hafner procedure, involving condensation of 1,3,4-trimethylpyridinium iodide with sodium cyclopentadienide.⁴¹ Another preparation from 5,6-dimethylindan via the diazoacetate ring-expansion method has recently been reported.⁴² In this preparation, a non-azulenic by-product (shown below) is formed in an amount nearly equal to that of the desired ring expanded material.

The isolation and identification of this sort of by-product indicates another of the problems with the diazoacetate ring-expansion method for the preparation of azulenes.

Hafner has reported the cycloaddition of 6-phenyl-5-azaazulene with diphenylacetylene.⁴³ The initially formed [4+2] adduct loses benzonitrile giving 5,6-diphenylazulene. 4,5,6-Triphenylazulene and hydrocyanic acid are also formed in lower yield.

Leaver and co-workers have independently discovered the reaction of thiophene dioxides with 6-dimethylaminofulvenes.⁴⁴ They recently reported the preparation of 5,6-dichloroazulene from the reaction of 3,4-dichlorothiophene dioxide with 6-dimethylaminofulvene. In addition to this reaction, the reaction of a number of 3,4-disubstituted thiophene dioxides with 6-dimethylaminofulvene have been studied and are reported here. This promises to provide a general route for the preparation of 5,6-disubstituted azulenes.

4,6,7-Trisubstituted Azulenes

There are no examples in the literature of the preparation of 4,6,7-trisubstituted azulenes. The Ziegler-Hafner method should be applicable starting with 2,4,5-trisubstituted pyridines. Several 4,6,7-trisubstituted azulenes have been prepared and are reported here. The reactions of 6-substituted-6-dimethylaminofulvenes with 3,4-disubstituted thiophene dioxides promises to provide a general route to the preparation of 4,6,7-trisubstituted azulenes.

4,6,8-Trisubstituted Azulenes

Dehydrogenation of the initial diazoacetate ring expansion product of 4,7-disubstituted indan produces a 4,8-disubstituted-6-azulene ester.⁴⁵ This can be elaborated to a variety of 4,6,8-trisubstituted azulenes.

The Hafner procedure has been applied to the preparation of 4,6,8-trimethylazulene.⁴⁶ Addition of 2,4,6-trimethylpyrilium perchlorate to sodium cyclopentadienide gives 4,6,8-trimethylazulene in good yield.

In the course of this work it has been discovered that reaction of 6-substituted-6-dimethylaminofulvenes with 2,4-disubstituted thiophene dioxides gives 4,6,8-trisubstituted azulenes. These reactions will be discussed in detail later.

1,4,6-Trisubstituted Azulenes

Attempted preparation of 1,4,6-trisubstituted azulenes by the diazoacetate ring expansion method, from 1,4,6-trisubstituted indans, produces a mixture of 1,4,6- and 1,4,7-trisubstituted azulenes.³⁸ These mixtures are separable only with great difficulty.

The Hafner method should give the desired substitution pattern if a monoalkyl substituted cyclopentadiene is substituted for cyclopentadiene, as 1-alkylazulenes are obtained in this manner, none of the 2-alkylazulene being formed. Thus, addition of an alkylated 2,4-disubstituted pyridine to a monoalkyl cyclopentadienide should give a variety of 1,4,6-trisubstituted azulenes. It is possible that the isomeric 1,6,8-trisubstituted product may also be formed in this reaction.

The reaction of 3,6-dimethyl-6-dimethylaminofulvene with 3-substituted thiophene dioxides has been found to produce 1,4,6-trisubstituted azulenes. These reactions will be discussed in detail later.

PART B. Thiophene Dioxides

1. Synthesis

The only general literature preparation of thiophene dioxides involves oxidation of the precursor thiophene having the desired substitution.⁴⁷ A large number of oxidizing agents and work-up procedures have been used,⁴⁸ but the oxidation procedure is only applicable to the preparation of higher substituted thiophene dioxides (at least disubstituted), apparently due to the high reactivity of the intermediate thiophene monoxides. Part of the work described here involved developing a general synthetic route to mono-substituted thiophene dioxides.

There are only two examples in the literature of the non-oxidative preparation of thiophene dioxides. The first is the preparation of the parent compound by Bailey and Cummins,⁴⁹ who reported the multistep route shown below beginning with butadiene.

Figure 4. Preparation of thiophene-S,S-dioxide⁴⁹

Cycloaddition with sulfur dioxide followed by treatment with bromine gives 3,4-dibromotetrahydrothiophene dioxide. Recently, it has been shown that treatment of this compound with a non-nucleophilic base leads directly to the desired thiophene dioxide.⁵⁰ The earlier workers treated the dibromide with excess dimethylamine, then in a stepwise fashion quarternized one amine function, treated with silver oxide, then quarternized the remaining amine function and finally generated the thiophene dioxide by a second treatment with silver oxide.

The preparation of 3,4-dichlorothiophene dioxide⁵¹ is the other non-oxidative process described in the literature.

Treatment of butadiene sulfone (the butadiene-sulfur dioxide cycloaddition product) with chlorine at room temperature in carbon tetrachloride gives 3,4-dichlorotetrahydrothiophene dioxide. Further chlorination is affected by treating the dichloride in refluxing carbon tetrachloride with a large excess of chlorine in the presence of uv irradiation (300 nm). The product thus obtained, 3,3,4,4-tetrachlorotetrahydrothiophene dioxide, is treated with two equivalents of ammonium hydroxide to give the desired thiophene dioxide.

In this work, the addition-elimination sequence used with

butadiene sulfone to prepare the parent thiophene dioxide has been extended and simplified to allow the preparation of a number of mono-substituted and di-substituted thiophene dioxides by a non-oxidative route. Treatment of a large number of substituted dienes with sulfur dioxide leads to a wide variety of 2,5-dihydrothiophene dioxides.⁵² These compounds can be brominated and then directly dehydrohalogenated by treatment with two equivalents of triethylamine. This method for the preparation of thiophene dioxides appears to be of general applicability. The major restrictions are due to the inability of sulfur dioxide to cycloadd to 1,4-disubstituted dienes, and the sluggish reaction of sulfur dioxide with dienes containing strongly electron withdrawing substituents. In these two cases, the attempted cycloaddition yields poly-diene or a copolymer of the diene and sulfur dioxide.

2. Reactions

Although the monosubstituted thiophene dioxides are not isolable, they have been characterized as their dimers.⁵³

Figure 5. Dimerization of thiophene dioxides

Extrusion of sulfur dioxide from the initially formed [4+2] cycloadduct gives a dihydrobenzothiophene dioxide derivative, which is the product isolated. This is also one of the products isolated when oxidation of a mono-substituted thiophene is attempted. Treatment of several of the dihydrobenzothiophene dioxide derivatives with base causes a (1,3)hydrogen shift followed by loss of sulfur dioxide resulting in the formation of styrenes.⁵³

The dimerization of thiophene dioxides indicates their ability to undergo cycloaddition reactions as either 2π or 4π electron systems. Examples of both modes of addition exist in the literature. For example, reaction of 3,4-dimethylthiophene dioxide with isoquinoline N-oxide gives a product consistent with initial 1,3-dipolar cycloaddition, involving the thiophene dioxide as a 2π addend.⁵⁴

A number of Diels-Alder reactions of thiophene dioxides reacting as dienes have also been reported. Bailey and Cummins⁵⁵ reported the formation of diethyl phthalate from reaction of thiophene dioxide and diethyl acetylenedicarboxylate. These same

workers also reported the reaction of thiophene dioxide as a dienophile when treated with 1,2-dimethylenecyclohexane.

The parent thiophene dioxide has also been characterized by its addition product with dimethylamine.⁴⁹ Recent work by Wrobel and Kabzinska⁵⁶ on the nucleophilic addition of amines to 3,4-dimethylthiophene dioxides indicates that isomerization as well as addition is promoted by base. These workers suggest that nucleophilic addition to alkylthiophene dioxides is preceded by isomerization to the 3-methyl-4-methylene derivative, 2.

PART C. Fulvenes

1. Theoretical Rationales of Periselectivity

The chemistry of fulvenes has been extensively studied, and several reviews have appeared.⁵⁷ In the realm of cycloaddition reactions, these compounds are capable of undergoing reactions as 2π , 4π , or 6π electron addends.⁵⁸

Examples of all possible modes of cycloaddition have been discovered. In reactions with most dienes, the fulvene reacts as a 2π addend. Fulvenes undergo reactions as 4π systems when treated with activated dienophiles. The most novel, and least studied of the cycloaddition possibilities is the reaction of the fulvene as a 6π moiety.

Recent work by Luskus⁵⁸ has led to the discovery of several [6+4] cycloaddition reactions of fulvenes. Treatment of a series of alkyl or arylfulvenes with tropone or diazomethane leads to formation of [6+4] cycloadducts.

In addition, Dunn¹³ is currently investigating the [6+4] cycloaddition of diethylaminobutadiene and several of its deriva-

tives with a variety of alkyl or aryl fulvenes. The products isolated in these reactions are dihydroazulenes, resulting from the loss of diethylamine from the initially formed cycloadduct (see Figure 3).

Several examples of [6+4] cycloaddition reactions involving 6-dimethylaminofulvene as the 6π electron component have been reported over the past few years. Treatment of this fulvene with benzonitrile oxide,⁵⁹ 3,6-diphenyltetrazine,⁶⁰ and coumalic esters⁶¹ yields cycloadducts consistent in all cases with initial [6+4] addition followed by loss of dimethylamine.

The reactions of coumalic esters with 6-dimethylaminofulvene give azulenes in low yields, and the activating ester group was required for reaction.⁶¹ The reactions of thiophene dioxides with amino-fulvenes investigated in this work provide a more general synthesis of azulenes.

A related 10π electrocyclization is the intramolecular condensation of the fulvene, **3**, to azulene, the final step of the Ziegler-Hafner azulene synthesis (see section I A).

The periselectivities (selectivities in formation of one of the Woodward-Hoffman thermally allowed⁶² products) observed in cycloadditions of dienes or other 4π addends to fulvene can be rationalized by applying the frontier molecular orbital theory.⁶³ The frontier orbitals for alkyl and amino fulvenes are shown below.

Figure 6. Frontier molecular orbitals of fulvene

The fulvenes will be expected to react as 2π components across the C-2, C-3 bond in reactions with electron-deficient dienes, because the transition state will be most stabilized when the sites of largest coefficients in the fulvene highest occupied molecular orbital (HOMO) overlap with the sites of largest coefficients in the diene lowest unoccupied molecular orbital (LUMO). A spiro compound indicating reaction of the fulvene as a 2π component across the C-1, C-6 bond is obtained only upon reaction of the sterically hindered 1,2,3,4-tetraphenylfulvene with substituted butadienes.⁶⁴ Reaction of the fulvene as a 6π component across the C-2 and C-6 positions will be less favored because of the node through C-6 in the fulvene HOMO.

With sufficiently electron-rich dienes, interaction of the fulvene LUMO with the diene HOMO becomes important, because these orbitals become closer in energy than the other pair of frontier orbitals. Due to the large coefficient on C-6 of the fulvene LUMO, overlap is greatest when the fulvene C-2 and C-6 positions (reaction as a 6π addend) overlap with the diene termini. Reaction in this sense is indeed observed for reactions of electron-rich aminobutadienes¹³ or diazoalkanes⁵⁸ with alkyl or aryl fulvenes.

The fulvenes react as 4π components in reactions with all alkenes, since the resulting 4π (fulvene) + 2π (alkene) reactions are the only ones allowed by orbital symmetry to occur in a concerted fashion.⁶² That is, with either an electron-rich alkene (high-lying symmetric HOMO) or an electron-deficient alkene (low-lying antisymmetric LUMO), interaction with the symmetric fulvene

LUMO or antisymmetric fulvene HOMO, respectively, across the fulvene 2 and 5 positions, to give [4+2] adducts are expected, and observed.

Aminofulvenes are formally trienamines and are expected to be very nucleophilic species. Reactions with dienes should involve interaction of the fulvene HOMO with the diene LUMO. However, attaching the strongly electron-donating dimethylamino group at the fulvene C-6 raises the energy of the second highest occupied orbital (SHOMO) such that the HOMO and SHOMO of 6-dimethylamino-fulvene are virtually degenerate (see Figure 6)⁶³. There is now a large coefficient on positions C-2 and C-6 of the HOMO "seen" by the attacking electrophilic diene. As already discussed, all known cycloaddition reactions of aminofulvenes with electrophilic dienes proceed by the [6+4] mode.

2. Synthesis of Aminofulvenes

The first preparation of 6-dimethylaminofulvene and several 6,6-disubstituted aminofulvenes was reported by Meerwein and co-workers.⁶⁵ They condensed N,N-dimethyldiethoxymethylamine, prepared from N,N-dimethylformamide and triethyloxonium tetrafluoroborate followed by treatment with sodium ethoxide, with cyclopentadiene.

The alkylation of a variety of amides by dimethyl sulfate⁶⁶ provides another route to the aminofulvenes. The amide-dimethyl sulfate complex is added to sodium cyclopentadienide, leading to a variety of aminofulvenes.⁶⁷

Use of a ring substituted cyclopentadiene will lead to formation of a ring substituted fulvene, which may be expected to be a mixture of the 2- and 3- substituted isomers.

3. Reactions of Aminofulvenes

In addition to the [6+4] cycloadditions of 6-dimethylaminofulvene mentioned earlier, a number of substitution reactions of the aminofulvenes have been reported. For example, addition of tetracyanoethylene occurs readily to yield 2-tricyanovinyl-6-dimethylaminofulvene.⁶⁸

Acylation is also reported to give the mono- and diacyl derivatives.⁶⁸

Mononuclear metallated products have been obtained by treating 6-dimethylaminofulvene and 6,6-bis(dimethylamino)fulvene with the hexacarbonyls of molybdenum and chromium.⁶⁹ The analogous initial product is proposed for similar treatment with iron pentacarbonyl. In this case, however, a bridged, binuclear product is isolated.

Sasaki and coworkers⁶⁰ reported that 6-dimethylaminofulvene undergoes substitution when treated with 3,4-diaza-2,5-diphenylcyclopentadienone or with diethyl azodicarboxylate.

In contrast, these reagents added to 6,6-dimethylfulvene and 6,6-diphenylfulvene in a [4+2] manner.⁶⁰ This difference in reaction mode of the fulvenes is due to the increased nucleophilicity of the aminofulvene and can readily be rationalized by consideration of the frontier molecular orbitals of fulvene.⁶⁰

Recently, Hafner and Suda⁷⁰ have reported the [6+2] cycloaddition of 6-dimethylaminofulvene with electron-deficient acetylene derivatives. Initial addition of the alkyne in a Michael fashion

is followed by cyclization and loss of dimethylamine to yield the pentalene shown.

II. RESULTS AND DISCUSSION

The cycloaddition reactions of fulvenes have been studied extensively in recent years by Houk and Luskus.⁵⁸ This study and current work by Dunn¹³ began with the goal of extending chemists' knowledge of fulvene cycloadditions. The work described herein developed from the discovery that thiophene dioxides and aminofulvenes react to give azulenes in one step. In order to investigate the scope and limitations of this synthetic reaction, a range of thiophene dioxides and aminofulvenes were prepared.

In the following sections, the preparations and characterizations of the starting materials for the azulene synthesis, the thiophene dioxides and aminofulvenes, are described. The reactions of these compounds to form azulenes will then be described.

PART A. Preparation of Thiophene Dioxides

A general procedure for the preparation of a wide range of thiophene dioxides was developed in the course of this work.

The route developed is shown below.

The thiophene dioxides prepared for this study by the route outlined above include the 2-methyl, 2-ethyl, 3-methyl, 3-ethyl, 3-phenyl, 2,4-dimethyl, 3,4-dimethyl, and 3,4-diphenyl substituted compounds, as well as the parent thiophene dioxide.

1. The Diene-Sulfur Dioxide Reaction

The reaction of a variety of dienes with sulfur dioxide gives a wide range of 2,5-dihydrothiophene dioxides.⁵² The diene and sulfur dioxide were sealed in heavy walled Pyrex tubes containing a small amount of hydroquinone (see experimental section for details). Depending on the diene, reaction conditions varied from room temperature for several days to moderate heating (70–100°C) for several hours. The yields were higher for the more electron-rich dienes when the reaction was carried out at room temperature. An electron-deficient diene such as chloropyrene, or a sterically hindered (1-substituted) diene such as piperylene, required heating to promote a significant degree of reaction.

When the reaction is complete, the reaction vessel is vented to release unreacted sulfur dioxide. Reaction conditions and

yields are given in Table VI. Solid products (the 3-substituted sulfones) were washed from the vessel with and recrystallized from methanol. All of these compounds have been previously reported,^{52,71} and were identified by comparison of melting points with published values, as well as by recording the 60 MHz nmr spectra in deuteriochloroform. For example, isoprene sulfone⁷² displays a broad singlet at about 1.9 δ (3H) corresponding to the methyl group, overlapping multiplets at 3.6-3.9 δ (4H) corresponding to the methylene units, and a poorly resolved triplet at 5.7 δ corresponding to the vinyl proton. Oily products (the 2-substituted sulfones) were poured into cold water, which caused precipitation of the polymer formed in the reaction. The product sulfone was extracted from the aqueous phase into chloroform. The instability of these compounds precludes their storage for extensive periods of time. Their identities were verified by 60 MHz nmr analysis, but these compounds were brominated, stored, and characterized as the dibromides.

The reactions of 2-substituted butadienes with sulfur dioxide were found to be much cleaner and to proceed more smoothly than cycloadditions with the corresponding 1-substituted butadiene systems. For example, the yield of piperylene sulfone⁷³ is only about 50% compared to an 80% yield of isoprene sulfone. Chloroprene produces a sulfone⁷⁴ in 60% yield when heated for an extended period of time with sulfur dioxide, in contrast to 1-chlorobutadiene which forms only polymeric material under the same reaction conditions.⁷⁵ 2-Phenylbutadiene reacts with sulfur

dioxide at room temperature over several days to give the expected sulfone⁷⁶ in greater than 80% yield, but 1-phenylbutadiene produces only polymeric material⁷⁷ under the same conditions, or when heated to 100° for 10-12 hours. 2-Ethylbutadiene produces the expected sulfone in high yield (80%), while 1,3-hexadiene gives only a 30% yield of the desired product.

The 2-ethyl-2,5-dihydrothiophene dioxide (1,3-hexadiene sulfone) has not been previously reported. It is an unstable oil that rapidly develops the smell of sulfur dioxide. For this reason, it was converted immediately to, and stored as, the dibromide. The nmr spectrum of the crude 1,3-hexadiene sulfone in carbon tetrachloride displays a singlet at 6.05 δ corresponding to the two olefinic protons, a singlet at 3.65 δ for the methylene unit adjacent to the sulfone group and a triplet at 3.50 δ corresponding to the methine proton. The ethyl group appears as a triplet at 1.1 δ (3H) and a multiplet at 1.8 δ (2H) corresponding to the methylene unit of the ethyl group.

The major side reactions observed in the diene-sulfur dioxide reaction were formation of polydiene and/or diene-sulfur dioxide copolymer (polysulfone).⁵² The addition of common polymerization inhibitors such as hydroquinone is necessary to prevent complete polymerization of the reaction mixture. The fact that 1-substituted butadienes polymerize more readily than the analogous 2-substituted compounds partially explains the yield difference noted above for the cycloaddition reaction with sulfur dioxide. Studies of the retro [4+2] reaction indicate that substituents at the 2-position of the sulfone destabilize

the adduct while substituents at the 3- and 4-positions stabilize the sulfone.⁷⁸

The propensity for polymerization, the destabilizing effect of 2- (and 5-) substituents, and steric factors account for the difficulty in obtaining cycloadducts when 1,4-disubstituted butadienes are treated with sulfur dioxide. 2,5-Dimethyl-2,5-dihydrothiophene dioxide is formed in low yield from 2,4-hexadiene.⁷⁹ The reactions of 3,4-diethyl-2,4-hexadiene⁸⁰ and 3,4-dimethyl-2,4-hexadiene⁸⁰ with sulfur dioxide have also been reported to give the expected sulfone in low yield.

2. Bromination of Sulfones

The bromination of the 2,5-dihydrothiophene dioxides is carried out by slow addition of a bromine/chloroform solution to a refluxing solution of the sulfone in chloroform. The dibromide begins to precipitate when the solution is cooled, and the product is isolated by removal of the chloroform solvent, followed by trituration of the resultant oily mass with methanol. The solid obtained in this way can be recrystallized from large volumes of methanol to give hard, white crystals that can be ground to a fine powder. All of the dibromotetrahydrothiophene dioxides have a very characteristic sweet aroma, and are moderately active skin irritants.

The bromination proceeds in the highest yield (80-90%) with 3-alkyl or 3-aryl substituted sulfones. 2-Substituted sulfones give dibromides in somewhat lower yield (20-40%). The sulfones of chloroprene and of 2,3-diphenylbutadiene resisted repeated

attempts at chlorination or bromination under a variety of reaction conditions.

A number of the dibromides prepared in the course of this work have been previously reported, and were identified by comparison with published melting points, satisfactory elemental analyses and reasonable nmr spectra. The nmr spectra of 2-substituted-3,4-dibromotetrahydrothiophene dioxides are quite complex as a result of the number of isomers possible. Assuming only anti addition, the four possible stereoisomers (two racemates) are shown below.

An additional difficulty encountered in the identification of the dibromides by nmr is the low solubility of these compounds in all common nmr solvents.

For example, the mixture of dibromide isomers prepared from piperylene sulfone melted over a 50° range, but gave a satisfactory elemental analysis, and the nmr spectrum indicated the absence of any vinyl protons. The spectrum in deuteriochloroform is not fully interpretable, displaying a doublet at 1.48 ($J=6\text{Hz}$, 3H), in addition to multiplets centered at 3.6, 3.9 and 4.85 δ , with a total area equivalent to five protons. Krug and Rigney⁷³ have reported the isolation of two dibromides from piperylene sulfone, melting at 89 and 145°, which they suggest are two racemic mixtures.

The bromination product of 1,3-hexadiene sulfone has an even more complex nmr spectrum. The ethyl group displays the

expected, although somewhat broadened, triplet at 1.14 δ (3H), and a multiplet centered at 1.99 δ (2H) corresponding to the methylene unit of the ethyl group. The five ring protons absorb from 2.95-4.7 δ . The absence of signal in the vinyl region of the dibromide spectrum is further evidence for the complete addition of bromine to the sulfone.

The analysis of the dibromides of 3-substituted sulfones is more straightforward since, if trans addition of bromine to the double bond is assumed, a single racemic product should be formed. Thus, these compounds give sharp melting points (1-2 $^{\circ}$ melting range) and less complex nmr spectra than the 2-substituted sulfone adducts. For example, the dibromide of isoprene sulfone⁸¹

has the following spectrum in deuterochloroform: a singlet at 2.17 δ (methyl protons), a doublet of doublets at 3.65 δ ($J=4$, 14Hz, H_a), a singlet at 3.75 δ (H_b), and two doublet of doublets centered at 4.26 δ ($J=6$, 14Hz, H_c (cis)) and 4.98 δ ($J=4$, 6Hz, H_d (trans)).

3. Dehydrobromination of 3,4-Dibromotetrahydrothiophene Dioxides

Treatment of the brominated sulfones described above with two equivalents of triethylamine in cold chloroform or benzene gives the corresponding thiophene dioxide. Backer and Melles⁸² reported in 1951 the preparation of 3,4-dimethyl-

thiophene dioxide by basically this same procedure. They treated 3,4-dibromo-3,4-dimethyltetrahydrothiophene dioxide with piperidine in benzene and obtained the thiophene dioxide. This thiophene dioxide and all other disubstituted thiophene dioxides studied in the course of this work were found to be stable and isolable compounds.

The starting dibromides are sparingly soluble in a large number of solvents, so it was found to be most convenient to carry out the reaction in chloroform. Due to the solubility of by-product triethylammonium bromide in chloroform, a crude indication of reaction progress was available by observing the uptake of starting dibromide into solution. The workup consisted of washing the chloroform solution several times with cold water, and drying over molecular sieves. The stable (disubstituted or greater substitution) thiophene dioxides can be isolated by evaporating the chloroform at this point. In general, this solution is used as is for further reaction with aminofulvenes, to be described below.

The elimination reaction has also been carried out in benzene solution, with the advantage that workup involves only filtration to remove the by-product triethylammonium bromide. The frequent clogging of a variety of fritted glass and paper filters by the triethylammonium bromide was a common problem, however. In addition, the low solubility of starting dibromide in benzene makes it quite difficult to determine when reaction is complete, since there is always some solid suspended in the solution. A further problem is the propensity of precipitated triethylammonium

bromide to coat undissolved dibromide, preventing complete reaction from occurring.

Due to the instability of the parent, unsubstituted thiophene dioxide, and the monosubstituted thiophene dioxides with respect to dimerization, these compounds were used in solution as produced. Dimerization is virtually complete if the solution of thiophene dioxide is allowed to stir overnight at room temperature.⁵³ Thus, these thiophene dioxides have been characterized as their dimers,⁵³ as discussed earlier (see Figure 5), and by their cycloaddition reactions with aminofulvenes, to be discussed shortly.

The preparation of the parent, 3,4-dichloro- and 3,4-dimethylthiophene dioxides has already been discussed. The commercially available 2,4-dimethyl-2,5-dihydrothiophene dioxide can be brominated⁸³ and dehydrobrominated as discussed earlier to give a previously unreported thiophene dioxide. This product was identified on the basis of its very simple nmr spectrum, and a satisfactory elemental analysis. The nmr spectrum in carbon tetrachloride displays a poorly resolved multiplet at 6.21 δ , arising from the olefinic protons at C-3 and C-5, which are long range coupled to the methyl groups. Two absorptions are observed for the methyl groups, one peak at 1.99 δ and the other at 2.01 δ .

PART B. Preparation of Aminofulvenes

All of the aminofulvenes used in this study were prepared by the reaction of an alkylated amide with sodium cyclopentadienide.⁶⁷ The amide is alkylated by dropwise addition of dimethyl sulfate to the neat amide at 30-40°C, then heated at 60-100° for 2-6 hours⁶⁶ (see Experimental section for details). The alkylated amide is then added dropwise to a sodium cyclopentadienide solution in tetrahydrofuran maintained at -20 to -30°C. When addition of the alkylated amide was complete, the reaction mixture was allowed to warm to room temperature and was stirred overnight. Sodium methyl sulfate by-product is removed by filtration, followed by evaporation of solvent to give the crude aminofulvene. In a number of cases, taking this material up in carbon tetrachloride and washing with water or filtering the solution served to partially purify the product. The carbon tetrachloride was then evaporated, and the residue was recrystallized from petroleum ether or cyclohexane. Cleaner product was obtained when petroleum ether was used, but large amounts of solvent are required.

The aminofulvenes prepared by the above procedure were the parent,⁶⁷ from N,N-dimethylformamide and cyclopentadiene, 6-methyl-6-dimethylaminofulvene,⁶⁵ from N,N-dimethylacetamide and cyclopentadiene, 6-phenyl-6-dimethylaminofulvene,⁸⁵ from N,N-dimethylbenzamide and cyclopentadiene, 6,6-bis(dimethylamino)-fulvene,⁸⁴ from N,N,N',N'-tetramethylurea and cyclopentadiene, compound 4,⁶⁵ from N-methyl-2-pyrrolidinone and cyclopentadiene, and 2,6- or 3,6-dimethyl-6-dimethylaminofulvene, 5, from N,N-dimethylacetamide and methylcyclopentadiene.

4

5

Compound 5 may be a mixture of up to four different positional and geometric isomers, 6, 7, 8, or 9 shown below. Hafner has obtained 2-substituted azulenes when methylcyclopentadienide is condensed with pyrilium salts,⁸⁶ indicating that the methyl is located as in 6 or 7 in the condensation product, but only 1-substituted azulenes are formed when alkylcyclopentadienes are reacted with Zincke's aldehyde¹⁰ (see Figure 2), indicating most likely formation of the pattern present in 8 or 9 in this reaction.

6

7

8

9

Compounds 6 and 7 differ only with respect to the geometry about the exocyclic double bond, as do compounds 8 and 9. The nmr spectrum of the reaction product in deuteriochloroform shows three different high field singlets. The dimethylamino protons absorb at 3.23 δ , the exocyclic methyl at 2.37 δ , and the ring methyl group appears as a broad singlet at 2.13 δ . The absorption pattern for the ring protons indicates the presence of a mixture of isomers, displaying a doublet of doublets at 6.07 δ (1H, J=2,5Hz), and multiplets at 6.15-6.3 δ (3H) and 6.38-6.58 δ (2H).

Downing, Ollis and Sutherland⁸⁵ have studied the barriers to rotational isomerization of the fulvene C-1, C-6 bond for a number of aminofulvenes. At low temperature, the ring protons of 6-substituted aminofulvenes give an ABCD spectrum which at elevated temperatures becomes an AA'BB' spectrum. These authors report that the coalescence of the ring protons of 6-methyl-6-dimethylaminofulvene occurs at 57° in deuteriochloroform. This suggests a means of determining whether 5 consists of a mixture of 6 and 7 only or 8 and 9 only, or if all possible isomers are formed. It was hoped that the spectrum of the vinyl region would simplify as the barrier for rotation about the C-1, C-6 bond was reached. Unfortunately, coalescence was not observed up to the boiling point of chloroform. Use of hexachlorobutadiene in attempts to attain the higher coalescence temperature were also unsuccessful due to rapid decomposition of the sample at elevated temperature. Coalescence in the nmr spectrum of 6-methyl-6-dimethylaminofulvene has also been observed at room temperature when the spectrum is recorded in dimethylsulfoxide-d₆-D₂O mixed solvent. Compound 5, however, precipitates from this solvent system before coalescence is observed.

Treatment of 6-dimethylaminofulvene with ethanol-d₁-D₂O in chloroform results in the rapid exchange of only two hydrogens.⁹⁹ Nmr analysis indicates exchange occurs mainly at the 2 and 5 positions of the aminofulvene.^{58c} This reaction was carried out to aid further characterization of 5. The two possible products, discounting the geometry about the exocyclic double bond, are

shown below.

The resolution of the absorption in the vinyl region of the nmr spectrum is insufficient to allow interpretation of this spectrum.

PART C. Reactions of Thiophene Dioxides and Aminofulvenes

1. Symmetrical Thiophene Dioxides

The first series of cycloaddition reactions carried out in this study was that of symmetrical thiophene dioxides with a number of aminofulvenes. The reactions to be discussed are summarized below.

Admixture of equimolar amounts of 6-dimethylaminofulvene and 3,4-dichlorothiophene dioxide in carbon tetrachloride led to almost immediate formation of a fast moving spot as determined by thin layer chromatography (tlc). The reaction mixture was stirred overnight at room temperature under a gentle stream of nitrogen. The solvent was removed on the rotary evaporator, and the crude product was dissolved in petroleum ether. Chromatography of the crude material on activated alumina with petroleum ether eluent gave, upon removal of the eluting solvent, a blue solid in 60% yield. The product was identified by 100 MHz nmr analysis as 5,6-dichloroazulene.

The azulene isomers are easily distinguished by 100 MHz nmr analysis.⁸⁷ The absorptions in the aromatic region (6.5–8.5 δ) are characteristic of the substitution pattern of the azulene under consideration. A complete analysis of the 100 MHz

nmr spectrum of the parent azulene in carbon tetrachloride will be useful here.

The absorption for protons 4 and 8 are always the lowest field resonances. In the parent, they appear approximately as a doublet, with some additional small splitting due to long-range coupling. The 2-proton appears as a characteristic triplet in all azulenes not substituted in the 5-membered ring. The 6-proton appears as a broadened triplet, coupled to the 5- and 7-protons by 9-11 Hz, and long-range coupled to the 4- and 8-protons by 1.5-

2.0 Hz. The 1- and 3-protons absorb as a sharp doublet, which becomes a pair of overlapping doublet of doublets when the azulene is unsymmetrically substituted in the 7-membered ring. The 5 and 7 protons usually appear furthest upfield. The chemical shifts and coupling constants for all azulenes obtained in the course of this work are compiled in Table I. The pertinent features of each spectrum will be described when appropriate.

For example, the spectrum of 5,6-dichloroazulene displays a singlet at 8.47 δ , corresponding to the 4-proton, a doublet at 7.96 δ corresponding to the 8-proton, which is coupled to the 7-proton by 11 Hz. The 7-proton absorbs at 7.37 δ . The characteristic pattern expected of the 1, 2 and 3 protons is observed. Additional structure proof for the azulene product is based on satisfactory elemental analysis and an ultraviolet/visible (uv/vis) spectrum consistent with published spectra (see below).

The reaction of 6-methyl-6-dimethylaminofulvene with 3,4-dichlorothiophene dioxide was carried out in the same way as the reaction described above, to give 4-methyl-6,7-dichloroazulene in 15% yield. Nmr analysis of this product in carbon tetrachloride reveals a singlet at 8.42 δ for the 8-proton, a singlet at 7.41 δ for the 5-proton, and a characteristic triplet for the 2-proton at 7.71 δ , while the 1 and 3-protons appear as a multiplet centered at 7.25 δ . This multiplet is the result of a 4 Hz coupling of the 1 and 3-protons with the 2-proton, and the long-range coupling of the 1 and 3-protons by 1-2 Hz. The methyl group at the azulene 4-position appears as a singlet at 2.82 δ .

TABLE I. 100 MHz nmr data for substituted azulenes

Azulene	Chemical Shifts (ppm)								Coupling Constants (Hz)									
	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈	J _{1,2}	J _{2,3}	J _{1,3}	J _{4,5}	J _{5,6}	J _{6,7}	J _{7,8}	J _{6,8}	J _{7,8}	J _{6,8}
Parent	H:7.27(d)	H:7.79(t)	H:7.27(d)	H:8.19(d)	H:6.99(t)	H:7.43(m)	H:6.99(c)	H:8.19(d)	4	4	--	9.5	10	10	9.5	1.5		
1-Methyl	H:7.28(dd)	H:7.69(t)	H:7.22(dd)	Me:2.86(s)	H:7.02(d)	H:7.41(dd)	H:6.98(dd)	H:8.19(d)	4	4	2	--	+	11	9	2		
3-Methyl	H:7.14(dd)	H:7.73(t)	H:7.11(dd)	H:8.11(s)	Me:2.57(s)	H:7.29(d)	H:6.88(c)	H:8.06(d)	4	4	1	--	--	10	10	2		
5-Methyl	H:7.18(d)	H:7.67(t)	H:7.18(d)	H:8.06(d)	H:6.94(d)	Me:2.60(s)	H:6.94(d)	H:8.06(d)	4	4	--	10	--	--	10	--		
5-Ethyl	H:7.11(d)	H:7.80(t)	H:7.11(d)	H:8.11(s)	Et:1.35(t) 2.84(q)	H:7.35(d)	H:6.92(c)	H:8.08(d)	4	4	--	--	--	10	10	2		
6-Ethyl	H:7.18(d)	H:7.67(t)	H:7.18(d)	H:8.10(d)	H:6.93(d)	Et:1.31(t) 2.78(q)	H:6.93(d)	H:8.10(d)	4	4	--	11	--	--	11	--		
1,4-Dimethyl	Me:2.59(s)	H:7.49(d)	H:7.15(d)	Me:2.77(s)	H:6.85(d)	H:7.29(dd)	H:6.85(dd)	H:8.05(d)	--	4	--	--	10	10	10	1		
4,5-Dimethyl	H:7.29(dd)	H:7.62(t)	H:7.11(dd)	Me:2.82(s)	Me:2.60(s)	H:7.45(d)	H:6.84(t)	H:8.08(d)	4	4	1	--	--	10	9	1		
1,6-Dimethyl	H:7.15(dd)	H:7.56(t)	H:7.11(dd)	Me:2.68(s)	H:6.80(s)	Me:2.42(s)	H:6.72(d)	H:7.91(d)	4	4	1	--	--	--	10	--		
4,7-Dimethyl	H:7.09(d)	H:7.64(c)	H:7.06(d)	Me:2.83(s)	H:6.91(dd)	H:7.32(dd)	Me:2.61(s)	H:8.12(d)	4	4	<1	--	10.5	--	--	1.5		
5,6-Dimethyl	H:7.09(d)	H:7.67(c)	H:7.09(d)	H:8.15(s)	Me:2.49(s)	Me:2.49(s)	H:6.99(d)	H:7.97(d)	4	4	<1	--	--	--	10	--		
4-Methyl-6-ethyl	H:7.18(dd)	H:7.57(t)	H:7.12(dd)	Me:2.82(s)	H:6.97(s)	Et:1.36(t) 2.76(q)	H:6.92(d)	H:8.07(d)	4	4	1.5	--	--	--	10	--		
1,4,5-Trimethyl	Me:2.59(s)	H:7.46(d)	H:7.20(d)	Me:2.78(s)	Me:2.57(s)	H:7.38(d)	H:6.76(dd)	H:7.99(d)	--	4	--	--	--	10	10	1		
1,4,6-Trimethyl	Me:2.56(s)	H:7.38(d)	H:7.09(d)	Me:2.72(s)	H:6.79(s)	Me:2.51(s)	H:6.74(d)	H:7.88(d)	--	4	--	--	--	--	10	--		
4,6,7-Trimethyl	H:7.06(dd)	H:7.55(t)	H:7.01(dd)	Me:2.77(s)	H:6.98(s)	Me:2.45(s)	Me:2.45(s)	H:8.09(s)	4	4	1.5	--	--	--	--	--		
4,6,8-Trimethyl	H:7.18(d)	H:7.48(t)	H:7.18(d)	Me:2.83(s)	H:6.90(s)	Me:2.59(s)	H:6.90(s)	Me:2.83(s)	4	4	--	--	--	--	--	--		
1,4-Dimethyl-6-ethyl	Me:2.57(s)	H:7.39(d)	H:7.08(d)	Me:2.75(s)	H:6.80(s)	Et:1.28(t) 2.70(q)	H:6.75(d)	H:7.94(d)	--	4	--	--	--	--	10	--		
1,4,6,7-Tetramethyl	Me:2.58(s)	H:7.38(d)	H:6.97(d)	Me:2.75(s)	H:6.92(s)	Me:2.50(s)	Me:2.50(s)	H:7.99(s)	--	4	--	--	--	--	--	--		

TABLE I cont'd.

	Chemical Shifts (ppm)					Coupling Constants (Hz)									
	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈	J _{1,2}	J _{2,3}	J _{1,3}	J _{4,5}	J _{5,6}	J _{6,7}	J _{7,8}
<u>Azuliene</u>															
2,4,6,7-Tetramethyl	H:6.86(d)	Me:2.55(s)	H:6.79(d)	Me:2.71(s)	H:6.92(s)	Me:2.48(s)	Me:2.48(s)	H:7.94(s)	--	--	1	--	--	--	--
2,4,6,8-Tetramethyl	H:6.94(s)	Me:2.56(s)	H:6.94(s)	Me:2.76(s)	H:6.87(s)	Me:2.56(s)	H:6.87(s)	H:2.76(s)	--	--	--	--	--	--	--
4-Dimethylamino	H:7.21(dd)	H:7.37(t)	H:7.01(dd)	NMe ₂ :3.21(s)	H:6.72(d)	H:7.25(m)	H:6.65(dd)	H:8.03(d)	4	4	2	--	11	9.5	2
4-Dimethylamino-6-methyl	H:7.13(dd)	H:7.27(t)	H:6.93(dd)	NMe ₂ :3.19(s)	H:6.63(s)	Me:2.55(s)	H:6.58(d)	H:7.87(d)	4	4	2	--	--	--	10
4-Dimethylamino-6-ethyl	H:7.12(dd)	H:7.27(t)	H:6.93(dd)	NMe ₂ :3.19(s)	H:6.65(s)	Et:1.31(t) 2.71(q)	H:6.59(d)	H:7.91(d)	4	4	2	--	--	--	10
4-Dimethylamino-6,7-dimethyl	H:7.04(dd)	H:7.26(t)	H:6.84(dd)	NMe ₂ :3.17(s)	H:6.71(s)	Me:2.40(s)	Me:2.47(s)	H:7.94(s)	4	4	2	--	--	--	--
4-Dimethylamino-6,8-dimethyl	H:7.17(dd)	H:7.25(t)	H:7.04(dd)	NMe ₂ :3.15(s)	H:6.66(s)	Me:2.56(s)	H:6.66(s)	Me:2.76(s)	4	4	2	--	--	--	--
4-Dimethylamino-6-phenyl	H:7.51(dd)	H:7.44(t)	H:7.02(dd)	NMe ₂ :3.22(s)	H:6.91(s)	Ph:7.1- 7.55(m)	H:6.84(d)	H:8.03(d)	2	2	1	--	--	--	19
5,6-Dichloro	H:7.52(d)	H:7.81(t)	H:7.52(d)	H:8.47(s)	-----	-----	H:7.37(d)	H:7.96(d)	4	4	--	--	--	--	11
4-Methyl-6,7-dichloro	H:7.27(dd)	H:7.71(t)	H:7.22(dd)	Me:2.82(s)	H:7.41(s)	-----	-----	H:8.42(s)	4	4	1.5	--	--	--	--
1,4-Dimethyl-6,7-dichloro	Me:2.57(s)	H:7.47(t)	H:7.12(d)	Me:2.69(s)	H:7.19(s)	-----	-----	H:8.19(s)	--	4	--	--	--	--	--
4-Dimethylamino-6,7-dichloro	H:7.15(dd)	H:7.32(t)	H:6.96(dd)	NMe ₂ :3.22(s)	H:7.03(s)	-----	-----	H:8.21(s)	4	4	1	--	--	--	--
6-Phenyl		H:7.74(t)		H:8.23(d)		Ph:7.15- 7.55(m)		H:8.23(d)	4	4	--	10	--	--	10
4-Methyl-6-phenyl		H:7.68(t)		Me:2.89(s)		Ph:7.1- 7.6(m)		H:7.18(d)	4	4	?	--	--	--	10
1,4-Dimethyl-6-phenyl	Me:2.59(s)	H:7.49(d)	H:7.15(d)	Me:2.81(s)	H:7.11(s)	Ph:7.23- 7.49(m)		H:7.06(d)	---	4	--	--	--	--	10
5,6-Diphenyl	H:7.26(d)	H:7.78(t)	H:7.26(d)	H:8.41(s)	Ph:7.04(s)	Ph:7.04(s)		H:7.17(d)	4	4	--	--	--	--	10

Additional structure proof is based on satisfactory elemental analysis and a uv/vis spectrum consistent with the proposed substitution pattern.

The uv/vis spectrum of azulene in hexane is reproduced in Figure 7. The spectrum consists of three sets of bands, the first having an absorption maximum of 580 nm, the second occurring at about 350 nm, and the third at about 275 nm. The fine structure in the visible band (first band) of the azulene spectrum is worth noting. The amount of fine structure decreases with increasing substitution of the azulene ring, and as the absorption maximum moves to shorter wavelength, regardless of the degree of substitution.

Extensive work done by Plattner in the 1930's and 1940's led to the compilation of a list of predicted shifts for the visible absorption maxima of alkylsubstituted azulenes^{19b} (Figure 8).

Predicted shifts, nm.

1	+28
2	-14
4	-12
5	+12
6	-15

Figure 8. Plattner's rules

The direction and magnitude of the observed shifts can be rationalized by consideration of the frontier molecular orbitals of azulene. Attaching an alkyl group to the 6-position of azulene for example, will have little effect on the energy of the HOMO, due to the node through the 6-position in this orbital. However, the donor methyl substituent will raise the energy of the LUMO

Figure 7. Uv/vis spectrum of azulene in hexane. Band 1, 450-700 nm ($1.03 \times 10^{-3}\text{M}$);
 Band 2, 300-360 nm ($1.03 \times 10^{-4}\text{M}$); Band 3, 250-290 nm ($1.03 \times 10^{-5}\text{M}$).

as a result of the large coefficient at the 6-position of the LUMO. The net effect is an increase in the HOMO-LUMO energy gap, therefore requiring more energy, or shorter wavelength irradiation, to effect the desired transition. Conversely, attaching an alkyl substituent to the 5-position of azulene raises the energy of the HOMO to a greater extent than the LUMO, decreasing the HOMO-LUMO energy gap, and decreasing the energy needed to effect the visible transition. Hence, a longer wavelength absorption is observed. The predicted and observed values for all alkyl azulenes that could have been or were obtained in the course of this study are tabulated in Table II. It is of interest to note the gradual drop off of additivity of predicted shifts with multiple substitution. Complete uv/vis data can be found in Table IV.

The absolute values indicated in Figure 8 apply only to alkyl substituted azulenes, but the trends indicated are observed for all electron donating substituents. Shifts in the opposite direction to those indicated are observed with electron withdrawing substituents.

The application of Plattner's rules can be extended to systems other than hydrocarbons as discussed so far. This is done by using the visible absorption maximum of the appropriately substituted azulenes as the starting point for calculating predicted maxima, in place of the absorption maximum for the parent azulene. This is equivalent to establishing a predicted shift for a given substituent as the difference in absorption maxima for the parent azulene and the heterosubstituted system. For example, 5,6-

Calculated and observed shifts in the visible spectra of
alkylsubstituted azulenes

Compound	λ_{max}^5 (nm) of band 1	
	calculated*	observed
Azulene	---	580
4-Methylazulene	568	570
5-Methylazulene	592	593
6-Methylazulene	565	569
4-Ethylazulene	568	---
5-Ethylazulene	592	591
6-Ethylazulene	565	568
1,4-Dimethylazulene	596	599
2,4-Dimethylazulene	554	---
4,5-Dimethylazulene	580	580
4,6-Dimethylazulene	557	557
4,7-Dimethylazulene	580	581
4,8-Dimethylazulene	556	---
5,6-Dimethylazulene	577	578
5,7-Dimethylazulene	604	---
4-Methyl-6-ethylazulene	557	557
4-Methyl-7-ethylazulene	580	---
1,4,5-Trimethylazulene	608	609
1,4,6-Trimethylazulene	581	586
1,4,7-Trimethylazulene	608	---
1,4,8-Trimethylazulene	584	---
4,5,7-Trimethylazulene	568	---
4,6,7-Trimethylazulene	565	568
4,6,8-Trimethylazulene	541	551
1,4-Dimethyl-6-ethylazulene	581	587
1,4-Dimethyl-7-ethylazulene	608	---
1,4,6,7-Tetramethylazulene	593	593
2,4,6,7-Tetramethylazulene	551	---
1,4,6,8-Tetramethylazulene	569	---
2,4,6,8-Tetramethylazulene	527	537

*Based on Plattner's rules (see Figure 8).

TABLE III

Calculated and observed shifts in the visible spectra of
heterosubstituted azulenes.

Compound	λ_{max}^5 (nm) of band 1	
	calculated*	observed
4-Dimethylaminoazulene	---	552
4-Dimethylamino-6-methylazulene	537	542
4-Dimethylamino-7-methylazulene	564	---
4-Dimethylamino-6-ethylazulene	537	543
4-Dimethylamino-7-ethylazulene	564	---
4-Dimethylamino-5,7-dimethylazulene	576	---
4-Dimethylamino-6,7-dimethylazulene	549	556
4-Dimethylamino-6,8-dimethylazulene	528	538
5,6-Dichloroazulene	---	599
4-Methyl-6,7-dichloroazulene	587	587
1,4-Dimethyl-6,7-dichloroazulene	615	616
2,4-Dimethyl-6,7-dichloroazulene	573	---
4-Dimethylamino-6,7-dichloroazulene	571	566
6-Phenylazulene	---	589
4-Methyl-6-phenylazulene	577	578
4-Dimethylamino-6-phenylazulene	561	563
1,4-Dimethyl-6-phenylazulene	605	607

*Based on Plattner's rules and "group" shifts of -28 nm for the 4-dimethylamino substituent; +19 nm for the 5,6-dichloro "group"; +9 nm for the 6-phenyl substituent.

TABLE IV cont'd.

4-Dimethylamino-6-methyl	-----	-----	-----	-----	542(2.79)	378(3.61)	-----	310(4.26)	276(4.81)
4-Dimethylamino-6-ethyl	-----	603(2.37)	-----	-----	543(2.65)	393(3.36)	369(3.43)	367(4.55)	263(4.14)
4-Dimethylamino-6,7-dimethyl	-----	-----	-----	-----	556(2.62)	-----	340(4.33)	310(4.23)	277(4.66)
4-Dimethylamino-6,8-dimethyl	-----	-----	-----	-----	538(2.02)	375(2.79)	-----	312(3.50)	281(4.01)
4-Dimethylamino-6-phenyl	-----	-----	-----	-----	563(2.80)	403(3.61)	382(3.71)	365(3.78)	345(3.92)
5,6-Dichloro	728(2.01)	696(2.01)	654(2.31)	622(2.28)	599(2.31)	353(3.48)	337(3.31)	307(3.64)	288(4.66)
4-Methyl-6,7-dichloro	707(2.31)	667(2.42)	638(2.70)	609(2.70)	587(2.72)	354(3.80)	340(3.69)	312(4.04)	283(4.84)
1,4-Dimethyl-6,7-dichloro	752(1.78)	714(1.88)	676(2.33)	-----	616(2.48)	360(3.34)	345(3.24)	295(4.73)	252(4.31)
4-Dimethylamino-6,7-dichloro	-----	-----	-----	-----	566(2.09)	396(2.88)	345(3.17)	318(3.46)	283(4.08)
6-Phenyl	713(2.11)	673(2.15)	642(2.44)	612(2.43)	589(2.47)	369(3.69)	350(3.72)	332(3.52)	292(4.84)
4-Methyl-6-phenyl	650(1.92)	656(2.17)	624(2.51)	594(2.54)	578(2.59)	370(3.71)	352(3.66)	338(3.75)	292(4.97)
1,4-Dimethyl-6-phenyl	712(1.89)	-----	651(2.46)	-----	607(2.62)	376(3.09)	359(3.19)	345(3.36)	299(5.00)
5,6-Diphenyl	714(2.20)	670(2.25)	644(2.59)	612(2.58)	591(2.60)	-----	353(3.80)	-----	292(3.85)

dichloroazulene, with a visible absorption maximum of 599 nm indicates a "group" shift of +19 nm for the 5,6-dichloro substitution. The absorption maximum for 4-methyl-6,7-dichloroazulene can now be predicted by either of two thought processes. Addition of a methyl group at the 4-position will shift the predicted absorption by -12 nm from the observed maximum of 599 nm for the appropriate "parent" structure, 5,6-dichloroazulene. Alternatively, the "group" shift of +19 nm can be added to the predicted absorption maximum of 568 nm for 4-methylazulene. Both considerations give the same prediction, an absorption maximum of 587 nm for 4-methyl-6,7-dichloroazulene, in agreement with the experimental value obtained. The predicted and observed values for a number of heterosubstituted and arylsubstituted azulenes that could have been or were obtained in the course of this study are tabulated in Table III.

When 6,6-bis(dimethylamino)fulvene was treated with 3,4-dichlorothiophene dioxide in chloroform or carbon tetrachloride solution, very slow formation of the expected fast running, intensely colored, azulene spot was observed by tlc. Allowing the reactants to stir for several days, or heating the solution to reflux overnight did not increase significantly the amount of azulene product obtained. Normal workup as described above gave only a trace amount of the expected 4-dimethylamino-6,7-dichloroazulene. In addition, a highly water soluble, but petroleum ether insoluble, residue is obtained. This residue may be a zwitterionic addition complex of the reactants, or may simply be decomposed fulvene, since the 6,6-bis(dimethylamino)fulvene

decomposes on the shelf at a moderate rate leaving a deep red-black, water soluble residue. The product azulene was identified by 100 MHz nmr spectroscopy. The 8-proton absorbs at 8.21 δ as a singlet, the 2-proton at 7.32 δ as a triplet, and the 5-proton at 7.03 δ as a singlet. The 1 and 3 protons appear as poorly resolved doublet of doublets at 7.15 δ and 6.96 δ , respectively. This absorption pattern results from the 4 Hz coupling between each of these protons and the 2-proton, and a long range coupling of the 1 and 3 protons by about 1 Hz. Additional structure confirmation is based on good agreement of the observed visible absorption maximum with that predicted in Table III. Insufficient sample was obtained to permit an elemental analysis to be performed.

The reactions of 6-phenyl-6-dimethylaminofulvene and the fulvene, 4, with 3,4-dichlorothiophene dioxide gave no azulene product despite the variety of reaction conditions tried. Reactions were carried out in benzene, chloroform, carbon tetrachloride and methanol solvents, at room temperature and under reflux, for a period of overnight to weeks. Evaporation of solvent, followed by extraction of the residue with large volumes of petroleum ether led to recovery of the majority of the unchanged fulvene.

The parent thiophene dioxide, prepared as described by Bailey and Cummins,⁴⁹ or by treating 3,4-dibromotetrahydrothiophene dioxide with triethylamine, reacted with the parent aminofulvene, 6-methyl-6-dimethylaminofulvene and 6,6-bis(dimethylamino)fulvene to give azulene,¹ 4-methylazulene¹ and 4-dimethylaminoazulene,⁸⁸ respectively. These reactions were carried out at room temperature under a gentle stream of nitrogen for six to twelve hours. Workup

and chromatography as described earlier gave the expected azulenes in 10-15% yield. The products were identified by comparisons of spectral data with literature values. The nmr spectra are very similar to the spectrum of the parent azulene. For example, 4-methylazulene displays a doublet at 8.19 δ of area equal to the characteristic triplet for the 2-proton at 7.69 δ . Protons 6 and 7 appear as a doublet of doublets centered at 7.41 δ and 6.98 δ , respectively. The 5-proton appears as a doublet centered at 7.02 δ . The major difference in the spectrum of the parent and 4-substituted azulene is the collapse of the absorption of the 1 and 3 protons from a very sharp doublet to a poorly resolved pair of doublet of doublets. In 4-methylazulene, these signals are centered at 7.22 δ and 7.28 δ . The visible absorption maximum of 568 nm for 4-methylazulene is in accord with prediction. The corresponding maximum at 552 nm for 4-dimethylaminoazulene indicates a "group" shift of -28 nm for attachment of the dimethylamino group at the azulene 4-position. The negative wavelength displacement is consistent with the electron donor properties of the dimethylamino group and the magnitude of the displacement is a qualitative indication of the very strongly electron donating properties of the dimethylamino group.

As above, reaction of the parent thiophene dioxide with 6-phenyl-6-dimethylaminofulvene and with fulvene 4 does not give any azulene products. Unreacted fulvene was again recovered upon workup.

Treatment of the parent aminofulvene, 6-methyl-6-dimethylaminofulvene and 6,6-bis(dimethylamino)fulvene with 3,4-dimethylthiophene dioxide in refluxing chloroform, benzene or carbon

tetrachloride for 24 hours gives, after workup and chromatography as described above, 5,6-dimethylazulene,^{41,42} 4,6,7-trimethylazulene and 4-dimethylamino-6,7-dimethylazulene,^{41,42} and the sample obtained here was identified by comparison with published nmr, uv/vis, and melting point data. The 4,6,7-trisubstituted azulenes are new compounds, and can readily be identified by 100 MHz nmr analysis.

The nmr spectra of 4,6,7-trimethylazulene (10) and 4-dimethylamino-6,7-dimethylazulene (11) are quite similar, but the entire spectrum is shifted slightly upfield in the amino compound. The 8-proton absorbs as a singlet at 8.09 δ for 10, and at 7.94 δ for 11. The characteristic triplet for the 2-proton appears at 7.55 δ for 10, and at 7.26 δ for 11. The 5-proton appears as a singlet at 6.98 δ for 10, and at 6.71 δ for 11. The 1 and 3 protons appear as a pair of doublet of doublets, very poorly resolved in 10, absorbing at 7.06 δ and 7.01 δ . These signals are better resolved in 11, absorbing at 7.04 δ and 6.84 δ . It is not possible to assign these signals specifically to proton 1 or proton 3 without more information. The amino group and the relative simplicity of the spectrum of 11, as well as the clean resolution of the two absorptions of interest, would make this an ideal system on which to carry out a shift reagent study, in order to assign the signals for the 1 and 3 protons. Interestingly, the methyl groups at the azulene 6 and 7-positions are not resolved in 10, absorbing as a singlet at 2.45 δ , twice the area of the singlet appearing at 2.77 δ for the methyl group at the azulene 4-position. Compound 11 has three methyl resonances: the methyl at the azulene 6-position

absorbs at 2.40 δ , that at the azulene 7-position at 2.47 δ , and the dimethylamino protons appear at 3.17 δ . Additional structure proof is based on the visible absorption maximum. 4,6,7-Trimethylazulene obeys Plattner's rules quite well, while 11 agrees reasonably well with the predicted value based on the "group" shift derived earlier for the dimethylamino substituent. Satisfactory elemental analyses served as confirmations of the products indicated.

The reaction of 3,4-diphenylthiophene dioxide, prepared by the non-oxidative route described earlier, with 6-dimethylamino-fulvene in refluxing chloroform gives 5,6-diphenylazulene⁴³ in at least 15% yield. Removal of solvent, followed by extraction of the residue with a 20% chloroform-petroleum ether mixture (V/V) and chromatography of the extract on activated alumina with 20% chloroform-petroleum ether eluent gave the azulene product which was identified by comparison of nmr and uv/vis spectra and melting point with published data. The residue, which was insoluble in chloroform-petroleum ether, was found to be 3,4-diphenyl-2,5-dihydrothiophene dioxide, the thiophene dioxide precursor, indicating that the dibromide used was not completely brominated. Subsequent attempts to repeat the bromination of 3,4-diphenyl-2,5-dihydrothiophene dioxide have been unsuccessful. The source of this difficulty is not clear.

The reaction of 2,5-dimethylthiophene dioxide, prepared by the oxidation of 2,5-dimethylthiophene,⁸⁹ with 6-dimethylamino-fulvene proceeds sluggishly in chloroform, even when heated to reflux. After 96 hours total reaction, solvent was removed, the

residue extracted with petroleum ether and chromatographed over activated alumina with petroleum ether eluent. The front running, bright blue band was identified as 4,7-dimethylazulene^{23,38} by comparison of nmr and uv/vis spectra with published data. The azulene was obtained in only 5% yield.

2. 3-Substituted Thiophene Dioxides

There are two orientations of addition possible when 3-substituted thiophene dioxides undergo [6+4] cycloaddition reactions with aminofulvenes, as shown below.

If addition occurs as drawn, the pseudo-meta product will result, giving a 6-monosubstituted or a 4,6-disubstituted azulene. The pseudo-meta designation relates to the 1,3-orientation of the substituents, as in a meta disubstituted benzene. This nomenclature is quite useful in comparing regiochemical results to those obtained in Diels-Alder reactions. If the orientation of the thiophene dioxide upon addition is opposite to that drawn, the pseudo-para product will result, giving a 5-monosubstituted or a 4,7-disubstituted azulene. The pseudo-para designation relates to the 1,4-orientation of the substituents, as in a para disubstituted benzene. The reactions of 3-methyl, 3-ethyl, and 3-phenylthiophene dioxide were studied. The results to be presented here are summarized below.

When 6-dimethylaminofulvene is treated with 3-methylthiophene dioxide in chloroform at room temperature under a gentle stream of nitrogen, reaction is complete within 24 hours, as determined by tlc. Evaporation of solvent, extraction of the resulting residue with petroleum ether, and column chromatography of this extract as described earlier gave a front running blue band in 25% yield based on the thiophene dioxide precursor, 3,4-dibromo-3-methyltetrahydrothiophene dioxide. This compound is identified as 6-methylazulene³³ by comparison with published nmr^{87d} and uv/vis spectra⁹¹ and melting point. The visible absorption maximum at 568 nm is in agreement with prediction based on Plattner's rules. The symmetrical substitution at the 6-position greatly simplifies the nmr absorption pattern. The 4 and 8 protons appear as a doublet furthest downfield, coupled to the 5 and 7 protons which appear highest upfield. The characteristic triplet for the 2-proton and the sharp doublet arising from protons 1 and 3 are unchanged in appearance from their absorptions in the parent. No other azulene products were obtained upon continued elution. The nmr and uv/vis spectra differ sufficiently so that the presence of the other possible isomer, 5-methylazulene,^{25,30,90} can be ruled out. In addition to the azulene product, α , meta-dimethylstyrene is observed in the crude workup by nmr spectroscopy.

The styrene displays a very characteristic pair of poorly resolved quartets at 4.97 δ and 5.27 δ (1H each) in addition to two methyl signals at 2.09 δ (doublet, J=1) and 2.28 δ , and a multiplet centered at 7.08 δ (4H).

The reaction of 6-methyl-6-dimethylaminofulvene with 3-methylthiophene dioxide in chloroform or benzene at room temperature under a gentle stream of nitrogen was followed by tlc. Reaction was complete after 48 hours. Standard workup as described above, followed by column chromatography on activated alumina with petroleum ether eluent gave a purple front running band, which upon removal of solvent gave a purple oil in 10% yield, based on starting dibromide. The product was identified as 4,6-dimethylazulene^{32,37} by analysis of its nmr spectrum. The other possible azulene product, 4,7-dimethylazulene,^{23,38} has been described earlier, and a number of characteristic differences in their nmr spectra are apparent. The 8-proton of the 4,6-disubstituted compound absorbs as a doublet (J=10), coupled to the 7-proton. In the 4,7-disubstituted isomer, however, the doublet observed is split only by 1.5 Hz, the result of long range coupling to the 6-proton. The 5-proton of the 4,6-disubstituted compound absorbs as a singlet, while in the 4,7-disubstituted isomer, the 5-proton appears as a doublet (J=10.5 Hz). Additional structure proof is afforded by uv/vis spectroscopy. The predicted visible absorption maximum for the 4,6-disubstituted isomer at 557 nm is the value observed for the azulene product obtained here.

Treating 6,6-bis(dimethylamino)fulvene with 3-methylthiophene dioxide in chloroform at room temperature led to rapid formation

of a fast running purple spot on tlc. The reaction was worked up as before after 24 hours. Column chromatography on activated alumina with 20% chloroform/petroleum ether (V/V) eluent gave a front running band which was an uncharacterizable pale blue oil in variable yield. This band was obtained in all azulene forming reactions of 6,6-bis(dimethylamino)fulvene. The second band obtained upon continued elution of the column was a deep purple oil. This compound has been identified as 4-dimethylamino-6-methylazulene by nmr spectroscopy. The alternate product possible, 4-dimethylamino-7-methylazulene, can be ruled out by nmr and uv/vis spectroscopy. The absorption for the 8-proton appears as a doublet, coupled to H-7 by 10 Hz, and the 5-proton appears as a singlet. These features are consistent only with a 4,6-disubstituted azulene. An additional feature to note is the general position and shape of the absorption of the 5 and 6-protons. The 5 (and 7) proton(s) generally appear(s) at highest field of the aromatic region, with little long range coupling, thus giving sharp peaks. In contrast, the absorption for the 6-proton generally appears between the signals for the 2-proton and the 1,3-protons. Due to long range coupling to the 4 and/or 8 proton(s), this signal usually appears somewhat broadened. The visible absorption maximum predicted in Table III for the 4,6-disubstituted product is in good agreement with the product of this reaction. The visible absorption band of this, and all other aminoazulenes prepared in the course of this work, displays none of the fine structure exhibited in band 1 of the azulene spectrum (see Figure 7).

Instead, the visible absorption appears as a single, very broad signal. Satisfactory elemental analysis serves as confirmation of the identity of the product indicated.

The reactions of 3-methylthiophene dioxide with 6-phenyl-6-dimethylaminofulvene and fulvene 4 gave no azulene product. As indicated earlier, a variety of reaction conditions led only to isolation of unchanged fulvene.

The reactions of 3-ethylthiophene dioxide with aminofulvenes are carried out and proceed in the same manner as already described for reactions of 3-methylthiophene dioxide. Thus, reaction of 3-ethylthiophene dioxide with 6-dimethylaminofulvene in chloroform at room temperature for 48 hours gave, upon normal workup and chromatography, a 12% yield of deep blue plates, mp. 50-52°, identified as 6-ethylazulene on the basis of the following data. The nmr of this material in carbon tetrachloride reveals an absorption pattern in the aromatic region virtually identical to that obtained for 6-methylazulene. The spectrum is quite simple, a doublet for protons 4 and 8 furthest downfield, coupled to the 5 and 7 protons highest upfield ($J=11$ Hz). The characteristic triplet for the 2-proton, and the sharp doublet for the 1 and 3 protons ($J=4$ Hz) to which it is coupled are identical with the same portion of the 6-methylazulene spectrum. The uv/vis spectra of the 6-alkyl (methyl and ethyl) substituted azulenenes are virtually identical and the predicted value for the visible absorption maximum of 565 nm is very close to the observed 568 nm. The melting point of this material is identical to the published

value,⁹² and satisfactory elemental analysis confirms the proposed structure.

6-Methyl-6-dimethylaminofulvene gave a purple oil in 12% yield when reacted with 3-ethylthiophene dioxide in chloroform at room temperature for 72 hours. This product was isolated as the front running band when the crude reaction mixture was chromatographed on activated alumina with petroleum ether eluent. Decomposition to an insoluble brown residue occurs readily on extended exposure to air, necessitating storage under argon. This material was identified by nmr and uv/vis spectroscopy to be 4-methyl-6-ethylazulene. No evidence for the formation of the other possible isomer, 4-methyl-7-ethylazulene, was obtained. The aromatic region of the nmr spectrum is indicative of a 4,6-disubstituted azulene, a doublet at 8.07 δ for H-8, coupled to H-7 which absorbs at 6.92 δ as a doublet ($J=10$ Hz); and the appearance of H-5 as a singlet at 6.97 δ . The uv/vis spectrum is characteristic of an azulene, and the observed visible maximum at 557 nm is exactly the value predicted for a 4,6-dialkyl substituted azulene. There is no chance that the presence of small amounts of the other possible isomer will be undetected by uv/vis spectroscopy. It would be possible for the major component of a mixture to mask the visible absorption of the minor component if the minor component absorbs at shorter wavelength than the major component. However, a 4,7-dialkyl substituted azulene, with a predicted visible absorption maximum of 580 nm, should give a maximum well-resolved from the 557 nm maximum observed for the

4,6-disubstituted compound. Satisfactory elemental analysis of this product serves as final confirmation for the proposed structure.

Reaction of 3-ethylthiophene dioxide with 6,6-bis(dimethylamino)fulvene was carried out at room temperature in chloroform or benzene, and was complete as determined by tlc after 48 hours. Evaporation of solvent, extraction of the residue with 20% chloroform-petroleum ether (V/V), and chromatography of the residue over activated alumina with 20% chloroform-petroleum ether (V/V) gave a pale blue leading band of unidentified composition, followed by a purple band consisting of a purple oil in 8% yield. This product was identified as 4-dimethylamino-6-ethylazulene on the basis of the now familiar nmr spectrum of a 4,6-disubstituted azulene. The doublet for the 8-proton ($J=10$ Hz) and the singlet for the 5-proton are the significant features of the nmr of this product. The perturbation by the 4-dimethylamino substituent is evidenced by the splitting of the signals for the 1 and 3 protons into two separate doublet of doublets, centered at 7.12 δ and 6.93 δ . The uv/vis spectrum confirms the formation of an azulene product, the visible absorption maximum falling reasonably close to the predicted value of 537 nm. The alternate substitution pattern possible would be predicted to give a visible absorption maximum of 564 nm, quite different from the 543 nm obtained experimentally. Additional structure proof is obtained from satisfactory elemental analysis.

The reactions of 3-ethylthiophene dioxide with 6-phenyl-6-dimethylaminofulvene and fulvene 4 gave no azulene product. As

indicated earlier, a variety of reaction conditions led only to the isolation of unchanged fulvene.

Reaction of 3-phenylthiophene dioxide with 6-dimethylamino-fulvene at room temperature in chloroform occurs quite readily, a fast running blue spot appearing on tlc a short time after the reagents were mixed. After 12 hours, the reaction mixture was evaporated to dryness, the residue extracted with 20% chloroform-petroleum ether (V/V), and the extract was chromatographed over activated alumina with 20% chloroform-petroleum ether (V/V) eluent. The front running band gave a dark blue solid, mp 80-95°, in 30% yield. The large mp range and the nmr spectrum of this compound indicate the formation of a mixture of azulene products. The pure 5-phenyl isomer has a literature mp of 99°, ⁹³ while the 6-isomer melts at 160°. ⁹⁴ Fractional sublimation, although not attempted, should allow separation of these two compounds. Sublimation of the product mixture gave two distinct crystal forms; a dense, dark blue material sublimes first, then a more flocculant, lighter blue material sublimes. Most of the aromatic region of the nmr spectrum of this compound is quite complicated due to interaction of the phenyl and azulene systems. The signal furthest downfield which usually arises from the 4 and 8 protons is resolved from the remainder of the aromatic absorptions, and displays both the doublet (J=10 Hz) expected of a 6-substituted compound and a doublet (J=2 Hz) even further downfield expected of a 5-substituted product. The integration of these two signals is about 20:1, indicating a product ratio of approximately 9-10:1,

since the 5-substituted product contributes to the area of the up-field doublet (from its 8-proton) in an amount equal to the area of the singlet downfield. The remainder of the area of the doublet represents the 4 and 8 protons of the 6-substituted isomer. Uv/vis and ir spectroscopy are not very useful in determining the site of substitution on the azulene products. The ir spectra of 5- and 6-phenylazulene are quite similar,⁹³ such that only the presence of the major product can be verified. The presence of minor amounts of the other possible isomer could be masked. Thus, ir analysis indicates only that 6-phenylazulene is the major product. Uv/vis analysis is similarly insensitive to phenyl substitution.⁹⁴ The visible absorption maximum in ethanol for 5 and 6-phenylazulene is 593 ± 2 nm. The longest wavelength absorption band for these two compounds is reported at 711-716 nm. Thus, the values of 589 and 713 nm, respectively, obtained in hexane in this study could be consistent with either isomer. Further evidence for the lack of sensitivity of the uv/vis spectrum to phenyl substitution is the absorption maximum and longest wavelength obtained for 5,6-diphenylazulene,⁴³ whose preparation has already been described. Values of 591 and 714 nm, respectively, are not significantly different from those obtained for either of the mono-substituted isomers.

The reaction of 6-methyl-6-dimethylaminofulvene with 3-phenylthiophene dioxide proceeded slower than the reaction with the parent aminofulvene. Development of the front-running spot on tlc increased for 48 hours, after which time no further reaction was observed. Evaporation of the reaction mixture, extraction

with 20% chloroform-petroleum ether, and column chromatography gave a front running purple band, which was evaporated to a purple oil, representing a 15% yield based on starting dibromotetrahydrothiophene dioxide. The nmr spectrum of this material, in addition to displaying features characteristic of azulene in the aromatic region, has a very sharp singlet at 5.2 δ , as well as a greatly enhanced absorption in the region 7.6-7.8 δ . These signals could arise from the styrene 12, resulting from thiophene dioxide dimerization, shown below.

The product was rechromatographed over activated alumina starting with pure petroleum ether eluent, then gradually increasing the solvent polarity by slow addition of chloroform (up to a maximum of 10% V/V). Isolation of the center fraction of the purple band thus obtained gave a 6% yield, based on starting dibromide, of an analytically pure mixture of azulene isomers. Analysis of the nmr spectrum of this material reveals both a doublet (J=10 Hz) at 8.21 δ expected for the 4,6-disubstituted isomer, as well as a doublet (J=2 Hz) further downfield (8.49 δ) expected for the 8 proton of the 4,7-disubstituted isomer. The product ratios can be determined by integration of the two different signals for the 8-protons, or by integration of the two different methyl signals observed, the major isomer absorbing at 2.89 δ , the minor at 2.85 δ . Either method indicates a product ratio of about

8:1, the 4,6-disubstituted isomer predominating. The uv/vis spectrum obtained is indicative of an azulene system, and the visible absorption maximum is shifted as predicted by Plattner's rules for attachment of an alkyl group to the 4-position of 6-phenylazulene (see Table III). Satisfactory elemental analysis serves as additional confirmation for the product mixture indicated.

6,6-Bis(dimethylamino)fulvene reacted readily with 3-phenylthiophene dioxide at room temperature to produce a fast running purple spot on tlc. The reaction was worked up as already described after stirring overnight. Chromatography on activated alumina with 20% chloroform-petroleum ether eluent gave the previously mentioned pale blue front running band, followed by a purple band that contains a mixture of azulene products and the styrene 12, as determined by nmr. Rechromatography of this mixture under these same conditions, and isolation of the center portion of the front running band gave in 7% yield, based on starting dibromide, a mixture of azulene isomers as a purple oil. The major isomer present, 4-dimethylamino-6-phenylazulene is identified by nmr. The doublets for the 7 and 8 protons at 6.84 and 8.03 δ ($J=10$ Hz) and the appearance of H-5 as a singlet at 6.91 δ are all features characteristic of a 4,6-disubstituted azulene. In addition, the doublet ($J=2$ Hz) for the 8 proton as well as the doublets for the 5 and 6-protons ($J=9$ Hz) of the 4,7-disubstituted isomer are visible in the spectrum of this mixture. Comparison of the signals for the 8-protons of the two different isomers indicates the 4,6-isomer predominates by a factor of about 3:1.

The uv/vis spectrum confirms the formation of the azulene system, and the visible absorption maximum is consistent with the value predicted in Table III by attaching a 4-dimethylamino substituent to 6-phenylazulene. Satisfactory elemental analysis serves as further structure proof for the product mixture indicated.

The reactions of 3-phenylthiophene dioxide with 6-phenyl-6-dimethylaminofulvene and fulvene 4 gave no azulene product. A variety of reaction conditions led only to the isolation of unchanged fulvene.

3. 2-Substituted Thiophene Dioxides

There are two orientations of addition possible when 2-substituted thiophene dioxides undergo [6+4] cycloaddition reactions with aminofulvenes, as shown below.

If addition occurs as drawn, the pseudo-meta product will result, giving a 4-monosubstituted or 4,8-disubstituted azulene. The pseudo-meta designation here relates to the 1,5-orientation of the substituents, as in a meta disubstituted benzene. If the orientation of addition of the thiophene dioxide is opposite to that drawn, the pseudo-ortho product will result, giving a 5-monosubstituted or a 4,5-disubstituted azulene. The pseudo-ortho designation relates to the 1,2-orientation of the substituents, as in an ortho disubstituted benzene. The reactions of 2-methyl

and 2-ethylthiophene dioxide were studied. Attempts to extend this series to include a 2-aryl substituted thiophene dioxide were unsuccessful for a number of reasons. As mentioned earlier, the precursor 1-phenylbutadiene does not cycloadd as desired with sulfur dioxide. The related 1-(p-nitrophenyl)butadiene does add sulfur dioxide to give the desired 2,5-dihydrothiophene dioxide, but treatment of the dibromide of this compound with a variety of bases under a variety of reaction conditions leads to ring opening with formation of a vinylacetylene system instead of the desired thiophene dioxide. The results to be presented here are summarized below.

Reaction of 2-methylthiophene dioxide with 6-dimethylamino-fulvene was quite slow at room temperature. By following the reaction by tlc, it was determined that a fast running blue spot did not appear until the reagents had stirred for almost 24 hours. A slow increase in the amount of this front running spot was then observed. Solvent was removed after 72 hours of reaction, and product was extracted into petroleum ether. The extract was chromatographed over activated alumina with petroleum ether eluent. The front running blue band yields a blue oil upon evaporation of solvent, representing a 5% yield based on starting dibromide. This product is identified as 5-methylazulene^{25,30,90} by com-

parison of its nmr^{87d} and uv/vis⁹¹ spectra with published data. The alternate azulene product possible in this reaction, 4-methylazulene, is ruled out on the basis of the spectral data. Although 5-methylazulene has a literature melting point of 27°, it was never obtained as a solid in the course of this work. One reason for this is the rapid decomposition of this azulene to a brown insoluble material on continued exposure to air. The nmr spectrum reveals a doublet ($J=10$ Hz) furthest downfield, centered at 8.06 δ , corresponding to the 8-proton. Superimposed on one of these absorptions is a singlet corresponding to the 4-proton at 8.11 δ . The 6-proton appears as a doublet ($J=10$ Hz) at 7.29 δ , and H-7 appears as a triplet, which is really composed of overlapping doublets, due to equal coupling to H-6 and H-8. The signal for H-1 and H-3, a sharp doublet in the parent and 6-substituted azulenes, has collapsed to a poorly resolved multiplet centered at 7.12 δ , the result of the overlapping of a doublet of doublets for each proton ($J=4,1$ Hz). The visible absorption maximum observed at 593 nm is in good agreement with literature values and the prediction based on Plattner's rules.

When 2-methylthiophene dioxide was reacted with 6-methyl-6-dimethylaminofulvene at room temperature or at reflux in chloroform, no fast running spot was ever observed by tlc analysis. However, a trace amount of a blue, fast running band was obtained when the reaction mixture was chromatographed on activated alumina with petroleum ether eluent following normal workup. This material was identified as 4,5-dimethylazulene³⁵ on the

strength of its nmr and uv/vis spectra. The alternate possible azulene product, 4,8-dimethylazulene, should have a very simple nmr spectrum due to its symmetrical substitution.

The appearance of a doublet ($J=9$ Hz) at $\delta 8.08$ could only represent the 8-proton of the 4,5-disubstituted isomer. The area of this signal is equal to the area of the characteristic triplet for the 2-proton, indicating the probable presence of only one azulene product. In addition, two methyl signals, at $\delta 2.82$ and $\delta 2.60$, are observed, indicating an unsymmetrically substituted product (or the symmetrically substituted product plus an unidentified impurity). The 6-proton absorbs as a doublet ($J=10$ Hz), consistent only with a 4,5-disubstituted azulene. The 7-proton appears as a triplet, the result of overlapping doublets ($J=9, 10$ Hz). The predicted visible absorption maximum for a 4,5-dialkyl substituted azulene is 580 nm, which would mask the absorption maximum of a 4,8-disubstituted azulene, predicted to fall at 556 nm. Thus, the observed absorption maximum at 580 nm indicates only that the 4,5-disubstituted isomer predominates. The absence of the 4,8-disubstituted isomer cannot be proven by uv/vis analysis.

Reaction of 2-methylthiophene dioxide with 6,6-bis(dimethylamino)fulvene similarly gave no indication of azulene formation by tlc analysis. Usual workup, followed by column chromatography led only to isolation of the pale blue front running band obtained in all azulene-forming reactions of this fulvene.

Treating 6-dimethylaminofulvene with 2-ethylthiophene dioxide led to very slow development of a pale blue fast running spot on tlc. Evaporation of solvent after 72 hours, extraction of the residue with petroleum ether followed by chromatography on activated alumina with petroleum ether eluent gave a blue oil in 2-3% yield. The two possible azulene products are 4- or 5-ethylazulene. The product was identified as 5-ethylazulene^{14d} on the basis of its nmr and uv/vis spectra, which are virtually identical with the spectra of 5-methylazulene. The predicted visible absorption maximum at 592 nm compares well with the observed value at 591 nm. Again, the formation of the 4-substituted isomer, with a predicted visible absorption maximum of 568 nm, cannot be ruled out on the basis of the uv/vis spectrum. The nmr spectrum reveals two down-field signals in the aromatic region, the 4-proton appears as a singlet at 8.11 δ while the 8-proton appears as a doublet ($J=10$ Hz) at 8.08 δ . Integration indicates these signals represent two protons when compared with the triplet for the 2 proton, which is well resolved. This information, and the appearance of the 6-proton as a doublet and the 7-proton as a triplet is consistent only with the exclusive formation of a 5-substituted azulene.

4. 2,4-Dimethylthiophene Dioxide

There are two orientations of addition possible when 2,4-dimethylthiophene dioxide undergoes [6+4] cycloaddition reactions with aminofulvenes, as shown below.

If the preference indicated by the 4-substituent (formally the 3-substituent in the absence of the 2-methyl group) is expressed, then addition will occur as drawn, and the pseudo-meta, meta product will result, giving a 4,6-disubstituted, or a 4,6,8-trisubstituted azulene. If, instead, the preference for addition expressed by the 2-substituent prevails, then addition will occur in a manner opposite to that drawn, giving the pseudo-ortho, para product, a 5,7-disubstituted or a 4,5,7-trisubstituted azulene. The results of the reactions of 2,4-dimethylthiophene dioxide with a series of aminofulvenes are presented here, and summarized below.

Reaction of 2,4-dimethylthiophene dioxide with 6-dimethylaminofulvene proceeds slowly at room temperature in chloroform, as indicated by tlc. The reaction can be sped up and the ultimate yield increased slightly by carrying out the reaction at reflux.

Evaporation of solvent after 24 hours at reflux, extraction of the residue with petroleum ether followed by column chromatography over activated alumina with petroleum ether eluent gave a blue oil that was identical in all respects with the 4,6-dimethylazulene obtained from the reaction of 6-methyl-6-dimethylaminofulvene with 3-methylthiophene dioxide. The formation of this azulene indicates the prevailing influence of the 3-substituent on the orientation of addition of 2,4-dimethylthiophene dioxide.

6-Methyl-6-dimethylaminofulvene reacts with 2,4-dimethylthiophene dioxide in refluxing chloroform over 48 hours, to give in 3% yield a solid purple material, isolated following usual workup and chromatography. The product, if an azulene, could be 4,5,7 or 4,6,8-trimethylazulene.^{46,95} The nmr and uv/vis spectra are in agreement with assignment as the 4,6,8-trisubstituted isomer. The predicted visible absorption maximum of 541 nm is reasonably close to the observed 551 nm, since strict additivity of Plattner's rules decreases as multiple substitution is obtained. The nmr spectrum is quite simple, indicative of a symmetrically substituted system. The triplet for the 2-proton, the doublet for the 1 and 3-protons, and a singlet for the 5 and 7 protons are the only signals in the aromatic region. Two methyl signals, in a 2:1 ratio, are observed at 2.83 and 2.59 δ . This is consistent with the general observation that an alkyl group at the 4- or 8 positions of azulene will absorb at lower field than the same group at the 5, 6, or 7 positions of azulene.

Refluxing 6,6-bis(dimethylamino)fulvene with 2,4-dimethyl-

thiophene dioxide in chloroform for 48 hours did not lead to the indication of formation of any fast running purple spot by tlc. However, a trace amount of purple material was obtained upon chromatography of the residue on activated alumina with 20% chloroform-petroleum ether (V/V) eluent. This material was identified as 4-dimethylamino-6,8-dimethylazulene by analysis of its nmr and uv/vis spectra. The predicted visible absorption maximum of 528 nm is reasonably close to the observed 538 nm. This difference is readily rationalized by two factors. First, the difference observed (10 nm) is the same as the difference obtained above (10 nm) for the predicted and observed values of 4,6,8-trimethylazulene. Second, the "group" shift used to calculate the predicted value is an approximation only, based on one measurement (4-dimethylaminoazulene). Regardless, the observed absorption maximum is shifted in the opposite direction from, and significantly different from the expected value should addition have occurred in the opposite manner (see Table III). The appearance in the nmr spectrum of a singlet for protons 5 and 7 indicates formation of a 4,6,8-trisubstituted product. Three methyl signals are obtained in ratio 2:1:1 at 3.15, 2.76 and 2.56 δ , respectively. The dimethylamino-group clearly corresponds to the signal furthest downfield. The resolution of the other two methyl signals by 0.20 ppm indicates that the signal downfield resides at the 8-position of azulene. As indicated earlier, substituents at the 4 and 8 positions of azulene generally absorb at significantly lower field than substituents at the 5, 6, or 7 positions. In addition, alkyl substituents at the 5, 6, and 7 positions are usually not

resolved or are resolved by a few Hz at best. Thus, the observed signals at 2.76 and 2.56 δ also indicate that both methyls do not reside on C-5, 6, or 7 only, which would rule out the 4,5,7-tri-substituted isomer. As in the other 4-dimethylaminoazulenes, the signals for H-1 and H-3 appear as doublet of doublets ($J=4, 2$ Hz) and are resolved one from another, centered at 7.04 and 7.17 δ . The triplet for the 2 proton appears unchanged despite the nonequivalence of H-1 and H-3.

The reactions of 2,4-dimethylthiophene dioxide with 6-phenyl-6-dimethylaminofulvene and fulvene 4 gave no azulene products. A variety of reaction conditions led only to the isolation of unchanged fulvene.

5. Reactions of Fulvene 5

As discussed earlier, fulvene 5 may consist of a mixture of ring-methylated aminofulvene isomers, 6-9.

The composition of 5 can be deduced by studying the [6+4] cycloaddition products of this compound. There are two modes of approach of thiophene dioxides to the 3-substituted isomers 6 and 7, as shown below.

Approach of the thiophene dioxide from face A will lead to formation of a 2,4-disubstituted azulene. If instead, the approach of the thiophene dioxide occurs from face B, a 1,4-disubstituted azulene will result. In this work, both modes of addition have been observed, with the approach from face B the more common mode of addition. Only one direction of addition of a thiophene dioxide to isomers 8 or 9 will lead to an azulene product.

The product resulting from addition to face C will be an azulene with a 1,8-disubstitution pattern. The product of addition to face D will be a dihydroazulene, unable to aromatize readily due to the presence of the bridgehead methyl group.

Reaction of compound 5 with the parent thiophene dioxide in chloroform proceeds smoothly at room temperature. Evaporation of solvent after 12 hours reaction, extraction of the residue with petroleum ether, and column chromatography of the extract on activated alumina with petroleum ether eluent gave, in 13%

yield, a blue oil as the front running band. The uv/vis spectrum of this material is consistent with the formation of an azulene product, based on the characteristic three absorption bands and the fine structure observed. The visible absorption maximum of 596 nm indicates the formation of a 1,4-¹⁵ or 1,8-disubstituted^{14b} azulene, the product of addition to face B of isomer 6 or 7, or addition to isomer 8 or 9, respectively. Analysis of the nmr spectrum of this material verifies the formation of a 1,4 or 1,8-disubstituted product, or a mixture of both, while excluding the formation of the 2,4-disubstituted product. It is not possible, however, to distinguish by nmr alone between the two isomeric possibilities. The nmr spectrum reported by Llinas, Roard, Derbesy and Vincent⁹⁶ for 1,4-dimethylazulene is very similar to that obtained here, but all chemical shifts reported differ from those obtained in this work by 0.01-0.10 ppm. This does not argue for either isomer since Llinas, et al⁹⁶ data for azulene itself also differ from the chemical shifts obtained here by 0.03-0.10 ppm. The characteristic features of the spectrum are the collapse of the triplet characteristic of the 2-proton in azulenes not substituted in the 5-membered ring to a doublet, coupled to the 3-proton, which appears as a sharp doublet despite the unsymmetrical substitution of the azulene. A 2,4-disubstituted azulene would instead have broad overlapping multiplets for the 1- and 3-protons, which would probably be long-range coupled to protons in the 7-membered ring. Of course, the characteristic signal for the 2-proton would disappear altogether. Llinas, et al.⁹⁶ also re-

ported a nuclear Overhauser experiment, which verified that the material they used was indeed the 1,4-isomer, but this was not done here.

Fulvene 5 reacts with 3-methylthiophene dioxide at room temperature in chloroform to give a fast running spot on tlc that continues to develop for 36-48 hours. Evaporation of solvent, extraction of the residue with petroleum ether and chromatography of the extract on activated alumina with petroleum ether eluent gave a fast moving blue band in 10% yield, based on starting dibromide. Assuming that the preference of the 3-substituted thiophene dioxide for addition in the pseudo-meta orientation is unchanged, there are three azulene products possible in this reaction. Fulvene 6 or 7 could give 2,4,6- or 1,4,6-trimethylazulene,³⁸ while fulvene 8 or 9 could give 1,6,8-trimethylazulene.⁹⁷ As above, it is not possible by nmr to distinguish between 1,4,6- and 1,6,8-trimethylazulene. The nmr is consistent with the formation of the 1,4,6- or 1,6,8-trisubstituted product. A doublet ($J=4$ Hz) for the 2-proton is observed at 7.38 δ , coupled to the 3-proton which appears at 7.09 δ . The appearance of the 5 (or 7)-proton as a singlet at 6.79 δ , and the 7 and 8 (or 5 and 4)-protons as doublets ($J=10$ Hz) at 6.74 and 7.88 δ , respectively, verifies the presence of a 6-substituent. The uv/vis spectrum is consistent with either a 1,4,6- or 1,6,8-trisubstituted azulene. The visible absorption maximum observed at 586 nm is in good agreement with the predicted value of 581 nm.

The reaction of 3-ethylthiophene dioxide with fulvene 5

proceeds in much the same manner as the reaction just described. The product is obtained following usual workup and chromatography as a blue oil in 12.5% yield. The nmr and uv/vis spectra of this compound are virtually identical with the spectra obtained and described above. The visible absorption maximum at 587 nm is consistent with the formation of 1,4-dimethyl-6-ethylazulene, but the isomeric 1,8-dimethyl-6-ethylazulene cannot be ruled out. Satisfactory elemental analysis serves as confirmation of the indicated product.

Fulvene 5 reacts with 3-phenylthiophene dioxide in chloroform at room temperature over a 24 hour period. Evaporation of solvent, extraction of the residue with 20% chloroform-petroleum ether and column chromatography of the extract gave a blue oil in 10% yield. Assuming, as observed earlier, that a mixture of 6- and 7-phenylazulene isomers will be obtained, and that only products of fulvene isomers 6 and 7 are present, a mixture of 1,4-dimethyl-6 or 7-phenylazulene and 2,4-dimethyl-6 or 7-phenylazulene is possible. Several other products are possible, but analysis of the data is simplified by narrowing the field of possibilities. The visible absorption maximum observed at 607 nm is consistent with a 1,4-dimethyl substitution pattern on a 6 (or 7)-phenylazulene. Thus, the product is proposed to be a mixture of 1,4-dimethyl-6-phenylazulene and 1,4-dimethyl-7-phenylazulene. The nmr spectrum is consistent with this. The downfield signal for the major isomer is a doublet ($J=10$ Hz) at 8.06 δ . Thus, the 1,4,6-trisubstituted compound is the major isomer. A

doublet ($J=2$ Hz) appears even further downfield at 8.26 δ , corresponding to the 8-proton of the minor, 1,4,7-trisubstituted isomer. Integration indicates the ratio of major to minor isomers is about 4:1. The pair of doublets ($J=4$ Hz) expected for the 2 and 3-protons are observed at 7.49 and 7.15 δ . The singlet for the 5-proton of the major isomer is observed at 7.11 δ . The styrene impurity, compound 12, obtained in other reactions of 3-phenylthiophene dioxide, is obtained on initial workup, so that a second chromatography is required to obtain an analytically pure azulene sample. Satisfactory elemental analysis of the sample thus purified verifies the composition of the product mixture.

When 2-methylthiophene dioxide in chloroform is stirred at room temperature with fulvene 5 for several days, no evidence of reaction is observed by tlc. Evaporation of solvent, extraction with petroleum ether and chromatography on activated alumina with petroleum ether eluent gave a trace amount of fast running blue material. Assuming only reactions of compounds 6 or 7, formation of 1,4,5- or 1,4,8-trimethylazulenes are possible. The uv/vis and nmr spectra indicate the formation of the 1,4,5-trisubstituted compound. The appearance of three methyl signals, two at higher field, are evidence for the 1,4,5-substitution pattern. If the 1,4,8-trisubstituted compound were formed, two methyl signals, if not equivalent, should be only slightly resolved and at lower field. In addition, the characteristic doublet ($J=10$ Hz) for the 8-proton appears furthest downfield in the aromatic region at 7.99 δ . The pair of doublets ($J=4$ Hz) for the

2 and 3-protons at 7.46 and 7.20 δ verifies the approach of the thiophene dioxide from face B of the fulvene, giving the 1,4 rather than the 2,4-substitution pattern. The predicted visible maximum of 608 nm for a 1,4,5-trialkylsubstituted azulene is in excellent agreement with the observed 609 nm.

Tlc analysis immediately after fulvene 5 and 3,4-dichlorothiophene dioxide are mixed in chloroform reveals a fast running blue spot already forming. The reaction mixture was allowed to stir overnight, then evaporated to dryness, extracted with 20% chloroform-petroleum ether (V/V) and chromatographed over activated alumina with petroleum ether eluent. The front running band was isolated in 16.5% yield as a soft blue solid. This material was identified as 1,4-dimethyl-6,7-dichloroazulene on the basis of its uv/vis and nmr spectra. The visible absorption maximum of 616 nm agrees quite well with the predicted value of 615 nm. The 2,4,6,7-tetrasubstituted isomer cannot be ruled out, however, since its predicted absorption maximum of 573 nm would be masked by the longer wavelength absorption. The nmr spectrum is quite clear, and readily interpreted in terms of a 1,4,6,7-tetrasubstituted azulene. The 5 and 8 protons appear as singlets at 7.19 and 8.19 δ , respectively. There are only two methyl absorptions, at 2.57 and 2.69 δ , representing the 1 and 4 substituents, respectively. The pair of doublets expected from the 2 and 3 protons of a 1-substituted azulene appear at 7.47 and 7.12 δ , respectively, $J=4$ Hz. Satisfactory elemental analysis serves as confirmation of the product proposed.

3,4-Dimethylthiophene dioxide reacts with fulvene, 5, in refluxing chloroform over a 48 hour period. Tlc of the reaction mixture indicates no further reaction occurs after that time. Evaporation of solvent, extraction of the residue with petroleum ether, followed by chromatography on activated alumina with petroleum ether eluent gave a blue oil in 5% yield. Assuming only the presence of fulvene isomers 6 and 7, there are two azulene products possible: 1,4,6,7- and 2,4,6,7-tetramethylazulene. The predicted visible absorption maximum for these are 593 and 551 nm, respectively. Thus, the observed absorption maximum at 593 nm indicates only that the 1,4,6,7-tetrasubstituted isomer is the major product. The presence of a lesser amount of the 2,4,6,7-tetrasubstituted isomer cannot be ruled out, since its visible absorption band would be masked by the major isomer. Indeed, the nmr spectrum of this material can be interpreted as a mixture of the two possible isomers:

The appearance of six different methyl groups is indicative of the mixture of products shown. Resolution of the 6 and 7 methyl groups is frequently not observed, so three methyl signals are expected from each isomer. The 4-methyls generally absorb furthest downfield, and they are observed at 2.75 and 2.71 δ for the major and minor isomers, respectively. The resolution of the other signals is about the same, the 6 and 7-methyls appearing at

2.50 and 2.48 δ for the major and minor isomers, respectively. The 1-methyl of the major isomer absorbs at 2.58 δ compared to the 2-methyl of the minor isomer at 2.55 δ . The appearance of two signals for the 8-proton, the major absorption at 7.99 δ and the minor at 7.94 δ serves as further confirmation for the mixture of products indicated. The ratio of these two isomers is revealed by integration of these signals to be about 5:1. That the mixture of products are isomeric with respect to the 1 and 2 positions of azulene is indicated by the observation of a pair of doublets ($J=4$) at 7.38 and 6.97 δ for the 2 and 3 protons of the major isomer, in addition to two poorly resolved multiplets at 6.86 and 6.79 δ for the 1 and 3 protons of the minor isomer. Only one signal, a singlet at 6.92 δ , is observed for the 5-proton.

Reaction of 2,4-dimethylthiophene dioxide with fulvene 5 in refluxing chloroform appears to be complete by tlc analysis after 24 hours reaction. Evaporation of solvent, extraction of the residue with petroleum ether followed by column chromatography with petroleum ether eluent gave a fast running purple band, producing a solid purple material in 10% yield upon evaporation of solvent. This material is identified as 2,4,6,8-tetramethylazulene⁹⁵ based on its very simple nmr spectrum and characteristic uv/vis spectrum. The 1 and 3 protons appear as a singlet at 6.94 δ , the 5 and 7 protons as a singlet at 6.87 δ . The 2 and 6-methyls absorb at 2.56 δ , while the 4 and 8 methyls appear at 2.76 δ . This very simple spectrum is consistent only with a symmetrically substituted compound. The visible absorption maximum at 537 nm

is reasonably close to the predicted 527 nm. The difference in predicted and observed values is the same as observed for the 4,6,8-trisubstituted azulenes discussed earlier. The alternate possible azulene product, a 1,4,6,8-tetrasubstituted compound, can be ruled out since its predicted visible absorption maximum of 569 nm would not be masked by the absorption of the major product. The 2,4,6,8-tetrasubstituted product observed here indicates the presence of only fulvene isomers 6 and 7. This substitution pattern could not arise from fulvenes 8 or 9. Only by approach of the thiophene dioxide to face A of the fulvene 6 or 7 can the observed product be formed. In the previous example discussed, reaction of 3,4-dimethylthiophene dioxide with fulvene 5, a mixture of products consistent with addition to both face A and B of fulvene 6 or 7 was indicated. All other examples discussed indicated approach of the thiophene dioxide to face B of fulvene 6 or 7. The reasons for this range of reactions will be discussed in the next section.

6. Discussion

a. Mechanism of Reaction

The patterns of reactivity and regioselectivity observed in the reactions of aminofulvenes and thiophene dioxides are best discussed in terms of the reaction mechanism. As with any cycloaddition, three possible mechanisms can be considered - a concerted one, in which both new bonds are partially formed in the transition state, as well as mechanisms involving diradical or zwitterionic intermediates. The lack of pronounced rate or

yield differences when the reaction is carried out in benzene, carbon tetrachloride, chloroform, and methanol suggest no zwitterionic intermediates are formed. However, the pronounced nucleophilicity of the 2 position of the aminofulvene should cause bond formation between this position and the thiophene dioxide 2 position to proceed faster than bond formation between the fulvene 6 and the thiophene dioxide 2' positions, so that some asymmetry in bond formation is expected, with accompanying partial charge development, even in a concerted reaction. Consideration of the reactivity and regioselectivity of this cycloaddition reaction should make it possible to distinguish among the mechanistic possibilities.

In a frontier molecular orbital analysis, the regioselectivity will be determined by the orientation of addition which affords the greatest overlap between those orbitals strongly interacting in the transition state,^{63,98} and the reactivity will be determined, to a first approximation, by the energy gap between the interacting orbitals.^{63,98} The orbitals important to this analysis are the fulvene SHOMO and HOMO (see Figure 6), as well as the LUMO of the thiophene dioxide, since these are the orbitals which should interact most strongly in the transition state. The fulvene orbitals "seen" by the approaching thiophene dioxide will be a composite of the HOMO and SHOMO shown in Figure 6. Since these orbitals are approximately degenerate,⁶³ positive and negative linear combinations of these orbitals may be taken, and the resulting orbitals will give a new pictorial representa-

tion (Figure 9), which is useful for considering the orbital interactions which occur between the fulvene and the thiophene dioxide.

Figure 9. Frontier molecular orbitals of aminofulvenes

Written as these linear combinations, the similarity of the aminofulvene orbitals to the HOMO and SHOMO of a simple triene is more apparent

In a normal [6+4] cycloaddition reaction, the symmetric HOMO of the triene can interact in a bonding fashion with the symmetric LUMO of the diene. The major stabilizing interaction in the aminofulvene-thiophene dioxide reaction arises from the bonding interaction of the composite HOMO + SHOMO ("HOMO") of the fulvene (see Figure 9) and the symmetric LUMO of the diene (see below). Additional stabilization will result from the interaction of the composite HOMO - SHOMO ("SHOMO") with the diene LUMO.

The latter interaction is net stabilizing despite the different localized symmetries of the interacting orbitals, because the bonding overlap across the fulvene 2-thiophene dioxide 2 positions is greater than the antibonding overlap across the fulvene 6-thiophene dioxide 2' positions. The greatest stabilization upon interaction of the aminofulvene and thiophene dioxide orbitals will probably be obtained when approach of the thiophene dioxide 2 and 2' positions to the fulvene 2 and 6 positions is non-symmetric, so the antibonding fulvene "SHOMO"-thiophene dioxide LUMO interaction will be minimized. Thus, an unsymmetrical transition state such as the one shown below is predicted by frontier orbital analysis, with bond formation at C-2 of the fulvene more advanced than that at C-6 in the transition state, even if the reaction is a one-step, concerted, reaction.

The shapes and relative energies of the thiophene dioxide LUMO's are indicated in Figure 10, where C represents a conjugating substituent, Z represents an electron withdrawing substituent, and R represents an alkyl substituent. This representation is essentially that of Houk⁹⁸ for simple dienes

with the following additional considerations. The thiophene dioxide vacant orbitals are more complicated than shown, due to various possible interactions of the diene orbitals with vacant orbitals of the SO_2 moiety. A simplified model will be used here, taking into account the large energy lowering effect of the electrophilic SO_2 group on the diene LUMO.

Figure 10. Lowest unoccupied molecular orbitals of substituted thiophene dioxides

b. Reactivity

Several qualitative patterns can be gleaned from inspection of Tables IX-XII. Thus, although rates have not been measured, the conditions and yields indicate qualitatively a reactivity order. Alkyl substitution on the thiophene dioxide slows the reaction, necessitating heating in order for reaction to proceed at all for the dialkyl examples. Phenyl or chloro substitution, however, accelerates the reaction. This is consistent with the proposal that the reactivity of a diene towards an aminofulvene increases as the diene is made more electrophilic. In frontier molecular orbital terms, alkyl substitution raises the energy of the thiophene dioxide LUMO (see Figure 10), thereby lowering its reactivity towards nucleophilic species.

Phenyl or chloro substitution, however, lowers the energy of the LUMO (see Figure 10), increasing the electron affinity of the thiophene dioxide and its reactivity towards nucleophilic species.

A more subtle observation is the difference in reactivity between 2 and 3-alkylsubstituted thiophene dioxides. The reactions of 3-substituted thiophene dioxides are faster, cleaner, and higher yield reactions than those of the analogous 2-substituted compounds. In molecular orbital terms, alkyl substitution at the 2-position has a greater energy raising effect on the LUMO than does similar substitution at the 3-position,⁹⁸ because the LUMO coefficient is larger at C-2 than at C-3 (see Figure 10). In addition, a steric effect should be considered, since one of the reactive centers of the 2-substituted isomer carries an added substituent, while the 3-substituted isomer retains relatively unhindered reactive termini.

Substitution of a 6-methyl or 6-dimethylamino substituent on 6-dimethylaminofulvene should increase the nucleophilicity of the fulvene by raising its HOMO energy. Experimentally, a rate increase is not observed, possibly due to several different types of steric effects. Substituents bulkier than hydrogen may force the dimethylamino group out of the optimal geometry for overlap of the nitrogen lone-pair with the fulvene π system. Thus, the ionization potentials of these 6,6-disubstituted fulvenes may be greater than that of 6-dimethylaminofulvene. The lack of reactivity of fulvene 4, however, with its con- strained

4

geometry, which holds the amine lone-pair in position to overlap with the fulvene π system, seems to discount this argument.

The decrease in reactivity as the steric requirements of the fulvene increase is consistent with a concerted reaction mechanism. The transition state of a concerted process will be greatly affected by increased bulk at any of the reactive termini. A mechanism involving diradical or zwitterionic intermediates should not be affected by increased steric bulk at fulvene C-6, if the formation of these intermediates is rate determining. In such a case, only the bond at the fulvene C-2, well removed from the bulk at C-6, is formed in the transition state.

The rate deceleration caused by substituents at C-6 does not, however, prove conclusively the operation of a concerted mechanism, since formation of the second bond might be the slow step, or competitive with the rate of formation of the first bond. Along the series of 6-methyl, 6-ethyl, 6-isopropyl ... to 6-phenyl-6-dimethylaminofulvene, the bulk of substituents at the 6-position becomes large enough to prevent reaction.

Ring substitution on the aminofulvene increases the reac-

tivity of the fulvene, as expected from frontier orbital considerations. The electron-donating substituent will enhance the nucleophilicity of the fulvene by raising the HOMO energy, with a minimal steric contribution since the added substituent is remote from the reactive centers.

As the electrophilicity of the thiophene dioxides or nucleophilicity of the aminofulvenes is increased by appropriate substitution, the reactivity of these species should increase. This increased reactivity may be expressed by enhanced reaction rate in the desired formation of azulenes, or it may be expressed by enhanced decomposition of starting materials by a variety of competing pathways. Very little information on reaction by-products has been obtained, but the possibilities include the known addition of nucleophiles such as the reaction by-product dimethylamine to thiophene dioxides, or the substitution of electrophiles such as by-product sulfur dioxide on the aminofulvenes, or the dimerization of thiophene dioxides (see Figure 5). The factors that will enhance cycloaddition behavior, but not the competitive reactions of the starting materials are not clear. That the substituents affect mainly cycloaddition reactivity, rather than side reactions, is consistent with the fact that the most reactive fulvenes decompose quite readily on prolonged storage, while the fulvenes that have the longest shelf life, 6-phenyl-6-dimethylaminofulvene and fulvene 4, are the compounds that are inert towards cycloaddition.

c. Regioselectivity

For reactions of the unsymmetrical thiophene dioxides, two regioisomers can be formed. In most reactions studied, only one of the possible regioisomers was observed. No one theoretical rationalization explains all of the observed results. Frontier orbital considerations^{63,98} correctly predict the pseudo-meta regioselectivity observed for the 3-alkylthiophene dioxides, but incorrectly predict the formation of pseudo-para products from arylthiophene dioxides. The predictions of frontier orbital theory are made by inspection of the orbitals in Figures 9 and 10. The favored regioisomer results from the orbital interaction which gives the greatest overlap, which is obtained upon interaction of the larger fulvene coefficient (at C-2) with the larger thiophene dioxide coefficient (at C-2 or C-5). At the same time, the bond resulting from union of these positions is predicted to be more advanced than the fulvene C-6-thiophene dioxide C-2' or C-5' bond in the transition state. Interaction in this sense leads to greater total overlap than interaction of the large coefficient of the HOMO of one molecule with the small coefficient on the LUMO of other, and vice versa. For reaction of a 3-substituted thiophene dioxide the possible diradical or zwitterionic intermediates are represented by 13 or 14, where the * represents a radical or a charged species (the negative charge would be expected to reside on the thiophene ring, the positive charge on the fulvene ring in the case of a zwitterion).

Preferential formation of the more stable diradical intermediate cannot explain the observed regiochemistry, since the isomer that would lead to 6-substituted azulenes is the less stable intermediate possible, 14. The more stable intermediate, 13, which has the alkyl or aryl substituent in position to better stabilize the allyl radical, would lead to formation of the unobserved, or minor azulene isomer. If a zwitterion were formed, 14 would be expected to be more stable for X = alkyl, but 13 for X = aryl. Experimentally, both thiophene dioxides give products formally arising from 14. In reactions of 2-alkyl substituted thiophene dioxides, frontier orbital theory predicts the formation of the "wrong" azulene isomer. This is the result of the large coefficient at the site of substitution in the 2-substituted thiophene dioxide (see Figure 10), so that initial bond formation is predicted to occur across the fulvene 2 and thiophene dioxide 2 positions. In this case, a satisfactory rationalization can be constructed by considering a diradical mechanism.

The more stable diradical, 15, would lead to the formation of the observed azulene product. A mechanism invoking zwitterionic intermediates would predict the formation of the "wrong" azulene isomer, since the intermediate 16 would be the more stable zwitterionic intermediate. Alkyl substitution would be expected to destabilize the allyl anion in zwitterionic 15.

For the "mixed", unsymmetrical system, 2,4-dimethylthiophene dioxide, the observed regiochemical preferences of the 2-mono-substituted and 3-monosubstituted systems are pitted against one another. The observed bis pseudo-meta, meta regioisomer is the product predicted by frontier orbital considerations, since the polarization caused by both substituents reinforces the large coefficient on the substituted terminus in the LUMO of the diene (see Figure 10). Although theory correctly predicts the observed orientation of addition in this example, the reactions of 2,4-dimethylthiophene dioxide are the only exceptions to the observation that the attack of the nucleophilic fulvene occurs preferentially at the less substituted thiophene dioxide double bond, as is the case for Diels-Alder reactions of electron-rich dienes with benzoquinones.¹⁰⁰

The observed orientation of addition to 3,6-dimethyl-6-dimethylaminofulvene, 5, is in most cases as expected. The 3-substituent on the ring would be expected to enhance the nucleophilicity at the neighboring 2-position by increasing the coefficient at C-2, in frontier orbital terms. The examples where attack is observed instead at fulvene C-5 can readily be explained in steric terms.

The thiophene dioxide terminus carrying a methyl group will attack at fulvene C-5 much more readily than at the hindered fulvene 2-position. The preparation of ring substituted aminofulvenes with substituents larger than methyl would be of interest. Based on the preceding arguments, the addition of thiophene dioxides to both faces or preferentially to the less hindered face of the fulvene should be observed.

The frontier orbital approach has been used to explain a great number of the results obtained in the course of this work. Problems arise in the application of this theory to reactions of unsymmetrical, electron-deficient dienes whose asymmetry results from electron-donating substituents. In these cases, invoking diradical intermediates sometimes correctly predicts the observed regiochemistry, but in analogy to other cycloadditions such as Diels-Alder reactions, the formation of diradical intermediates is rather unlikely. Clearly, a good theoretical explanation of regioselectivity observed with substituted thiophene dioxides has not been devised.

PART D. Conclusions

The synthetic reaction for the preparation of azulenes described in this dissertation has been shown to be a versatile means for the synthesis of azulenes. The reactions studied are summarized in Table V. Inspection of this table indicates the wide variety of azulene substitution patterns obtainable by application of the cycloaddition reaction of thiophene dioxides with aminofulvenes. In the course of this work, a wide range of reactivity has been observed, and limitations on the usefulness of this particular synthetic method have been defined.

The reaction has been shown to be regioselective in most cases, only one of the possible isomers being formed. 3-Phenylthiophene dioxide and fulvene 5 give various product mixtures, depending on the co-reactants studied. Reaction conditions are mild, proceeding in most cases at room temperature. The most vigorous reaction conditions require refluxing chloroform. Reaction workup is simple and straightforward, since the by-products and reactants are all much more polar materials than the azulenes.

In the previous section, a number of experiments were proposed to extend our knowledge of the usefulness and the limitations of the cycloaddition reaction of aminofulvenes with thiophene dioxides. In addition to those reactions, the preparation of other ring substituted fulvenes and thiophene dioxides with varied substituents and substitution patterns would be of interest in furthering the potential utility of this synthetic method.

TABLE V. Summary of cycloaddition reactions carried out in this study*

	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
✓	✓	✓	✓	✓	—	✓	✓	—	✓	—
✓	✓	✓	✓	X	—	✓	✓	—	✓	—
✓	✓	✓	✓	✓	—	✓	✓	—	✓	—
X	X	X	X	X	—	X	X	—	X	—
X	X	X	X	X	—	X	X	—	X	—

*

✓ - Azulene obtained

X - No azulene product

— Reaction not carried out

III. EXPERIMENTAL

PART A. Introduction

The syntheses and reactions described herein were carried out utilizing solvents and reagents of commercial reagent grade.

Microanalyses were performed by Mr. Ralph Seab, Louisiana State University, Baton Rouge, Louisiana, and Galbraith Laboratories, Inc., Knoxville, Tennessee.

Melting points were determined on a Thomas-Hoover Capillary Melting Point Apparatus and are uncorrected.

Infrared spectra (ir) were taken on a Perkin-Elmer Model 621 Grating Infrared Spectrophotometer. The 3.30, 6.24, and 9.27 μ bands of polystyrene were used as calibration standards.

Electronic spectra (uv/vis) were recorded on a Cary 14 Spectrometer.

60 MHz nuclear magnetic resonance (nmr) spectra were recorded on a Varian Associates Model A-60A Spectrometer or a Perkin-Elmer Model R12-B Spectrometer in CCl₄ (unless otherwise stated) with tetramethylsilane (TMS) as internal reference.

100 MHz spectra were recorded by Mr. John Martin on a Varian HA-100 Spectrometer. Chemical shifts are reported in ppm downfield from TMS (δ), and coupling constants are measured in Hz. The usual notation is used to describe the splitting patterns, i.e., s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad, etc.

Photolysis was carried out in a Rayonet RPR-204 Preparative Photochemical Reactor.

PART B. Starting Materials

1. Synthesis of Thiophene Dioxides

3,4-Dichlorothiophene dioxide was prepared according to the procedure of Bluestone, *et al.*⁵¹

mp 112° (lit⁵¹ 112-113°)

Nmr (CDCl₃): 6.71δ(s)

The rest of the thiophene dioxides were prepared via the dehydrobromination of the corresponding 3,4-dibromotetrahydrothiophene dioxide. The following procedure is illustrative:

Preparation of 3-Methylthiophene dioxide. A quantity of 3 ml (20 mmol) triethylamine was added to a solution of 3.0 g (10 mmol) 3-methyl-3,4-dibromotetrahydrothiophene dioxide in 75 ml chloroform chilled to 0°C. The solution was stirred for several hours, then washed 4 times with 50 ml aliquots of ice water, dried over molecular sieves (Type 4A), and maintained at 0°C until ready for use.

2. Syntheses of 3,4-Dibromotetrahydrothiophene dioxides

The 3,4-dibromotetrahydrothiophene dioxides were prepared from the 2,5-dihydrothiophene dioxides obtained on reaction of sulfur dioxide and an appropriate diene by the general method of Bailey and Cummins.⁴⁹ Conversion of a number of dienes to 3,4-dibromotetrahydrothiophene dioxides is summarized in Table VI.

The brominations were carried out by the slow addition of an equimolar amount of bromine in chloroform to a refluxing solution of sulfone in chloroform. The reaction mixture was allowed to reflux overnight, then nitrogen was bubbled through

the solution to effect cooling and to remove unreacted bromine and by-product HBr. Solvent was removed on the rotary evaporator, and the residue was taken up in methanol, which caused crystallization. Very clean product was obtained upon recrystallization of the crude dibromide from large volumes of methanol.

3. Syntheses of 2,5-Dihydrothiophene dioxides

The dienes used were obtained from commercial sources or prepared by literature routes. The dienes were then sealed in heavy walled Pyrex tubes with a pinch of hydroquinone and liquid sulfur dioxide, in ratios ranging from equimolar to a 4:1 excess of sulfur dioxide (see Table VI for details). A variety of reaction times and temperatures were tried, and the optimal conditions found are reported in Table VI.

The reaction was terminated by breaking open the tubes and allowing evaporation of the excess sulfur dioxide overnight. If the product was a solid, it was washed out of the tube with, and recrystallized from methanol. If the product was an oil, the reaction mixture was poured into cold water, polymeric material was removed by filtration, and the product sulfone was extracted into chloroform. Due to the instability of the 2-substituted-2,5-dihydrothiophene dioxides, bromination was generally carried out directly on the chloroform extract.

TABLE VI. Preparation of dibromotetrahydrothiophene dioxides from dienes

Diene	Sulfone preparation ⁵²			Bromination ⁴⁹	
	Diene: SO ₂ ratio	Reaction time, temp.	Yield, % (Ref.)	Reaction Time ¹⁾	Yield % (Ref.)
Isoprene ^{a)}	1:4	8 hrs., 75°	72 (72)	8	85 (81)
Piperylene ^{a)}	1:1	24 hrs., 70°	79 (73)	8	67 (73)
2,3-Dimethylbutadiene ^{a)}	1:2	12 hrs., 80°	100 (78)	2	84 (80)
1,3-Hexadiene ^{a)}	1:1	10 days, 25°	55	24	10 ^{g)}
2-Ethylbutadiene ^{a)}	1:1	10 days, 25°	84 (71)	8	70 ^{g)}
2-Phenylbutadiene ^{b)}	1:3	8 days, 25°	82 (76)	2	87 ^{g)}
2,3-Diphenylbutadiene ^{c)}	1:2	8 days, 25°	74 (80)	4-48	?
Chloroprene ^{d)}	1:1	16 days, 80°	64 (74)	48	0
1-Phenylbutadiene ^{e)}	1:1	10 days, 25°	0 (77)		---
1-Chlorobutadiene ^{f)}	1:2	14 days, 70°	0 (75)		---
2-Methyl-1,3-pentadiene ^{h)}	---	---	---	4	90 (83)

TABLE VI cont'd

- a) Aldrich Chemical Co. Inc., Milwaukee, Wisconsin.
- b) E. G. E. Hawkins and R. D. Thompson, J. Chem. Soc., 370 (1961).
- c) J. M. Johlin, J. Am. Chem. Soc., 39, 292 (1917).
- d) Pfaltz and Bauer, Inc., Stanford, Conn.
- e) O. Grummitt and E. I. Becker, J. Am. Chem. Soc., 70, 149 (1948); C. F. Koelsch and A. F. Steinhauer, J. Org. Chem., 18, 1516 (1953).
- f) A. S. Onishchenko and N. I. Aronova, Dokl. Akad-Nauk SSSR, 132, 138 (1960); Chem. Abst., 54, 20916e (1960).
- g) Table VII for analytical data on new compounds.
- h) Obtained from Aldrich Chemical Co. Inc., as the sulfone.
- i) Followed by reflux overnight.

TABLE VII. Analytical data for new starting materials

<u>Compound</u>	<u>MP, °C</u>	<u>NMR</u>	<u>Analysis</u>	
			Calculated	Found
3,4-Dibromo-2-ethylhydrothio- phenene dioxide	105-108	(CDCl ₃): 1.14(3H,t,J=7); 1.99 (2H,m); 2.95-4.7(5H,m).	C-23.54 H-3.27	C-23.85 H-3.49
3,4-Dibromo-3-ethyltetrahydro- thiophene dioxide	150-151	(CDCl ₃): 1.18(3H,t,J=7); 2.23 (2H,q,J=7); 3.68(2H,s); 3.63 (1H,dd,J=2,14); 4.35(1H,dd,J=6, 14); 4.92(1H,dd,J=2,6).	C-23.54 H-3.27	C-23.76 H-3.36
3,4-Dibromo-3-phenyltetrahydro- thiophene dioxide	108-110 (dec.)	(CDCl ₃): 3.67-4.75 (4H,m); 5.52(1H,dd,J=3,6); 7.52(5H,s).	C-33.91 H-2.85	C-33.92 H-3.00
3,6-Dimethyl-6-dimethylamino- fulvene (5)	55-57	(CDCl ₃): 2.13(3H,s); 2.37(3H, s); 3.23(6H,s); 6.07(1H,dd, J=2,5); 6.15-6.30(2.5H,m); 6.38- 6.58(2H,m).	C-80.48 H-10.13	C-80.61 H-10.40

4. Syntheses of Aminofulvenes

The aminofulvenes were prepared by the condensation of sodium cyclopentadienide (or sodium methylcyclopentadienide) with an alkylated amide as described by Hafner, *et al.*⁶⁷ Slow addition of the alkylated amide (preparation described below) to the cyclopentadienide salt in THF maintained at -20 to -30° was followed by stirring overnight at room temperature. The reaction mixture was filtered to remove sodium methyl sulfate. Solvent was removed on the rotary evaporator and the residue was recrystallized from petroleum ether or cyclohexane.

Alkylated amides were prepared by treating the amide with dimethyl sulfate at 60-100° for 2-6 hours as described by Brederick, Effenberger, and Simchen.⁶⁶ Dimethyl sulfate was added dropwise to an equimolar amount of the amide held at 30-40°. When addition was complete, the mixture was heated to the desired temperature which was maintained for the prescribed period of time. The conditions for preparation of the dimethyl sulfate-amide complex and the yields of the resulting aminofulvenes are summarized in Table VIII.

Deuteration of 3,6-Dimethyl-6-dimethylaminofulvene (5)

Fulvene 5 was treated with ethanol-d₁ and D₂O in chloroform as described by Luskus.^{58c} After standing for four days in the dark under nitrogen, all solvents were removed on the rotary evaporator. The residue was then washed several times with carbon tetrachloride, and was then evaporated to dryness.

TABLE VIII. Aminofulvene preparations

Amide	Conditions for Amide-Dimethylsulfate Reaction ⁶⁶		Fulvene		
	Temperature, °C.	Time, hrs.	mp, °C.	Yield, %	Ref.
N,N-Dimethylformamide	60-80	2	66-67.5	70	67
N,N-Dimethylacetamide	60-80	2	86-87.5	60	65
N,N-Dimethylacetamide*	60-80	2	55-57	40	--
N,N-Dimethylbenzamide	70-80	4	82-85	20	85
N,N,N',N'-Tetramethylurea	100	4	81-83	25	84
N-Methyl-2-pyrrolidinone	100	2	99-100	30	65

* Added to sodium methylcyclopentadienide

PART C. Cycloadditions of Aminofulvenes and Thiophene Dioxides

Cycloaddition reactions were carried out in 100 ml 3-neck round bottom flasks equipped with a nitrogen inlet tube, a reflux condenser with exit bubbler, and a thermometer. The reactions were maintained under a gentle stream of nitrogen and monitored by thin layer chromatography (tlc). Tlc was performed using aluminum sheets coated with EM silica gel F-254. The eluent consisted of X% ethyl acetate in cyclohexane (V/V) and is reported as (X%, Y elutions). Unless otherwise stated, one elution with 10% ethyl acetate is assumed.

The cycloaddition reactions were worked up by removing the solvent on the rotary evaporator, extracting the crude product with petroleum ether or 20% chloroform-petroleum ether (V/V). Reaction products were purified by column chromatography using MCB Chromatographic Grade Activated Alumina, 80-325 mesh, with petroleum ether or 20% chloroform-petroleum ether (V/V) eluent. Further purification for analysis was effected by re-chromatography with re-distilled benzene eluent. Unless otherwise noted, the azulene was the front running band.

The reactions of six aminofulvenes were studied. A sample procedure for the cycloaddition of each aminofulvene is described. The procedures for most of the remaining reactions are very similar. Thus, the experimental details and product data are summarized in tabular form. Other cycloadditions will be described separately.

1. Cycloadditions of 6-Dimethylaminofulvene

6-Dimethylaminofulvene was reacted with a variety of thiophene dioxides. The exemplary preparation of 6-methylazulene is given below. Table IX gives a summary of reaction conditions and yields starting from the corresponding dibromotetrahydrothiophene dioxide. Complete nmr and uv/vis data can be found in Tables I and IV, respectively. Elemental analysis and infrared data for new azulenes are tabulated in Tables XIII and XIV, respectively.

Preparation of 6-Methylazulene. 3-Methyl-3,4-dibromotetrahydrothiophene dioxide (3.0 g, 10 mmol) was dissolved in 75 ml of chloroform. The solution was chilled to 0-5°, and triethylamine (3 ml, 20 mmol) was added in one portion. This solution was stirred for two hours, then washed 4 times with 50 ml aliquots of ice water, and finally dried over molecular sieves. The dried solution was added to dimethylaminofulvene (1.5 g, 12.5 mmol) and stirred at room temperature under a gentle stream of nitrogen for 72 hours. The reaction mixture was evaporated to dryness, and the crude product was dissolved in petroleum ether. Insoluble material was filtered off, and the solution was chromatographed on alumina with petroleum ether eluent. The first fraction consisted of 6-methylazulene (0.36 g, 25% yield, based on dibromotetrahydrothiophene dioxide).

TABLE IX. Cycloaddition reactions of 6-dimethylaminofulvene and thiophene dioxides*

<u>Thiophene dioxide</u>	<u>Azulene</u>	<u>Conditions</u>			<u>Workup**</u>	<u>Ref.</u>
		<u>Time, h</u>	<u>T, °C.</u>	<u>Yield, %</u>		
Parent	Parent	12	25	10	A/A	1
2-Methyl-	5-Methyl-	72	25	4	A/A	25, 30, 32, 90
3-Methyl-	6-Methyl-	72	25	25	A/A	32, 33
3,4-Dimethyl-	5,6-Dimethyl-	48	reflux	8	A/A	32, 41, 42
2,4-Dimethyl-	4,6-Dimethyl-	48	reflux	10	A/A	32, 37
2,5-Dimethyl-	4,7-Dimethyl-	72	reflux	5	A/A	23, 32, 38
3-Phenyl-	5 and 6-Phenyl-	12	25	30	B/B	93, 94
3,4-Diphenyl-	5,6-Diphenyl-	24	25	15	B/B	43
2-Ethyl-	5-Ethyl-	48	25	2	A/A	14d
3-Ethyl-	6-Ethyl-	48	25	12	A/A	*** (92)
3,4-Dichloro-	5,6-Dichloro-	12	25	60	A/A	***

* In all cases, reaction involved admixture of 10 mmol thiophene dioxide with 12.5 mmol aminofulvene.

** Indicates solvent system used for crude product extraction and as eluent for column chromatography, where A represents pure petroleum ether and B is 20% chloroform-petroleum ether (V/V), reported as X/Y.

*** See Tables I, IV, XIII and XIV for complete analyses of new compounds.

2. Cycloadditions of 6-Methyl-6-dimethylaminofulvene

6-Methyl-6-dimethylaminofulvene was reacted with a variety of thiophene dioxides. The exemplary preparation of 4-methyl-6-ethylazulene is given below. Table X gives a summary of reaction conditions and yields starting from the corresponding dibromotetrahydrothiophene dioxide. Complete nmr and uv/vis data can be found in Tables I and IV, respectively. Elemental analyses and infrared data for new azulenes are tabulated in Tables XIII and XIV, respectively.

Preparation of 4-Methyl-6-ethylazulene. 3-Ethyl-3,4-dibromotetrahydrothiophene dioxide (3.1 g, 10 mmol) was dissolved in 75 ml of chloroform. The solution was chilled to 0-5°, and triethylamine (3 ml, 20 mmol) was added in one portion. The solution was stirred for two hours, then washed 4 times with 50 ml aliquots of ice water, and finally dried over molecular sieves. The dried solution was added to 6-methyl-6-dimethylaminofulvene (1.7 g, 12.5 mmol) and stirred at room temperature under a gentle stream of nitrogen for 72 hours. The reaction mixture was evaporated to dryness, and the crude product was dissolved in petroleum ether. Insoluble material was filtered off, and the solution was chromatographed on alumina with petroleum ether eluent. The first fraction consisted of 4-methyl-6-ethylazulene (0.21 g, 12% yield, based on dibromotetrahydrothiophene dioxide).

TABLE X. Cycloaddition reactions of 6-methyl-6-dimethylaminofulvenes and thiophene dioxides*

<u>Thiophene dioxide</u>	<u>Azulene</u>	<u>Conditions</u>		<u>Yield, %</u>	<u>Workup**</u>	<u>Ref.</u>
		<u>Time, h</u>	<u>T, °C.</u>			
Parent	4-Methyl	12	25	4	A/A	1, 32
2-Methyl	4,5-Dimethyl	96	25	trace	B/A	32, 35
3-Methyl	4,6-Dimethyl	72	25	15	A/A	32, 37
3,4-Dimethyl	4,6,7-Trimethyl	48	reflux	7	A/A	***
2,4-Dimethyl	4,6,8-Trimethyl	48	reflux	3	A/A	46, 95
3-Phenyl	4-Methyl-6-phenyl (major)	24	25	10	B/B	***
	4-Methyl-7-phenyl (minor)					
3-Ethyl	4-Methyl-6-ethyl	48	25	12	A/A	***
3,4-Dichloro	4-Methyl-6,7-dichloro	12	25	15	A/A	***

* In all cases, reaction involved admixture of 10 mmol thiophene dioxide with 12.5 mmol aminofulvene.

** Indicates solvent system used for crude product extraction and as eluent for column chromatography, where A represents pure petroleum ether and B is 20% chloroform-petroleum ether (V/V), reported as X/Y.

*** See Tables I, IV, XIII, and XIV for complete analyses of new compounds.

3. Cycloadditions of 6,6-Bis(dimethylamino)fulvene

6,6-Bis(dimethylamino)fulvene was reacted with a variety of thiophene dioxides. The exemplary preparation of 4-dimethylaminoazulene is given below. Table XI gives a summary of reaction conditions and yields starting from the corresponding dibromotetrahydrothiophene dioxide. Complete nmr and uv/vis data can be found in Tables I and IV, respectively. Elemental analyses and infrared data for new azulenes are tabulated in Tables XIII and XIV, respectively.

Preparation of 4-Dimethylaminoazulene. 3,4-Dibromotetrahydrothiophene dioxide (2.9 g, 10 mmol) was dissolved in 75 ml of chloroform. The solution was chilled to 0-5°, and triethylamine (3 ml, 20 mmol) was added in one portion. This solution was stirred for two hours, then washed 4 times with 50 ml aliquots of ice water, and finally dried over molecular sieves. The dried solution was added to 6,6-bis(dimethylamino)fulvene (2.0 g, 12.5 mmol) and stirred at room temperature under a gentle stream of nitrogen for 12 hours. The reaction mixture was evaporated to dryness, and the crude product was dissolved in 20% chloroform-petroleum ether (V/V). Insoluble material was filtered off, and the solution was chromatographed on alumina with 20% chloroform-petroleum ether eluent. The first, pale blue fraction, was discarded; the second, purple fraction, consisted of 4-dimethylaminoazulene (0.17 g, 10% yield, based on dibromotetrahydrothiophene dioxide).

All azulene forming reactions of 6,6-bis(dimethylamino)-fulvene were characterized by a front running non-azulene pale

blue band upon chromatographic workup. The desired azulene was always the second band eluted.

Attempted reaction of 2-Methylthiophene dioxide and 6,6-bis-(dimethylamino)fulvene. 2-Methyl-3,4-dibromotetrahydrothiophene dioxide (3.0 g, 10 mmol) was dissolved in 75 ml of chloroform and chilled to 0-5°. Triethylamine (3 ml, 20 mmol) was added in one portion and the solution stirred for two hours, then washed 4 times with 50 ml aliquots of ice water, and finally dried over molecular sieves. The dried solution was added to 6,6-bis-(dimethylamino)fulvene (2.0 g, 12.5 mmol) and stirred at room temperature under a gentle stream of nitrogen for 96 hours. The reaction mixture was evaporated to dryness, and the residue extracted with 20% chloroform-petroleum ether (V/V). Insoluble material was filtered off and the solution was chromatographed on alumina with 20% chloroform-petroleum ether eluent. The first, pale blue fraction was discarded as before, and the second, pale purple fraction was collected. The nmr displayed a multiplet at 7.35-7.75 δ and a doublet (or two singlets) at 4.10 and 4.20 δ . This nmr spectrum as well as the uv/vis spectrum was not azulene-like, so this material was not investigated further.

TABLE XI. Cycloaddition reactions of 6,6-bis(dimethylamino)fulvene and thiophene dioxides*

<u>Thiophene Dioxide</u>	<u>Azulene</u>	Conditions				<u>Ref.</u>
		<u>Time, h</u>	<u>T, °C.</u>	<u>Yield, %</u>	<u>Workup**</u>	
Parent	4-Dimethylamino	12	25	10	B/B	88
2-Methyl	-----			0	B/B	
3-Methyl	4-Dimethylamino-6-methyl	24	25	5	B/B	***
3,4-Dimethyl	4-Dimethylamino-6,7-dimethyl	72	reflux	4	B/B	***
2,4-Dimethyl	4-Dimethylamino-6,8-dimethyl	72	reflux	trace	B/B	†
3-Phenyl	4-Dimethylamino-6-phenyl (major)	12	25	6	B/B	***
	4-Dimethylamino-7-phenyl (minor)				B/B	
3-Ethyl	4-Dimethylamino-6-ethyl	48	25	12	B/B	***
3,4-Dichloro	4-Dimethylamino-6,7-dichloro	96	25	trace	B/B	†

* In all cases, reaction involved admixture of 10 mmol thiophene dioxide with 12.5 mmol aminofulvene.

** Indicates solvent system used for crude product extraction and as the eluent for column chromatography, where A represents pure petroleum ether and B is 20% chloroform-petroleum ether (V/V), reported as X/Y.

*** See Tables I, IV, XIII, and XIV for complete analyses of new compounds.

† Insufficient sample for complete analyses. Nmr and uv/vis obtained only.

4. Cycloadditions of 3,6-Dimethyl-6-dimethylaminofulvene (5)

Fulvene 5 was reacted with a variety of thiophene dioxides. The exemplary preparation of 2,4,6,8-tetramethylazulene is given below. Table XII gives a summary of reaction conditions and yields starting from the corresponding dibromotetrahydrothiophene dioxide. Complete nmr and uv/vis data can be found in Tables I and IV, respectively. Elemental analyses and infrared data for new azulenes are tabulated in Tables XIII and XIV, respectively.

Preparation of 2,4,6,8-Tetramethylazulene. 2,4-Dimethylthiophene dioxide (1.4 g, 10 mmol) and fulvene 5 (1.8 g, 12.5 mmol) were dissolved in 75 ml of chloroform. The solution was heated to reflux and stirred for 24 hours under a gentle stream of nitrogen. The reaction mixture was evaporated to dryness, and the crude product was dissolved in petroleum ether. Insoluble material was filtered off, and the solution was chromatographed on alumina with petroleum ether eluent. The first fraction consisted of 2,4,6,8-tetramethylazulene (0.19 g, 10% yield).

TABLE XII. Cycloaddition reactions of 3,6-dimethyl-6-dimethylaminofulvene (5) and thiophene dioxides*

<u>Thiophene Dioxide</u>	<u>Azulene</u>	<u>Conditions</u>		<u>Yield, %</u>	<u>Workup**</u>	<u>Ref.</u>
		<u>Time, h</u>	<u>T, °C.</u>			
Parent	1,4-Dimethyl	12	25	13	A/A	15, 96
2-Methyl	1,4,5-Trimethyl	96	25	2	A/A	†
3-Methyl	1,4,6-Trimethyl	48	25	10	A/A	***
3,4-Dimethyl	1,4,6,7-Tetramethyl (major)	48	reflux	5	A/A	†
	2,4,6,7-Tetramethyl (minor)					
2,4-Dimethyl	2,4,6,8-Tetramethyl	24	reflux	10	A/A	95
3-Phenyl	1,4-Dimethyl-6-phenyl (major)	48	25	10	B/B	***
	1,4-Dimethyl-7-phenyl (minor)					
3-Ethyl	1,4-Dimethyl-6-ethyl	48	25	12.5	A/A	***
3,4-Dichloro	1,4-Dimethyl-6,7-dichloro	12	25	16.5	A/A	***

* In all cases, reaction involved admixture of 10 mmol thiophene dioxide with 12.5 mmol aminofulvene.

** Indicates solvent system used for crude product extraction and as the eluent for column chromatography, where A represents pure petroleum ether and B is 20% chloroform-petroleum ether (V/V), reported as X/Y.

*** See Tables I, IV, XIII, XIV for complete analyses of new compounds.

† Insufficient sample for complete analyses. Nmr and uv/vis obtained only.

TABLE XIII. Elemental analyses of new azulene

<u>Azulene (mp)</u>	<u>calculated</u>			<u>found</u>		
6-Ethyl (50-51°)	C: 92.26	H: 7.69		C: 92.11	H: 7.67	
5,6-Dichloro (56-58°)	C: 60.95	H: 3.07	Cl: 35.98	C: 60.78	H: 3.14	Cl: 35.86
4,6,7-Trimethyl	C: 91.71	H: 8.29		C: 91.80	H: 8.14	
4-Methyl-6-phenyl	C: 93.54	H: 6.46		C: 93.46	H: 6.48	
4-Methyl-6-ethyl	C: 91.71	H: 8.29		C: 91.64	H: 8.19	
4-Methyl-6,7-dichloro (43-45°)	C: 62.59	H: 3.82		C: 62.48	H: 4.21	
4-Dimethylamino-6-methyl	C: 84.28	H: 8.16	N: 7.56	C: 84.47	H: 8.16	N: 7.43
4-Dimethylamino-6,7-dimethyl	C: 84.37	H: 8.60	N: 7.03	C: 84.50	H: 8.73	N: 6.94
4-Dimethylamino-6-phenyl	C: 87.41	H: 6.93	N: 5.66	C: 87.31	H: 7.05	N: 5.51
4-Dimethylamino-6-ethyl	C: 84.37	H: 8.60	N: 7.03	C: 84.56	H: 8.69	N: 7.10
1,4-Dimethyl-6-phenyl	C: 93.06	H: 6.94		C: 92.95	H: 6.88	
1,4,6-Trimethyl	C: 91.71	H: 8.29		C: 91.59	H: 8.32	
1,4-Dimethyl-6-ethyl	C: 91.25	H: 8.75		C: 91.36	H: 8.71	
1,4-Dimethyl-6,6-dichloro (38-40°)	C: 64.03	H: 4.48		C: 63.98	H: 4.59	

TABLE XIV. Principal infrared absorptions of new azulenes, μ .^{a,b}

<u>Azulene (phase)</u>													
6-Ethyl (CCl ₄)	3.24	<u>3.38</u>	3.48	<u>6.34</u>	6.79	6.91	<u>7.18</u>	7.68	<u>8.00</u>	9.50	10.3	<u>11.6</u>	
		12.0	<u>13.7</u>	14.4									
5,6-Dichloro (CCl ₄)	3.24	3.42	3.50	<u>6.37</u>	6.65	6.83	<u>7.15</u>	<u>7.18</u>	7.64	8.36	<u>9.6</u>	10.5	
		10.9	12.0										
4,6,7-Trimethyl (film)	3.24	3.36	3.40	<u>3.43</u>	6.29	6.45	6.52	6.78	6.90	<u>7.10</u>	7.32	8.28	
		9.8	<u>13.4</u>										
4-Methyl-6-phenyl (film)	3.25	3.27	3.31	<u>6.34</u>	<u>6.38</u>	6.43	6.76	7.00	7.37	11.8	<u>13.2</u>	14.3	
4-Methyl-6-ethyl (film)	3.24	<u>3.37</u>	3.41	3.48	<u>6.31</u>	6.40	6.73	7.00	7.18	<u>7.38</u>	9.5	10.0	
		11.8	<u>13.4</u>										
4-Methyl-6,7-dichloro (CCl ₄)	3.23	3.42	3.50	6.36	<u>6.62</u>	6.80	<u>7.02</u>	<u>7.12</u>	7.32	7.80	8.46	<u>9.2</u>	
		9.8	10.1	10.5									
4-Dimethylamino-6-methyl (film)	3.24	3.32	3.40	3.43	3.46	3.51	3.57	6.26	<u>6.55</u>	6.73	6.89	6.98	
		7.18	7.34	<u>7.45</u>	8.00	8.37	8.58	<u>8.92</u>	9.6	10.5	12.1	12.7	13.4
4-Dimethylamino-6,7-dimethyl (film)	3.24	<u>3.42</u>	3.47	3.57	6.25	<u>6.48</u>	6.76	6.90	7.14	7.20	<u>7.36</u>	<u>7.48</u>	
		8.46	8.82	<u>9.12</u>	9.42	9.83	<u>10.62</u>	11.8	13.5	14.0			
4-Dimethylamino-6-phenyl (film)	3.24	3.27	3.31	3.40	3.48	3.52	3.58	6.30	<u>6.58</u>	6.78	6.90	7.00	
		7.14	<u>7.52</u>	8.25	8.71	<u>8.92</u>	9.7	10.7	11.8	14.3			
4-Dimethylamino-6-ethyl (film)	<u>3.37</u>	3.42	3.48	<u>6.29</u>	<u>6.40</u>	6.61	6.85	6.92	7.06	7.22	7.33	9.5	
		9.8	12.1	<u>13.0</u>	14.1								

TABLE XIV cont'd

1,4-Dimethyl-6-phenyl (film)	3.27	3.31	3.43	3.50	6.32	<u>6.38</u>	6.44	6.63	<u>6.71</u>	6.92	7.07	7.25
	7.34	13.0	<u>13.3</u>	<u>14.3</u>								
1,4-Dimethyl-6,7-dichloro (CCl ₄)	3.25	3.30	<u>3.36</u>	<u>3.42</u>	3.50	6.37	<u>6.63</u>	<u>7.02</u>	7.20	7.30	7.71	7.87
	8.32	8.50	8.68	9.2	9.6	9.75	10.0	10.3	<u>10.5</u>	11.0	11.3	
	11.8	<u>14.3</u>										

- a) Infrared spectra of numerous azulenes are given in Hs. H. Günthard and Pl. A. Plattner, Helv. Chim. Acta, 32, 284 (1949).
- b) Intense absorptions are underlined.

5. Attempted Cycloadditions of 6-Phenyl-6-dimethylaminofulvene

6-Phenyl-6-dimethylaminofulvene was treated with a variety of thiophene dioxides in the same manner already described in sections 1-4 above. In all cases, extraction of the reaction mixture with petroleum ether gave only unchanged fulvene. Column chromatography of the reaction mixture with 20% chloroform-petroleum ether (V/V) yields thiophene dioxide dimer and the resultant styrene, identified by nmr spectroscopy. Since these were not the desired products, these reactions were not studied further. The reactions that were attempted are summarized in Table V.

6. Attempted Cycloadditions of Fulvene 4

Fulvene 4 was treated with a variety of thiophene dioxides in the same manner already discussed. In all cases, extraction of the reaction mixture with petroleum ether gave only unchanged fulvene. The reactions that were attempted are summarized in Table V.

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APPENDIX

Aromatic region of selected 100 MHz azulene spectra
in carbon tetrachloride.

VITA

Stephen Elliott Reiter was born on August 30, 1950 in Miami, Florida. He attended the public schools in Miami, graduating from Miami Senior High School in 1968. He was granted a B.S. degree in chemistry from the University of Florida in 1972, and enrolled in the Graduate School of the Louisiana State University in 1973. He is currently a candidate for the degree of Doctor of Philosophy in the Department of Chemistry, Louisiana State University.

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EXAMINATION AND THESIS REPORT

Candidate: Stephen Elliott Reiter

Major Field: Chemistry

Title of Thesis: The Synthesis of Azulenes by the [6+4] Cycloadditions of
6-Aminofulvenes to Thiophene-S,S-Dioxides

Approved:

Major Professor and Chairman

Dean of the Graduate School

EXAMINING COMMITTEE:

Date of Examination:

September 20, 1977