1977

The (6+4) Cycloaddition Reactions of Fulvenes and Aminobutadienes.

Lee C. Dunn

Louisiana State University and Agricultural & Mechanical College

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THE [6+4] CYCLOADDITION REACTIONS OF
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A Dissertation

Submitted to the Graduate Faculty of the
Louisiana State University and
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in

The Department of Chemistry

by

Lee C. Dunn
B.S., Louisiana State University, 1971
M.S., San Diego State University, 1973
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Abstract

Prior to this work only diazomethane and an azomethine ylide were sufficiently electron rich to undergo predominately [6+4] cycloaddition reactions with fulvenes. Houk, et al., predicted, on the basis of molecular orbital theory, that 1-diethylaminobutadiene should also be electron rich enough to give [6+4] cycloadducts, specifically dihydroazulenes. This prediction has now been verified experimentally and numerous [6+4] adducts have been prepared by reacting 6,6-dimethylfulvene with 1-diethylaminobutadiene, 1-diethylamino-1,3-hexadiene, and 1-diethylamino-3-methylbutadiene. In all of the reactions studied, the C-1 terminus of the diene added to the C-2 carbon of fulvene and the C-4 terminus of the diene added to the C-6 carbon of fulvene.

The regioselectivity for this reaction, with respect to secondary bond formation, was investigated by reacting 2,6,6- and 3,6,6-trimethylfulvene with 1-diethylaminobutadiene. With 3,6,6-trimethylfulvene, the observed product, 2,4,4-trimethyl-4,5-dihydroazulene, was the same product predicted by frontier molecular theory. In the case of 2,6,6-trimethylfulvene, the observed product, 3,4,4-trimethyl-4,5-dihydroazulene, was formed exclusively; although, frontier molecular theory predicted that the product should have been 4,4,9-trimethyl-4,5-dihydroazulene. In the latter case, it was observed that the diene added across the less hindered side of the fulvene.

Since the products of these reactions were dihydroazulenes, it followed that 6-monosubstituted fulvenes should give azulenes after
dehydrogenation of the dihydroazulene. Experimentally, this was found to be the case, and numerous 4,5-, 4,6-, and 4,7-disubstituted azulenes were prepared by reacting 6-phenyl-, 6-isopropyl- and 6-methylfulvene with 1-diethylaminobutadiene, 1-diethylamino-1,3-hexadiene, 1-diethylamino-3-methylbutadiene, and 2-ethyl-1-pyrrolidinobutadiene.

The three possible mechanisms for the [6+4] cycloaddition reaction are zwitterionic, diradical, and concerted. To distinguish between a zwitterionic and a concerted mechanism, the cycloaddition reaction of 6,6-dimethylfulvene and 1-diethylaminobutadiene was studied in two solvents (benzene and acetonitrile) of different polarity. The results of this study indicate only a small rate enhancement in the more polar solvent, acetonitrile. Thus, the possibility of going through a zwitterionic intermediate seemed small. The diradical mechanism could not be unequivocally ruled out; however, this mechanism appeared unlikely since no precedent for this type of behavior has been observed in other fulvene cycloaddition reactions. The conclusion reached in this study was that the [6+4] cycloaddition reaction occurred by a concerted pathway, in which one bond was formed to a greater extent than the other one in the transition state.
CHAPTER I
INTRODUCTION

Fulvenes are non-aromatic cyclic polyolefins which undergo a variety of reactions, including free radical, electrophilic, nucleophilic, and concerted cycloaddition reactions.\(^1\) Fulvene is shown in Figure 1. Houk et al., have shown the relationship between the frontier molecular orbitals of fulvene and the periselectivity in cycloaddition reactions of fulvene with dienes and 1,3-dipoles.\(^2\),\(^3\) Periselectivity refers, in general, to the competition between various allowed cycloaddition reactions,\(^4\) or in the case of reactions between fulvenes and \(4\pi\) systems, the competition between \([6+4]\) and \([4+2]\) cycloadditions. Fulvenes can undergo concerted cycloaddition reactions with \(4\pi\) systems as either \(6\pi\) or \(2\pi\) addends as shown in Figure 1. Both of these cases are thermally allowed by the Woodward-Hoffmann rules,\(^5\) as long as the cycloadditions are suprafacial on both addends. The \([4+4]\) reaction is thermally forbidden for a concerted process.

FULVENE:

\[
\begin{array}{c}
\text{[4+2]} \\
\text{[6+4]} \\
\text{[4+4]}
\end{array}
\]

Figure 1
One can gain deeper understanding into the factors which favor one of these cycloadditions over the other by consideration of the energy and coefficients of the $\pi$ molecular orbitals of fulvene. In the frontier molecular orbital theory of reactivity, the transition state stabilization arises mainly (not exclusively) from the interaction of the highest occupied molecular orbital (HOMO) of one molecule with the lowest unoccupied molecular orbital (LUMO) of the other molecule and vice versa. This interaction results in stabilization of the filled orbitals, and the net transition state stabilization is increased as the energy difference between the orbitals decreases, and the overlap between them increases.

Two frontier orbital interactions are possible. For fulvene cycloadditions, one involves mixing of the HOMO of fulvene with the LUMO of the diene or 1,3-dipole. The second interaction involves the mixing of the LUMO of fulvene with the HOMO of the diene or 1,3-dipole. In cases where neither molecule is clearly a donor or acceptor with respect to the other, then both interactions are important. However, if the fulvene is clearly the nucleophile with respect to the diene, then the first interaction is most important. If the fulvene is the electrophile, then the second type of interaction is most important.

As shown in Figure 2, the HOMO of fulvene has a node through C-1 and C-6 (i.e., the coefficients are zero at these two positions); the fulvene HOMO resembles that of butadiene. Stabilization from overlap of the fulvene HOMO with the LUMO of a diene can only occur if the fulvene acts as a $2\pi$ or $4\pi$ addend.
Thus with electron deficient dienes or 1,3-dipoles, simple (alkyl or aryl) fulvenes should prefer to react in a [4+2] fashion or [2+4] fashion using the 4π electrons of fulvene. In the LUMO of fulvene, the largest coefficients are centered at C-6 and C-2. This orbital resembles the exocyclic ethylene π* orbital, mixed with the diene LUMO in a bonding fashion. The C-6 coefficient is larger than the C-2 coefficient, because the LUMO also has some of the ethylene π orbital mixed with the diene LUMO in an antibonding fashion. The interaction of the diene HOMO with the fulvene LUMO will be most stabilizing if the diene adds across the C-2 and C-6 positions. In reactions where fulvene is clearly electrophilic, that is, in reactions with electron-rich dienes or 1,3-dipoles, the preferred reaction should be the [6+4] reaction. The preference...
here is not as great as that for the $[4+2]$ reaction when the fulvene HOMO is in control, since the C-3 coefficient is reasonably large.²

Figure 2 shows the HOMO's and LUMO's of dimethylfulvene and 1,3-butadiene. The energies of the HOMO of dimethylfulvene and 1,3-butadiene are the negatives of the ionization potentials (I.P.'s) and the energies of the LUMO's are estimated from the electron affinities (E.A.). For both of these estimates, the connection between orbital energies and experimental quantities is made via Koopmans' theorem.⁶ The I.P.'s of dimethylfulvene and 1,3-butadiene are 8.03 eV² and 9.1 eV⁷ respectively. The E.A. for dimethylfulvene has been estimated as -0.6 eV, and has been measured as -0.62 eV for butadiene (refer to Figure 2). Although the fulvene LUMO-butadiene HOMO interaction is slightly more important than the other frontier orbital interaction, the $[4+2]$ reaction is the only one found experimentally for such cases. This results from the fact that the fulvene HOMO interaction strongly favors the $[4+2]$ reaction, while the fulvene LUMO interaction slightly favors the $[6+4]$ addition, but can also stabilize the $[4+2]$ addition. In most cases one need consider only the HOMO-LUMO interactions; however, Paddon-Row et al., have pointed out that other types of interactions should be considered as well. For example, the importance of the second highest occupied molecular orbital (SHMO) and/or the second lowest unoccupied molecular orbital (SLUMO) has been stressed in some reactions.⁹
In almost all cases, it has been experimentally observed that the cycloaddition reaction of fulvenes to dienes give exclusively the \([1+2]\) adduct (Figure 3). For example, Luskus and Houk\(^{10}\) investigated the cycloaddition reactions of fulvenes to a variety of dienes. In this study, they reacted mono- and disubstituted fulvenes with \(\alpha\)-pyrone, cyclopentadiene, 2,4-cycloheptadieneone and 2,5-dimethyl-3,4-diphenylcyclopentadienone. They observed exclusive formation of Diels-Alder type adducts with fulvene acting as the dienophile, as shown in Figure 3.

\[
\begin{align*}
\text{Diene} & \quad \text{Diene} \\
\text{Dienes:} & \\
\text{a} & \quad \text{b} \\
\text{c} & \quad \text{d}
\end{align*}
\]
Figure 4
Prior to this work, only two unequivocal examples of predominant [6+4] cycloadditions of fulvenes to dienes were known. Diazomethane$^{5,11}$ and an azomethine ylide$^{12}$ were the only 1,3-dipoles that were investigated which were sufficiently electron rich to add in a [6+4] fashion, as shown in Figure 4.

In these two examples, the HOMO energy of the 1,3-dipole is sufficiently high so that the energy difference between the HOMO of the 1,3-dipole and the LUMO of the fulvene is much less than the energy difference between the HOMO of fulvene and the LUMO of the 1,3-dipole. During the course of this work, Padwa and Nobs$^{13}$ reported that nitrile ylides also add in a [6+4] fashion to fulvenes, as had been predicted earlier$^{5}$. 

![Diagram showing the reaction of a 1,3-dipole with a fulvene](image-url)
The purpose of this investigation was to determine whether or not fulvenes would cycloadd in a $[6+4]$ fashion to butadienes more electron rich than those studied by Luskus. In Figure 5, the HOMO and LUMO energies and coefficients of diethylaminobutadiene and dimethylfulvene are shown. The diethylamino group lowers the I.P. and decreases the E.A. of butadiene. In this case, one can clearly see that the energy difference between the LUMO of the fulvene and the HOMO of the diene will be much less than the energy difference between the HOMO of the fulvene and the LUMO of the diene. This will make the $[6+4]$ cycloaddition reaction
more favorable.

It should be pointed out that the same conclusion could be reached using classical assignments. An attacking nucleophile would prefer to attack the electrophilic C-6 position and generate the aromatic cyclopentadienide anion. The frontier molecular orbital approach and the classical approach both predict similar results, although the frontier molecular orbital approach more clearly predicts results for concerted cycloadditions.

Recent Literature on Fulvene Cycloadditions

Cycloaddition reactions of fulvenes as $6\pi$ or $2\pi$ addends have now been well established. Luskus' dissertation reviews the cycloaddition reactions of fulvenes up until 1971. Since that time, Luskus and Houk have published two papers dealing with the cycloaddition of tropone to dimethylfulvene.\textsuperscript{4,15} The 2:1 adduct (\(\tilde{3}\)) and precursor 1:1 adduct (\(\tilde{2}\)) formed in these reactions must arise from the unisolable $[6+4]$ adduct (\(\tilde{1}\)). However, it is
possible that \(~ \) arises via a Cope rearrangement from the unisolable [6+4] adduct (\(~ \) ). In 1972, Tanida et al.\textsuperscript{16} reported the cycloaddition of 8,8-dimethylisobenzofulvene to tropone. Because the 1,5-sigmatropic shift, which converts \(~ \) to \(~ \), was impossible in \(~ \), the unrearranged adduct \(~ \) was isolated. In 1973, Warrener\textsuperscript{17} et al. showed that this reaction gave the [6+4] adduct \(~ \) at room temperature, but that under the conditions of Tanida's reaction, a Cope rearrangement of \(~ \) to \(~ \) occurred. Thus, tropone was the 6π component. It was possible that the dimethylfulvene-tropone reaction followed the same course, although Houk, Luskus and Bhacca\textsuperscript{18} had reported \(~ \) as the primary adduct in this reaction.
on the basis of cycloadduct stereochemistry of 6-monosubstituted fulvene to tropone reaction. It has recently been shown by Houk and Tegmo that 4 was actually the primary adduct, and that Houk's original stereochemical arguments were incorrect.

In 1973, the cycloaddition of diphenylfulvene to tropone was investigated by Sasaki and co-workers. They reported formation of a single [4+2] adduct in 60% yield. Houk independently studied this reaction and found that three other Diels-Alder ([4+2]) adducts were also formed. In each case tropone added as the diene across an endocyclic fulvene double bond. The exclusive formation of [4+2] adducts was probably due to the large steric bulk of the two phenyl rings at the C-6 position.

Cornelis and Laszlo studied the reaction of dicyclopentylfulvene with tetracyanoethylene (TCNE). They observed the expected [4+2] Diels-Alder adduct 5 in almost quantitative yield at 0°C. At a slightly higher temperature, 5 rearranged to give a [2+2] cyclobutane adduct 6. Since this compound has considerable strain, it rearranges to form a [2+6] cycloadduct 7, which undergoes a 1,5-sigmatropic shift to give 8.

Sasaki et al., in 1975, investigated the periselectivity of reactions involving fulvenes with heterodienes and heterodienophiles. They studied the cycloaddition reactions of 6,6-dimethylfulvene, 6,6-diphenylfulvene, and 6-dimethylaminofulvene with 3,6-diphenyltetrazine, 3,4-diaza-2,5-diphenylcyclopentadienone, and diethyl azodicarboxylate (shown in Figure 6 on page 13). In the reaction of
6-dimethylaminofulvene with 3,6-diphenyltetrazine, they observed the formation of 4,7-diphenyl-5,6-diazaazulene  
resulted from initial [6+4] cycloaddition, followed by loss of nitrogen and diethylamine. When 6,6-diphenylfulvene was reacted with 3,6-diphenyltetrazine, only the [4+2] cycloadduct was observed. With 6,6-dimethylfulvene, a mixture of products was obtained which decomposed during attempted isolation. With 6-dimethylaminofulvene and 3,4-diaza-2,5-diphenylcyclopenta
dienone, they observed formation of compound 11, which
Figure 6
presumably arose from initial \([4+2]\) cycloaddition followed by loss of carbon monoxide and hydrogen. The reaction of diethyl azodicarboxylate with dimethyl- and diphenylfulvene gave only the \([4+2]\) adduct \(12\). Diethyl azodicarboxylate, tetrazine, and diazacycopentadienone are very electron-deficient heteropolypenes and interaction of their LUMO's with the HOMO's of the alkyl fulvenes are the most important interactions. This interaction leads to the expected \([4+2]\) cycloaddition products. In the case of 6-dimethylaminofulvene (an electron-rich fulvene), the important interaction to consider is that of the fulvene HOMO with the 3,6-diphenyltetrazine LUMO.

Takeshita, et al. studied the cycloaddition reaction of isobenzofuran with 6,6-dimethyl- and 6,6-diphenylfulvene.\(^{24}\) Isobenzofuran reacted with 6,6-diphenylfulvene to give two endo \([4+2]\) cycloadducts: an endo 1:1 adduct \(13a\), and an endo-anti-endo 1:2 adduct \(13b\). With isobenzofuran and dimethylfulvene, they observed a single \([6+4]\) endo cycloadduct, \(14\).

Friedrichsen et al. have published numerous papers, which deal with the cycloadditions of fulvenes with a variety of reagents. In two papers appearing in 1974\(^{25}\) and 1976\(^{26}\), they reacted 6,6-disubstituted fulvenes (alkyl or aryl) with substituted o-benzoquinones (\(x=0\)). With these compounds, they obtained exclusively the \([4+2]\) adducts \(15\) and \(16\). Formation of these adducts is understandable, since the electron-deficient quinones should have low-lying LUMO's, so that there will be strong fulvene
HOMO-quinone LUMO interaction. In 1974, these authors reported that the reaction of 6,6-disubstituted fulvenes with substituted o-benzoquinone dibenzimines (X=NR') gave pyrazines.\textsuperscript{27} In every case except one, R' was an electron-withdrawing COPh group. In the single case, R' was the even stronger electron-withdrawing COC$_6$H$_4$(p-NO$_2$) group. The only compounds formed in these reactions were the [4+2] adducts \textsuperscript{16}. In continuation of this study, they investigated the reaction of substituted
N,N'-dibenzoylsulfonyl-o-benzoquinone dibenzimines (X=NSO₂R') with 6,6-disubstituted fulvenes (alkyl and aryl). In these reactions they observed formation of both the [4+2] cycloadduct 16 and the [6+4] cycloadduct 17. Recently, they reported the reaction of 6,6-bis(p-methoxyphenyl)fulvene with N,N'-dibenzolsulfonyl-o-benzoquinone diimines (X=NSO₂R'). In this case, they reported the formation of the [6+4] cycloadduct 17 and the [4+4] cycloadduct 18 which rearranged to the [4+2] cycloadduct 16. Although no electronic explanation is available, these products may arise from a non-concerted process, such as formation of a zwitterionic intermediate.
CHAPTER II

Results and Discussion

The initial study of the reaction of 6,6-dimethylfulvene and l-diethylamino-1,3-butadiene was carried out by Chang, who obtained an impure product, which was shown in this work to arise from the desired [6+4] adduct. In the present study, the prediction that l-aminobutadiene can cycloadd in a [6+4] fashion based on frontier molecular theory, has been verified experimentally, and numerous adducts have been prepared. In the following section will be described: (1) preparation of substituted l-aminobutadienes, (2) elucidation of the [6+4] cycloadduct structures via trapping of intermediates with dimethyl acetylenedicarboxylate, (3) synthesis of azulenes using reactions, and (4) a discussion of the possible mechanisms for the cycloaddition of 6,6-dimethylfulvene and l-aminobutadiene.

Preparation of Dienes

Numerous methods exist for the preparation of enamines, including dienamines. Hünig and Kahane prepared 1-diethylamino-3-butadiene at 0°C, by the sodium carbonate catalyzed condensation of diethylamine and crotonaldehyde. Azeotropic removal of water using benzene was used to prepare 1-diethylamino-1,3-hexadiene from diethylamine and hex-2-enal. The nmr spectrum of this product indicated that a mixture of cis and trans isomers existed. A complex vinyl region extended from δ 4.50 to 6.20, two overlapping quartets due to CH₂-N protons were centered at δ 2.97 and 3.00, the aliphatic CH₂ protons appeared as a complex pattern centered at δ 2.01, and the
aliphatic CH₃ resonances overlapped the N-CH₂CH₃ resonances in the region from δ 0.8 to 1.20. The most convincing evidence that there were indeed two stereoisomers, was from the overlapping quartets of the NCH₂ protons. By inspection, an approximate ratio of 1:1 (E:Z) could be ascertained.

cis-1,3-Pentadiene, as well as the corresponding trans isomer, exist in both cisoid and transoid conformations as shown on the following page. In the cis isomer, the equilibrium is shifted almost completely to the right in favor of the transoid conformation to relieve steric repulsion between the terminal H and the terminal methyl group. In the trans isomer, equilibrium still favors the transoid conformation but not as much, since the steric interaction in the cisoid conformation involves only hydrogens. In Diels-Alder reactions, the cis-substituted butadienes reacts slowly or not at all; the trans dienes are much more reactive.³² Thus, in Diels-Alder reactions and presumably in other cycloaddition, only the trans compound is expected to react. In the reaction of fulvenes with 4-ethyl-1-diethylaminobutadiene, two equivalents of diene were used to make sure that at least one equivalent of the trans compound was present.

Both the parent compound and the 4-ethyl derivative could be stored for months in the freezer with only a slight decomposition.

The 3-methyl-1-diethylaminobutadiene, 10, was readily obtained
from 3-methylcrotonaldehyde and was converted to the corresponding aminobutadiene in 27-40% yield by azeotropic removal of water. In the nmr spectrum of 19, the vinyl methyl was a singlet at $\delta 1.52$. The CH$_3$ protons of the ethyl group appeared as a triplet at $\delta 1.10$ and the CH$_2$ protons was a quartet at $\delta 3.00$ ($J=7$Hz). H$_1$ resonated as a doublet centered at $\delta 6.03$ ($J=14$ Hz), H$_2$ was a doublet at $\delta 4.99$ ($J=14$ Hz) and both H$_3$ and H$_3'$ appeared as a broad complex multiplet centered at $\delta 4.32$.

In the preparation of 2-ethyl-1-pyrrolidino-1,3-butadiene, one equivalent of 2-ethylcrotonaldehyde in toluene was treated with three equivalents of pyrrolidine in the presence of one equivalent of anhydrous potassium carbonate, and the water was removed by azeotropic distillation. After 12-14 hours, the excess reagents and solvent were removed under reduced pressure, ~ 0.5g phenanthrenequinone was added, and the product was distilled to give (65%) 2-ethyl-1-pyrrolidino-butadiene 20, as a pale yellow liquid.
The nmr spectrum of this compound in deuterobenzene, indicated that both cis(Z) and trans(E) isomers were present in a ratio of ~4:1 (Z/E) based on the relative intensities of the H₃ proton signals in both isomers. That the Z-isomer was the major isomer, was indicated by the disappearance of this isomer during the course of the cycloaddition reaction with 6-monosubstituted fulvenes. The methyl protons absorbed as a triplet at δ 1.15 (J = 8 Hz) and the methylene protons exhibited as a quartet at δ 2.4 (J = 8 Hz). Complex multiplets due to the pyrrolidine ring protons appeared at δ 1.50 and δ 3.10, with the four protons nearest the nitrogen resonating at lower field. In the major isomer, the H₃ proton appeared as a doublet of doublets at δ 6.15 and δ 6.40 (J = 11, 17 Hz) and in the minor isomer, H₃ appeared as a doublet of doublets at δ 6.80 and δ 7.10 (J = 11, 17 Hz). The H₁ proton in both isomers represented a sharp singlet at δ 5.95. The H₄ proton appeared as a doublet of doublets at δ 4.70 (J = 1.5, 11 Hz) and the H₄' proton was a doublet of doublets at δ 4.90 (J = 1.5, 17 Hz).

The 1,4-bis-(dimethylamino)-1,3-butadiene was prepared according to the procedure of Pegley, Bortnick and McKeever.
and the structure was verified by carrying out a Diels-Alder reaction with fumaronitrile.$^{34}$

**Cycloadditions of Dienamines to Dimethylfulvene**

In the initial study, 3 equivalents of 6,6-dimethylfulvene were reacted with 1 equivalent of 1-diethylaminobutadiene at room temperature without solvent. After two days, thin layer chromatography, (tlc) showed the presence of a new red spot which moved with the solvent front ($R_f \approx 0.9$). In the first attempts to isolate the new compound, the sample was chromatographed on neutral alumina, resulting in decomposition of the sample. Successful separations were carried out on silica gels columns. The yield of this product was generally less than 30%. In an attempt to increase the yield, methyl iodide was added to quaternize any amines present. Since this methylation reaction was exothermic, the reaction mixture was diluted with methylene chloride and cooled in an ice bath before addition of methyl iodide. After stirring for one hour, the reaction mixture was filtered, and the solution was extracted several times with 4% aqueous potassium hydroxide. This procedure increased the isolated yield of the red oil to 65%, presumably by making it easier to chromatograph the reaction mixture since water soluble ammonium salts would be easily removed in the extraction step.

There are several possible thermally allowed products obtained from the cycloaddition reaction of dimethylfulvene and aminobutadienes which are shown on the next page.
The nmr spectrum of this new red component exhibited a sharp singlet at δ 1.10, indicative of the protons of methyl groups attached to a saturated carbon, a doublet at δ 2.25 (J=5 Hz) due to two allylic protons, and a complex multiplet ranging from δ 5.80 to 6.50 due to six vinyl protons. The coupling constant of 5 Hz for the allylic protons was in accord with the value observed for an allylic proton coupled with a vinyl proton.\(^3\) These data support structure 21 for the adduct. In particular, the uv spectrum of this compound had \(\lambda_{\text{max}}\) (cyclohexane) at 317 nm (\(\log \epsilon = 4.10\)). These values are similar to the uv spectral data of 6-vinylfulvenes shown in Table I.\(^3\)~

<table>
<thead>
<tr>
<th>(\lambda_{\text{max}}) nm (cyclohexane)</th>
<th>(\log \epsilon)</th>
</tr>
</thead>
<tbody>
<tr>
<td>305</td>
<td>4.30</td>
</tr>
<tr>
<td>317</td>
<td>4.31</td>
</tr>
<tr>
<td>307</td>
<td>4.25</td>
</tr>
<tr>
<td>313</td>
<td>4.26</td>
</tr>
</tbody>
</table>

Table I
In order to provide further evidence for the dihydroazulene structure, 21 was reacted with dimethyl acetylenedicarboxylate, DMAD, since DMAD is known to undergo Diels-Alder reactions with dienes. A solution of 21 and DMAD in carbon tetrachloride was refluxed overnight. After removal of solvent and excess DMAD, followed by chromatography, a white crystalline solid (23), mp 62-63°C was obtained in 79% yield. Evidence for the formation of 23 from a [4+2] cycloaddition of DMAD across the butadiene moiety in the five membered ring of compound 21 was provided as follows.

The nmr spectrum of 23, shown in Figure 7, was confusing at first because it indicated the presence of at least two different compounds. This confusion was cleared up by studying the temperature dependence of the nmr spectrum. This study indicated
Figure 7
that actually consisted of two conformations which only slowly interconvert at room temperature. The temperature dependent nmr spectrum will be discussed after presentation of the room temperature nmr data.

The nmr spectrum of compound in CDCl$_3$, had methyl singlets at δ 1.00 and 1.17 which were twice as intense as those at δ 1.09 and 1.35. Resonances for the two methylene hydrogens (H$_3$) appeared at δ2.82 and 2.98 for the major isomer and at δ 2.49 and 2.63 for the minor isomer. Two peaks due to the methoxy methyl protons incidentally overlapped at δ 3.72 and two others absorbed at δ3.81 and 3.82. The bridgehead protons in both adducts accidentally have the same chemical shift and appeared as a doublet of doublets at δ4.11 (J = 3.2, 1.1 Hz), coupled to the olefinic protons on the norbornadiene moiety. In the major isomer, H$_{10}$ was a doublet of doublets centered at δ 6.60 (J = 5.5, 1.5 Hz) and H$_9$ resonated as a doublet of doublets centered at δ 7.06 (J = 5.5, 3.2 Hz). In the minor isomer H$_{10}$ was a doublet of doublets centered at δ 6.94 (J = 5.5, 1.1 Hz) and H$_9$ appeared as a doublet of doublets centered at δ 7.19 (J = 5.5, 3.2 Hz). The three cycloheptadiene vinyl protons were partially resolved multiplets centered at δ 4.85 (one proton from each isomer) and 5.60 (two protons from each isomer). These assignments were confirmed by the following decoupling experiment. When the bridgehead proton H$_8$ was irradiated at δ4.04, the complex vinyl region from δ6.55 to 6.96
simplified to form three doublets centered at $\delta 6.62$, $6.78$ and $6.91$, respectively, each having $J = 5.5$ Hz. The doublet at $\delta 6.62$ was assigned to $H_{10}$ in the major isomer and the doublet at $6.91$ was due to $H_9$ in the minor isomer. $H_{10}$ in the minor isomer and $H_9$ in the major isomer were accidentally equivalent and appeared as a doublet centered at $\delta 6.78$. The long range couplings between $H_{10}$ and $H_9$ ($J = 1.5$ Hz) and the coupling between $H_9$ and $H_8$ ($J = 3.2$ Hz) disappeared. Irradiation of the vinyl region at $6.64$ caused collapse of the overlapping doublet of doublets due to the bridgehead proton, $H_8$, giving a doublet centered at $\delta 4.03$. Thus, the vinyl region at $6.64$ was attributed to $H_{10}$. When the resonance at $\delta 4.65$ was irradiated, the complex vinyl region centered at $5.60$ simplified but gave no definite information about the couplings involved. Irradiation of the vinyl region at $5.50$ caused collapse of the complex multiplet centered at $4.63$ to give a broad singlet. The absorptions at $4.63$ were assigned to $H_6$ and the vinyl region at $5.60$ was assigned to $H_4$ and $H_5$. The latter two protons could not be further resolved from each other. In deuterobenzene, the four high field methyl singlets changed their relative positions. The methyl resonances due to the major isomer now appeared at $0.98$ and $1.17$ while the methyl resonances of the minor isomer appeared at $1.23$ and $1.38$ (Figure 7). Also note in Figure 7, that the methylene protons in the major isomer were shifted to lower field and appeared at $3.03$ and $3.19$. To determine the
correspondence between the methyl resonances in CDCl₃ and C₆D₆, the nmr spectrum was determined first in CDCl₃, and then a few drops of C₆D₆ were added. The nmr spectrum was rerun and this procedure was repeated several times until the spectrum resembled that of 23 in pure C₆D₆.

The couplings and the chemical shifts of the norbornadiene protons in 23 are similar to those of the corresponding protons in 24. In the nmr spectrum of 24 in carbon tetrachloride, the bridgehead protons Hb Hb' appear as an apparent triplet (AA' XX') centered at δ 4.30 and the vinyl protons Ha and Ha' appear as an apparent triplet at 6.92. Both J_ab and J_a'b', are approximately equal to 2 Hz. The methoxy protons appear as a singlet at δ 3.70.

The chemical shifts and coupling constants for the DMAD adducts described in this section are given in Table II.
Table II

Chemical Shifts (ppm)
for
DMAD Adducts

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>R_2</th>
<th>R_3</th>
<th>R_4</th>
<th>R_5</th>
<th>R_6</th>
<th>R_7</th>
<th>R_8</th>
<th>R_9</th>
<th>R_10</th>
<th>J_5,6</th>
<th>J_8,9</th>
<th>J_8,10</th>
<th>J_9,10</th>
</tr>
</thead>
<tbody>
<tr>
<td>23a</td>
<td>Me:1.00(s)</td>
<td>H:2.82(s)</td>
<td>H:5.60(m)</td>
<td>H:5.60(m)</td>
<td>H:4.63(m)</td>
<td>H:4.11(dd)</td>
<td>H:7.06(dd)</td>
<td>H:6.64(dd)</td>
<td>-</td>
<td>3.2</td>
<td>1.1</td>
<td>5.5</td>
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<tr>
<td>23b</td>
<td>Me:1.09(s)</td>
<td>H:2.48(s)</td>
<td>H:5.60(m)</td>
<td>H:5.60(m)</td>
<td>H:4.63(m)</td>
<td>H:4.11(dd)</td>
<td>H:7.19(dd)</td>
<td>H:6.91(dd)</td>
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<td>1.1</td>
<td>5.5</td>
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<tr>
<td>29a</td>
<td>Me:0.99(s)</td>
<td>H:3.07(s)</td>
<td>H:5.55(m)</td>
<td>H:5.55(m)</td>
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<td>H:3.69(d)</td>
<td>Me:1.74(d)</td>
<td>H:6.12(q)</td>
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<td>2.0</td>
<td>-</td>
<td>2.0</td>
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</tr>
<tr>
<td>29b</td>
<td>Me:1.24(s)</td>
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<td>H:5.55(m)</td>
<td>H:5.55(m)</td>
<td>H:4.67(d)</td>
<td>H:3.69(d)</td>
<td>Me:1.70(d)</td>
<td>H:6.26(q)</td>
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<td>-</td>
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</tr>
<tr>
<td>32a</td>
<td>Me:1.00(s)</td>
<td>H:2.82(s)</td>
<td>H:5.57(m)</td>
<td>H:5.57(m)</td>
<td>H:4.78(d)</td>
<td>H:3.84(d)</td>
<td>H:6.56(dd)</td>
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<td>H:5.57(m)</td>
<td>H:4.86(d)</td>
<td>H:3.89(d)</td>
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<td>Me:2.10(d)</td>
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<td>3.5</td>
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<tr>
<td>35a</td>
<td>Me:0.96(s)</td>
<td>H:2.82(s)</td>
<td>Me:1.79(m)</td>
<td>H:5.30(m)</td>
<td>H:4.68(d)</td>
<td>H:4.05(d)</td>
<td>H:6.99(dd)</td>
<td>H:6.73(dd)</td>
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<td>1.0</td>
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<tr>
<td>35b</td>
<td>Me:1.03(s)</td>
<td>H:2.48(s)</td>
<td>Me:1.76(m)</td>
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<td>H:3.99(d)</td>
<td>H:7.13(dd)</td>
<td>H:6.93(dd)</td>
<td>7.0</td>
<td>3.0</td>
<td>1.0</td>
<td>5.5</td>
<td></td>
</tr>
</tbody>
</table>

s=singlet; m=multiplet; d=doublet; dd=doublet of doublets

* These are couplings between the methyl group and the vinyl proton.
The temperature dependence of the nmr spectrum of compound \( \sim 2^3 \) was studied in the following way (refer to Figure 8).

The sample was dissolved in hexachlorobutadiene and disiloxane was added as an internal lock. The temperature was increased in increments of 10°C from 40°C to 60°C, the four peaks due to methoxy protons collapsed to form two singlets at δ 3.40 and 3.60. The four peaks due to methyl protons collapsed at 121°C to form a singlet at δ 1.10. This singlet was accidental due to exchange between the highest field and lowest field methyl protons and exchange between the two inner methyl proton peaks.

The other peaks in the nmr spectrum also became less complex. When the sample was cooled to room temperature, the original spectrum was obtained. This study indicated that \( \sim 2^3 \) actually consisted of two conformations, \( \sim 2^3a \) and \( \sim 2^3b \), which interconvert slowly at room temperature. The ratio of methyl resonances indicated that the two isomers were present in a ratio of 2:1. The major isomer was assigned structure \( \sim 2^3a \) on the basis of the following evidence:
Figure 8

$\text{C}_4\text{Cl}_6\ 40^\circ\text{C}$

$\text{C}_4\text{Cl}_6\ 121^\circ\text{C}$
A Dreiding model indicated closer approach of one of the ring methyls and one of the methoxyl groups in 23b than in 23a. Thus, the structure 23a was assigned as the major isomer and 23b as the minor isomer. The observed ratio of 2:1 (23a:23b) was attributed to the preference by the methyl group for the sterically unhindered side of the norbornadiene moiety, away from the 2,3-dicarboxylic acid dimethyl ester substituents.

The energy barrier to conformational interconversion is estimated from the coalescence temperatures observed in the temperature dependent nmr spectrum. At the coalescence temperature, $T_c$, the rate constant can be determined approximately from the relationship:

$$K_c = \frac{\pi \Delta \nu}{\sqrt{2}}$$

(1)

where $\Delta \nu$ is the difference in chemical shift of resonances of exchanging hydrogens at a temperature where exchange is slow. From $K_c$, the free energy to interconversion can be determined:

$$\Delta G^\ddagger = 4.57 T_c \left(10.32 + \log \frac{T_c}{K_c} \right)$$

(2)
In 23, the methoxy protons coalesced at $60 \pm 5^\circ C$ and the ring methyls coalesced at $100 \pm 5^\circ C$. From the nmr spectrum at $40^\circ C$, the outer methyl peaks were separated by $37.5\text{Hz}$ and the inner methyl peaks were separated by $8.5\text{Hz}$. The first and third methoxy methyl peaks were separated by $6\text{Hz}$ and the second and fourth peaks were separated by $7\text{Hz}$. Using this information, the $\Delta G^\ddagger$ for conformational inversion can be calculated in four independent ways, shown in Table III.

**TABLE III**

<table>
<thead>
<tr>
<th>$K_c$</th>
<th>$T_c$</th>
<th>$\log \frac{T_c}{K_c}$</th>
<th>$10.32 + \log \frac{T_c}{K_c}$</th>
<th>$(4.57 \times T_c)$</th>
<th>$\Delta G^\ddagger$</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.33</td>
<td>$60^\circ$</td>
<td>1.398</td>
<td>11.718</td>
<td>1521.8</td>
<td>17.83</td>
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<tr>
<td>15.55</td>
<td>$60^\circ$</td>
<td>1.331</td>
<td>11.651</td>
<td>1521.8</td>
<td>17.73</td>
</tr>
<tr>
<td>83.3</td>
<td>$121^\circ$</td>
<td>0.675</td>
<td>10.995</td>
<td>1800.6</td>
<td>19.80</td>
</tr>
<tr>
<td>18.88</td>
<td>$121^\circ$</td>
<td>1.321</td>
<td>11.641</td>
<td>1800.6</td>
<td>20.96</td>
</tr>
</tbody>
</table>

ave 19.08

This relatively high barrier to conformational change in a cycloheptadiene ring probably results from the high barrier to rotation about the C-C bond which joins two quaternary centers. Dibenzobarrelenes, which have quaternary centers attached to quaternary bridgehead positions, have even larger barriers.\(^37\)
The conclusion reached, based on the experimental data given above, leaves no doubt that the reaction of 6,6-dimethylfulvene and 1-diethylaminobutadiene occurred by a [6+4] cycloaddition reaction.

To test the regioselectivity of the [6+4] cycloaddition reaction of 1-aminobutadienes to fulvenes, both 2,6,6-trimethylfulvene and 3,6,6-trimethylfulvene were reacted with 1-aminobutadiene. These fulvenes were prepared by the base-catalyzed condensation of methylcyclopentadiene and acetone according to the procedure of Crane, Boord, and Henne. Two isomers, 24 and 25, were formed in a 3:1 ratio and were readily separated by gas chromatography.

Assignments of structure were made by spectral analysis of the products formed by reaction of the major isomer and a mixture, consisting of both isomers, with DMAD.

![Chemical structures and reactions](attachment:image.png)
In the nmr spectrum of the adduct, 26, formed from the major isomer 24, the exocyclic methyl peaks resonated as a singlet at δ 1.40, the ring methyl was a doublet (J = 1.5 Hz) centered at δ 1.85, and the methoxy peaks resonated at δ 3.62 and δ 3.72. The vinyl protons were a complex multiplet centered at δ 6.30. One of the bridgehead protons appeared as a doublet at 4.00 (J = 1.5 Hz) and the other bridgehead proton absorbed as a doublet (J = 3 Hz) at 4.15. Since 26 had the ring methyl attached to a double bond, a single vinyl proton and two bridgehead protons, this compound had to have the structure shown and could only be formed from the 3-methyl isomer.

By comparing the nmr spectrum of 26 to the nmr of the mixture containing both 26 and 27, peaks due to the minor isomer were assigned. The methoxy peaks appeared at δ 3.62 and 3.72, the exocyclic methyls were at δ 1.50 and 1.56, and the ring methyl appeared at 1.70. The olefinic protons appeared as two complex multiplets centered at δ 6.60 and δ 6.90, and the single bridgehead proton appeared as a complex pattern at δ 4.35. From the nmr data, structure 27 was assigned to the minor isomer since this compound had two vinyl protons and only one bridgehead proton.

The major isomer, 3,6,6-trimethylfulvene, may react with 1-diethylaminobutadiene, to give two possible [6+4] adducts, 28a and 28b, differing only in the position of the methyl substituent in the five membered ring. One equivalent of fulvene 24 was heated without solvent at 35-40°C with two equivalents of the 1-diethyl aminobutadiene without solvent.
Two equivalents of 1-diethylaminobutadiene were used since this diene readily decomposes. After four days, eight equivalents of methyl iodide were added and the reaction mixture was worked up in the same manner as the 6,6-dimethylfulvene reaction described previously, to give compound 28 in a 40% yield.

The nmr spectrum of this compound had a sharp singlet at δ 1.08 due to the six methyl protons at the saturated carbon and a doublet centered at δ 1.85 (J = 2 Hz) due to three hydrogens of the methyl group attached to a vinyl carbon. A doublet appeared at δ 2.23 (J = 5 Hz) due to the two allylic methylene protons. However, this was not a clean-cut doublet and had some virtual coupling associated with it. In the vinyl region, there was a broad multiplet extending from δ 5.40 to 6.20 due to four olefinic protons. Since the individual vinyl protons could not be assigned, these data were consistent with either structure 28a or 28b. To identify the product, 28 was reacted with DMAD in refluxing CCl₄ (80° C) overnight. The product of this reaction, 29, was once again found to exist as two slowly interconverting conformators 29a and 29b in a ratio of 2:1.
Figure 9

C₆D₆ 40°C

C₄Cl₆ 40°C
The 2,6,6-trimethylfulvene $25$ can also add to 1-aminobutadienes to give two possible [6+4] cycloadducts, which after loss of diethylamine would give $30$, $31$, or both.

Using the same procedure as before, the intermediate cycloadduct was trapped with DMAD to yield (9 %) a single product. On the basis of nmr (Figure 10) uv, and ir data, this compound was assigned structure $32$. This compound, like the two previous DMAD adducts, consisted of two conformational isomers, $32a$ and $32b$. Nmr data are given in Table II.
The reaction of 6,6-dimethylfulvene with 3-methyl-1-diethylamino-butadiene was then studied. The two possible [6+4] adducts that could form after loss of amine, are $33$ and $34$. 

$\text{R}_2\text{N}$

$\text{R}_2\text{N}$

$33$
A 1:1 mixture of aminobutadiene and dimethylfulvene was kept at room temperature for two days, after which the product was worked up in the usual way to give a dark red oil in a 20% yield. In the nmr spectrum of the isolated product, there was a sharp singlet at $\delta 1.10$ due to the two methyl groups attached to a saturated carbon, a broad singlet at $\delta 1.90$ arising from the methyl attached to an olefinic carbon, and a complex 5-proton olefinic region extending from $\delta 5.80$ to 6.50. The two allylic methylene protons appeared as a broad singlet at $\delta 2.25$. On the basis of the allylic proton pattern, the product was assigned structure $\text{33}$, since in compound $\text{34}$, the allylic protons would have appeared as a doublet. Further proof for the correctness of the structural assignment was obtained from the nmr spectrum of the DMAD adduct $\text{35}$, shown in
Figure 11

Acetone - d6

CCl₄
Other attempts were made to obtain [6+4] cycloadducts from fulvene but these were unsuccessful. When one equivalent of 6,6-diphenyfulvene and one equivalent of 1-diethyl-aminobutadiene were maintained at room temperature, no reaction occurred. The reaction mixture was slowly heated up until the temperature reached 155°C; however nmr spectra taken at different temperatures indicated that no reaction had occurred. At 155°C, the nmr spectrum still indicated the presence of both starting materials. After work up, only 6,6-diphenyfulvene was recovered. This reaction did not work presumably because of the large steric bulk of the two phenyl substituents on the terminus of the exocyclic double bond. The reaction of 6,6-dimethylfulvene and 1-methoxy-1,3-butadiene at 125°C produced one or more [4+2] cycloadducts. In the nmr spectrum of the isolated product in deuterobenzene, the methyl peaks appeared at δ1.47 and δ1.51. This was indicative of methyl groups attached to a vinyl carbon. In the [6+4] cycloadducts formed from 6,6-dimethylfulvene and aminobutadienes, the methyl groups attached to a saturated carbon center absorbed at δ1.0.
When 6,6-dimethylfulvene was heated several days at 70°C in the presence of \(\text{36}\), prepared from the corresponding dienoic acid by Overman, et al., no product was formed and the diene remained essentially unchanged. An attempt was also made to react 1,4-bis-(dimethylamino)-1,3-butadiene with 6,6-dimethylfulvene; however, the reaction was much slower than expected and the results were inconclusive. It was hoped that this 1,4-diamino compound would react with 6-monosubstituted fulvenes to form a \([6+4]\) cycloadduct, which would undergo subsequent loss of two equivalents of diethylamine and form the azulene directly, thus avoiding the dehydrogenation step.

**Conclusions**

The studies discussed in this section established that the cycloaddition of dimethylfulvene and aminobutadiene was regioselective and occurred to give exclusively the \([6+4]\) adduct in which the most nucleophilic terminus of the aminobutadiene (C-4) became attached to the most electrophilic position of the fulvenes, the exocyclic C-6 position, as predicted by frontier molecular orbital treatment presented in the introduction. A second type of regioselectivity, namely regioselectivity with respect to secondary bond formation on the fulvene ring was also observed. In the reaction of ring substituted fulvenes, only one product was observed for each fulvene. In the case of 3,6,6-trimethylfulvene, the \([6+4]\) cycloadduct formed, based on frontier molecular orbital theory, (i.e., HOMO of the diene interacting with the LUMO of the fulvene) would be the one in which the largest coefficient of the fulvene
at C-6 would interact with the largest coefficient on the aminobutadiene at C-4, and the second largest coefficients at C-5 on the fulvene would interact with the C-1 terminus of the aminobutadiene. This was verified experimentally and is shown below.

The same reasoning should hold for 2,6,6-trimethylfulvene, where the largest coefficient, on the cyclopentadiene ring is at the carbon C-1, to which the methyl substituent is attached, should interact with the C-1 terminus of the aminobutadiene. Experimentally, this was not observed and the C-1 terminus of the diene added to the C-5 carbon of the fulvene (shown below).

One plausible explanation for the 2,6,6-trimethylfulvene case is that the steric interaction between the ring methyl of the fulvene and aminobutadiene is too great to allow formation of the predicted product shown above.
Cycloaddition of Dienamines to Monosubstituted Fulvenes: A New Synthesis of Azulenes

In the preceding section, the cycloaddition reaction between 6,6-dimethylfulvene and various aminobutadienes was found to give only [6+4] adducts. Since the products of these reactions were dihydroazulenes, it was of interest to determine whether this reaction could be used for the preparation of azulenes, by dehydrogenation of the dihydroazulene formed by the [6+4] cycloaddition reaction of 6-monosubstituted fulvenes.

Azulenes are non-benzoid aromatic compounds with the general structure. Azulenes have been reported to have a number of interesting properties including anti-inflammatory activity, useful anti-oxidant properties in cosmetics, and lubricant properties. Certain reduced and functionalized derivatives of azulene, particularly the guaianolide sesquiterpene lactones, have anti-tumor and hypnotic activity. Azulenes undergo substitution reactions with free radicals, electrophiles, and nucleophiles. Several azulenes, such as chamazulene (1,4-dimethyl-7-ethyl azulene) and guaiazulene (1,4-dimethyl-
7-isopropylazulene) (38) have been obtained from plants and essential oils. Other azulenes have been obtained from the degradation of naturally occurring sesquiterpenes.

Azulenes have been extensively reviewed by Heilbronner, Haagen-Smit, Gordon, Hafner, and Ito. Reiter, in his Ph.D. dissertation, has reviewed azulene synthesis from 1959 to 1977 and has prepared a number of new azulenes.

The methods used for the preparation of azulenes had used both direct routes in which the azulene was formed in a one step process and indirect routes that required dehydrogenation of the hydroazulene in the last step. The latter methods generally gave low yields because of the conditions required for dehydrogenation and the number of double bonds that had to be formed. However, Hafner reported the synthesis of 4-methylazulene from 4-methyl-4,5-dihydroazulene in a 67% yield using chloranil as the dehydrogenating agent.

The most versatile method for the preparation of azulenes has been the Ziegler-Hafner synthesis, which involves
thermal cyclization of an aminodienylfulvene (40):

\[
\begin{align*}
\text{[Diagram]} & \quad \Delta \\
\text{[Structure]} & \quad \text{[Structure]} \\
\end{align*}
\]

The fulvene is prepared by the hydrolysis of an alkylated pyridine or dihydropyran derivative to yield a Zincke aldehyde, 1\(\lambda\), which is condensed with sodium cyclopentadienide:

\[
\begin{align*}
\text{[Pyridine]} & \quad \rightarrow \\
\text{[Structure]} & \quad \text{[Structure]} \\
\end{align*}
\]

In the present study, 6-monosubstituted fulvenes are reacted with aminobutadienes to produce \(4\)-substituted dihydroazulenes, which are subsequently dehydrogenated to the corresponding \(4\)-substituted azulene, 2\(\lambda\). This reaction is essentially an

\[
\begin{align*}
\text{[Fulvene]} & \quad + \\
\text{[Butadiene]} & \quad \rightarrow \\
\text{[Azulene]} & \quad \text{[Azulene]} \\
\end{align*}
\]
intermolecular version of the Ziegler-Hafner synthesis. Other methods used to synthesize \( \beta \)-substituted azulenes are also known. The first method involves oxidation of tetralin followed by aldol condensation to give a bicyclo-[5,3,0] decan-2-one system, \( (43)^{52,53} \).

\[
\begin{array}{c}
\text{tetralin} \rightarrow \text{bicyclo-[5,3,0] decan-2-one system} \rightarrow \text{azulene}
\end{array}
\]

Compound \( ^{43} \) could also be prepared by ring closure of cyclopentane-1-carboxylic-2-\( \gamma \)-valeric acid

\[
\begin{array}{c}
\text{cyclopentane-1-carboxylic-2-\( \gamma \)-valeric acid} \rightarrow \text{azulene}
\end{array}
\]

Grignard addition to \( ^{43} \), followed by dehydration and dehydrogenation gives the corresponding \( \beta \)-substituted azulene:

\[
\begin{array}{c}
\text{azulene} \xrightarrow{RMgX} \text{azulene} \xrightarrow{-H_2O} \text{azulene} \xrightarrow{-3H_2} \text{azulene}
\end{array}
\]
A second method involves a modified Hafner procedure utilizing 2-substituted pyridines to synthesize the appropriately substituted aminodienylfulvene (similar to compound $\text{H}_1$) which thermally cyclized to the $\text{H}_1$-substituted azulene. Hafner$^{51}$ was also able to prepare $\text{H}_1$-substituted azulenes by reacting azulene with an organolithium compound, followed by dehydrogenation.

In azulene, $\text{H}_2$, there is a plane of symmetry which bisects the molecule and passes through C-2 and C-6. Thus, in unsubstituted azulene $\text{H}_1$ is equivalent to $\text{H}_3$, $\text{H}_4$ is equivalent to $\text{H}_9$, and $\text{H}_5$ is equivalent to $\text{H}_7$. This is reflected in the nmr spectrum shown below.$^{47}$ Protons $\text{H}_1$ and $\text{H}_3$ appear as a doublet centered at $\delta 7.39$ ($J = 4$ Hz); $\text{H}_2$ appears as a triplet centered at $\delta 7.92$ ($J = 4$ Hz); $\text{H}_4$ and $\text{H}_9$ are a doublet centered at $\delta 7.57$ ($J = 9.5$ Hz); $\text{H}_5$ and $\text{H}_7$ appear as a triplet centered at $\delta 7.11$ ($J = 10$ Hz), and $\text{H}_8$ is a triplet centered at $\delta 7.57$ ($J = 10$ Hz). However, it should be pointed out that these splitting patterns are somewhat more complex due to long range couplings. For example, in the
nmr spectrum of azulene, note that the H₄ and H₈ doublet is partially split again due to long range couplings. The chemical shifts and coupling constants for the azulenes described in this section are summarized in Table IV.

In the uv-visible spectrum of azulene, three absorptions are typically observed. These regions are shown in Table V along with
<table>
<thead>
<tr>
<th>AZULENE</th>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>R₄</th>
<th>R₅</th>
<th>R₆</th>
<th>R₇</th>
<th>R₈</th>
<th>J₁,₂</th>
<th>J₂,₃</th>
<th>J₃,₄</th>
<th>J₄,₅</th>
<th>J₅,₆</th>
<th>J₆,₇</th>
<th>J₇,₈</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent</td>
<td>H:7.39(d)</td>
<td>H:7.92(t)</td>
<td>H:7.39(d)</td>
<td>H:8.22(d)</td>
<td>H:7.11(t)</td>
<td>H:7.57(s)</td>
<td>H:7.11(t)</td>
<td>H:8.22(d)</td>
<td>4</td>
<td>4</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>1.5</td>
<td>10</td>
</tr>
<tr>
<td>4-Phenyl</td>
<td>---</td>
<td>H:7.68(t)</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>4</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>10</td>
</tr>
<tr>
<td>5-Ethyl-4-phenyl</td>
<td>---</td>
<td>H:7.53(t)</td>
<td>H:6.38(d)</td>
<td>---</td>
<td>1.05(t)</td>
<td>2.48(q)</td>
<td>---</td>
<td>---</td>
<td>H:8.12(d)</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>-</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>6-Methyl-6-phenyl</td>
<td>H:7.22(dd)</td>
<td>H:7.57(c)</td>
<td>H:6.88(dd)</td>
<td>---</td>
<td>H:6.94(a)</td>
<td>Me:2.60(s)</td>
<td>H:6.90(d)</td>
<td>H:8.10(d)</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9.5</td>
</tr>
<tr>
<td>7-Ethyl-4-phenyl</td>
<td>---</td>
<td>H:7.70(t)</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Et:1.35(t)</td>
<td>2.85(q)</td>
<td>H:8.25(d)</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4-Isopropyl</td>
<td>H:7.28(d)</td>
<td>H:7.72(t)</td>
<td>H:7.28(d)</td>
<td>Me:1.47(d)</td>
<td>H:3.98(h)</td>
<td>H:7.03(a)</td>
<td>H:7.50(t)</td>
<td>H:6.96(c)</td>
<td>4</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>4-Isopropyl-6-methyl</td>
<td>H:7.36(d)</td>
<td>H:7.59(t)</td>
<td>H:7.19(d)</td>
<td>Me:1.43(d)</td>
<td>H:3.94(h)</td>
<td>H:7.05(a)</td>
<td>Me:2.59(s)</td>
<td>H:6.82(d)</td>
<td>H:8.01(d)</td>
<td>4</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>10</td>
</tr>
<tr>
<td>7-Ethyl-4-Isopropyl</td>
<td>H:7.48(d)</td>
<td>H:7.65(t)</td>
<td>H:7.41(d)</td>
<td>Me:1.30(d)</td>
<td>H:3.85(h)</td>
<td>---</td>
<td>---</td>
<td>Et:1.20(t)</td>
<td>2.55(q)</td>
<td>H:8.15(d)</td>
<td>4</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>7-Ethyl-4-Methyl</td>
<td>---</td>
<td>H:7.67(t)</td>
<td>---</td>
<td>Me:2.82(s)</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Et:1.32(t)</td>
<td>2.79(q)</td>
<td>H:8.12(d)</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table IV

Chemical Shifts (ppm)

Coupling Constants (Hz)
the corresponding log $\varepsilon$ values.

**TABLE V**

<table>
<thead>
<tr>
<th>$\lambda$ (nm)</th>
<th>log $\varepsilon$</th>
</tr>
</thead>
<tbody>
<tr>
<td>580</td>
<td>2.50</td>
</tr>
<tr>
<td>400</td>
<td>3.60</td>
</tr>
<tr>
<td>270</td>
<td>4.65</td>
</tr>
<tr>
<td>240</td>
<td>4.35</td>
</tr>
</tbody>
</table>

Plattner\textsuperscript{55} has studied numerous examples of alkyl substituted azulenes and has developed an empirical method for predicting the expected wavelength shift due to alkyl substituents at any position on azulene. This is based on $\lambda_{\text{max}}$ observed in the first band in the visible region, which for azulene is at 580 nm. These substituent effects are shown in Table VI.

**TABLE VI**

<table>
<thead>
<tr>
<th>Substituent Position</th>
<th>Shift (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or 3</td>
<td>+ 28</td>
</tr>
<tr>
<td>2</td>
<td>- 14</td>
</tr>
<tr>
<td>4 or 8</td>
<td>- 12</td>
</tr>
<tr>
<td>5 or 7</td>
<td>+ 12</td>
</tr>
<tr>
<td>6</td>
<td>- 15</td>
</tr>
</tbody>
</table>

For example, 4-methylazulene has a $\lambda_{\text{max}}$ at 568 nm and Plattner's rules predict a value of 580 nm - 12 nm or 568 nm. The observed and calculated values of all azulenes obtained in the course of this work are given in Table VII.
<table>
<thead>
<tr>
<th>Compound</th>
<th>$\lambda_{\text{max}}$ (nm) of band 1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Observed</td>
</tr>
<tr>
<td>4-Phenylazulene</td>
<td>588</td>
</tr>
<tr>
<td>5-Ethyl-4-phenylazulene</td>
<td>592</td>
</tr>
<tr>
<td>6-Methyl-4-phenylazulene</td>
<td>570</td>
</tr>
<tr>
<td>7-Ethyl-4-phenylazulene</td>
<td>595</td>
</tr>
<tr>
<td>4-Isopropylazulene</td>
<td>568</td>
</tr>
<tr>
<td>4-Isopropyl-6-methylazulene</td>
<td>560</td>
</tr>
<tr>
<td>7-Ethyl-4-isopropylazulene</td>
<td>585</td>
</tr>
<tr>
<td>7-Ethyl-4-methylazulene</td>
<td>580</td>
</tr>
</tbody>
</table>
The success of Plattner's empirical method for predicting the observed \( \lambda_{\text{max}} \) in the visible spectrum of azulenes can be rationalized by considering the frontier molecular orbitals of azulene \(^{47}\) shown below.

Substitution of a methyl at C-4 or C-8 raises the energy of the LUMO more than that of the HOMO, since the increase in orbital energy is related to the size of the orbital coefficient at the site of substitution. This results in an increase in the HOMO-LUMO energy gap, and more energy for the transition to occur. Thus, the shift to shorter wavelength in the visible spectrum can be rationalized. A methyl substituent at the C-1 (or C-3) position will have little effect on the energy of the LUMO since the coefficients at these sites are small; however, the energy of the HOMO will be increased as a result of the large coefficient at the C-1 (or C-3) position; a decrease in the energy gap and a
shift to longer wavelength is observed.

In the following section, the preparation of various substituted azulenes by the [6+4] cycloaddition reaction of 6-phenyl-, 6-isopropylfulvene, and 6-methylfulvene to aminobutadienes will be discussed. In addition, this section will focus on the generality of this reaction, the regioselectivity observed in the cycloadditions, and the possible mechanism(s) of the [6+4] cycloaddition reaction.

The first azulene to be prepared by the [6+4] cycloaddition reaction was 4-phenylazulene. After two days at room temperature, the nmr spectrum of a 1:1 mixture of 6-phenylfulvene and 1-diethylaminobutadiene indicated that the 6-phenylfulvene was no longer present. In addition, tlc showed a new dark red spot (Rf = 0.5, cyclohexane). The reaction mixture was diluted with dichloromethane (~200 ml) and methyl iodide (1 equivalent) was added to quaternize any amines present. After stirring for 1 hr. at room temperature, the reaction mixture was extracted several times with 4% aqueous NaOH and the excess reagents were removed under reduced pressure. After chromatography, 4,5-dihydro-4-phenylazulene(44) was obtained in 62% yield.
In the 60 MHz nmr spectrum of 45, there was a complex pattern from δ 2.35 to 2.95 due to two allylic protons, another complex multiplet from δ 3.50 to 4.00 due to one benzylic proton, a vinyl region extending from 5.30 to 6.60 due to six vinyl protons, and a sharp singlet at 7.10 due to five phenyl protons. The dehydrogenation step was carried out by refluxing the dihydroazulene with one equivalent of chloranil in benzene for fifteen minutes. Tlc showed the appearance of a royal blue component (Rf = 0.5). The reaction mixture gave, after chromatography, 110 mg (11 %) 4-phenylazulene (45). The nmr spectrum is shown in Figure 12.

Pfau and Plattner52 first reported the synthesis of 4-phenylazulene in 1936. The ir spectrum of 45 obtained via the [6+4] cycloaddition route was identical to that reported in the literature by Bergmann and Ikan.56

To test the generality of this reaction as well as verify the direction of addition of 1-aminobutadiene, 4-ethyl, 3-methyl, and the 2-ethyl derivatives of 1-aminobutadiene were prepared and reacted with 6-phenyl-, 6-methyl-, and 6-isopropylfulvene.

The cycloaddition reaction of two equivalents 1-diethylamino-1,3-butadiene and one equivalent of 6-phenylfulvene was carried out at room temperature under nitrogen. After two days the solvent was removed under reduced pressure and the resultant dar-red oil was chromatographed to give the dihydroazulene 46 in a 43 % yield.
In the nmr spectrum of 46, there was a singlet at δ7.20 due to five phenyl protons and a complex vinyl region extending from δ5.70 to 6.65. The allylic hydrogens could not be readily identified because of trace amounts of impurity in the same region.

Several attempts were made to dehydrogenate with chloranil, but the results were not consistent. One difficulty, that was believed to occur, was addition of chloranil (a tetrachloroquinone) to the azulene. Eugster et al. have reported the electrophilic substitution of azulenes by methoxycarbonyl-1,4-benzoquinones.

Compound 46 was dehydrogenated by refluxing for one hour in triglyme (triethylene glycol dimethyl ether, bp 220°C) in the presence of sulfur. After the residue was chromatographed, the crude azulene was further purified by sublimation. The 5-ethyl-4-phenylazulene was obtained in 1% yield as a bright blue solid. The H₈ proton was easy to
Figure 13
identify in the nmr spectrum, since it appeared at a lower field than any other proton in azulene. This proton appeared as a doublet at $\delta 8.12$ ($J = 9 \text{ Hz}$). If the [6+4] cycloaddition reaction had occurred with the opposite regioselectivity, the resonance due to H$_3$ would not have been observed in the nmr spectrum, since this proton would have been replaced by an ethyl group. H$_3$ was shifted from its normal position at $\delta 7.39$ in azulene to a higher field at $6.38$ ($J = 4 \text{ Hz}$). This large shift was thought to arise from shielding by the phenyl ring, oriented in such a way that H$_3$ was in its shielding zone. The nmr spectrum is shown in Figure 13.

The reaction of 6-phenylfulvene and 3-methyl-1-diethylaminobutadiene was used to prepare 6-methyl-4-phenylazulene. One equivalent of the aminobutadiene was reacted with one equivalent of 6-phenylfulvene without solvent to give 48 in a 21% yield. The nmr spectrum of 48 exhibited a broad singlet at $\delta 1.80$ due to the methyl protons, a complex pattern extending from $\delta 2.40$ to 2.95 due to benzylic and allylic hydrogens, a complex vinyl region from $\delta 5.50$ to 6.70, and a sharp singlet at 7.20 due to five aromatic protons.

Dehydrogenation was carried out with sulfur by refluxing in triglyme for one hour. After work up, 6-methyl-4-phenylazulene 48 was obtained in a 28% yield. The trinitrobenzene (TNB) adduct was prepared by refluxing equivalent amounts of the azulene and TNB in absolute ethanol ethanol to give dark purple needles. The TNB adduct was recrystallized from absolute ethanol and gave a satisfactory elemental analysis. The azulene was recovered by chromatography and the nmr spectrum is shown in Figure 14.
For the preparation of 7-ethyl-4-phenylazulene, one equivalent of 6-phenylfulvene was reacted with one equivalent 2-ethyl-1-pyrrolidinobutadiene in benzene under a nitrogen atmosphere at room temperature for 12 hours. The reaction was worked up to give the dihydroazulene (47) in a 47% yield. Compound 47 was dehydrogenated by refluxing in triglyme (1 hour) in the presence of an equimolar amount of sulfur to give 7-ethyl-4-phenylazulene (50) in low yield. The nmr spectrum is
Figure 15

60 MHz
in Figure 15.

Analogous 4-isopropylazulenes were prepared from 6-isopropylfulvene and 1-aminobutadienes. Although 4-isopropylazulene was not found in the literature, 1-isopropyl-, 5-isopropyl-, and 6-isopropylazulenes were known.\textsuperscript{46c} The parent compound (51) was prepared by reacting a 2:1 mixture of 1-diethylaminobutadiene and 6-isopropylfulvene at room temperature for two days. After dehydrogenation of the dihydroazulene, 4-isopropylazulene was obtained in 23% yield. This blue oil was converted to the TNB adduct, which was recrystallized several times to give dark purple needles. The TNB adduct gave a satisfactory elemental analysis. The azulene was recovered by chromatography and the nmr spectrum is shown in Figure 16.
The reaction of 6-isopropylfulvene and 3-methyl-1-aminobutadiene (1:1) at room temperature for two days without solvent, followed by the usual work up gave 52, which was converted directly to the azulene by dehydrogenation with sulfur. The resulting 4-isopropyl-6-methylazulene was purified by preparation of the TNB adduct and the azulene (53) was recovered by chromatography. The nmr spectrum is shown in Figure 16.

The 4,5-dihydro-7-ethyl-4-isopropylazulene (54) was prepared by reacting 2-ethyl-1-pyrrolidinobutadiene with 6-isopropylfulvene at room temperature without solvent for 24 hours. The reaction was worked up in the usual way to give 54 in a 34% yield. This dihydroazulene was converted to the corresponding azulene 55 in a 17% yield, by refluxing in triglyme in the presence of sulfur. The dark blue 7-ethyl-4-isopropylazulene (55) was converted to the TNB adduct, which gave a satisfactory elemental analysis, and the azulene was recovered by chromatography. The spectroscopic data were determined on the azulene and the nmr
The 4,5-dihydro-7-ethyl-4-methylazulene (56) was synthesized by reacting 6-methylfulvene with 2-ethyl-1-pyrrolidinobutadiene at room temperature under nitrogen for 24 hours. The 6-methylfulvene\(^5\) was prepared from 6-dimethylaminofulvene\(^6\) and methyl lithium and used without further purification. The dihydroazulene 56 was obtained in a 52% yield. Dehydrogenation with 10% Pd on carbon provided 7-ethyl-4-methylazulene (57) in a 17% yield.
The NMR spectrum is shown in Figure 18.

**Conclusions**

Azulenes can be prepared by the \([6+4]\) cycloaddition reaction of fulvenes and aminobutadienes. In 6-mono-substituted fulvenes, the diene adds in such a way that the C-1 terminus to which the amine is attached adds to the C-2 carbon of the fulvene and the C-4 terminus of the diene adds to the C-6 carbon of the fulvene:

![Diagram showing the cycloaddition reaction of fulvene and aminobutadiene](image)

The regiochemical results found here for trimethylfulvenes indicate that neither the 2-alkyl- nor 3-alkyl-6-substituted fulvenes with a single 6-substituent will give rise to 1-alkyl substituted azulenes. Instead, they would give 3,4- and 2,4-disubstituted azulenes respectively. This fact is important in the synthesis of azulenes isolated from natural sources, such as chamazulene or guaiatzulene, which have the 1,4,7-trisubstitution pattern. The 1-methyl substituent must be added after the 4,7-disubstituted azulene has been prepared. Dr. Mukherjee, working in our laboratory, has been able to convert 7-ethyl-4-methylazulene (described in the last section) into chamazulene by introducing...
a methyl group at the C-1 position. This procedure involved reacting 7-ethyl-4-methylazulene with the Vilsmeier reagent to introduce a CHO unit, chromatographic separation of the two isomers, and Wolff-Kishner reduction of the aldehyde:

\[
(CH_3)_2NCHO + POCl_3 \rightarrow (CH_3)_2N=CHCl \quad Cl_2PO_2
\]

The [6+4] cycloaddition reaction described in this work has been used to prepare 4,5-, 4,6-, and 4,7-disubstituted azulenes, where the C-4 substituent is predetermined by the 6-mono-substituted fulvene used. Preparation of a 4,8-disubstituted
azulene by this method is theoretically possible, but unlikely because the aminobutadiene precursor is not likely to exist in the cisoid conformation, shown below.

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{R} & \quad \text{NR}_2 \\
\end{align*}
\]

However, this presents no problem since nucleophiles such as organolithium compounds are known to add to the C-4 and C-8 positions of azulene; thus, 4,8-disubstituted azulenes can be readily obtained from 4-substituted azulenes. Azulenes without a 4-substituent are possible but are not easily obtained due to the difficulty in preparing unsubstituted fulvene.

**Mechanism(s)**

Cycloaddition reactions usually occur by one of three mechanisms. The cycloadduct can be formed in a one step or concerted process in which both new bonds are partially formed in the transition state, or in a non-concerted process consisting of two or more steps. The non-concerted pathways proceed via zwitterionic or diradical intermediates. These three mechanistic possibilities are shown below for the aminobutadiene-fulvene cycloaddition.

If the cycloaddition were to occur by the zwitterionic
mechanism, the rate of the reaction should be very sensitive to the polarity of the solvent used for the reaction. For example, Gompper studied the effect of solvent on the rates of the following cycloadditions:

1. $\text{p-CH}_3\text{OC}_6\text{H}_4\text{-CH=CH}_2 + \text{TCNE}$
   
   $$k_1/k_2 = 6.3 \times 10^4$$

2. \( \text{NR}_2 + \text{CS}_2 \rightarrow \text{NR}_2 \text{CS}_2 \)
   
   $$k_1/k_2 \approx 10^3$$

3. \( \text{NR}_2 + \text{PhN}_3 \rightarrow \text{NR}_2 \text{PhNPh} \)
   
   $$k_1/k_2 \leq 10$$

4. \( \text{NR}_2 + \text{NPh} \rightarrow \text{NPh} \text{NR}_2 \)
   
   $$k_1/k_2 \leq 10$$

\( k_1 \text{ in CH}_3\text{CH}_2 \quad k_2 \text{ in cyclohexane} \)

Table VIII
For reactions 1 and 2, large rate enhancements were observed
in going from cyclohexane to acetonitrile ($k_{rel} \geq 10^3$). This
was indicative of a zwitterionic intermediate, in which the charge
developing in the transition state was stabilized by the more
polar solvent, acetonitrile. Reactions 3 and 4 had small rate
enhancements and were relatively insensitive to a change in solvent
polarity. Thus, these two reactions proceeded by a concerted
cycloaddition. It must be pointed out that only large rate
enhancements should be used to distinguish between concerted
reactions and reactions which proceed through a zwitterionic inter-
mediate.

In order to gain some insight into the mechanism of the
fulvene-aminobutadiene reaction, the effect of solvent on the rate
of cycloaddition was determined in two solvents of widely different
polarities, benzene and acetonitrile. The rates were measured
by nmr spectroscopy. One difficulty encountered was the instability
of the aminobutadiene, which rapidly decomposed in $CCl_4$, $CDCl_3$,
$CD_3OD$ and slowly decomposed in $CD_3CN$. In the last two solvents
cited, the decomposition of the diene is believed to be due to
acid catalyzed polymerization. Thus, the rate of decomposition
of the aminobutadiene, as well as the rate of the cycloaddition
reaction had to be determined in both benzene and acetonitrile.

The integrated form of the second order rate constant is
$k = \frac{1}{A_0 t^{1/2}}$, when the initial concentration of the two reactants,
$A_0$ is equal. The half life of the reaction is $t^{1/2}$. In the pre-
sent study, two equivalents of aminobutadiene were used because
the diene was found to slowly decompose during the course of
the reaction. Since this equation cannot be used directly
because of diene decomposition, half lives of the reaction in
benzene and acetonitrile were compared. Under these conditions,
the half-lives can be used to compare, approximately, the
relative rates in different solvents. The reactant concentrations
were assumed to be proportional to peak heights in the nmr
spectrum; thus, $t_{1/2}$ was a measure of the time required for the
peak height to decrease to half of the initial height.

In the experiment using benzene as solvent, one equivalent of 6,6-
dimethylfulvene was added to two equivalents of diethylaminobuta-
diene in 0.5 ml benzene. In a parallel experiment, the same amount
of diethylaminobutadiene was added to a nmr tube containing
only benzene (0.5 ml). The aminobutadiene in benzene did not
decompose noticeably during the course of this experiment. In
the other nmr tube, the half life of the cycloaddition reaction
was determined by following the disappearance of the methyl peak
of the fulvene at δ1.90. By measuring this peak height at
various times, $t_{1/2}$ was found to be $1.52 \times 10^5$ sec.

Identical experiments were conducted in acetonitrile. The
half life for the decomposition of aminobutadiene was determined
by measuring the change in peak height at δ5.33 in the olefinic
region of the nmr spectrum. The half life for this decomposition
was $7.7 \times 10^4$ sec. The half life for the cycloaddition reaction
was determined in the same way as the reaction in benzene
(following the fulvene methyl signal) and was found to be
Note that the half life for aminobutadiene decomposition was approximately equal to the half life for the cycloaddition reaction. If one considered the extreme case in which half of the diene was reacting with the fulvene and half of it was decomposing, then the effective concentration of diene in acetonitrile would be about half that in benzene. If it is assumed, in order to estimate an upper limit to the rate difference, that the concentration of aminobutadiene was 2 to 5 times less in acetonitrile than benzene, then equal half-lives would indicate an approximate rate 2 - 5 fold greater in acetonitrile than in benzene. The ratio of half-lives is actually,

\[
\frac{t_{1/2}^{CD_3CN}}{t_{1/2}^{C_6D_6}} = \frac{1.5 \times 10^5 \text{ sec}}{0.8 \times 10^5 \text{ sec}} = 1.9,
\]

that the range of relative reaction rates, \(k_{CD_3CN}/k_{C_6D_6}\), is crudely estimated to be \(4 - 10\). Although there is some acceleration by the more polar solvent, acetonitrile, the possibility of the reaction proceeding through a zwitterionic intermediate is low, since the example described earlier indicated a much larger dependence on solvent polarity.

The other possible non-concerted process would involve formation of a diradical intermediate which subsequently undergoes cyclization to form the \([6+4]\) adduct. Luskus\(^{10}\) has shown that simple dienes, such as cyclopentadiene and \(\alpha\)-pyrone, react with fulvenes to form \([4+2]\) cycloadducts. In a preliminary study carried out here, the reaction of 1-methoxybutadiene and 6,6-dimethylfulvene
indicated the formation of only [4+2] cycloadduct. If these reactions proceed via diradical intermediates to yield [4+2] cycloadducts, then it is difficult to explain why the reaction of aminobutadienes and fulvenes would not also give [4+2] cycloadducts if diradical intermediates were involved. By looking at the heats of reaction for the formation of ethyl, methoxymethyl, and aminomethyl radicals shown below, it was hoped that some insight into the relative stabilities of diradical intermediates such as,

\[ X = \text{CH}_3, \text{CH}_3\text{O}, \text{NH}_2 \]

might be gained.

\[
\begin{array}{ccc}
\text{Reagent} & \rightarrow & \text{Products} \\
\text{CH}_3-\text{CH}_3 & & \text{CH}_3\text{CH}_2^{\cdot} + \text{H}^{\cdot} & 98.7 \\
\text{CH}_3-\text{OCH}_3 & & \text{CH}_3\text{O}-\text{CH}_2^{\cdot} + \text{H}^{\cdot} & 94.0 \\
\text{NH}_2-\text{CH}_3 & & \text{NH}_2-\text{CH}_2^{\cdot} + \text{H}^{\cdot} & 91.0 \\
\end{array}
\]

However, the trend is what one would expect. That is, the ease of formation of these radicals increases as the electron donor ability, which parallels the radical stabilizing ability of the substituent, increases. Although the diradical mechanism does not seem likely to occur, it cannot be unequivocally ruled out as a mechanism for this cycloaddition.
In the concerted process, both new bonds are partially formed in the transition state. In the case of unsymmetrical dienes such as 1-aminobutadiene, in which the C-1 and C-4 coefficients are of unequal size, reacting with fulvene, where the C-6 and C-1 coefficients are also different in size, an unsymmetrical transition state is expected. The bond resulting from overlap of the two largest coefficients, C-6 in fulvene and C-4 in aminobutadiene, would be expected to form slightly faster than the bond formed by overlap of the C-1 orbital of the fulvene and the C-4 terminus of the aminobutadiene. This is shown below.

The conclusion reached is that the aminobutadiene-fulvene reaction does not proceed via a zwitterionic process as indicated by the insensitivity to solvent polarity but may involve a diradical intermediate, although the evidence does not support this mechanism. The most likely mechanism seems to be a concerted process in which one of the bonds is formed slightly faster than the other.
CHAPTER III

EXPERIMENTAL

Part A. Introduction

All the reactions described in this section were done using reagent grade chemicals and solvents which were commercially available.

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

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

The Ultraviolet and Visible spectra were recorded on a Cary-14 Spectrophotometer.

The 60 MHz nmr spectra were recorded on a Varian A-60A Spectrometer and the 100 MHz nmr spectra were recorded on a Varian HA-100 Spectrometer. All nmr spectra were run in CCl$_4$ (unless stated otherwise), and tetramethylsilane (TMS) was used as an internal reference. The chemical shift values are reported in ppm and coupling constants are reported in Hz. The splitting patterns are designated s for singlet, d for doublet, t for triplet, q for quartet, h for heptet, and m for multiplet.

Part B. Starting Materials

1. Preparation of Fulvenes. The fulvenes used in this study of [6+4] cycloaddition reactions were described and referenced in a recent review.\textsuperscript{2}
Base Catalyzed Condensation of Cyclopentadiene With Aldehydes and Ketones

This method\(^{1a}\) was used to prepare 6,6-dimethylfulvene, 6-phenylfulvene, 6-isopropylfulvene, 2,6,6-trimethylfulvene, and 3,6,6-trimethylfulvene.

A. Preparation of 6,6-Dimethylfulvene\(^{1a}\)

To 80g (1.4 mol) of acetone and 66g (1.0 mol) of freshly distilled cyclopentadiene was added dropwise, with stirring, 100 ml of methanol, containing 27.5g KOH. The reaction mixture was cooled in an ice bath during the addition, allowed to warm up to room temperature, and stirred overnight at room temperature. The methanol was removed under reduced pressure and the resultant red oil was taken up in methylene chloride. The organic phase was washed twice with water and once with saturated sodium chloride solution. The methylene chloride was removed under reduced pressure, and the resulting oil was vacuum distilled at 25°C (0.35 mm). The product (55.7g, 53%) had sharp singlets at 62.00 and 6.30 in the nmr spectrum due to methyl protons and olefinic protons, respectively.

B. Preparation of 6-Phenylfulvene

This compound was prepared according to the procedure reported in Luskus's dissertation.\(^{64}\) Starting with 99.0g (1.50 mol) of freshly distilled cyclopentadiene and 106g (1.00 mol) benzaldehyde the reaction was carried out the same way as 6,6-dimethylfulvene. After the reaction was complete, the excess reagents were removed in vacuo, and the pH was adjusted between 6 and 7 with 6M HCl.
The red oil was taken up in methylene chloride, washed twice with water, and once with aqueous sodium chloride. The solvent was removed under reduced pressure, and the resulting red oil was carefully vacuum distilled. The pot temperature was maintained below 115°C (using an oil bath), and the product distilled at a head temperature of 60-70°C. The product (27% yield) solidified and clogged the condenser if the temperature of the condenser was not kept above room temperature (mp 27-29°C). The nmr spectrum showed two complex multiplet centered at 66.30 and 7.30, in the ratio of 1:1.

C. Preparation of 6-Isopropylfulvene

This compound was prepared in the same way as 6,6-dimethylfulvene. Distillation at 42°C (0.15 mm Hg) gave the yellow product a 30% yield. In the nmr spectrum of this compound, there was a doublet at 81.0 (J = 7 Hz) due to six methyl protons, a broad singlet at 85.40 due to the exocyclic vinyl proton, and a complex multiplet from 85.75 to 6.50 due to the vinylic ring protons. A complex pattern, due to the tertiary proton appeared at 83.00.

D. Preparation of 6-Methylfulvene

To 9g (75 mmol) 6-dimethylaminofulvene in 200 ml absolute diethyl ether was added 95 ml (76 mmol) of a 0.8 M methyllithium solution in ether at 0°C. All of the amine dissolved during the course of the addition. After the exothermic reaction was complete, the reaction mixture was stirred at room temperature for one hour and extracted with ice water. The ether layer was dried over anhydrous potassium carbonate at 0°C. This entire
experimental procedure must be carried out in the absence of air, or else, the fulvene formed will rapidly decompose. The ether was carefully removed at -30°C (12 torr) and the resultant orange oil was chromatographed on neutral alumina (Activity II) using petroleum ether (30-60°C) and diethyl ether in a ratio of 2:1. The fast moving yellow 6-methylfulvene was eluted first and the solvent was removed at -30°C with a water aspirator. The 6-methylfulvene was used without further purification.

Preparation of 2,6,6- and 3,6,6-Trimethylfulvenes (24 and 25)

To 65g (0.75 mol) of freshly distilled methylcyclopentadiene in ~500 ml methanol was added 43g (0.74 mol) of acetone. A solution containing 20g KOH in 100 ml of methanol was added dropwise with stirring. After addition was complete, the reaction mixture was stirred overnight at room temperature. The methanol was removed under reduced pressure by distilling through a short Vigreux column, and the yellow product distilled at 68-69°C and 1.7 mm Hg in a 47% yield. The product was a mixture of the two isomers, in a ratio of 3:1 (3,6,6-trimethylfulvene: 2,6,6-trimethylfulvene). These isomers were separated by gas chromatography on a 12 foot column using Carbowax 20-M Chrom-W adsorbent.

Preparation of α,β-Unsaturated Aldehydes

Preparation of 3-Methylcrotonaldehyde

The 3-methyl derivative of crotonaldehyde was prepared from 3-methylcrotonic acid in the following way. To 150g (1.50 mol) of 3-methylcrotonic acid in 3l of benzene, 692g (2.40 mol)
of Red-Al (70% solution of bis(2-methoxyethoxy) aluminum hydride in benzene) diluted with an equal volume of benzene was added. The reaction mixture was stirred with a mechanical stirrer, cooled in an ice bath, and maintained under a nitrogen atmosphere. During the addition of Red-Al, a white gelatinous precipitate formed which resisted stirring. After the addition of Red-Al was complete, the reaction mixture was heated to reflux for 30 min. and became a clear golden yellow solution. The reaction was stirred overnight and the aluminum complexes were hydrolyzed with 500 ml of a saturated solution of ammonium chloride. The solution was filtered to remove the aluminum salts, the precipitate was washed with 1L diethyl ether, and the solvent was removed in vacuo. The allylic alcohol was used without further purification.

The aldehyde was obtained by oxidizing the allylic alcohol with pyridinium chlorochromate using a procedure developed by Corey. 66

The alcohol obtained above was added dropwise with stirring to a chilled solution of dichloromethane containing 4.13g (1.90 mol) pyridinium chlorochromate and 29.5g (0.360 mol) anhydrous sodium acetate (as a buffer). After the addition was complete, the reaction mixture was stirred overnight at room temperature, the dark brown solution was filtered, and the solvent was removed under reduced pressure. The reaction mixture was filtered through a 1L, pear-shaped separatory funnel filled with Florsil (60-200 mesh), and the product was eluted with chloroform.
After distilling off the chloroform, the dark green solution remaining was distilled to yield 95g (75%) of 3-methylcrotonaldehyde.

\[
\text{Nmr(CCl}_4\text{): } \delta 1.90 (s, 3H); \delta 2.10 (s, 3H); \delta 5.80 (d, 8 Hz, 1H); \delta 7.80 (d, 8 Hz, 1H)
\]

**Preparation of 2-Ethylcrotonaldehyde**

To freshly prepared lithium diisopropylamide\(^{68}\) (0.204 mol) at 0°C in tetrahydrofuran, 31.3g (0.204 mol) butylidencyclohexylamine (prepared by reacting 1 equivalent of butyraldehyde and 1 equivalent cyclohexylamine at 0°C) was added. The reaction mixture was cooled to -78°C using a dry ice-acetone bath. After 30 min., 9.00g (0.204 mol) acetaldehyde was added dropwise with stirring. The reaction mixture was kept at -78°C for an additional hour, then allowed to warm up to room temperature and stirred overnight. The reaction mixture was cooled down to 0°C with ice and hydrolyzed with 100 ml H\(_2\)O. Methylene chloride was added, the two phases were separated, and the aqueous phase was extracted three times with methylene chloride. The organic phases were combined and washed once with saturated sodium bicarbonate solution and once with saturated aqueous sodium chloride solution. The solvent was removed \textit{in vacuo} and the resulting oil was hydrolyzed to the aldehyde by stirring in the presence of 5% H\(_2\)SO\(_4\). The product was distilled at 130-131°C to yield 9.6g (0.098 mol; 48%) of 2-ethylcrotonaldehyde.
Nmr (CCl₄): δ 0.85 (t, 7 Hz, 3H); δ 1.95 (d, 7.5 Hz, 3H); δ 2.20 (q, 7 Hz, 2H)
δ 6.45 (q, 7.5 Hz, 1H); δ 9.20 (s, 1H)

This compound can also be obtained from Chemical Samples Company, Columbus, Ohio.

Preparation of Dienamines

Dienamines were prepared by one of the following methods:

1. Addition of potassium (sodium) carbonate as a catalyst.
2. Addition of potassium (sodium) carbonate as a catalyst combined with azeotropic removal of water with benzene.

Preparation of 1-Diethylaminobutadiene

This dienamine was prepared according to the method of Hünig and Kahanek.³¹ To 100 ml of a benzene solution containing 140g (2.00 mol) crotonaldehyde and 34g (0.24 mol) K₂CO₃, cooled to 0°C with dry ice-acetone bath under a nitrogen atmosphere, 211g (2.90 mol) diethylamine were added dropwise with stirring. The temperature was maintained below - 5°C during the addition of the amine. The reaction mixture was allowed to warm up to room temperature and stirred overnight. The excess reagents were removed under reduced pressure, and the dark red oil was vacuum distilled after addition of 1g of phenanthrenequinone.

Distillation at 27°C (0.5 mm) afforded 100g (40%) of a pale yellow liquid.

Nmr (CCl₄): δ 1.00 (t, 7 Hz, 6H); δ 2.90 (q, J = 7 Hz, 4H);
Vinyl Protons δ 4.15 to δ 5.20 and δ 5.70 to δ 6.50 (m, 4H)
Preparation of 1-Diethylamino-1,3-hexadiene

This compound was prepared in the same way as described above. Starting with 25.0g (0.255 mol) trans-2-hexenal, 16.2g (41.5%) 1 diethylamino-1,3-hexadiene were obtained, bp 47-49°C (0.2 mm).

Nmr (CCl₄): δ 1.01 (t, J = 7.5 Hz, 3H); δ 1.05 (t, J = 7.0 Hz, 6H); δ 2.00 (m, 2H);
δ 2.98 (q, J = 7.0 Hz, 2H); δ 3.00 (q, J = 7.0 Hz, 2H); Vinyl Protons δ 4.50 to δ 6.20 (m, 4H)

Preparation of 1-Diethylamino-3-methyl-1,3-butadiene (19)

To 12.2g (0.149 mol) 3-methylcrotonaldehyde and 15.0g (0.141 mol) Na₂CO₃ in benzene was added 25.6g (0.35 mol) diethylamine. The reaction mixture was refluxed for 2-3 hours, and the water formed was azeotroped into a Dean Stark trap. At the end of this time, the excess reagents were removed under reduced pressure, 0.5g of phenanthrenequinone was added, and the product was distilled at 33-34°C (0.25mm) to give 6.0g (30%) of 3-methyl-1-diethylaminobutadiene.

Nmr (CCl₄): δ 1.00 (t, J = 7.5 Hz, 3H); δ 2.70 (d, J = 1 Hz, 3H); δ 3.00 (q, J = 7.5 Hz, 4H);
δ 4.35 (m, 2H); δ 5.00 (d, J = 14 Hz, 1H);
δ 6.05 (d, J = 14 Hz, 1H)

Preparation of 2-Ethyl-1-Pyrrolidinobutadiene (20)

To 10.0g (0.102 mol) 2-ethyl-2-butenal in toluene was added 20.0g (0.281 mol) pyrrolidine and 14.0g (0.102 mol) anhydrous
potassium carbonate. The reaction mixture was equipped with a Dean Stark trap, kept under an atmosphere of nitrogen, and refluxed for 24 hours. At the end of this time, the solvent was removed under reduced pressure, and 0.5g phenanthrenequinone was added. The pale yellow liquid distilled at 2mm Hg and 65-70°C to give a 65% yield of 2-ethyl-1-pyrroolidinobutadiene. The product consisted of both cis and trans isomers in a ratio of 3:1.

Nmr (C₆D₆): δ 1.15 (t, J = 8 Hz, 3H); δ 1.50 (m, 4H);
δ 2.40 (q, J = 8 Hz, 2H); δ 3.00 (m, 4H);
δ 4.55 (d, J = 2Hz, 1H); δ 4.70 (d, J = 2 Hz, 1H);
δ 5.00 (d, J = 2 Hz, 1H) δ 5.95 (s, 1H);
δ 6.10 (d, J = 11 Hz, 1H); δ 6.40 (d, J = 11 Hz, 1H) δ 6.75 (d, J = 11 Hz, 1H); 7.05 (d, J = 11 Hz, 1H).

Reaction of 6,6-Dimethylfulvene and 1-Diethylaminobutadiene (20)

To 42.0g (0.396 mol) of 6,6-dimethylfulvene was added 16.5g (0.132 mol) 1-diethylaminobutadiene. After 2 days at room temperature, the excess 6,6-dimethylfulvene was removed in vacuo, and the reaction mixture was diluted with dichloromethane. Methyl iodide was added to facilitate removal of amines, and the reaction mixture was stirred at room temperature. After 1 hour, the dichloromethane was removed under reduced pressure and the reaction mixture was chromatographed on silica gel (cyclohexane) to give 13.5g (65% yield) of a dark-red oil. This oil was further
purified by short path distillation, with the major fraction distilling at 36-37° C (0.5 mm).

Nmr: \( \text{(CDCl}_3 \\delta \) 1.10 (s, 6 H); \( \delta \) 2.25 (d, \( J = 5 \) Hz, 2H); 5.80 to 6.50 (m, 6H)

Uv: \( \lambda_{\text{max}} \) (hexanes): 428 nm (log \( \varepsilon = 3.20 \)); 317 nm (log \( \varepsilon = 4.10 \))

**Reaction of \( 4,4\)-dimethyl-\( 4,5\)-dihydroazulene with DMAD \((\text{E})\)**

To 2.0 g (0.013 mol) of the dihydroazulene in ~ 5 ml CCl\(_4\), 3.7 g (0.026 mol) DMAD was added. After refluxing overnight and removal of the solvent under reduced pressure, the reaction mixture was chromatographed on silica gel (CHCl\(_3\)) to give 2.34 g (79% yield) of a white crystalline solid, mp 62-63° C, which could be further purified by recrystallization from petroleum ether (30-60° C).

Anal. Calc. for C\(_{16}\)H\(_{20}\)O\(_4\): C, 71.98; H, 6.71

Found: C, 72.06; H, 6.85

Nmr: \( \text{(CDCl}_3 \))

Uv: \( \lambda_{\text{max}} \) (hexanes): 320 nm (log \( \varepsilon = 2.95 \)); 257 nm (log \( \varepsilon = 4.07 \))
Reaction of 3,6,6-Trimethylfulvene with 1-Diethylaminobutadiene (28)

To 2.60g (0.0216 mol) 3,6,6-trimethylfulvene, 5.40g (0.0432 mol) 1-diethylaminobutadiene was added in the absence of solvent. After stirring under nitrogen overnight, an additional 5.40g (4.32 x 10^{-2} mol) 1-diethylaminobutadiene was added to the reaction mixture. This procedure was repeated for three additional days. After the last day, the reaction mixture was diluted with ~200 ml dichloromethane, and 27.0g (0.193 mol) CH₃I was added to quaternize any amines present and facilitate their removal in the work-up procedure. After stirring at room temperature for one hour, the dichloromethane solution was extracted with three 200 ml portions of 4% NaOH and washed once with aqueous sodium chloride solution. The solvent was removed under reduced pressure and the resultant dark brown oil chromatographed (silica gel: pet ether, 30-60°C) to give 1.48g (40%) of 2,4,4-trimethyl-4,5-dihydroazulene. This oil was used without further purification.

Reaction of 2,4,4-Trimethyl-4,5-dihydroazulene with DMAD (29)

To 1.00g (5.81 x 10^{-3} mol) of the dihydroazulene prepared above in ~5 ml CCl₄, 0.82g (5.8 x 10^{-3} mol) DMAD was added and the reaction mixture refluxed overnight. After preparative tlc chromatography, 0.61g of a white crystalline compound, mp 79.5 - 80.5°C was obtained in a 33% yield.

Anal. Calc. for C₁₉H₂₃O₄:  C, 72.59; H, 7.05
Found:  C, 72.77; H, 7.23

Nmr: Spectrum No. 2
Uv: \( \lambda_{\text{max}} \) (hexanes) 255 nm \((\log c = 3.99)\), 314 nm \((\log c = 2.93)\)

Ir: CH stretch 3.37\(\mu\); CH bend, 6.97\(\mu\); gem dimethyl, 7.87 \(\mu\); CH\(_3\)-O, 8.37\(\mu\); Unsat. Ester, 5.88\(\mu\).

**Reaction of 2,6,6-Trimethylfulvene with 1-Diethylaminobutadiene**

To 3.0g \((2.5 \times 10^{-2} \text{ mol})\) 2,6,6-trimethylfulvene, 9.4g \((7.5 \times 10^{-2} \text{ mol})\) 1-diethylaminobutadiene was added and the reaction mixture was stirred at room temperature under nitrogen for one week. An additional 3.2g \((2.6 \times 10^{-2} \text{ mol})\) of 1-diethylaminobutadiene was added, and the reaction mixture was stirred for two more days. The reaction mixture was diluted with \(\sim\) 200 ml dichloromethane and 14.5g \((0.102 \text{ mol})\) CH\(_3\)I was added. After stirring at room temperature for one hour and extracting four times with 200 ml 4\% NaOH, the dichloromethane was removed under reduced pressure. Addition of petroleum ether \((30-60^\circ\text{C})\) precipitated out the ammonium salts, which were removed by filtration. The petroleum ether was removed under reduced pressure and the resultant brown oil was chromatographed (silica petroleum ether, \(30-60^\circ\text{C}\)) to give 0.364g (% mol) of the 3,4,4-trimethyl-4,5-dihydroazulene. This compound was dissolved in CCl\(_4\), 0.30g \((2.1 \times 10^{-3} \text{ mol})\) DMAD was added and the mixture was refluxed overnight to give 60 mg \((9.1\% \text{ yield})\) of the DMAD adduct.

Nmr: Number 3

Uv: \( \lambda_{\text{max}} \) (hexanes) 260 nm \((\log c = 3.82)\), 312 nm \((\log c = 2.76)\)
Reaction of 6,6-Dimethylfulvene and 1-Diethylamino-3-methylbutadiene (33)

To 5.2g (0.037 mol) 1-diethylamino-3-methylbutadiene, 10g (0.094 mol) 6,6-dimethylfulvene was added with stirring under nitrogen. After 24 hours, the reaction mixture was diluted with ~200 ml dichloromethane, and 6.0g (0.042 mol) CH₃I was added. The reaction mixture was stirred at room temperature for one hour and extracted three times with 200ml of 4% NaOH. The solvent was removed in vacuo and the resultant dark brown oil was chromatographed on silica gel (petroleum ether, 30-60°C) to give 2.7g (43%) of 4,4,6-trimethyl-4,5-dihydroazulene (43% yield) as a red oil.

Nmr (CCl₄): δ 1.10 (s, 6H); δ 1.90 (s, 3H); δ 2.25 (s, 1H); δ 5.80 to δ 6.50 (m, 5H)

Reaction of 4,4,6-Trimethyl-4,5-dihydroazulene with DMAD (35)

To 10ml CCl₄, 2.7g (0.016 mol) of 4,5-dihydro-4,6,6-trimethylazulene and 2.50g (0.0176 mol) DMAD were added. The reaction mixture was refluxed for one hour, the solvent was removed under reduced pressure, and the light brown oil was chromatographed on preparative tlc plates (CHCl₃) to give 2.1g (42%) of the DMAD adduct. Several attempts were made to crystallize this compound but were unsuccessful.

Nmr: Spectrum No. 4

Hydrolysis of the Diester

To 1.0g (3.2 x 10⁻³ mol) of the DMAD adduct, in a mixed
methanol-water solvent (in a ratio of 1:1), 10 ml of a 20% KOH solution was added. After refluxing for 2 hours, the reaction mixture was diluted with ~50 ml water, extracted with three 50 ml portions of diethyl ether to remove any ester present and the aqueous phase was carefully acidified at 0°C with 6M HCl to precipitate out the diacid derivative. The aqueous phase was extracted with diethyl ether and the ether was removed under reduced pressure to give 0.3g (33% mol) of the diacid, mp 190-192°C.

Nmr: Spectrum No. 4

**Preparation of 4-Phenylazulene (4g)**

To 3.6g (0.029 mol) 1-diethylaminobutadiene, 4.6g (0.029 mol) 6-phenylfulvene was added in the absence of solvent. The next day, 4.1g (0.029 mol) CH$_3$I was added to the reaction mixture in ~200 ml dichloromethane, and the reaction mixture was stirred at room temperature for one hour. The reaction mixture was extracted several times with 4% NaOH and chromatographed (silica gel, petroleum ether) to yield 3.7g (62%) of the corresponding dihydroazulene. Dehydrogenation was carried out by reacting 1.0g ($4.5 \times 10^{-3}$ mol) of the dihydroazulene with 1.1g chloranil in xylene and refluxing for fifteen minutes. The xylene was removed under reduced pressure to give, after column chromatography (silica gel: petroleum ether, 30-60°C) 0.11g (12% mol) of 4-phenylazulene starting from the dihydroazulene.

Nmr: Spectrum No. 5
Preparation of 5-Ethyl-4-Phenylazulene

To 3.1g (0.020 mol) 6-phenylfulvene in CCl₄, 6.0g (0.039 mol) 1-diethylamino-1,3-hexadiene was added. The reaction mixture was stirred at room temperature for two days under nitrogen. The reaction mixture was diluted with ~ 200 ml dichloromethane, and 5.6g (0.039 mol) CH₃I was added. After stirring at room temperature for one hour and extracting with 4% NaOH, the solvent was removed under reduced pressure and the resulting dark brown oil was chromatographed on silica gel (petroleum ether, 30-60°C) to give 2.0g (8.6 x 10⁻³ mol) of the 4,5-dihydro-5-ethyl-4-phenylazulene (43% yield).

The dihydroazulene was dissolved in ~ 5 ml of triglyme (triethylene glycol dimethyl ether), and 0.26g (8.0 x 10⁻³ mol) sulfur was added. After refluxing for one hour, a noticeable smell of H₂S developed. The reaction mixture was allowed to cool to room temperature and was diluted with ~ 50 ml of water. The water layer was repeatedly extracted with petroleum ether (30-60°C) until the ether layer remained clear and colorless. The petroleum ether was removed in vacuo and the reaction mixture chromatographed (silica gel: pet ether, 30-60°C) twice to give 5-ethyl-4-phenylazulene in poor yield (< 5%), which was subsequently sublimed to give bright blue crystals, mp 74-75°C.

Anal. Calc. for C₁₈H₁₆: C, 93.06; H, 6.94

Found: C, 93.01; H, 7.36
Nmr (CCl₄): δ 1.05 (t, J = 8 Hz, 3H); δ 2.48 (q, J = 8 Hz, 2H); δ 6.38 (d, J = 4 Hz, 1H);
δ 7.53 (t, J = 4 Hz, 1H); δ 8.12 (d, J = 9 Hz, 1H). Spectrum No. 8

Uv: λₘₐₓ (hexanes) 592 nm (log ε = 2.75); 346 nm (log ε = 3.72); 282 nm (log ε = 4.67).

Preparation of 6-Methyl-1-Phenylazulene (48)

To 3.4g (0.024 mol) 3-methyl-1-diethylaminobutadiene, 3.7g (0.024 mol) 6-phenylfulvene in ~ 5 ml CCl₄ was added. The reaction mixture was stirred overnight under a nitrogen atmosphere and was then diluted with ~ 200 ml dichloromethane. To this solution 3.5g (0.024 mol) CH₃I was added and the mixture was stirred at room temperature for one hour. At the end of this time, the solution was extracted 3-4 times with 4% NaOH, the solvent was removed in vacuo, and the resultant dark brown oil chromatographed on silica gel (petroleum ether, 30-60°C) to give 1.1g (21%) of the dark red oil, 4,5-dihydro-6-methyl-1-phenylazulene.

To the dihydroazulene in ~ 10 ml of benzene, 1.2g (5 x 10⁻⁵ mol) chloranil was added and the suspension was stirred at room temperature for several days. The reaction mixture was filtered to remove the insoluble material and the solvent removed under reduced pressure to give 0.3g of the dark purple oil, 6-methyl-1-phenylazulene.
Nmr: Number 7

$\lambda_{\text{max}}$ (hexanes), 570 nm ($\log \varepsilon = 2.61$); 350 nm ($\log \varepsilon = 3.56$); 288 nm ($\log \varepsilon = 4.58$)

This azulene was converted to the trinitrobenzene (TNB) complex by refluxing 0.101 g ($4.60 \times 10^{-4}$ mol) of the azulene with 0.987 g ($4.60 \times 10^{-4}$ mol) TNB in a small quantity of absolute ethanol ($\sim 5$ ml). After cooling off, the TNB adduct crystallized out of solution as dark purple needles, mp 114-115°C, in a 50% yield.

Anal. Calc. for $C_{23}H_{17}N_3O_6$: C, 64.03; H, 3.97; N, 9.74
Found: C, 63.99; H, 3.89; N, 9.75

Preparation of 7-Ethyl-4-Phenylazulene (50)

To 2.40 g (0.0156 mol) 6-phenylfulvene in a small quantity of benzene ($\sim 3$ ml), 2.40 g (0.0156 mol) 2-ethyl-1-pyrrolidinobutadiene was added. The reaction mixture was allowed to stir at room temperature under nitrogen for approximately 12 hours. At the end of this time, 2.30 g (0.0162 mol) methyl iodide was added to the reaction mixture, diluted in 200 ml dichloromethane. After stirring one hour at room temperature, the reaction mixture was extracted with three 200 ml portions of 4% NaOH, the solvent was removed under reduced pressure, and the reaction mixture was chromatographed on silica gel (cyclohexane) to give the 4,5-dihydro-7-ethyl-4-phenylazulene in a 46% yield. Dehydrogenation was effected by refluxing 1.70 g ($7.2 \times 10^{-3}$ mol) of the dihydroazulene and 0.23 g ($7.2 \times 10^{-3}$ mol) sulfur in 5 ml triglyme for one hour. This procedure gave 7-ethyl-4-phenylazulene in low
yield (< 4%). This compound was purified by column chromatography (petroleum ether, 30-60°C) and on tlc prep plates (cyclohexane).

\[ \text{Nmr (CCl}_4\): } \delta 1.15 \text{ (t, } J = 7.5 \text{ Hz, } 3\text{H); } \delta 2.85 \text{ (q, } J = 7.5 \text{ Hz, } 2\text{H); } \delta 6.90 - \delta 7.80 \text{ (m, } 11\text{H); } \delta 8.20 \text{ (d, } J = 1 \text{ Hz, } 1\text{H)} \]

Spectrum No. 8

\[ \text{Uv: } \lambda_{\text{max}} \text{ (hexanes): } 595 \text{ nm (log } e = 2.46); 350 \text{ nm (log } e = 3.51) \]

290 nm (log e = 5.43); 280 nm (log e = 5.43).

**Preparation of 4-Isopropylazulene (51)**

The initial cycloadduct was prepared by reacting 4.0 g (0.033 mol) 6-isopropylfulvene with 8.4 g (0.066 mol) 1-diethylaminobutadiene. After 24 hours, an additional 4.0 g (0.033 mol) of 1-diethylaminobutadiene was added. After two more days, the reaction mixture was diluted with ~200 ml dichloromethane, and 14 g (0.099 mol) methyl iodide was added. After stirring at room temperature for one hour, the reaction mixture was extracted with three 200 ml portions of 4% NaOH, the solvent removed under reduced pressure, and the resulting oil chromatographed on silica gel (petroleum ether, 30-60°C) to give 1.3 g (23%) of 4,5-dihydro-4-isopropylazulene.

The corresponding azulene was obtained by taking the dihydroazulene prepared above in ~5 ml triglyme and adding 0.24 g (7.6 x 10^-3 mol) sulfur. After refluxing for one hour and chromatographing on silica gel (cyclohexane), the 4-isopropylazulene was obtained as a purple oil in a 23% yield.

This was converted to the TNB adduct by adding 0.30 g
(1.8 x 10^{-3} \text{ mol}) of the azulene to 0.38g (1.8 x 10^{-3} \text{ mol})
trinitrobenzene in \sim 5 \text{ ml absolute ethanol and refluxing until all the TNB was dissolved. The solution was allowed to cool to room temperature and the precipitate was collected by gravity filtration. The elemental analysis was performed on the TNB adduct, and the azulene was recovered by dissolving the TNB adduct in benzene and eluting it through a silica gel column. The spectroscopic data were determined on the azulene.

Anal. Calc. for C_{19}H_{17}N_{3}O_{6}: C, 59.23; H, 4.47; N, 10.96

Found: C, 59.36; H, 4.57; N, 10.81

Nmr: Number 9

Uv: \lambda_{\text{max}} (hexanes) 277\text{ nm} (\log \epsilon = 4.62); 342 \text{ nm}

(\log \epsilon = 3.64); 568 \text{ nm} (\log \epsilon = 2.57).

**Preparation of 4-Isopropyl-6-Methylazulene (53)**

The reaction was carried out by reacting 13.9g (0.0998 \text{ mol})
of 1-diethylamino-3-methylbutadiene with 5.00g (0.0416 \text{ mol})
6-isopropylfulvene without solvent, under nitrogen for two days.

At the end of this time, the reaction mixture was diluted with
\sim 200 \text{ ml dichloromethane, 14.2g (0.100 \text{ mol}) methyl iodide was added, and the mixture was stirred at room temperature for one hour. The dichloromethane was then removed in vacuo and petroleum ether (30-60^{\circ}\text{C}) was added, resulting in the precipitation of insoluble ammonium salts which were removed by filtration. The solvent was again removed in vacuo and the resultant dark brown oil chromatographed on silica gel (petroleum ether, 30-60^{\circ}\text{C}) to give
1.6 g (21% yield) of 4,5-dihydro-4-isopropyl-6-methylazulene as a dark red oil.

The dihydroazulene was dissolved in triglyme (~5 ml) and 0.37 g (0.012 mol) sulfur added. After refluxing the solution for hour, 50 ml of water were added, and the water layer repeatedly extracted with petroleum ether (30-60°C) until the ether layer remained clear and colorless. The extracts were combined, the solvent removed under reduced pressure, and the resultant oil was chromatographed twice on silica gel (petroleum ether, 30-60°C). The blue oil that was obtained was converted to the TNB complex by refluxing the azulene and TNB (1:1) together in absolute ethanol, to give purple needles, mp 155.5-156.6°C.

Anal. Calc. for C_{20}H_{19}N_{3}O_{6}: C, 60.45; H, 4.82; N, 10.58
Found: C, 60.27; H, 4.92; N, 10.54.

The azulene was recovered by chromatographing the TNB adduct on silica gel (benzene).

Nmr: Number 9

Uv: \( \lambda_{\text{max}} \) (hexanes), 282 nm (log \( \varepsilon = 4.63 \)); 348 (log \( \varepsilon = 3.67 \))
560 nm (log \( \varepsilon = 2.57 \)).

Preparation of 7-ethyl-4-isopropylazulene (55)

To 5.0 g (0.033 mol) freshly prepared 2-ethyl-1-pyrrolidino-butadiene was added 3.5 g (0.029 mol) 6-isopropylfulvene. The reaction was stirred overnight at room temperature under nitrogen.
After 24 hours, 4.7 g (0.033 mol) methyl iodide was added to the reaction mixture, dissolved in 200 ml dichloromethane. After stirring one hour at room temperature, the solution was extracted three times with 4% NaOH and the solvent removed under reduced pressure. The resultant red oil was chromatographed to give 4,5-dihydro-7-ethyl-4-isopropylazulene in a 34% yield. The dihydroazulene was converted to the corresponding azulene by refluxing 2.0 g (0.010 mol) of this compound and 0.32 g (0.010 mol) sulfur in triglyme (~5 ml) for one hour. After column chromatography, 300 mg (15% yield) of 7-ethyl-4-isopropylazulene were obtained. The azulene was converted to the TNB adduct by refluxing 0.071 g (3.8 x 10^{-4} mol) of the azulene and 0.80 g (3.8 x 10^{-4} mol) TNB in ethanol to give 0.140 g of the TNB adduct as purple needles, mp 103-104°C.

Anal. Calc. for TNB adduct, C_{21}H_{19}N_{3}O_{6}: C, 61.31; H, 5.15

N, 10.21

Found: C, 61.00; H, 5.22; N, 9.95

This adduct was recrystallized from ethanol and chromatographed on silica gel (benzene) to recover the azulene.

Nmr (benzene): Number 10

Uv: \lambda_{\text{max}} (hexanes) 282 nm (log \epsilon = 4.63); 348 nm (log \epsilon = 3.67); 560 nm (log \epsilon = 2.57)
Preparation of 7-Ethyl-4-methylazulene

The 6-methylfulvene was prepared from 15.0g (0.124 mol) 6-dimethylaminofulvene and was used without further purification. The yields were based on the amount of diene used. To the 6-methylfulvene, 12.3g (0.0813 mol) 2-ethyl-1-pyrrolidinobutadiene was added. The reaction mixture was stirred overnight, under a nitrogen atmosphere at room temperature. The reaction was diluted with 200 ml diethyl ether and 12.0g (0.0847 mol) CH_3I was added. After stirring for one hour and extracting 3-4 times with 4% NaOH, the solvent was removed in vacuo and the resulting oil chromatographed (silica gel, petroleum ether, 30-60°C) to give 7.0g (52% yield) of the 4,5-dihydro-7-ethyl-4-methylazulene.

Nmr: Number 11

The dihydroazulene was dehydrogenated by refluxing 1.1g (6.4 x 10^{-3} mol) of the dihydroazulene for fifteen minutes in triglyme in the presence of 1.1g 5% Pd on carbon. After column chromatography (silica gel, petroleum ether, 30-60°C), 0.18g (17% yield) of 7-ethyl-4-methylazulene was obtained as a purple oil.

Nmr: Number 18

\[ \lambda_{\text{max}} \text{(hexanes)} = \begin{align*} 580nm \quad (\log \epsilon = 2.54), \quad 340nm \quad (\log \epsilon = 3.6), \quad 285nm \quad (\log \epsilon = 4.55). \end{align*} \]
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VITA

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Major Field: Organic Chemistry

Title of Thesis: The \([6+4]\) Cycloaddition Reactions of Fulvenes and Aminobutadienes

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