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AN INTRAMOLECULAR [8+6] CYCLOADDITION

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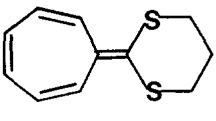
Abstract: An intramolecular [8+6] cycloaddition of a heptafulvene linked to a fulvene by a trimethylene chain has been observed.

Interest in the discovery of cycloadditions involving more than 6π electrons has been sustained for the twenty years since the creation of the Woodward-Hoffmann selection rules for concerted cycloadditions.[2] An [8+2] cycloaddition of heptafulvene was discovered by Doering and Wiley in 1960,[3] and many other examples of [8+2] cycloadditions involving substituted heptafulvenes have been found.[4] A variety of [6+4] cycloadditions have been discovered.[5] Prinzbach has reported several [12+2] cycloadditions.[6] A $[_{\pi}14_a + _{\pi}2_s]$ *cycloaddition involving heptafulvene and TCNE was discovered by Doering,*[7] *and has become* rather legendary in this field. Since suprafacial cycloadditions involving (4n+2)π electrons can occur in a concerted fashion, and because we had experience with both intramolecular heptafulvene (8π)[4] and fulvene (6π)[8] cycloadditions, we undertook a search for an [8+6] cycloaddition. An intramolecular 14π electron [8+6] cycloaddition reaction is reported here.

Since dimethylfulvene undergoes concerted cycoadditions to electron-rich dienes exclusively as a 6π addend, we first attempted an intermolecular [8+6] cycloaddition of dimethylfulvene to the electron-rich 8,8-dithioheptafulvene, **1**.[9] Heating a 1:1 mixture of these in refluxing xylene failed to give any [8+6] adduct, but gave only polymerization of the addends.



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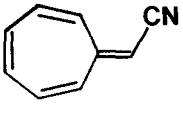

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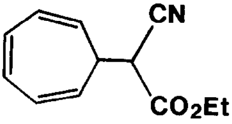
Similarly, no reaction was observed with this heptafulvene and the electron-rich 6-(dimethylamino)fulvene. The attempted reaction of 8-cyanoheptafulvene, **2**, with *dimethylfulvene or 6-(dimethylamino)-fulvene in refluxing xylene yielded complex reaction* mixtures and decomposition. No products of these reactions have been identified. Since intermolecular [8+6] cycloadditions failed, a fulvene connected to a heptafulvene was synthesized, in order to attempt an intramolecular cycloaddition.

The heptafulvene-fulvene, **8**, was prepared from the intermediates shown below.



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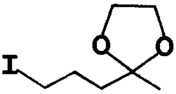

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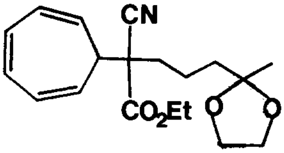

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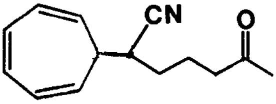

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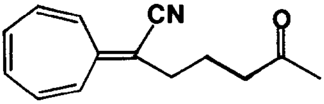

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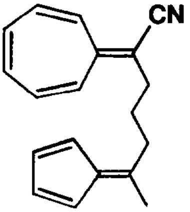
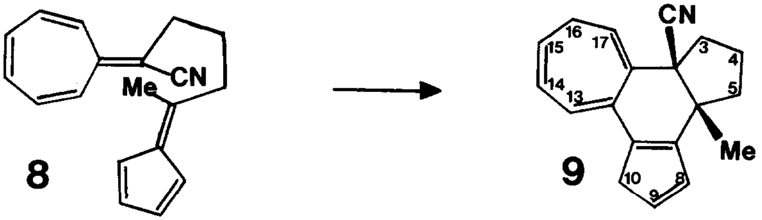


8

Cycloheptatriene **5** was obtained in 78% yield by treating ethyl tropylcyanoacetate, **3**, with sodium ethoxide and 5-iodo-2-pentanone ethylene ketal, **4**,[10] in dry ethanol. Hydrolysis and decarboxylation of **5** gave **6** in 46% yield after column chromatography. Thermal isomerization of **6**, followed by treatment with trityl fluoroborate and triethylamine[11] gave heptafulvene, **7** in 31% yield, which was converted to **8**[12] in 81% yield by reaction with cyclopentadiene and methylamine in dry methanol.[13]

Thermolysis of **8** in toluene at 185°C for 2 h in a sealed tube in the presence of BHT gave **9** in 48% yield, along with 32% yield of a mixture of compounds. The major product, **9**, proved to be the result of an intramolecular [8+6] cycloaddition, followed by 1,5-sigmatropic shifts in both the cycloheptatriene and cyclopentadiene moieties.



The structure of **9** was confirmed by analysis of the 300 MHz ^{1}H NMR spectrum. A sharp singlet at δ 1.32 is assigned to the methyl group. A six-proton signal at δ 1.75-2.29 is assigned to H-3-H-5. The doublet at δ 6.59 ($J_{13,14}$ = 5.5 Hz) is assigned to H-13. On irradiation at δ 6.17, the multiplet at δ 5.57 collapsed to a triplet ($J_{15,16}$ = 7 Hz) and the doublet at δ 6.59 ($J_{13,14}$ = 5.5 Hz) collapsed to a sharp singlet. Therefore, one-proton signals at δ 6.17 and δ 5.57 are assigned to H-14 and H-15, respectively. On irradiation at δ 5.57 (H-15), the multiplet at δ 6.17 (H-14) collapsed to a doublet ($J_{13,14}$ = 5.5 Hz), the multiplet at δ 2.82 collapsed to a doublet of doublets (J_{gem} = 13 Hz, $J_{16a,17}$ = 8 Hz), and the multiplet at δ 2.0 is simplified. On irradiation at δ 2.82, the multiplet at δ 5.57 (H-15) collapses to a doublet of doublets ($J_{14,15}$ = 9 Hz, $J_{15,16b}$ = 7 Hz), the doublet of doublets at δ 5.97 is collapsed to a doublet ($J_{16b,17}$ = 6 Hz), and the multiplet at δ 2.0 is simplified. Therefore, the multiplet at δ 2.82 ($J_{16a,17}$ = 7 Hz), the multiplet at δ 2.0, and the doublet of doublets at δ 5.97 ($J_{16a,17}$ = 8 Hz, $J_{16a,17}$ = 6 Hz) are assigned to H-16a, H-16b and H-17 respectively. The doublets at δ 3.11 (J_{gem} = 22 Hz, $J_{9,10}$ = 1 Hz) and δ 3.35 (J_{gem} = 22 Hz, $J_{9,10}$ = 1 Hz) are assigned to H-10. The doublet of triplets at δ 6.48 ($J_{8,9}$ = 5.5 Hz, $J_{8,10}$ = 1 Hz) and δ 6.41 ($J_{8,9}$ = 5.5 Hz, $J_{9,10}$ = 1 Hz) are assigned to H-8 and H-9, respectively.

The cis stereochemistry of **9** was inferred from the relatively low-field position of the quaternary methyl resonance, which indicates that the methyl group resides in the deshielding zone of the vicinal group.[14]

Four double bond isomers have structures which are compatible with nmr spectral data given above. A series of NOE experiments at 600 MHz led to the assignment of regiochemistry. Upon irradiation of the methyl singlet at δ 1.32, a large positive enhancement at δ 6.48 (H-8) and a small positive enhancement at δ 5.97 (H-17) were observed. No enhancement was observed at δ 3.11 (H-10), 3.35 (H-10) or for the rest of the cycloheptatriene ring system. These results are consistent with the regiochemistry of the cyclopentadiene and cycloheptatriene units shown in structure **9**. This was supported by the positive enhancement at δ 2.19 (H-5) and δ 1.32 (methyl), upon irradiation at δ 6.48 (H-8). A small positive enhancement at δ 5.97 (H-17) was also observed, which seems surprising in light of the larger distance between H-8 and H-17. Upon irradiation at δ 6.59 (H-13), only positive enhancement at δ 3.11 (H-10) and δ 3.35 (H-10) was observed. Irradiation at δ 5.97 (H-17) produces a negative enhancement at both δ 6.48 (H-8) and δ 1.32 (methyl), confirming the results stated above. However, no enhancement was observed between δ 1.75-2.29 (H-3-H-5). This suggests the presence of a cis-fused ring junction, in which the cyano group, methyl group, H-17 and H-8 are all above the six-membered ring, while the saturated five-membered ring is down. On the basis of these data, structure **9** is proposed for the major adduct. The minor product of the thermolysis appears, from NMR coupling patterns and mass spectral data, to be a mixture of intramolecular [8+6] cycloaddition products in which the positions of the five- and seven-membered ring methylenes differ.

Prinzbach[15] has made a similar benzenoid dihydrocyclopept[e]indene via thermal 14π-electron electrocyclization of sesquifulvalene. Both regioisomers arising from [1,5]-sigmatropic hydrogen shifts in the five-membered ring were observed and were shown to be non-interconvertible.

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