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Stereoselectivity, Periselectivity and Regioselectivity in the Intramolecular Cycloadditions of Heptafulvene-Fulvenes ※

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Abstract: The side-chain and substituent control of stereoselectivity, periselectivity and regioselectivity in the intramolecular [8 + 6] and [4 + 2] cycloadditions of electron-deficient 8-cyanoheptafulvenes connected at C-8 by trimethylene or tetramethylene chains to C-6 of electron-rich 6-methyl- or 6-phenylfulvenes are discussed.

INTRODUCTION

The competition among thermally allowed [4 + 2], [6 + 4], [8 + 2], and [8 + 6] cycloaddition reactions has prompted much investigation. Houk *et al.* have reported the periselective formation of *syn*-[8 + 6] adduct **2**, in the intramolecular cycloaddition of 8-cyanoheptafulvene connected at C-8 by a trimethylene chain to C-6 of 6-methylfulvene, eq 1.[1] We recently reported that the intermolecular cycloadditions of 8,8-dicyanoheptafulvene (**3a:** $R^1 = R^2 = CN$) and 8,8-bis(methoxycarbonyl)heptafulvene (**3b:** $R^1 = R^2 = CO_2Me$) with 6,6-dimethylfulvene (**4a:** $R^3 = R^4 = Me$) and 6,6-diphenylfulvene (**4b:** $R^3 = R^4 = Ph$) give *anti*-endocyclic [8 + 2], *anti*- and/or *syn*-endocyclic [4 + 2], and/or *anti*-[6 + 4] adducts, eq 2.[2] We had also found that the exocyclic substituent effects exerts a significant controlling influence upon the stereoselectivity, periselectivity and regioselectivity of these cycloadditions, eq 2.[3,4] No [8 + 6] adduct was obtained. The differing behaviors of these cycloadditions seem to indicate that the side-chain conformational effects have a controlling influence upon the periselectivity and regioselectivity of these cycloaddition reactions.

In this paper, we report the intramolecular cycloadditions of heptafulvene-fulvenes **1**, **7**, and **16** (Schemes 1 and 3) and the analogous intermolecular cycloadditions of 8-cyano-8-methylheptafulvene (**3c**) with 6,6-dimethylfulvene (**4a**)[4] and 6-methyl-6-phenylfulvene (**4c**) (Scheme 4). The side-chain and substituent control of stereoselectivity, periselectivity and regioselectivity in these intramolecular cycloadditions are discussed.

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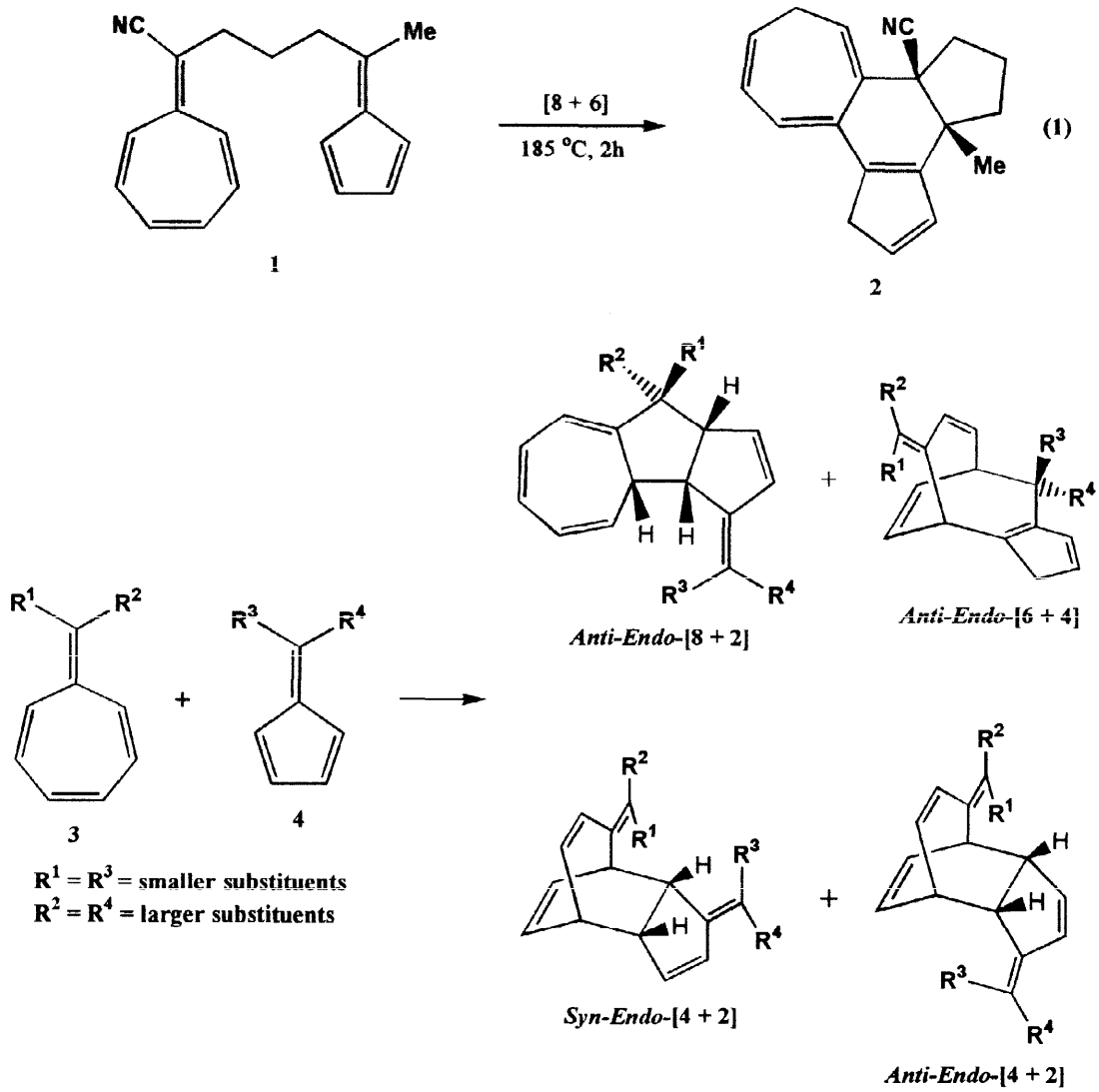
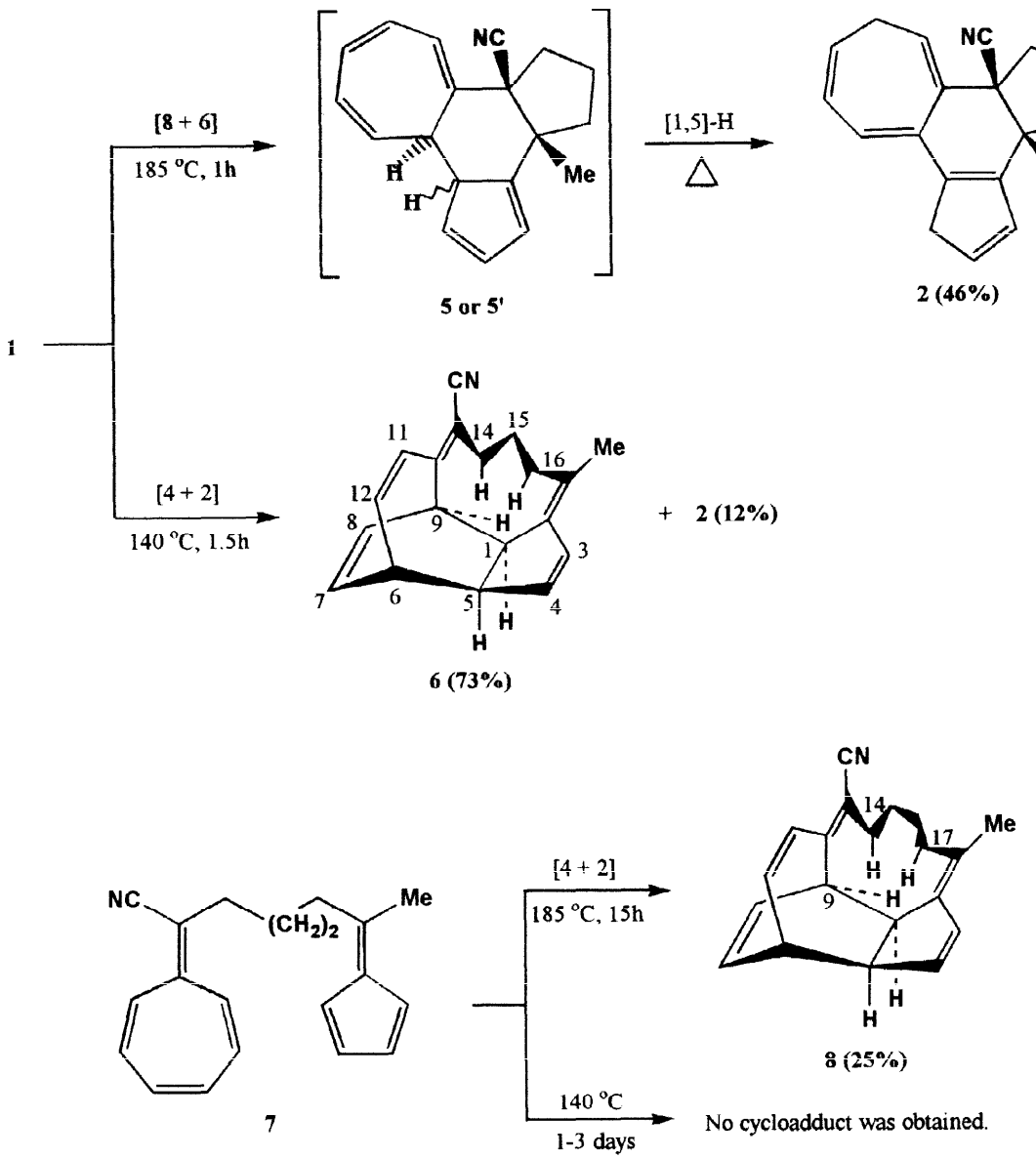


RESULTS

Sealed-tube thermolysis of a solution of **1** in xylene at 185 °C for 1 hour in the presence of BHT (butylated hydroxytoluene) gave **2** in 46% yield (Scheme 1). Adduct **2** proved to be the result of an intramolecular [8 + 6] cycloaddition to form **5** (or **5'**, see Figure 2 and discussion below), followed by 1,5-sigamatropic hydrogen shifts in both the cycloheptatriene and cyclopentadiene moieties.[1]

When the reaction was carried out in refluxing xylene for 1.5 hours, **6** and **2** were formed in 73% and 12% yield, respectively (Scheme 1). The major adduct, **6**, proved to be the result of an intramolecular [4 + 2] cycloaddition. The IR spectrum of adduct **6** showed a characteristic α,β-unsaturated cyano absorption at about 2215 cm^{-1}. Its structure was assigned on the basis of a careful analysis of its NMR spectrum, double-resonance experiments, and comparison of its spectrum with those of related compounds.[2-4] The ^1H NMR spectrum showed a sharp singlet at δ 1.74 for the methyl group on the unsaturated carbon, a broad multiplet for H-15 at δ 1.60-1.85, a broad multiplet for H-16 at δ 1.92-2.26, a broad multiplet for H-14 at δ 2.28-2.68,

Scheme 1

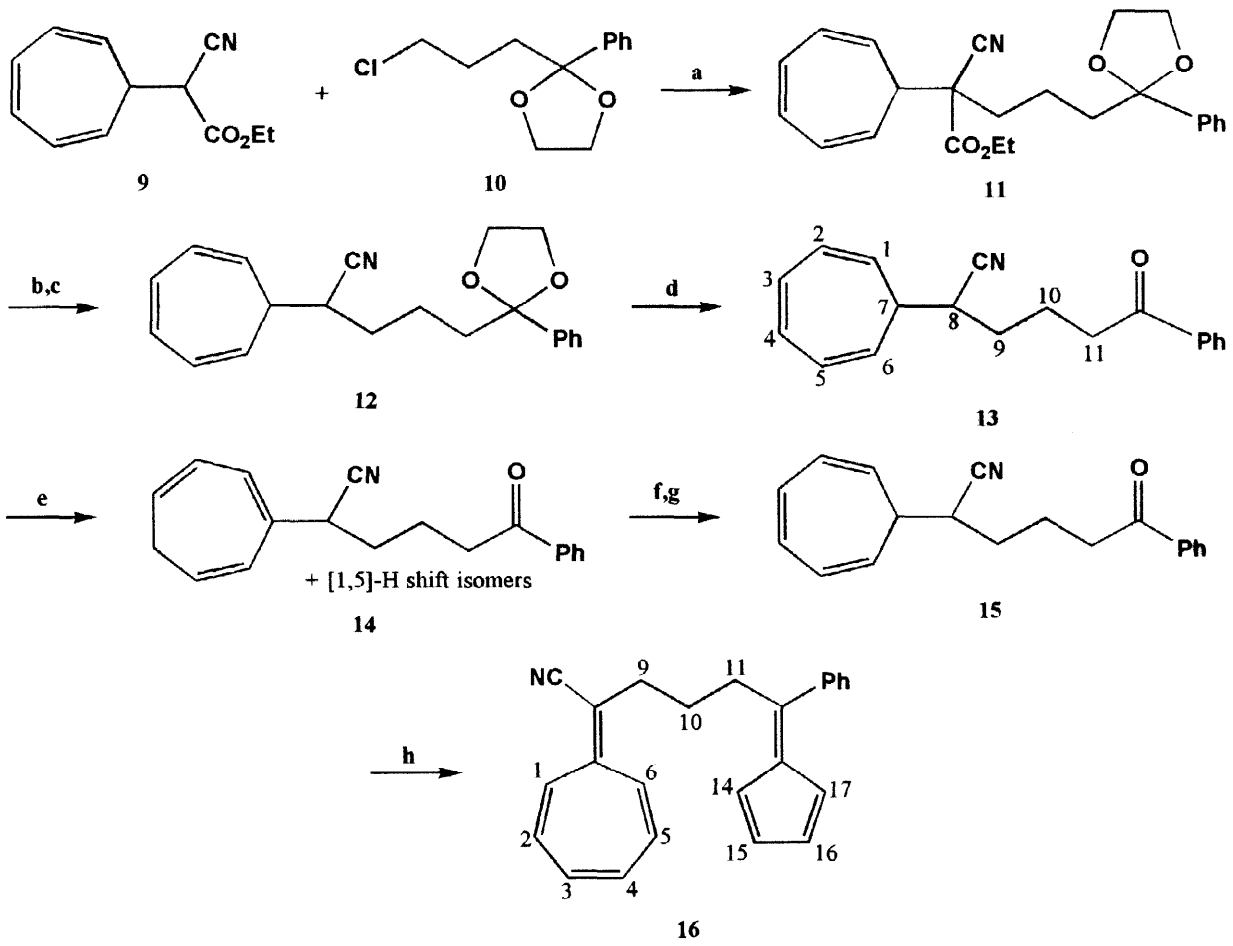


a broad multiplet for H-1 and H-6 at δ 3.20-3.39, a broad multiplet for H-5 at δ 3.53, and a broad triplet for H-9 at δ 4.05 ($J_{1,9}$ = $J_{8,9}$ = 7.4 Hz). The appropriate six olefinic resonances for H-3-4, H-7-8, and H-11-12 were also observed. The large coupling constant of 7.4 Hz between H-1 and H-9 is compatible only with an *exo* stereochemistry for this adduct.[2-5] Furthermore, H-5 was coupled to H-1, H-3, H-4, and H-6, respectively, indicating a *syn* regiochemistry of the cyanomethylene and methylmethylene groups. A series of NOE experiments further confirmed these structural assignments.

Upon irradiation at δ 1.74 (the methyl group on the unsaturated carbon), only a large enhancement at δ 6.33 (H-3) was observed. Upon irradiation at δ 4.05 (H-9), large enhancements at both δ 2.60 (H-14) and 5.92 (H-8), a moderate enhancement at δ 2.18 (H-16), and a small enhancement at δ 3.30 (H-1) were observed. All these results are consistent with the stereochemistry and regiochemistry shown in structure 6.

Another heptafulvene-fulvene **7**, with one more methylene in the connecting chain, was synthesized by analogous techniques[1] in order to get more information about the side-chain conformational effects. In contrast to the intramolecular cycloadditions of heptafulvene-fulvenes **1** and **16** (see below), the attempted thermolysis of **7** in refluxing xylene for 1 day did not proceed, and after a longer time (3 days) only decomposition products were formed. Sealed-tube thermolysis of a solution of **7** in xylene at 185 °C for 15 hours in the presence of BHT gave *syn-exo*-[4 + 2] adduct **8** in 25% yield (Scheme 1). Its structure was assigned on the basis of a careful analysis of its NMR spectrum, double-resonance experiments, NOE experiments, and comparison of its spectrum with those of related adducts **6** and **17** (Scheme 3). At higher temperatures, **7** decomposed to a black mass without any conversion to adducts. We were unable to detect the existence of any [8 + 6] adduct.

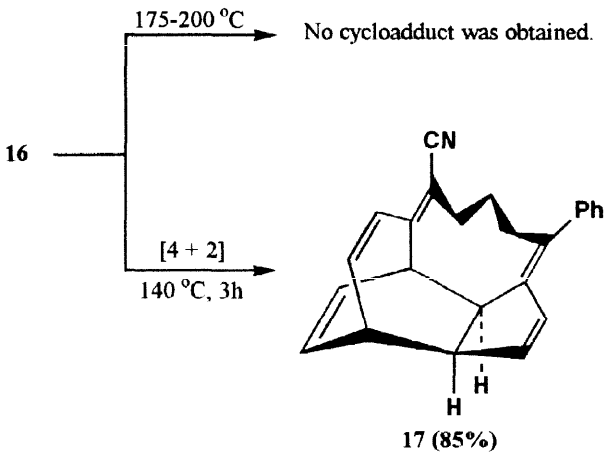
Scheme 2



(a) NaOEt, EtOH, reflux, 16h (43%); (b) KOH, aq. EtOH (100%); (c) Cu, xylene, reflux, 2h (43%); (d) H_3O^+, THF, 24h (89%); (e) 205 °C, 9h (70%); (f) $(C_6H_5)_3C^+BF_4^-$, $CHCl_3$, 1h; (g) Et_3N, CH_2Cl_2 1h (51% from 14); (h) cyclopentadiene, t-BuO^-K^+, CH_3OH, 6h (80%).

In order to establish whether the methyl group, the exocyclic alkyl substituent on the fulvene, has a influence upon the intramolecular periselectivity observed for reaction of **1**, we synthesized the phenyl substituted heptafulvene-fulvene **16** as shown in Scheme 2. Alkylation of ethyl tropylcyanoacetate (**9**)[6] with sodium ethoxide and 4-chlorobutyrophenone ethylene ketal (**10**) in dry ethanol gave **11** in 43% yield. Hydrolysis and decarboxylation of **11** gave **12** in 43% yield after careful flash chromatography. Acid hydrolysis of **12** gave the corresponding ketone **13** (85%). Thermal rearrangement of **13** gave a mixture of 1- and 3-substituted cycloheptatrienes **14** (70%), which provides a satisfactory starting material for hydride abstraction, whereas the 7-substituted compounds are unreactive.[1,4,7-8] The mixture of nitrile **14** was dehydrogenated with trityl fluoroborate followed by triethylamine[1,4,7-8] to give heptafulvene **15** in 51 % yield, which was converted to **16** in 80% yield by reaction with cyclopentadiene and potassium *tert*-butoxide in methanol.

Scheme 3

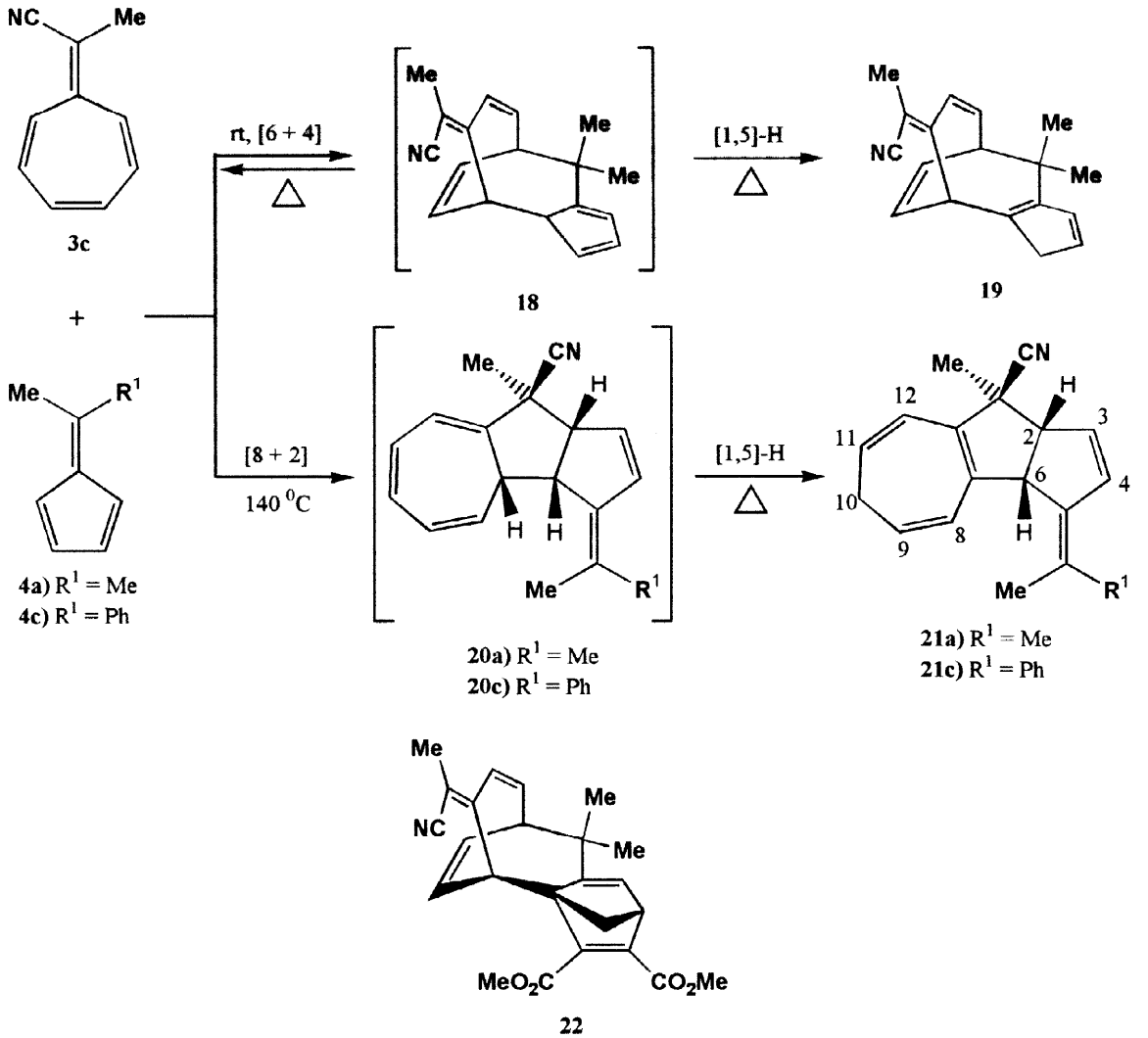


17 (85%)

Upon thermolysis in refluxing xylene for 3 hours, **16** undergoes only intramolecular [4 + 2] cycloaddition, leading to **17** in 85% yield (Scheme 3). Its structure was assigned on the basis of a careful analysis of its NMR spectrum, double-resonance experiments, NOE experiments, and comparison of its spectrum with those of related adducts **6** and **8**. However, **16** decomposed to a black mass without any conversion to products upon attempted sealed-tube thermolysis from 175 to 200 °C in xylene containing BHT. No [8 + 6] adduct was obtained.

In order to establish whether the side-chain conformational effects have a significant influence upon the intramolecular stereoselectivity, periselectivity, and regioselectivity observed for reactions of **1**, **7**, and **16**, the analogous intermolecular cycloadditions of 8-cyano-8-methylheptafulvene (**3c**) with 6,6-methylfulvene (**4a**)[4] and 6-methyl-6-phenylfulvene (**4c**) have been studied (Scheme 4). The reactions of fulvenes **4a** and **4c**, respectively, with heptafulvene **3c** in refluxing xylene gave only the *anti-endo*-[8 + 2] adducts **21a** and **21c**, respectively (Scheme 4). When the reaction of **4a** with **3c** was carried out in refluxing chloroform, only the *anti-endo*-[6 + 4] adduct **19** was obtained.[4] Adducts **21a** and **21c** were believed to come from [8 + 2]

Scheme 4



cycloadditions to form **20a** and **20c**, respectively, followed by 1,5-sigmatropic hydrogen shifts.[1-4] As expected,[2-4] the [6 + 4] adduct **19**, although formed under milder conditions, mainly reverted back to starting materials **3c** and **4a** at higher temperatures and in turn recombined to form the thermodynamically more stable [8 + 2] adduct **21a**.[4] The stereochemistry and regiochemistry of these adducts were assigned on the basis of a careful analysis of their NMR spectra, double-resonance experiments, NOE experiments, and comparison of their spectra with those of related compounds.[2-4] Additional structural evidence for **19** is the [4 + 2] cycloaddition reaction of **19** with DMAD, which gave **22**.[4] We were unable to detect the existence of any [4 + 2] or [8 + 6] adduct.

DISCUSSION

The intermolecular cycloadditions of heptafulvene **3c** with fulvenes **4a,c** gave [8 + 2] and/or [6 + 4]

adducts (Scheme 4). Like observations made in earlier studies,[2-4] these cycloaddition reactions took place with exclusive *endo* diastereoselectivity and *anti* regioselectivity. The *endo* stereochemistry of these reactions is controlled by secondary orbital interactions, and the preferred *anti* regioselectivity could be attributed to the steric repulsion between the exocyclic substituents on the heptafulvenes and fulvenes.

In contrast, the analogous intramolecular cycloadditions of heptafulvene-fulvenes **1**, **7**, and **16** gave no [8 + 2] or [6 + 4] adducts. Heptafulvene-fulvene **1** undergoes intramolecular [4 + 2] and [8 + 6] cycloadditions to give the *syn-exo* adduct **6** and the *syn-endo* adduct **2**, respectively (Scheme 1). The phenyl substituent shifts the intramolecular cycloaddition of **16** exclusively to give the *syn-exo* [4 + 2] adduct **17** (Scheme 3). However, the methyl substituted heptafulvene-fulvene **7**, with one more methylene in the connecting chain, undergoes only intramolecular [4 + 2] cycloaddition, under more drastic reaction conditions than those of **1** and **16**, to give the *syn-exo* adduct **8** (Scheme 1).

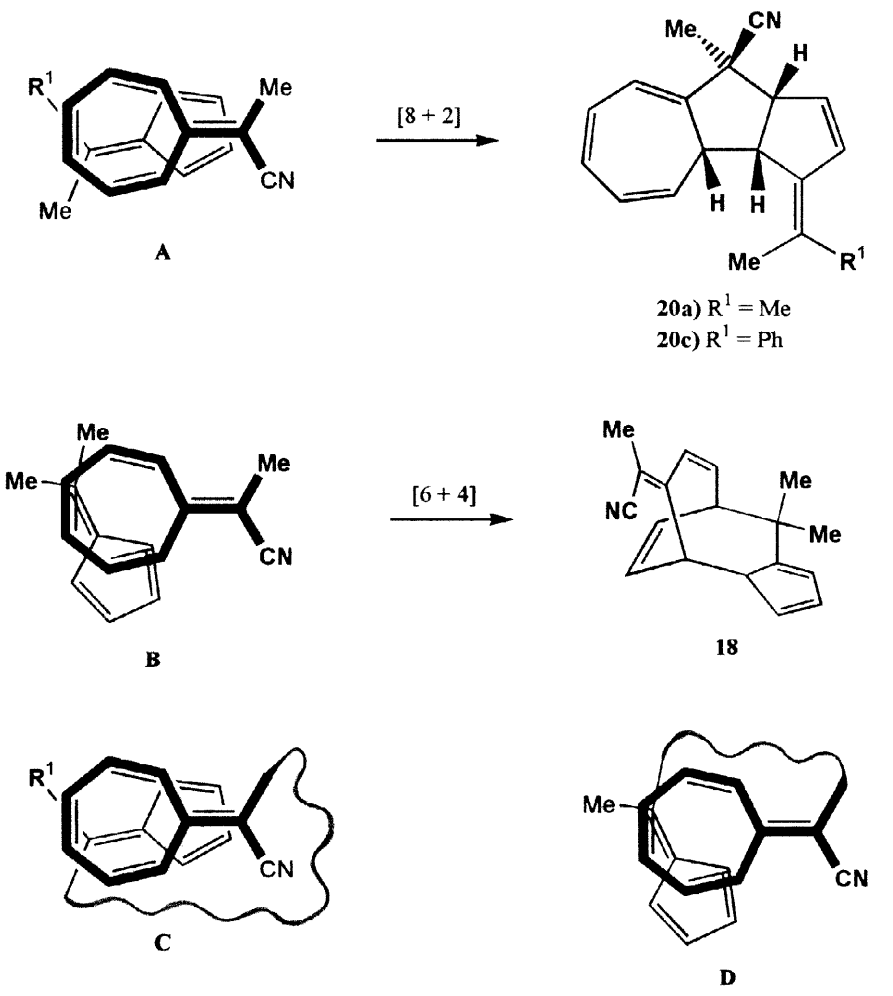


Figure 1. *Anti-endo* transitionstates of the intermolecular [8 + 2] (**A**) and [6 + 4] (**B**), and the analogous intramolecular [8 + 2] (**C**) and [6 + 4] (**D**) cycloadditions.

All these results show that the substituent and the side-chain conformational effects exert significant controlling influences upon the stereoselectivity, periselectivity, and regioselectivity of these intramolecular cycloadditions. These can be explained by comparing the various transition states involved in the cycloadditions. Since the steric repulsion between the exocyclic substituents on the heptafulvenes and fulvenes destabilizes the *syn* transition states relative to the *anti* transition states of the [8 + 2] and [6 + 4] cycloaddition reactions, as has been found in earlier examples,[2-4] the possible transition-state geometries (*anti-endo*) for these intermolecular cycloadditions (**A** and **B**)[4] and the analogous intramolecular cycloadditions (**C** and **D**) are sketched in Figure 1. Examination of molecular models indicates that the restricted geometry imposed by the trimethylene or tetramethylene side-chain makes these *anti* transition-state conformations required for intramolecular cycloadditions impossible to achieve. Indeed, no such intramolecular [8 + 2] or [6 + 4] cycloadditions were observed.

The possible transition-state geometries for [8 + 6] intramolecular cycloadditions of **1** and **16**, which has a three-carbon connecting chain, are sketched in Figure 2. Examination of these transition states indicates

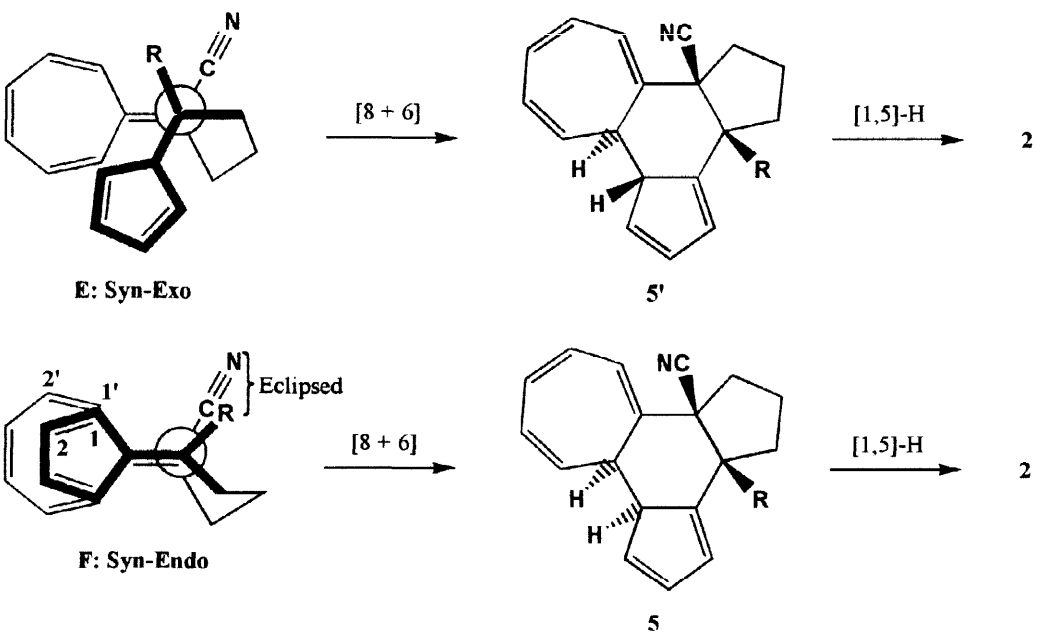


Figure 2. Transition states of the intramolecular [8 + 6] cycloadditions with a three-carbon connecting chain.

that the [8 + 6] cycloaddition via the *syn-endo* transition state **F** can occur with the forming five-membered ring in a favorable envelope conformation.[9] This transition state can also benefit from favorable secondary orbital interactions (C-1 and C-1'). In the *syn-exo*- [8 + 6] transition state, **E**, the connecting side-chain must take a more strained conformation, with a much larger dihedral angle in the cyclopentane about the forming internal bond.[9] Thus, the transition state conformation required for cycloaddition via **E** should have a much higher activation energy than that via **F**. However, the thermal 1,5-sigmatropic hydrogen shift of adduct 2 of

1 prevents full determination of the stereochemistries of this reaction. No initial [8 + 6] adduct 5 or 5' was obtained. In addition, there is an alkyl-cyano eclipsing interaction in the *syn-endo* transition state F. Increasing steric bulk of the exocyclic alkyl substituent, R, on the fulvene should destabilize this transition state, and result in a higher activating energy barrier for this cycloaddition. Indeed, heptafulvene-fulvene 16, with a large exocyclic alkyl substituent, Ph, did not undergo [8 + 6] cycloaddition.

The possible transition-state geometries for [4 + 2] intramolecular cycloadditions of 1 and 16, which has a three-carbon connecting chain, are sketched in Figure 3. Carefully analysis of molecular models indicates

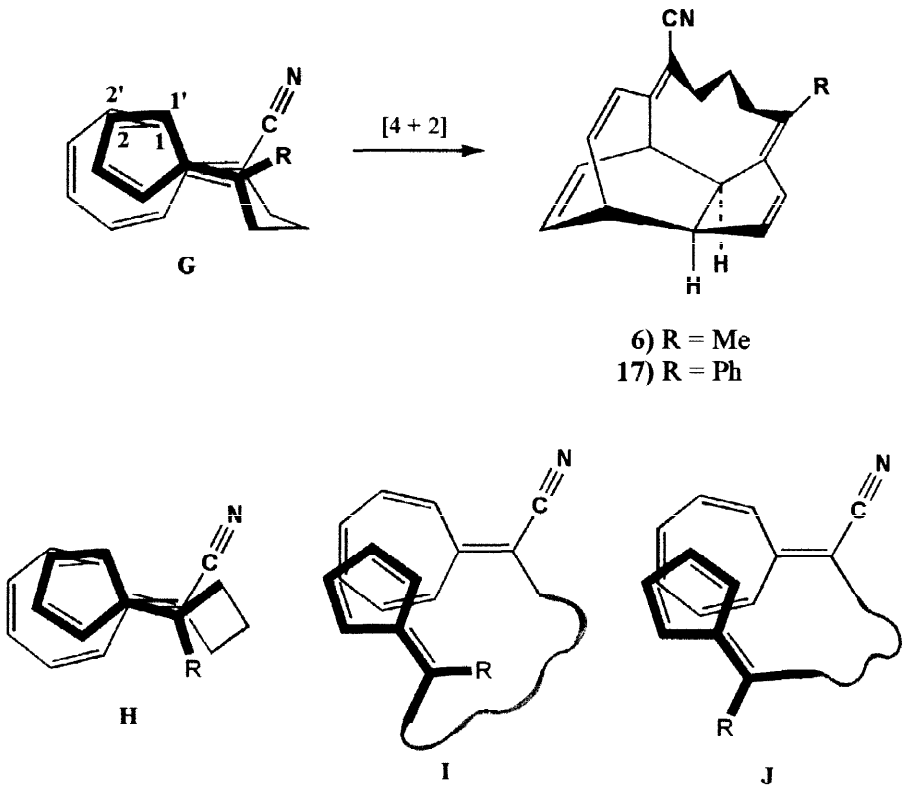


Figure 3. Transition states of the intramolecular [4 + 2] cycloadditions with a three-carbon connecting chain.

that *syn-exo*-[4 + 2] transition state, G, has a less eclipsed (skewed) conformation (R vs CN) than the *syn-endo*-[8 + 6] transition state, F (Figure 2). Similar to F, this transition state, G, can also benefit from favorable secondary orbital interactions (C-1 and C-1'). Thus, the transition state conformation required for cycloaddition via G should have a lower activation energy than that via F. Indeed, [4 + 2] cycloadditions proceed much easier than [8 + 6] cycloadditions (e.g., 1 → 6, 16 → 17, and 1 → 2, Schemes 1 and 3). In accord with examination of molecular models, severe steric or nonbonded interactions were observed in the connecting side-chain, making all other three transition-state conformations (H, I, and J) required for intramolecular cycloadditions impossible to achieve.

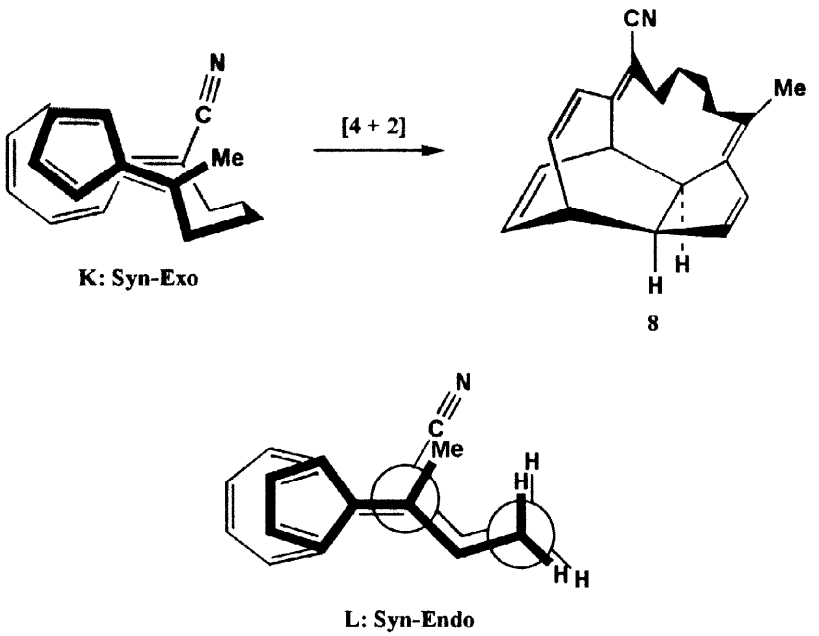


Figure 4. Transition states of the intramolecular [4 + 2] (**K**) and [8 + 6] (**L**) cycloadditions with a four-carbon connecting chain.

The possible transition-state geometries for [4 + 2] (**K**) and [8 + 6] (**L**) intramolecular cycloadditions of **7**, which has a four-carbon connecting chain, are sketched in Figure 4. The *syn-exo*-[4 + 2] transition state **K** should be prefered, since significant steric strain and torsional strain are present in the connecting side-chain in the boat cyclohexane about the forming internal bond in the *syn-endo*-[8 + 6] transition atate **L**. Even with a twist-boat like conformation, transition state **K** is still much more strained than the *syn-exo*-[4 + 2] transition state, **G** (Figure 3). Thus heptafulvene-fulvene **7**, with four-carbon in the connecting chain, undergoes only intramolecular [4 + 2] cycloaddition, under more drastic reaction conditions than those of **1** and **16**, which have three-carbon in the connecting chain, to give the *syn-exo* adduct **8** (Scheme 1).

EXPERIMENTAL SECTION

General Methods. ^{1}H NMR spectra were determined with tetramethylsilane as the internal standard and $CDCl_3$ as the solvent. All reagents were of reagent grade and were purified prior to use. All reactions were performed under an inert atomsphere of nitrogen. The preparations of heptafulvene-fulvene **1**[1] and fulvene **4c**[10] were by literature procedures. Heptafulvene-fulvene **7** was prepared by the same procedure of Houk[1] starting with 6-bromo-2-hexanone ethylene ketal.[11]

Intramolecular Cycloaddition Reaction of Heptafulvene-Fulvene 1. Thermolysis of **1** (60 mg, 230 mmol) in 20 mL of xylene at 185 °C for 1 h in a sealed tube in the presence of BHT afforded a yellow oil. Purification by silica gel flash chromatography, using 5% EtOAc in n-hexane as eluant, gave **2** (27.5 mg, 46%)

as a yellowish oil.[1] When the reaction was carried out in refluxing xylene for 1.5 h, **6** and **2** were formed in 73% and 12% yield, respectively: **6** (a yellow oil) : ^{1}H NMR δ 1.60-1.85 (m, 2 H, H-15), 1.74 (s, 3 H, Me), 1.92-2.08 (m, 1 H, H-16), 2.10-2.26 (m, 1 H, H-16), 2.28-2.41 (m, 1 H, H-14), 2.51-2.68 (m, 1 H, H-14), 3.20-3.39 (m, 2 H, H-1, H-6), 3.53 (m, 1 H, H-5), 4.05 (bt, 1 H, $J_{1,9} = J_{8,9} = 7.4$ Hz, H-9), 5.39 (dd, 1 H, $J_{3,4} = 5.9$ Hz, $J_{4,5} = 2.6$ Hz, H-4), 5.70 (dd, 1 H, $J_{6,12} = 8.5$ Hz, $J_{11,12} = 11.0$ Hz, H-12), 5.92 (bt, 1 H, $J_{7,8} = J_{8,9} = 7.4$ Hz, H-8), 6.30 (dd, 1 H, $J_{9,11} = 2.4$ Hz, $J_{11,12} = 11.0$ Hz, H-11), 6.33 (dd, 1 H, $J_{3,4} = 5.9$ Hz, $J_{3,5} = 1.9$ Hz, H-3), 6.52 (dd, 1 H, $J_{6,7} = J_{7,8} = 7.4$ Hz, H-7); IR 2215 (CN) cm^{-1}; MS *m/z* 261 (M^+); exact mass cacld for $C_{19}H_{19}N$ 261.1519, found 261.1515.

Intramolecular Cycloaddition Reaction of Heptafulvene-Fulvene 7. The attempted thermolysis of **7** (60 mg, 218 mmol) in refluxing xylene (20 mL) for 1 day did not proceed, and after a longer time (3 days) only decomposition products were formed. Sealed-tube thermolysis of **7** (60 mg, 218 mmol) in 20 mL of xylene at 185 °C for 15 h in a sealed tube in the presence of BHT afforded a yellow oil. Purification by silica gel flash chromatography, using 5% EtOAc in n-hexane as eluant, gave **8** (15 mg, 25%) as a yellowish oil. At higher temperatures, **7** decomposed to a black mass without any conversion to adducts. **8:** ^{1}H NMR δ 1.60-2.00 (m, 4 H, H-15-16), 1.66 (s, 3 H, Me), 2.10-2.55 (m, 4 H, H-14, H-17), 3.18-3.28 (m, 1 H, H-1), 3.31-3.41 (m, 1 H, H-6), 3.43-3.51 (m, 1 H, H-5), 4.31 (bt, 1 H, $J_{1,9} = J_{8,9} = 7.5$ Hz, H-9), 5.54 (dd, 1 H, $J_{3,4} = 5.9$ Hz, $J_{4,5} = 2.5$ Hz, H-4), 5.90 (dd, 1 H, $J_{6,12} = 8.5$ Hz, $J_{11,12} = 11.0$ Hz, H-12), 5.97 (bt, 1 H, $J_{7,8} = J_{8,9} = 7.5$ Hz, H-8), 6.38 (dd, 1 H, $J_{9,11} = 2.4$ Hz, $J_{11,12} = 11.0$ Hz, H-11), 6.39 (dd, 1 H, $J_{3,4} = 5.9$ Hz, $J_{3,5} = 1.9$ Hz, H-3), 6.54 (dd, 1 H, $J_{6,7} = J_{7,8} = 7.5$ Hz, H-7); IR 2215 (CN) cm^{-1}; MS *m/z* 275 (M^+); exact mass cacld for $C_{20}H_{21}N$ 275.1675, found 275.1664.

Preparation of Ethyl Alkyltropylcyanoacetate 11. To a solution of 10.0 g (49.3 mmol) of ethyl tropylcyanoacetate (**9**)[6] in 25 mL of anhydrous ethanol was added 19.5 mL (52.3 mmol, 21 wt. % solution in denatured ethanol) of NaOEt. After being stirred at room temperature for 1 h, 12.0 g (53.0 mmol) of 4-chlorobutyrophenone ethylene ketal (**10**) was added, and the mixture was refluxed for 16 h. Water (10 mL) was then added. The mixture was concentrated *in vacuo* and extracted with Et_2O (3 × 30 mL). The combined organic extracts were washed with 30 mL of brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel flash chromatography, using 20% EtOAc in n-hexane as eluant, gave **11** (8.32 g, 43%) as a yellowish oil: ^{1}H NMR δ 1.20 (t, 3 H, J = 7.5 Hz, -O-CH_2-C$\boldsymbol{H}_3$), 1.61-2.25 (m, 7 H, H-7, H-9-11), 3.61-3.80 (m, 2 H, ketal-H), 3.89-401 (m, 2 H, ketal-H), 4.20 (q, 2 H, J = 7.5 Hz, -O-C$\boldsymbol{H}_2$-CH_3), 5.18-5.35 (m, 2 H, H-1, H-6), 6.12-6.32 (m, 2 H, H-2, H-5), 6.60-6.71 (m, 2 H, H-3-4), 7.19-7.42 (m, 5 H, Ph); IR 1740 (C=O), 2243 (CN) cm^{-1}; MS *m/z* 393 (M^+); exact mass cacld for $C_{24}H_{27}NO_4$ 393.1941, found 393.1938.

Preparation of 5-Cyano-5-tropylvalerophenone Ethylene Ketal (12). To a solution of 5.00 g 12.7 mmol) of **11** in 40 mL of ethanol at 0 °C was added a solution of 3.4 g (59.6 mmol) of potassium hydroxide in 20 mL of water. After being stirred at room temperature for 0.5 h, the solution was neutralized and further acidified with 6N HCl. The mixture was concentrated *in vacuo* and extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with 20 mL of water, dried over anhydrous

$MgSO_4$, filtered, and concentrated *in vacuo* to give quantitatively the acid as a very viscous yellow oil. A mixture of the crude acid (3.95 g, 10.8 mmol) and 0.8 g of copper in 20 mL of xylene was refluxed for 2 h. The mixture was filtered, concentrated *in vacuo*, and extracted with Et_2O (3 × 30 mL). The combined organic extracts were concentrated *in vacuo* and purified by silica gel flash chromatography, using 20% EtOAc in n-hexane as eluant, gave **12** (1.49 g, 43%) as a yellow oil: ^1H NMR δ 1.14-1.98 (m, 7 H, H-7, H-9-11), 2.65-2.78 (m, 1 H, H-8), 3.63-3.75 (m, 2 H, ketal-H), 3.89-4.01 (m, 2 H, ketal-H), 5.10-5.20 (m, 1 H, H-6), 526-5.39 (m, 1 H, H-1), 6.11-6.29 (m, 2 H, H-2, H-5), 6.52-6.69 (m, 2 H, H-3-4), 7.19-7.41 (m, 5 H, Ph); IR 2245 (CN) cm^{-1}; MS *mlz* 321 (M^+); exact mass cacld for $C_{21}H_{23}NO_2$ 321.1730, found 321.1725.

Preparation of 5-Cyano-5-tropylvalerophenone (13). A mixture of 1.50 g (4.67 mmol) of **12** in 30 mL of THF, 15 mL of water, and 8 mL of 37% HCl was thoroughly stirred at room temperature for 24 h. The mixture was concentrated *in vacuo* and extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with 20 mL of saturated aqueous $NaHCO_3$, 20 mL of brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel flash chromatography, using 20% EtOAc in n-hexane as eluant, gave **13** (1.10 g, 85%) as a yellowish oil: ^1H NMR δ 1.69-2.09 (m, 5 H, H-7, H-9-10), 2.77-2.91 (m, 1 H, H-8), 3.01 (bt, 2 H, $J_{10,11}$ = 6.5 Hz, H-11), 5.18-5.28 (m, 1 H, H-6), 5.31-5.45 (m, 1 H, H-1), 6.18-6.34 (m, 2 H, H-2, H-5), 6.58-6.71 (m, 2 H, H-3-4), 7.21-7.93 (m, 5 H, Ph); IR 1683 (C=O), 2237 (CN) cm^{-1}; MS *mlz* 277 (M^+); exact mass cacld for $C_{19}H_{19}NO$ 277.1468, found 277.1465.

Preparation of Ketone 14. Thermal isomerization of **13** (1.10 g, 3.97 mmol) in 30 mL of xylene at 205 °C for 9 h in a sealed tube in the presence of BHT afforded a yellow oil. Purification by silica gel flash chromatography, using 20% EtOAc in n-hexane as eluant, gave **14** (70 mg, 70%) as a yellow oil: ^1H NMR δ 1.61-1.95 (m, 4 H, H-9, H-10), 2.20-2.25 (m, 2 H, H-4), 2.90-3.10 (m, 2 H, H-11), 3.35-3.55 (m, 1 H, H-8), 5.30-5.60 (m, 2 H), 6.05-6.21 (m, 2 H), 6.48-6.71 (m, 2 H), 7.40-7.97 (m, 5 H, Ph); IR 1685 (C=O), 2238 (CN) cm^{-1}; MS *mlz* 277 (M^+); exact mass cacld for $C_{19}H_{19}NO$ 277.1468, found 277.1466.

Preparation of Heptafulvene 15. A solution of **14** (0.75 g, 2.70 mmol) in 30 mL of chloroform was added to a solution of triphenylmethyl fluoroborate (1.09g, 3.32 mmol) in 50 mL of chloroform. After being stirred at room temperature for 2 h, excess triethylamine was added. Purification by silica gel flash chromatography, using 20% EtOAc in n-hexane as eluant, gave **15** (0.38 g, 51 %) as a red oil: ^1H NMR δ 1.92-2.10 (m, 2 H, H-10), 2.33 (t, 1 H, $J_{9,10}$ = 7.0 Hz, H-9), 3.07 (t, 2 H, $J_{10,11}$ = 6.9 Hz, H-11), 6.07-6.21 (m, 4 H, H-3-H-6), 6.38-6.49 (m, 1 H, H-2), 6.79 (bd, 1 H, $J_{1,2}$ = 11 Hz, H-1), 7.40-8.01 (m, 5 H, Ph); IR 1682 (C=O), 2185 (CN) cm^{-1}; MS *mlz* 275 (M^+); exact mass cacld for $C_{19}H_{17}NO$ 275.1311, found 275.1308.

Preparation of Heptafulvene-Fulvene 16. A solution of 0.31 g (2.76 mmol) of potassium *tert*-butoxide, 0.20 g (3.03 mmol) of freshly distilled cyclopentadiene, and 0.38 g (1.38 mmol) of **15** in 20 mL of methanol was stirred at room temperature for 6 h. Water (5 mL) was then added. The mixture was concentrated *in vacuo* and extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with 20 mL of brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by silica gel flash chromatography, using 20% EtOAc in n-hexane as eluant, gave **16** (0.36 g, 80%)

as a red oil: ^{1}H NMR δ 1.54-1.69 (m, 2 H, H-10), 2.09 (t, 1 H, $J_{9,10}$ = 8.5 Hz, H-9), 2.95 (t, 2 H, $J_{10,11}$ = 7.4 Hz, H-11), 5.98-6.13 (m, 4 H, H-3-6), 6.40-6.47 (m, 1 H, H-2), 6.48-6.59 (m, 4 H, H-14-17), 6.68 (bd, 1 H, $J_{1,2}$ = 11.5 Hz, H-1), 7.35-7.95 (m, 5 H, Ph); IR 2186 (CN) cm^{-1}; MS *mlz* 323 (M^+); exact mass cacld for $C_{24}H_{21}N$ 323.1675, found 323.1671.

Intramolecular Cycloaddition Reaction of Heptafulvene-Fulvene 16. Thermolysis of **16** (60 mg, 186 mmol) in refluxing xylene (20 mL) for 3 h in the presence of BHT afforded a yellowish oil. Purification by silica gel flash chromatography, using 10% EtOAc in n-hexane as eluant, gave **17** (51 mg, 85%) as a yellowish oil. Heptafulvene-fulvene **16** decomposed to a black mass without any conversion to products upon attempted sealed-tube thermolysis ftom 175 to 200 °C in xylene containing BHT. **17:** ^{1}H NMR δ 1.32-1.72 (m, 2 H, H-15), 2.24-2.46 (m, 2 H, H-14), 2.49-2.73 (m, 2 H, H-16), 3.24-3.37 (m, 1 H, H-6), 3.47 (bt, 1 H, $J_{1,9} = J_{1,5}$ = 7.5 Hz, H-1), 3.52-3.62 (m, 1 H, H-5), 4.19 (bt, 1 H, $J_{1,9} = J_{8,9}$ = 7.5 Hz, H-9), 5.38 (dd, 1 H, $J_{3,4}$ = 5.8 Hz, $J_{4,5}$ = 2.5 Hz, H-4), 5.77 (dd, 1 H, $J_{6,12}$ = 8.6 Hz, $J_{11,12}$ = 11.0 Hz, H-12), 5.94 (dd, 1 H, $J_{3,4}$ = 5.8 Hz, $J_{3,5}$ = 1.5 Hz, H-3), 5.98 (bt, 1 H, $J_{7,8} = J_{8,9}$ = 7.5 Hz, H-8), 6.47 (dd, 1 H, $J_{9,11}$ = 1.9 Hz, $J_{11,12}$ = 11.0 Hz, H-11), 6.57 (t, 1 H, $J_{6,7} = J_{7,8}$ = 7.5 Hz, H-7), 7.05-7.32 (m, 5 H, Ph); IR 2195 (CN) cm^{-1}, MS *mlz* 323 (M^+); exact mass cacld for $C_{24}H_{21}N$ 323.1675, found 323.1668.

Intermolecular Cycloaddition Reaction of 8-Cyano-8-methylheptafulvene (3c) with 6-Methyl-6-phenylfulvene (4c). A solution of the crude heptafulvene **3c** (0.50 g, 3.50 mmol) and **4c** (0.59 g, 3.50 mmol) in xylene (10 mL) was heated under reflux for 3 days afforded a yellow oil. Purification by silica gel flash chromatography, using 5% EtOAc in n-hexane as eluant, gave **21c** (149 mg, 48%) as a yellowish oil: ^{1}H NMR δ 1.57 (s, 3 H, Me), 2.25 (s, 3 H, Me), 2.19-2.40 (m, 2 H, H-10), 3.84 (m, 1 H, H-2), 4.47 (d, 1 H, $J_{2,6}$ = 5.7 Hz, H-6), 5.29-5,51 (m, 2 H, H-9, H-11), 5.73 (dd, 1 H, $J_{2,3}$ = 2.3 Hz, $J_{3,4}$ = 5.7 Hz, H-3), 6.13 (d, 1 H, $J_{8,9}$ = 9.9 Hz, H-8), 6.14 (dd, 1 H, $J_{2,4}$ = 2.3 Hz, $J_{3,4}$ = 5.7 Hz, H-4), 6.32 (d, 1 H, $J_{11,12}$ = 9.5 Hz, H-12), 7.11-7.32 (m, 5 H, Ph); IR 2245 (CN) cm^{-1}; MS *mlz* 311 (M^+); exact mass cacld for $C_{23}H_{21}N$ 311.1690, found 311.1685.

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REFERENCES AND NOTES

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1. Liu, C. -Y.; Smith, D. A.; Houk, K. N. *Tetrahedron Lett.* **1986**, 27, 4881.
2. Liu, C. -Y.; Ding S. -T. *J. Org. Chem.* **1992**, 57, 4539.
3. Liu, C. -Y.; Ding, S. -T.; Chen, S. -Y.; You, C. -Y.; Shie, H. -Y. *J. Org. Chem.* **1993**, 58, 1628.
4. Liu, C. -Y.; Shie, H. -Y.; Chen, S. -Y.; You, C. -Y.; Wang, W. -C.; Hua, L. -N.; Yang, H. -J.; Tseng, C. -M. *Tetrahedron* **1997**, 51, 17275.
5. (a) Ito, S.; Sakan, K; Fujise, Y. *Tetrahedron Lett.* **1969**, 10, 775. (b) Ito, S.; Takeshita, H.; Shoji, Y. *Tetrahedron Lett.* **1969**, 10, 815. (c) Ito, S.; Sakan, K; Fujise, Y. *Tetrahedron Lett.* **1970**, 11, 2873.

6. Nozoe, T.; Mukai, T.; Osaka, K.; Schishido, N. *Bull. Chem. Soc. Japan* **1961**, 34, 1384.
7. Oda, M.; Kitahara, Y. *Chem. Commun.* **1969**, 352.
8. Liu, C. -Y.; Houk, K. N. *Tetrahedron Lett.* **1987**, 28, 1371.
9. Reviews of the intramolecular Diels-Alder reaction: (a) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, 80, 63. (b) Funk, R.; Vollhardt, K. P. C. *Chem. Soc. Rev.* **1980**, 9, 41. (c) Ciganek, E. *Org. React.* **1984**, 32, 1. (d) Fallis, A. G. *Can. J. Chem.* **1984**, 62, 183. (e) Taber, D. F. *Intramolecular Diels-Alder and Alder Ene Reactions;* Springer Verlag: New York, **1984**. (f) Craig, D. *Chem. Soc. Rev.* **1987**, 16, 187. (g) Roush, W. R. in *Advances in Cycloaddition;* Curran, D. P. Eds.; Jai Press, Greenwich, CT, **1990**, 2, 91. (h) Roush, W. R. in *Comprehensive Organic Synthesis;* Trost. B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, **1991**, 4, 513.
10. (a) Thiele, J. *Ber.* **1900**, 33, 666. (b) Yates, P. *Adv. Alcycl. Chem.* **1968**, 2, 59.
11. Anderson, E. P.; Crawford, J. V.; Sherrill, M. L. *J. Am. Chem. Soc.* **1946**, 68, 1294.