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Reaction of 2,2-Bis(trifluoromethyl)-1,1-dicyanoethylene with 6,6-Dimethylfulvene: Cycloadditions and a Rearrangement

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Reaction of 2,2-bis(trifluoromethyl)-1,1-dicyanoethylene (BTF; **1**) with 6,6-dimethylfulvene (**2**) affords the expected Diels−Alder cycloadduct, 7-(1-methylethylidene)-3,3-bis(trifluoromethyl)bicyclo[2.2.1]-hept-5-ene-2,2-dicarbonitrile (**3**), in good yield. The cycloadduct **3** is unstable and exists in equilibrium with the starting materials in less polar solvents. In more polar environment, the [4 + 2] adduct **3** either reverts to starting materials, or, in a competing process, is converted to the formal [2 + 2] adduct, 2-(1-methylethylidene)-7,7-bis(trifluoromethyl)bicyclo[3.2.0]hept-3-ene-6,6-dicarbonitrile (**6**). In the presence of acid, **3** is converted to a third isomeric form, 1,3a,5,6-tetrahydro-7-methyl-5,5-bis(trifluoromethyl)-4*H*-indene-4,4-dicarbonitrile (**8**). Both **6** and **8** are formed with complete regiospecificity. Quantum mechanical calculations and X-ray crystallographic studies of this ensemble of reactions by BTF, and the analogous set of reactions by its progenitor, tetracyanoethylene (TCNE), reveal several interesting facets. The conversion of **3** to **6** occurs in certain polar solvents, in the presence of silica gel and alumina, as well as in the solid state. Single crystals of **3** were observed by X-ray crystallography to undergo crystal-to-crystal rearrangement to **6**. The conversion of **3** to **8** proceeds by the initial retro-Diels−Alder reaction followed by isomerization of the fulvene to 1-isopropenyl-1,3-cyclopentadiene that then reacts with BTF to give the alternative Diels−Alder product as a single regioisomer. A hybrid density functional theory (DFT) method at the B3LYP/6-31G(d) level of theory gave calculated relative energies of 0.0, −9.0, and −18.8 kcal/mol for **3**, **6**, and **8**, respectively. The same method was also used to correctly predict the regiochemical outcome of the cycloaddition of BTF with 1-isopropenyl-1,3-cyclopentadiene. Finally, an explanation is offered for the preference of the persubstituted cyanoolefins BTF and TCNE to add to the exocyclic diene portion of 1-isopropenyl-1,3-cyclopentadiene and the contrasting preference of 2-acetyloxy-2-propenenitrile to add to the endocyclic diene.

Introduction

Cyanoolefin Reactivity. The discovery of tetracyanoethylene[1] (TCNE) over 40 years ago spurred a sustained interest in the chemistry of polycyanoolefins that has revealed many varied and unique modes of reactivity.[2] On a practical level, cycloadducts of polycyanoolefins are noteworthy for their biological activity.[3] Polycyclic dinitriles have been identified as a novel class of potent antagonists of the γ-aminobutyric acid (GABA) receptor.[3a] Since certain of these *gem*-dinitriles exhibit toxicity to invertebrate pests at levels comparable to commercial insecticides, there is interest in structure−activity relationships, and a unified pharmacophore model has been developed.[3b] The perfluoroalkyldicyanoolefins, a much less-studied subclass of polycyanolefins, have similarly exhibited intriguing chemical behavior.[4] This subclass, as exemplified by 2,2-bis(trifluoromethyl)-1,1-dicyanoethylene (BTF; **1**),[5] is characterized by additional modes of reactivity not seen in other cyanoolefins. While both TCNE (**4**) and BTF (**1**) are highly electrophilic, their

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(1) Cairns, T. L.; Carboni, R. A.; Coffman, D. D.; Engelhardt, V. A.; Heckert, R. E.; Little, E. L.; McGreer, E. G.; McKusick, B. C.; Middleton, W. J.; Scribner, R. M.; Theobald, T. W.; Winberg, H. E. *J. Am. Chem. Soc.* **1958**, *80*, 2775−2778.

(2) (a) Dworczak, R.; Junek, H. In *The Chemistry of Triple-Bonded Functional Groups*; Patai, S., Ed.; John Wiley & Sons Ltd: Chichester, U.K., 1994; Vol. 2, pp 789−871. (b) Fatiadi, A. J. *Synthesis* **1986**, (4), 249−284. (c) Fatiadi, A. J. *Synthesis* **1987**, *9*, 749−789. (d) Fatiadi, A. J. *Synthesis* **1987**, *11*, 959−978.

(3) (a) Rauh, J. J.; Benner, E.; Schnee, M. E.; Cordova, D.; Holyoke, C. W.; Howard, M. H.; Bai, D.; Buckingham, S. D.; Hutton, M. L.; Hamon, A.; Roush, R. T.; Sattelle, D. B. *Br. J. Pharmacol.* **1997**, *121*, 1496−1505. (b) Rauh, J. J.; Holyoke, C. W.; Kleier, D. A.; Presnail, J. K.; Benner, E. A.; Cordova, D.; Howard, M. H.; Hosie, A. M.; Buckingham, S. D.; Baylis, H. A.; Sattelle, D. B. *Invertebr. Neurosci.* **1997**, *3*, 261−268.

(4) (a) Fokin, A. V.; Tyutin, V. Y.; Chkanikov, N. D. *Usp. Khim.* **1992**, *61* (8), 1395−1421. (b) Ciganek, E.; Linn, W. J.; Webster, O. W. In *The Chemistry of the Cyano Group*; Rappoport, Z., Ed.; Wiley-Interscience: London, 1970; pp 484−490.

(5) Middleton, W. J. *J. Org. Chem.* **1965**, *30* (5), 1402−1407.

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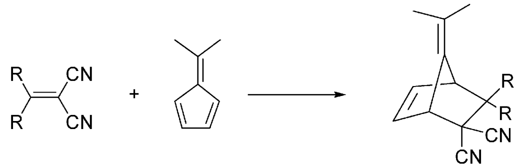
behaviors diverge as a consequence of the latter compound's enhanced polarizability and greater steric demand. Cyanoolefins are known to be reactive enophiles, but BTF undergoes ene reactions with terminal, unactivated alkenes via allylic hydrogen transfer, while TCNE is unreactive toward such substrates.[6] Early spectrophotometric studies of TCNE showed it to have the highest electron affinity of any π-acid studied up to that time.[7] Electron-rich aromatic rings undergo electrophilic substitution by both BTF and TCNE. Ketones react via their enol tautomers with TCNE and added catalyst or with BTF without added catalyst—a consequence of the even higher electron affinity of BTF.[8] In [2 + 2] cycloadditions with enol ethers[8b] and vinyl sulfides,[9] BTF reacts 3 orders of magnitude faster than TCNE. The rate difference between the two cyanoolefins in Diels–Alder reactions is much less pronounced since the acceleration due to the electronic effect of the CF_3 groups in **1** is largely canceled out by the concomitant increase in steric hindrance.[5,10]

Fulvene Chemistry. The diverse reactivity of fulvenes made them the subject of considerable interest from both a mechanistic and synthetic standpoint over the entire 20th century.[11] Possessing a cyclic diene system cross-conjugated with an exocyclic double bond, these trienes are isomeric with the corresponding benzenoid series. The resonance energy of fulvene is approximately 12 kcal/mol, considerably less than that of benzene.[12] The reactivity of fulvenes therefore falls somewhere between that observed in aromatic and olefinic systems.[13] Fulvenes are versatile partners in cycloaddition reactions with olefins and can serve as 2π, 4π, or 6π species depending on the substitution pattern of the reacting components.[11a] With so many modes of reaction available to each partner, the outcome of the interaction of BTF with fulvenes seemed bound to produce challenges to mechanistic and theoretical understanding.

Results

Diels–Alder Reaction. Addition of BTF (**1**) to a bright yellow solution of 6,6-dimethylfulvene (**2**) in hexanes (Scheme 1) results in a transient red color indicative of a charge transfer complex between the two species. Once a stoichiometric amount of BTF has been added, the yellow color fades and a white solid precipitates from the mildly exothermic reaction. Analysis of the precipitate showed it to be the [4 + 2] cycloadduct **3**.

SCHEME 1[a]



1 R = CF_3
4 R = CN

2

3 R = CF_3
5 R = CN

[a] Conditions: hexanes, rt (R = CF_3); acetone, −60 °C (R = CN).

In less-polar solvents, the [4 + 2] adduct **3** exists in equilibrium with its starting materials. The ratio of the [4 + 2] product **3** to the fulvene **2** is easily measured using ^1H NMR spectroscopy to compare the integrals for well-separated peaks of each compound in either the vinyl or methyl region. The equilibrium constant (K_{eq}) for **3** was determined to be 11.2 M^{-1} in toluene-d_8 at 20 °C, and this value is very close to that observed in other less-polar solvents such as $CDCl_3$ and benzene-d_6. In these solvents, the cycloadduct **3** is stable for over 1 month. In acetone, a solvent of intermediate polarity, no Diels–Alder reaction is observed between **1** and fulvene **2** at room temperature, in contrast to the reaction of **2** with TCNE (**4**), which occurs rapidly. When dissolved in more polar solvents, **3** reverts to a mixture of starting materials **1** and **2** and a rearrangement product (vide infra) that is formed in a competing process.

Single crystals of **3** can be obtained by careful crystallization from diethyl ether/petroleum ether or, more easily, by sublimation under high vacuum at slightly elevated temperature. X-ray crystallography of the single crystals gave the structure shown in Figure 1a.

Reaction of 6,6-dimethylfulvene (**2**) with equimolar TCNE also gives the expected [4 + 2] cycloadduct **5** as shown in Scheme 1.[14] A transient dark blue color was noted in the acetone solution as the reactants were mixed. A solvent-dependent equilibrium for this reaction is evident from the NMR spectrum of the product. The equilibrium constant in acetone-d_6 is 11.5 at room temperature. X-ray diffraction of single crystals of this compound gave the structure shown in Figure 1b.

Based on an accumulating wealth of successful precedents for its use in the study of Diels–Alder reactions, we decided to use B3LYP/6-31G(d) method to examine the reaction between 6,6-dimethylfulvene and the two cyanoolefins under consideration in this work.[15–18] The bond lengths and angles for the calculated transitions states for the reaction of fulvene **2** with the two cyanoolefins and ethylene are given in Table 1. Several attempts to locate biradical intermediates using UB3LYP/6-31G-

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(6) Huisgen, R.; Brückner, R. *J. Org. Chem.* **1991**, *56* (5), 1679–1681.

(7) Merrifield, R. E.; Phillips, W. D. *J. Am. Chem. Soc.* **1958**, *80*, 2778–2782.

(8) (a) Brückner, R.; Huisgen, R. *Tetrahedron Lett.* **1991**, *32* (16), 1871–1874. (b) Brückner, R.; Huisgen, R. *Tetrahedron Lett.* **1990**, *31* (18), 2557–2560.

(9) Brückner, R.; Huisgen, R. *Tetrahedron Lett.* **1990**, *31* (18), 2561–2564.

(10) Brückner, R.; Huisgen, R. *Tetrahedron Lett.* **1994**, *35* (20), 3285–3288.

(11) (a) Neuenschwander, M. In *Chemistry of Double-bonded Functional Groups*; Patai, S., Ed.; Wiley: Chichester, U.K., 1989; Vol. 2, pp 1131–1268. (b) Zeller, K.-P. In *Houben-Weyl, Methoden der Organischen Chemie*; Georg Thieme Verlag: Stuttgart, Germany, 1985; Vol. 5/2c, pp 504–508. (c) Yates, P. *Adv. Alicycl. Chem.* **1968**, *2*, 59–184. (d) Hamb, F. L. *Org. Chem. Bull.* **1966**, *38* (1), 1–6. (e) Day, J. H. *Chem. Rev.* **1953**, *53*, 167–189.

(12) Day, J. H.; Oestreich, C. *J. Org. Chem.* **1957**, *22*, 214–216.

(13) Hafner, K.; Häfner, K. H.; König, C.; Kreuder, M.; Ploss, G.; Schulz, G.; Sturm, E.; Vöpel, K. H. *Angew. Chem., Int. Ed. Engl.* **1963**, *2* (3), 123–134.

(14) (a) Kresze, G.; Rau, S.; Sabelus, G.; Goetz, H. *Annalen* **1961**, *648*, 57–63. (b) Smith, W. B.; Biesemeier, S.; Deavenport, D. L. *J. Org. Chem.* **1971**, *36* (19), 2853–2855. (c) Knight, D. B.; Hartless, R. L.; Jarvis, D. A. *J. Org. Chem.* **1972**, *37*, (5), 688–692.

(15) (a) Houk, K. N.; Gonzalez, J.; Li, Y. *Acc. Chem. Res.* **1995**, *28* (2), 81–90. (b) Dewar, M. J. S.; Olivella, S.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1986**, *108* (19), 5771–5779.

(16) Goldstein, E.; Beno, B.; Houk, K. N. *J. Am. Chem. Soc.* **1996**, *118*, (25), 6036–6043.

(17) Jursic, B. S. *THEOCHEM* **1995**, *358*, 139–43.

(18) Tian, J.; Houk, K. N.; Klaerner, F. G. *J. Phys. Chem. A* **1998**, *102* (39), 7662–7667.

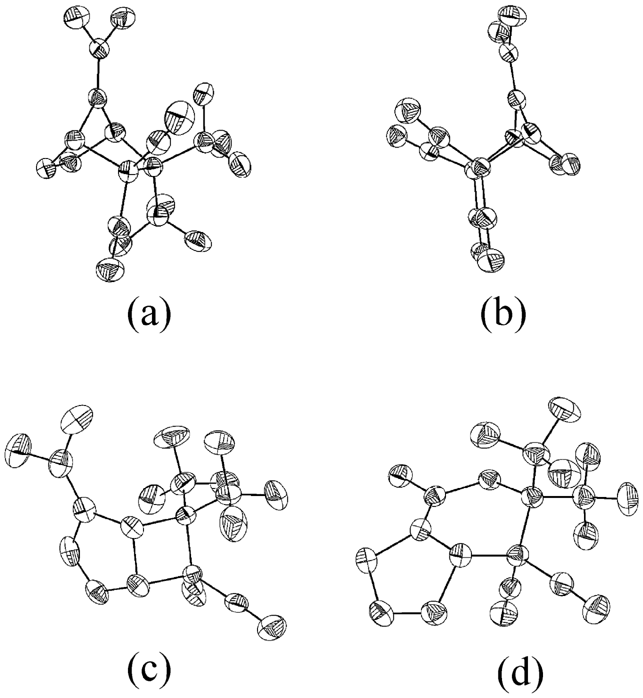


FIGURE 1. X-ray crystal structures of (a) 7-(1-methylethylidene)-3,3-bis(trifluoromethyl)bicyclo[2.2.1]hept-5-ene-2,2-dicarbonitrile **(3)**, (b) 7-(1-methylethylidene)bicyclo[2.2.1]hept-5-ene-2,2,3,3-tetracarbonitrile (**5**), (c) 2-(1-methylethylidene)-7,7-bis(trifluoromethyl)bicyclo[3.2.0]hept-3-ene-6,6-dicarbonitrile (**6**), and (d) 1,3a,5,6-tetrahydro-7-methyl-5,5-bis(tri-fluoromethyl)-4*H*-indene-4,4-dicarbonitrile (**8**).

TABLE 1. Calculated Geometrical Parameters for the Transition States of the Diels–Alder Reactions of 6,6-Dimethylfulvene with Ethylene, TCNE, and BTF

parameter	ethylene	TCNE	BTF
forming C- - -C bond (Å)	2.204	2.114	1.890[a]
	2.204	2.112	2.664[b]
angle around C2 (deg)	354.5[c]	349.2[c]	359.0[d]
angle around C3 (deg)	354.4[c]	349.0[c]	337.6[e]

[a] C3–C4 (see Supporting Information for atom numbering). [b] C1–C2 (see Supporting Information for atom numbering). [c] Angle around the dienophilic C-atom. For a planar carbon center, the angle is 360°. [d] Angle around the dienophilic C-atom with the two CN groups attached. [e] Angle around the dienophilic C-atom with the two CF_3 groups attached.

(d) failed, indicating the reaction in the gas phase is probably concerted.

The calculated potential energy surface is schematically displayed in Figure 2. The theoretical calculations indicate relatively deep minima that we attribute to π-complexes based on the experimentally observed color changes noted above. The intermolecular distance in the π-complex of BTF and fulvene is longer than that in the complex of TCNE and fulvene. A graphical rendering of the calculated π-complex is included in the Supporting Information.

The calculated reaction barrier for the reaction of BTF and fulvene **2** is about 8.2 kcal/mol. The overall reaction is calculated to be exothermic; however, the heat of reaction appears to be underestimated. Since the calculated forward barrier is very reasonable, the underestimation of the heat of reaction must be due to underestimation of the stability of the product. The same consideration applies to the reaction of TCNE and fulvene **2**.

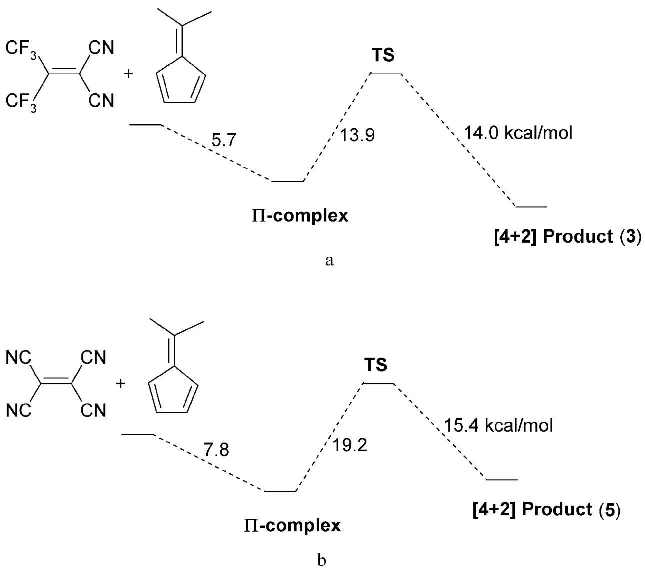
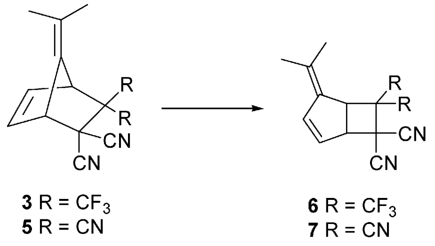


FIGURE 2. Calculated potential energy surface for the Diels–Alder reactions of 6,6-dimethylfulvene with BTF (a) and TCNE (b) at the B3LYP/6-31G(d) level of theory.

SCHEME 2. Rearrangement of the Norbornenes 3 and 5 to the Bicyclo[3.2.0]heptenes 6 and 7[a]

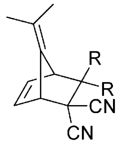
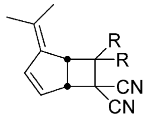
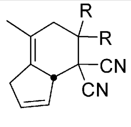


[a] Conditions: see text.

Rearrangement of the Diels–Alder Product. On standing in polar solvents such as methyl sulfoxide (DMSO) and acetonitrile, the [4 + 2] product **3** gradually converts in low yield to a new structure (Scheme 2), along with starting materials **1** and **2** from retro-Diels–Alder reaction. Combustion analysis of the new product gave the same elemental composition as the starting material. The ^1H NMR spectrum of the new product in $CDCl_3$ indicated that a skeletal rearrangement had occurred. The two sets of multiplets in the range 6.63–6.71 ppm for the two vinyl protons (H5, H6) of **3** were replaced by two well-separated signals, one at 6.9 ppm (doublet, 1H) and the other at 6.0 ppm (doublet of doublets, 1H). Furthermore, the signals at 4.34 (s, 1H) and 3.99 (t, 1H) ppm due to the bridgehead protons (H1 and H4, respectively) of **3** were replaced by signals at 4.24 (dd, 1H) and 4.06 (d, 1H) ppm in the new product. Unequivocal assignment of structure **6** to the new product was obtained by single-crystal X-ray crystallography (Figure 1c).

We have found that the fastest and highest yielding method for converting **3** to **6** is contact with silica gel. Passing the [4 +2] product **3** through a column of silica

TABLE 2. Calculated Relative Energies (kcal/mol) at the B3LYP/6-31G(d) Level of Theory

Structure	Relative Energy
	0.0 (**3**, R = CF_3) 0.0 (**5**, R = CN)
	-9.0 (**6**, R = CF_3) -4.9 (**7**, R = CN)
	-18.8 (**8**, R = CF_3) -16.4 (**9**, R = CN)

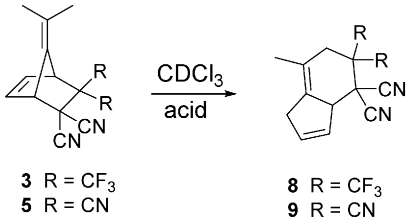
gel using ethyl acetate/hexanes as eluent gives a 90% yield of **6**. The same result was obtained on contacting solutions of **3** with acidic, neutral or basic alumina. The fused-ring cyclobutane product **6** is stable and does not revert to **3** upon heating (see the Experimental Section), nor is there any evidence for the presence of the fulvene **2** seen in solutions of purified **6**.

Rearrangement of the TCNE [4 + 2] adduct **5** to the formal [2 + 2] adduct **7** occurs in polar media but is much more sluggish than in the BTF case. For instance, treatment of **5** with silica gel under the same conditions used to convert **3** to **6** gave only 25% yield of material that was a 1:1 mixture of **5** and **7**. Results from density functional theory calculations of the rearrangement products **6** and **7** are presented in Table 2. While both rearrangements reactions are exothermic, the process leading to **6** is more favorable by 4.1 kcal/mol.

It is also worth noting that solid samples of **3** undergo clean conversion to **6** after standing at room temperature for as little as a few days, with or without exposure to ambient light. The solid state rearrangement of the microcrystalline precipitate from the reaction of BTF with **2** was verified by powder diffraction studies. By containing a single crystal of **3** in a sealed glass capillary, the formation of crystals of **6** was observed to occur adjacent to the original crystal of **3**. Photographic images of the crystal-to-crystal transformation are included in the Supporting Information.

Alternative Diels−Alder Reaction. In the presence of certain acids, a different pathway becomes available to the [4 + 2] cycloadduct **3**. While **3** is stable for extended periods in chloroform, exposure to strong protic acids (hydrochloric acid, trifluoroacetic acid, and *p*-toluenesulfonic acid) results in conversion to an entirely new product (Scheme 3). In chloroform solution containing either excess or substoichiometric amounts of these acids, all peaks in the ^{1}H NMR spectrum of **3** (including those of equilibrium partner **2**) disappear and are replaced cleanly by an isomeric structure that is distinct from the formal [2 + 2] cycloadduct **6**. Acetic acid was not effective in promoting the conversion. Conversion of **3** to the new product is best achieved in 18 h by use of 20 mol % of *p*-toluenesulfonic acid. Single-crystal X-ray crystallography of the new product established the unexpected structure **8** shown in Figure 1d.

SCHEME 3. Acid-Catalyzed Conversion of Norbornenes 3 and 5 to Tetrahydroindenes 8 and 9, Respectively[a]



[a] Conditions: see text.

Conversion of the TCNE Diels−Alder adduct **5** to an analogous cycloadduct **9** (Scheme 3) proceeds more slowly than in the BTF case. No reaction occurs between **5** and *p*-toluenesulfonic acid in chloroform at room temperature, but after 1 h at reflux clean conversion to **9** was obtained. This compound has been reported previously by isolation from a mixture obtained by TCNE trapping of mixed isomers resulting from kinetic protonation of the carbanion of **2**.[14c]

The calculated relative energies of these unexpected cycloadducts (**8** and **9**) were considerably lower than those of the corresponding fulvene cycloaddition products (**3** and **5**) and are reported in Table 2.

Given the necessity of acid catalysis to effect the conversion of **3** to fused bicycle **8**, the likely mechanism of the reaction involves the intermediacy of 1-isopropenyl-1,3-cyclopentadiene (see the Discussion). To gain a better understanding of the regiochemical outcome of this reaction, the transition state for the Diels−Alder reaction between 1-isopropenyl-1,3-cyclopentadiene (Chart 1) and BTF (**1**) was located using a hybrid density functional theory method at the B3LYP/6-31G(d) level of theory. Two alternative Diels−Alder reaction pathways were investigated. One involves reaction with the endocyclic diene system (a) and the other involves reaction with the exocyclic double bond and the adjacent ring double bond (b). The calculated structures and relative energies of the transition states are shown in Figure 3. According to the calculations, the Diels−Alder reaction involving the exocyclic double bond is favored by about 13.7 kcal/mol. The calculated preference for the transition state leading

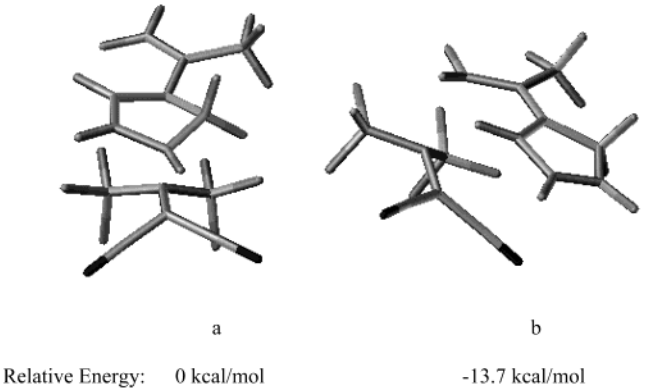
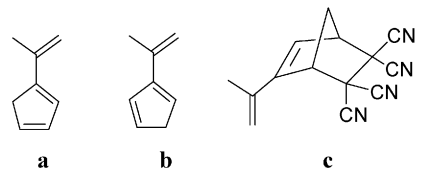


FIGURE 3. Transition states and relative energies for the reaction of the endocyclic (a) and exocyclic (b) diene system of 1-isopropenyl-1,3-cyclopentadiene with BTF (**1**).

CHART 1. Structures of 6,6-Dimethylfulvene Tautomers (a) 1-Isopropenyl-1,3-cyclopentadiene, (b) 2-Isopropenyl-1,3-cyclopentadiene, and TCNE Adduct (c) 2-Isopropenyl-5,5,6,6-tetracyanonorbornene



to the tetrahydroindene ring system is consistent with the observed formation of **8** as the sole product.

Discussion

The reaction of 6,6-dimethylfulvene with BTF and TCNE to give the [4 + 2] cycloadducts **3** and **5**, respectively, is expected on the basis of frontier molecular orbital theory[19] which predicts the dominant interactions in this reaction to be between the HOMO of the fulvene and the LUMO of the olefins.[20] In certain solvents, these products exist in equilibrium with their respective starting materials. The reversibility of Diels−Alder reactions of fulvenes was established by Kohler,[21] who observed that in dilute solution the cycloadducts with maleic anhydride dissociate almost completely. We observed a strong solvent dependence for the reaction of BTF (**1**) with fulvene **2**. While the forward reaction occurs readily in nonpolar solvents to give Diels−Alder product **3**, no reaction occurs in solvents of intermediate to high polarity.

The crystal structure of **3** reveals some striking features. The one-atom bridge (C7) forms a 95° angle with the bridgehead carbons (C1 and C4). The strain energy that accompanies this very acute angle may account for the instability of this structure. The slightly elongated single bonds (1.59−1.60 Å) between the bridgehead carbons and the trifluoromethyl- and cyano-bearing carbons (C3 and C2, respectively) in **3** may be further manifestations of this strain. The bond angles and lengths in the TCNE cycloadduct **5** show the same trends as in the BTF cycloadduct **3**.

Despite this structural similarity, the TCNE cycloadduct **5** is more stable than the BTF adduct **3** in all solvents studied. For instance, in chloroform solution BTF adduct **3** shows appreciable dissociation, whereas the TCNE adduct **5** has an equilibrium constant for association of 32×10^3 M^{-1} in the same solvent.[14a] Also, **5** exists in a stable equilibrium with **2** in acetone while **3** undergoes cycloreversion to **2** in less than 2 days.

To gain insight into the reaction of the cyanoolefins **1** and **4** with the fulvene **2**, quantum mechanics calculations were carried out. The mechanism of Diels−Alder reactions has been intensively investigated by computational methods.[15] The hybrid density functional theory with the 6-31G(d) basis set (B3LYP/6-31G(d) level of theory) has been demonstrated to be an effective method in dealing with the Diels−Alder reaction.[16] The B3LYP/6-31G(d) method also gives reasonable activation barrier for the Diels−Alder reaction of cyclopentadiene with 1,1-dicyanoethylene.[17] The retro-Diels−Alder reaction of isopropylidenenorbornene was recently studied by the B3LYP/6-31G(d) method: the computational results, in conjunction with experimental observation of stereospecificity, support a synchronous concerted mechanism.[18]

From the theoretical calculations, the most interesting feature of the potential energy surfaces (Figure 2) is the existence of relatively deep minima attributable to π-complexes. The π-complex formed between TCNE and fulvene is more stable than that of BTF and fulvene, which is consistent with the trend reported for the π-complexes of TCNE and BTF with aromatic π-bases.[5,7]

As expected, the intermolecular distance in the π-complex of BTF and fulvene is longer than that in the complex of TCNE and fulvene (3.3−3.4 versus 3.2 Å). The relative orientation of the BTF and TCNE to fulvene in these π-complexes suggests that the dominant interactions in these complexes to be between the HOMO of fulvene and the LUMO of the BTF and TCNE.

The results from density functional theory treatment of the reactions between fulvene **2** and ethylene, TCNE (**4**) and BTF (**1**) show strong contrast between the transition state for the first two dienophiles and that of the more polarizable perfluoroalkylcyanoolefin. The geometrical parameters from the calculated transition states are given in Table 1. The reaction of fulvene **2** with TCNE is concerted in the gas phase, and the two developing C−C bonds in the transition state are around 2.11 Å. In the reaction with BTF, the calculated transition-state bond lengths differ by 0.75 Å and the angles around the dienophilic carbon atoms differ by 22 degrees. Compared to the TCNE reaction, the developing bond between the diene carbon atom and the *gem*-bis(trifluoromethyl)-substituted carbon atom of BTF is shorter still by another 0.2 Å while the *gem*-dicyano-substituted carbon atom is barely distorted from planarity. This evidence indicates that fulvene **2** and BTF combine in a highly asynchronous Diels−Alder reaction. Similar findings have recently been reported for other polar asymmetrical Diels−Alder reac-

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[19] Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: London, 1976.

[20] Houk, K. N.; George, J. K.; Duke, R. E., Jr. *Tetrahedron* **1974**, *30* (4), 523−533.

[21] Kohler, E. P.; Kable, J. *J. Am. Chem. Soc.* **1935**, *57* (5), 917−918.

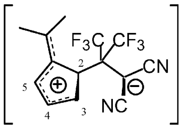

FIGURE 4. Proposed zwitterionic intermediate in the conversion of norbornene **3** to bicyclo[3.2.0]heptene **6**.

tions.[17,22] The calculated structures for the products are in good agreement with the X-ray crystal structures, with the calculated C1−C2 and C3−C4 distances (1.627 and 1.596 Å, respectively) being slightly longer than the experimentally determined distances for **3**.

In competition with the equilibrium between the bridged bicyclic product **3** and the starting materials **1** and **2** is the conversion to the isomeric ring-fused cyclobutane **6**. The rate and extent of the conversion of **3** to **6** depends on the polarity of the medium. Empirical measurements of solvent polarity such as E_T have provided valuable insights into the mechanisms of medium-dependent organic reactions.[23] None of the rearrangement product **6** is formed in less polar solvents such as toluene (E_T 33.9), benzene (E_T 34.5), and chloroform (E_T 39.1). In acetone (E_T 42.2) the bridged bicycle **3** simply undergoes an irreversible retro-Diels−Alder reaction. The rearrangement product **6** is finally formed in polar solvents DMSO (E_T 45.0) and acetonitrile (E_T 46.0), although the process is complicated by competing retro-Diels−Alder reaction of **3**. These observations, combined with the excellent conversion of **3** to **6** in the presence of silica gel and alumina, point to the importance of polarity of the medium and therefore suggest a dipolar mechanism.

Two earlier mechanistic studies of the reactions of fulvenes with electron-deficient olefins provide precedent for the BTF reaction. The weak effect of solvent polarity on the rate of reaction of 4-methyl-1,2,4-triazoline-3,5-dione with 6,6-diphenylfulvene led Olsen to conclude that the intermediate species was likely a resonance hybrid having both zwitterionic and diradical character.[24] Support for a zwitterionic mechanism comes from the laboratory of Laszlo where a strong dependence of reaction rate on solvent dielectric was observed in the fascinating cascade reaction between 6,6-dicyclopropylfulvene and TCNE.[25]

We favor a zwitterionic intermediate of the form depicted in Figure 4 in which the two ends of the dipole are highly stabilized through charge delocalization. Huisgen has presented strong evidence for analogous dipolar intermediates in the reaction of BTF with enol ethers.[8b,9]

We also used theoretical methods to examine the zwitterionic intermediate in solution. The Onsager solvation model[26] was used and the dielectric constant used is that of DMSO (ca. 46.7). The calculated structure at the HF/6-31G(d) level using the Onsager solvation model is consistent with the proposed zwitteronic intermediate.

Unimolecular solid-state organic reactions are rare.[27] X-ray crystallographic analysis of single crystals of the reaction components in a solid-state transformation can yield valuable insight into the extent that the required atomic motions force deformation in the reaction cavity.[28] Single crystal-to-single-crystal reactions are referred to as topotactic when at least one crystallographic axis is maintained between the starting material and the product.[27f] Sublimation of the crystalline material in the capillary tube experiment prevents us from determining any such details about the physical rearrangement of the solid. Comparison of the crystal packing in structures **3** and **6** did not reveal structural similarities. Because pure, intact crystals of **3** can also be grown by sublimation of the microcrystalline precipitate from the Diels−Alder reaction, we do not believe that the rearrangement of **3** to **6** is occurring during the sublimation process in the capillary. Rather, we propose that a solid-state transformation of **3** to **6** at the surface of the crystal is accompanied by deterioration of the reactant lattice thereby allowing the newly formed product **6** to sublime and reform adjacent to the original crystal. To the best of our knowledge, this reaction is the first example of a dipolar rearrangement occurring in the solid state. In the mid-1980s, magic angle spinning ^{13}C NMR studies proved that the degenerate Cope rearrangements of the well-studied bullvalene system occur in the crystalline state.[29]

The structure of the tetrahydroindene products **8** and **9** and the conditions under which they are formed suggest that an alternative [4 + 2] cycloaddition manifold is available when the fulvene **2** undergoes acid-catalyzed isomerization. Under neutral conditions, the 1- and 2-isopropenyl-1,3-cyclopentadiene tautomers (Chart 1) are very minor contributors and 6,6-dimethylfulvene (**2**) accounts for 98% of the equilibrium mixture.[30] At elevated temperatures, tetra- and pentamethylene fulvene have been shown to undergo isomerization.[31] In strong acid, fulvenes protonate at 2-position[32] and tautomerization then leads to the isomeric triene intermediate 1-isopropenyl-1,3-cyclopentadiene, shown in Scheme 4.

The acid-catalyzed isomerization of cross-conjugated **2** to give the fully conjugated 1-isopropenyl-1,3-cyclopentadiene has been reported by Oku and co-workers.[33] Reaction of 2-acetyloxy-2-propenenitrile (**10**) with **2** gave **11** (Scheme 5) as the minor component in a mixture with the normal [4 + 2] cycloadduct (**12**). In this case the captodative cyanoolefin[34] behaves as would be expected

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[22] Garcia, J. I.; Martinez-Merino, V.; Mayoral, J. A.; Salvatella, L. *J. Am. Chem. Soc.* **1998**, *120* (10), 2415−2420.

[23] (a) Reichardt, C., Ed.; *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; VCH Verlagsgesellschaft: Weinheim, Fed. Rep. Ger, 1988. (b) Reichardt, C. *Angew. Chem.* **1979**, *91* (2), 119−131.

[24] Olsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21* (5), 383−384.

[25] Cornelis, A.; Laszlo, P. *J. Am. Chem. Soc.* **1975**, *97* (1), 244−245.

[26] Onsager, L. *J. Am. Chem. Soc.* **1936**, *58*, 1486-1493.

[27] (a) Desiraju, G. R.; Goud, B. S. In *React. Solids: Past, Present Future*; Boldyrev, V. V., Ed.; Blackwell, Oxford, U.K., 1996; pp 223−236. (b) Toda, F. In *Reactivity in Molecular Crystals*; Ohashi, Y., Ed.; VCH Publishers: Weinheim, 1993; pp 177−201. (c) Curtin, D. Y.; Paul, I. C. *Chem. Rev.* **1981**, *81* (6), 525−541. (d) Curtin, D. Y.; Paul, I. C.; Duesler, E. N.; Lewis, T. W.; Mann, B. J.; Shiau, W.-I. *Mol. Cryst. Liq. Cryst.* **1979**, *50* (1−4), 25−41. (e) Paul, I. C.; Curtin, D. Y. *Accounts Chem. Res.* **1973**, *6* (7), 217−225. (f) Keating, A. E.; Garcia-Garibay, M. A. *Mol. Supramol. Photochem.* **1998**, *2* (Organic and Inorganic Photochemistry), 195−248.

[28] Kim, J. H.; Hubig, S. M.; Lindeman, S. V.; Kochi, J. K. *J. Am. Chem. Soc.* **2001**, *123* (1), 87−95.

[29] Meier, B. H.; Earl, W. L. *J. Am. Chem. Soc.* **1985**, *107* (19), 5553−5555.

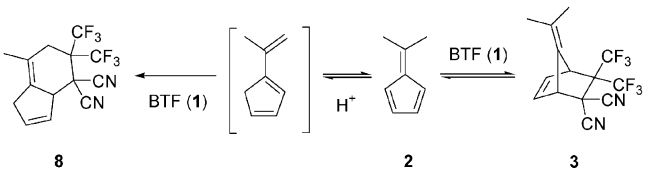
[30] Knox, G. R.; Pauson, P. L. *J. Chem. Soc.* **1961**, 4610−4615.

[31] Nair, V.; Kumar, S. *Tetrahedron* **1996**, *52*, 4029−4040.

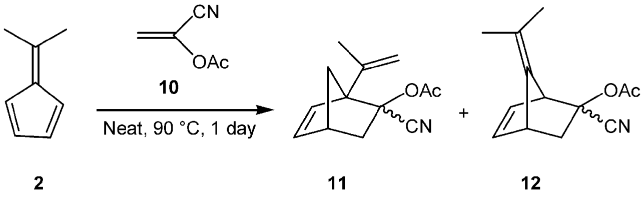
[32] Olah, G. A.; Reddy, P. V.; Prakash, G. K. S. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; John Wiley & Sons Ltd.: Chichester, U.K., 1995; Vol. 2, pp 813−859.

[33] Oku, A.; Nozaki, Y.; Hasegawa, H.; Nishimura, J.; Harada, T. *J. Org. Chem.* **1983**, *48* (23), 4374−4377.

SCHEME 4. Proposed Mechanism for the Acid-Catalyzed Conversion of Norbornene 3 to Tetrahydroindene 8 in Chloroform Solution



SCHEME 5. Reaction of 6,6-Dimethylfulvene (2) with 2-Acetyloxy-2-propenenitrile[33] [a]



[a] Formation of the minor product (**11**) is suppressed by addition of pyridine to the reaction mixture.

for a normal, less reactive dienophile and adds to the inner-ring diene system of 1-isopropenyl-1,3-cyclopentadiene to give **11** in what is most likely a synchronous cycloaddition.

The regioselectivity of the cycloaddition leading to **11** can be qualitatively explained by the fact that cyclopentadiene is a better dienophile than 1,3-butadiene. For instance, the experimentally measured activation energy for the reaction between cyclopentadiene and ethylene is about 5 kcal/mol lower than that of 1,3-butadiene (22.5 vs 27.5 kcal/mol).[35] Thus, reaction of **11** with 1-isopropenyl-1,3-cyclopentadiene occurs at the cyclopentadiene moiety. However, the reaction of the tetrasubstituted cyanoolefin BTF is sterically more demanding. Therefore, cycloaddition of BTF (**1**) occurs at the less crowded exocyclic diene moiety.

The formation of the tetrahydroindene **8** is itself a regiospecific process: the BTF adds so as to minimize steric interactions between the CF_3 groups and the bridgehead methine (H3a). The high conformational demand of the trifluoromethyl groups (A value = 2.4−2.5 kcal/mol) relative to the cyano groups (0.2 kcal/mol) is most likely the determining factor.[36] The same sense of regiochemistry is observed in the [4 + 2] product from the reaction of BTF with styrenes.[37] The preference for orienting the cyano-bearing end of BTF toward the more crowded end of the diene system is also operative in linear dienes as well: see, for example, the case of 2,4-dimethyl-1,3-pentadiene, which reacts with BTF to give the product cyclohexene regioisomer in which the carbon bearing the cyano groups is attached to the carbon bearing the *gem*-dimethyl groups.[10]

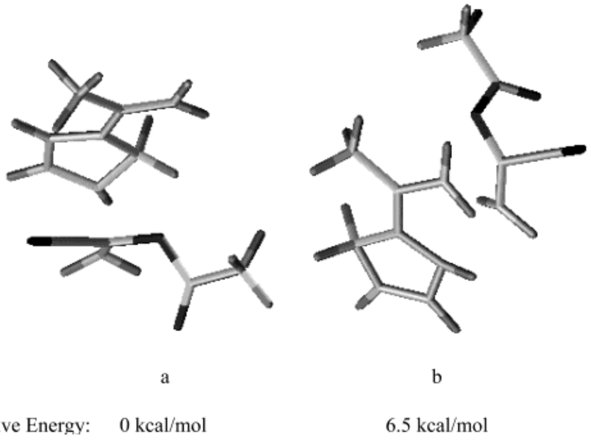


FIGURE 5. Transition states and relative energies for the reaction of the endocyclic (a) and exocyclic (b) diene system of 1-isopropenyl-1,3-cyclopentadiene with 2-acetyloxy-2-propenenitrile (**10**).

Our acid-catalyzed conversion of the TCNE cycloadduct **5** to the indene product **9**, while slower than the analogous reaction in the BTF series, provides clean access to a product that was previously only obtained as a mixture with two other isomeric structures. In addition to a 66% yield of **9** and a 10% yield of **5** from the TCNE reaction with the resulting C_8H_{10} triene isomer mixture obtained upon kinetic protonation of the carbanion of 6,6-dimethylfulvene, a 25% yield of 2-isopropenyl-5,5,6,6-tetracyanonorbornene (Chart 1) was also reported.[14c] Although the authors of the study made no comment on the matter, it is interesting that their results show that TCNE adds to the endocyclic diene system of 2-isopropenyl-1,3-cyclopentadiene to give 2-isopropenyl-5,5,6,6-tetracyanonorbornene, while adding to the opposite diene system in 1-isopropenyl-1,3-cyclopentadiene to give **9**. These results are consistent with our explanation based on dienophile structure (above) and also confirm that the greater steric hindrance of 1-isopropenyl-1,3- cyclopentadiene relative to 2-isopropenyl-1,3-cyclopentadiene prevents access to the normally more reactive endocyclic diene system by these two tetrasubstituted cyanoolefins.

The two cyanoolefins, BTF (**1**) and 2-acetyloxy-2-propenenitrile (**10**), add with opposite regiospecificities to the same diene, 1-isopopenyl-1,3-cyclopentadiene. To examine the transition state of the latter reaction, we again turned to hybrid density functional theory at the B3LYP/6-31G(d) level of theory. The same two alternative Diels−Alder pathways as in the BTF reaction were investigated, one involving reaction with the endocyclic diene system and the other involving reaction with the exocyclic double bond and the adjacent ring double bond. The calculated structures and relative energies of the transition states for the 2-acetyloxy-2-propenenitrile reaction are shown in Figure 5. According to our calculations, addition of **10** to the endocyclic diene system of 1-isopropenyl-1,3-cyclopentadiene is favored by 6.5 kcal/mol. Thus, the density functional theory predictions for both reactions are consistent with experimental observations.

The calculations suggest that both orientations of the 2-acetyloxy-2-propenenitrile transition state (Figure 5) are relatively late compared to the corresponding BTF

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(34) (a) Viehe, H. G.; Janousek, Z.; Merenyi, R.; Stella, L. *Acc. Chem. Res.* **1985**, *18* (5), 148−154. (b) Viehe, H. G.; Merenyi, R.; Stella, L.; Janousek, Z. *Angew. Chem.* **1979**, *91* (12), 982−997.

(35) (a) Walsh, R.; Wells, J. M. *J. Chem. Soc., Perkin Trans. 2* **1976** (1), 52−55. (b) Rowley, D.; Steiner, H. *Discuss. Faraday Soc.* **1951**, *10*, 198−213.

(36) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; John Wiley & Sons: New York, 1994.

(37) Brückner, R.; Huisgen, R.; Schmid, J. *Tetrahedron Lett.* **1990**, *31* (49), 7129−7132.

transition states (Figure 3). The two forming C−C bonds are 2.742 (for the bond forming to C2 of **10**) and 1.965 Å (for the bond forming to C1 of **10**) in Figure 5a and 2.143 (for the bond forming to C1 of **10**) and 2.349 Å (for the bond forming to C2 of **10**) in Figure 5b. Similarly, the two forming C−C bonds are 2.359 (for the bond forming to C2 of BTF) and 2.098 Å (for the bond forming to C1 of BTF) in Figure 3a and 2.988 (for the bond forming to C1 of BTF) and 2.122 Å (for the bond forming to C2 of BTF) in Figure 3b.

Conclusions

The perfluoroalkyldicyanoolefin BTF (**1**) reacts rapidly with 6,6-dimethylfulvene (**2**) to give the [4 + 2] cycloaddition product **3**. The cycloadduct exists in equilibrium with the starting materials in certain solvents. Density functional theory calculations of the Diels−Alder reaction suggest an asynchronous process with much greater formation of C3−C4 than C1−C2 in the transition state leading to **3**.

While the BTF adduct **3** exists in a stable equilibrium with its precursors in less-polar solvents, it converts to the formal [2+2] adduct **6** in certain polar solvents and on contact with silica gel or alumina. Although a mechanism involving a radical species cannot be unequivocally ruled out based on the evidence at hand, the necessity of a polar medium to effect the conversion of the bridged bicycle **3** to the fused-ring cyclobutane system of **6** suggests a zwitterionic intermediate stabilized by delocalization of the positive charge over the pentadiene system of the fulvene ring and the negative charge over the geminal-dicyano moiety. The rearrangement of **3** to **6** also occurs upon standing at room temperature in the absence of solvent. An experiment designed to determine whether this transformation is topotactic was complicated by the fact that the two compounds could not be observed as a solid solution.

In the presence of acid, an entirely different reaction manifold becomes available to the kinetic product **3**. The BTF present in the equilibrium mixture reacts with the fulvene isomer, 1-isopropenyl-1,3-cyclopentadiene, to give the indene **8**. The process by which **8** is formed is regiospecific in two senses. First, given the choice between the diene system consisting of the two double bonds in the cyclopentadiene ring or the diene consisting of the exocyclic double bond and the adjacent endocyclic bond, the BTF adds across the latter diene system. This regiospecificity is opposite to that seen for the captodative cyanoolefin, 2-acetyloxy-2-propenenitrile, and is predicted by density functional theory calculations. Second, BTF adds so as to give exclusively the regioisomer in which the bulky CF_3 groups are placed away from the more hindered bridgehead carbon.

The cycloaddition product **5** from the reaction of tetracyanoethylene with 6,6-dimethylfulvene undergoes the same rearrangement and alternative Diels−Alder reactions as the BTF cycloadduct **3**, albeit at slower rates. As reported in other reactions of BTF with olefinic systems, greater polarizability and the steric demand of the trifluoromethyl groups result in rate acceleration relative to TCNE. Hybrid density functional theory performed well in modeling the transition states and predicting the relative energies of the products.

Experimental Section

General Methods. Melting points were in open capillaries and are uncorrected. All reactions were carried out under an atmosphere of dry nitrogen. Reagent grade solvents were purchased from commercial sources and used as received. 6,6-Dimethylfulvene was either prepared by the literature method[38] or purchased from Aldrich Chemical Co. Cyclopentadiene was obtained by cracking the dimer according to the literature procedure.[39] TCNE (Aldrich) was recrystallized from 1,2-dichloroethane. Reactions were monitored by thin-layer chromatography (TLC) using glass-backed silica gel TLC plates. Visualization was done with iodine vapor and/or staining with phosphomolybdic acid (PMA, 5% solution in ethanol) followed by heating. Concentrations were performed by rotary evaporation using water aspirator vacuum. Low-pressure chromatography (LPC) was carried out by applying air pressure to Pyrex columns packed with EM Science silica gel 60 (0.040−0.063 mm particle size, 230−400 mesh). Routine ^{1}H NMR spectra were recorded at 500 MHz. Broad-band ^{1}H decoupled ^{13}C NMR spectra were recorded at 125 MHz. ^{19}F NMR spectra were recorded at 377 MHz. ^{1}H chemical shifts are reported in ppm downfield from internal tetramethylsilane. ^{13}C chemical shifts are reported in ppm relative to $CDCl_3$ (77.0 ppm). Freon-11 was used as an internal standard for ^{19}F spectra. Significant ^{1}H NMR data are tabulated in order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; dist., distorted; br, broad), number of protons, coupling constant(s) in hertz (Hz), assignment.

X-ray Diffraction Studies (Structures). All of the crystal structure data were collected using a Rigaku RU300 diffractometer (Mo Kα radiation) equipped with a Raxis-II image plate detector and MSC low-temperature unit. No absorption corrections were applied. A total of 180° of ω-scans were performed for each compound with a crystal-to-plate distance of 85 mm. The structures were solved by direct methods (MULTAN or teXsan)[40] and the final refinement was done using the Z-refinement package.[40] Refinement by full-matrix least squares on F with the R-indices defined as $R1 = \Sigma(||F_o| - |F_c||)/\Sigma|F_o|$ and $Rw = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2}$ with w proportional to $[\sigma^2(I) + 0.0009I^2]^{-1/2}$. For the final refinements, the hydrogen atoms were idealized close to the previously refined positions. Atomic scattering factors were taken from the *International Tables for X-ray Crystallography*, Vol. IV.

Theoretical Procedures. All calculations were carried out using either the Gaussian 94 or 98 programs.[42] Geometry optimization and transition state search were carried out using the B3LYP hybrid density functional theory method[43] with the 6-31G(d) basis set. Frequency calculations were carried out to characterize the Diels−Alder transition states.

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[38] Stone, K. J.; Little, R. D. *J. Org. Chem.* **1984**, *49* (11), 1849−1853.

[39] Korach, M.; Nielsen, D. R.; Rideout, W. H. Dihydroxycyclopentene. In *Organic Syntheses*; Baumgarten, H. E., Ed.; John Wiley and Sons: New York, 1973; Collect. Vol. V, pp 414−418.

[40] *TeXsan Structure Solution Software*; Molecular Structure Corp.: 1985, 1992.

[41] Calabrese, J. C. *Z Structure Solution Software*; E. I. DuPont de Nemours & Co.: Wilmington, Delaware, 1994.

[42] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; J. A. Montgomery, J.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; J. Tomasi; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian*, Revision A.5; Gaussian, Inc.: Pittsburgh, PA, 1998.

[43] (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98* (7), 5648−5652. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B: Condens. Matter* **1988**, *37* (2), 785−789.

7-(1-Methylethylidene)-3,3-bis(trifluoromethyl)bicyclo[2.2.1]hept-5-ene-2,2-dicarbonitrile (3). 2,2-Bis(trifluoromethyl)-1,1-dicyanoethylene[5] (**1**; 1.88 g, 8.78 mmol) was added dropwise via syringe over 1 min to a magnetically stirred solution of 6,6-dimethylfulvene (**2**; 1.0 g, 9.4 mmol) in hexanes (10 mL) at room temperature. As each drop was added a bright red color was noted, which then quickly dissipated. A white precipitate began to form before the addition was complete. After 10 min the reaction mixture was filtered. The collected precipitate was washed with hexanes and pumped under high vacuum. Yield: 2.0 g (71%). Mp: 104−105 °C. IR (KBr press): 2249 (w), 1274 (s), 1245 (m), 1233 (m), 1206 (s) cm^{-1}. The ^{1}H NMR spectrum of this product in CDCl$_3$ indicated it to be a mixture of the desired bicycle (**3**) and 6,6-dimethylfulvene (**2**) in a ratio of 91:9, respectively. The NMR spectroscopic data for **3** only are reported here. ^{1}H NMR (500 MHz, CDCl$_3$) δ: 1.63 (s, 3H, CH$_3$), 1.73 (s, 3H, CH$_3$), 3.99 (t, $J = 2.3$ Hz, 1H, H4), 4.34 (s, 1H, H1), 6.63−6.68 (m, 1H, H5), 6.68−6.71 (m, 1H, H6). ^{13}C NMR (125 MHz, CDCl$_3$) δ: 19.71 (CH$_3$), 20.01 (CH$_3$), 38.75 (C2), 48.08 (C4 or C1), 57.75 (C1 or C4), 66.91 (septet, $J = 24$ Hz, C3), 111.74 (CN), 112.42 (CN), 121.45 (C1′), 122.23 (q, $J = 288$ Hz, CF$_3$), 122.71 (q, $J = 288$ Hz, CF$_3$), 135.82 (C5), 137.67 (C7), 139.35 (C6). ^{19}F NMR (377 MHz, CDCl$_3$) δ: −63.69 (q, $J = 13$ Hz, 3F), −58.36 (q, $J = 13$ Hz, 3F). MS (APCI, negative ion): m/z 320 (M$^+$), 273, 214. Anal. Calcd for $C_{14}H_{10}N_2F_6$: C, 52.51; H, 3.15; N, 8.75; F, 35.60. Found: C, 52.65; H, 3.01; N, 8.76; F, 35.67.

The product was crystallized from Et$_2$O/petroleum ether at 0 °C to give X-ray quality crystals. X-ray data for $C_{14}H_{10}N_2F_6$ (**3**) were collected at −50 °C using a colorless crystal with dimensions of ∼ 0.25 × 0.35 × 0.40 mm. A total of 6239 reflections were collected and merged using Z[41] ($R_m = 0.021$) to yield 2974 unique reflections with $I > \sigma 3(I)$. All of the observed data were used to calculate the triclinic cell parameters: $a = 12.442(1)$ Å, $b = 12.661(1)$ Å, $c = 8.621(1)$ Å, $\alpha = 90.118(6)°$, $\beta = 99.075(5)°$, and $\gamma = 94.220(3)°$. For $Z = 4$, the calculated density is 1.592 g/mL and μ(Mo) = 1.47 cm^{-1}. The full-matrix least squares refinement of 397 parameters in space group P-1 (no. 2) converged at R1 = 0.040, Rw = 0.044 with the goodness of fit = 1.58. The data/parameter ratio was 7.41. An ORTEP diagram is shown in Figure 1a with thermal ellipsoids drawn to the 50% probability level.

X-ray quality crystals of **3** could also be obtained by water-cooled, coldfinger sublimation of the microcrystalline precipitate from the Diels−Alder reaction at 0.06 mmHg vacuum with heating to 35 °C in an oil bath.

7-(1-Methylethylidene)bicyclo[2.2.1]hept-5-ene-2,2,3,3-tetracarbonitrile (5).[14] A solution of TCNE (1.48 g, 11.6 mmol) in acetone (15 mL) was added dropwise over 10 min to a solution of **2** (1.34 g, 12. 6 mmol, 109 mol %) in acetone (20 mL) at −60 °C. A white precipitate formed in approximately 5 min. The reaction mixture was allowed warm to room temperature over 4 h. The clear, colorless solution was cooled to −30 °C, and the resulting precipitate was collected by filtration and washed with hexanes. The analytically pure white solid (1.95 g, 72%) thus obtained had spectroscopic data identical to those previously reported for bicycle **5**. Mp: 137−9 °C dec (lit.[14a] mp 138−9 °C). IR (KBr press): 2252 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$) δ: 1.82 (s, 6H), 4.45 (t, 2H, $J = 2.0$ Hz, H1/H4), 6.77 (t, 2H, $J = 2.0$ Hz, H5/H6). ^{13}C NMR (125 MHz, CDCl$_3$) δ: 20.08 (CH$_3$), 46.07 (C2/C3), 55.11 (C1/C4), 110.81 (CN), 111.41 (CN), 127.37 (C1′ or C7), 135.46 (C7 or C1′), 137.98 (C5/C6). MS (APCI, negative ion): m/z 234 (M$^{\bullet}$), 128. Anal. Calcd for $C_{14}H_{10}N_4$: C, 71.78; H, 4.30; N, 23.92. Found: C, 71.87; H, 4.34; N, 24.05.

X-ray quality crystals of **5** were grown by slow diffusion of hexanes into an ethyl acetate solution of the above solid at room temperature. X-ray data for $C_{14}H_{10}N_4$ (**5**) were collected at −100 °C using a colorless crystal with dimensions of ∼0.26 × 0.37 × 0.40 mm. A total of 13704 reflections were collected and merged using Z[41] ($R_m = 0.020$) to yield 2838 unique reflections with $I > \sigma 3(I)$. All of the observed data were used to calculate the orthorhombic cell parameters: $a = 14.592(1)$ Å, $b = 14.909(1)$ Å, $c = 11.280(1)$ Å. For $Z = 8$, the calculated density is 1.268 g/mL and μ(Mo) = 0.75 cm^{-1}. The full-matrix least squares refinement of 325 parameters in space group $P2_12_12_1$ (no. 19) converged at R1 = 0.048, Rw = 0.051 with the goodness of fit = 2.49. The data/parameter ratio was 8.70. An ORTEP diagram is shown in Figure 1b with thermal ellipsoids drawn to the 50% probability level.

2-(1-Methylethylidene)-7,7-bis(trifluoromethyl)bicyclo[3.2.0]hept-3-ene-6,6-dicarbonitrile (**6**). Silica gel (5 g) was added to a solution of the bridged bicycle (**3**) (1.85 g, 5.78 mmol) in CH$_2$Cl$_2$ (25 mL), and the solvent was removed by rotary evaporation. The resulting powder was applied to a column containing 150 g of silica gel slurry-packed in hexanes. The column was eluted with 10% EtOAc in hexanes (2 L) to give 1.66 g (90%) of pure cyclobutane (**6**) as a white powder after evaporation of the eluent. Mp: 90−91 °C. IR (KBr press): 2253 (w), 1329 (m), 1283 (s), 1208 (s), 1197 (m) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 1.72 (s, 3H, H10), 1.88 (s, 3H, H9), 4.06 (d, $J = 8.2$ Hz, 1H, H1), 4.24 (dd, $J = 2.0, 8.2$ Hz, 1H, H5), 6.00 (dd, $J = 3, 5$ Hz, 1H, H4), 6.94 (d, $J = 5$ Hz, 1H, H3). NOE-difference experiment (400 MHz, CDCl$_3$): irradiation of the singlet at δ 1.88 caused enhancement of the doublet at δ 6.94 (H3), irradiation of the singlet at δ 1.72 caused enhancement of the doublet at δ 4.06 (H1). ^{13}C NMR (100 MHz, CDCl$_3$, peak assignments based on HETCOR experiments) δ: 21.22 (C2′), 21.87 (C3′), 34.11 (C6), 39.88 (C1), 51.51 (C5), 58.72 (septet, $J = 26.9$ Hz, C7), 109.76 (CN), 111.51 (CN), 120.95 (q, $J = 285$ Hz, CF$_3$), 122.64 (q, $J = 285$ Hz, CF$_3$), 126.03 (C4), 132.92 (C2), 133.78 (C1′), 140.79 (C3). ^{19}F NMR (377 MHz, CDCl$_3$) δ: −69.40 (q, $J = 10.7$ Hz, 3F), −64.46 (q, $J = 10.7$ Hz, 3F). MS (APCI, negative ion): m/z 320 (M$^+$), 293, 214. Anal. Calcd for $C_{14}H_{10}N_2F_6$: C, 52.51; H, 3.15; N, 8.75; F, 35.60. Found: C, 52.32; H, 3.38; N, 8.69; F, 35.51.

A small sample of the product was crystallized from Et$_2$O/petroleum ether to give X-ray quality crystals. X-ray data for $C_{14}H_{10}N_2F_6$ (**6**) were collected at −52 °C using a colorless crystal with dimensions of ∼0.35 × 0.15 × 1.10 mm. A total of 3127 reflections were collected and merged using Z[41] ($R_m = 0.039$) to yield 1090 unique reflections with $I > \sigma 3(I)$. All of the observed data were used to calculate the triclinic cell parameters: $a = 9.357(3)$ Å, $b = 12.235(4)$ Å, $c = 6.691(2)$ Å, $\alpha = 99.86(6)°$, $\beta = 109.11(2)°$, and $\gamma = 85.38(3)°$. For $Z = 2$, the calculated density is 1.492 g/mL and μ(Mo) = 1.38 cm^{-1}. The full-matrix least squares refinement of 199 parameters in space group P-1 (no. 2) converged at R1 = 0.068, Rw = 0.066 with the goodness of fit = 1.85. The data/parameter ratio was 5.43. An ORTEP diagram is shown in Figure 1c with thermal ellipsoids drawn to the 50% probability level.

X-ray Diffraction Capillary Experiment. In an attempt to determine if the transformation from **3** to **6** occurs as a topotactic rearrangement, a single crystal of **3** was mounted and sealed in a glass capillary. For this experiment, crystals were obtained by the sublimation procedure given above in the experimental procedure for **3**.

First, the cell parameters of the singular piece were quickly matched to those of **3** using a Bruker CCD system. The capillary was then stored at room temperature for 14 days when it was observed that the same crystal was reduced in size and two smaller pieces had started to form near the endpoints of the original crystal. By translating the capillary to center first the original crystal and then the smaller crystallites, the unit cell parameters for the original piece and one of the smaller pieces were determined. While the cell parameters for the larger original piece still matched those of **3**, the smaller subset of reflections from the newly sublimed crystals matched the cell parameters of **6**. After 6 weeks of storage at room temperature, the transformation was observed to be complete. The original crystal was gone and the two smaller crystallites had grown in size. The unit cell parameters of both the two individual crystals were matched to **6**.

Stability Test of Cyclobutane (6). The bicyclic cyclobutane product **6** (12 mg) was placed in a 5 mm NMR tube and dissolved in 0.6 mL of DMSO-d_6. The ^{1}H NMR spectrum at room temperature showed only the cyclobutane product **6** with no detectable fulvene present. ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.66 (s, 3H), 1.85 (s, 3H), 4.28 (d, 1H, $J = 8.2$ Hz), 4.48 (br d, 1H, $J = 8.1$ Hz), 6.12 (dd, 1H, $J = 3.1$, 5.4 Hz), 7.06 (d, 1H, $J = 5.6$ Hz).

The tube was immersed in an oil bath at 100 °C for 15 min and then cooled to room temperature. The ^{1}H NMR spectrum was recorded and showed a mixture of cyclobutane **6** and 6,6-dimethylfulvene (**2**) in a ratio of 73:27, respectively (based on integration of the proton signals in the vinyl region of the spectrum). The NMR tube was then immersed in an oil bath at 120 °C for 20 min and then cooled to room temperature. The ^{1}H NMR spectrum was recorded and showed a mixture of cyclobutane **6** and 6,6-dimethylfulvene (**2**) in a ratio of 1:1. Finally, the NMR tube was immersed in an oil bath at 140 °C for 15 min, then cooled to room temperature. The ^{1}H NMR spectrum was recorded and showed a mixture of cyclobutane **6** and 6,6-dimethylfulvene (**2**) in a ratio of 24:76, respectively. No peaks attributable to the formal [6 + 2] adduct were observed.

1,3a,5,6-Tetrahydro-7-methyl-5,5-bis(trifluoromethyl)-4*H*-indene-4,4-dicarbonitrile (8). To a solution of bridged bicycle (**3**) (1.0 g, 3.1 mmol) in $CDCl_3$ (20 mL) was added *p*-toluenesulfonic acid monohydrate (119 mg, 0.62 mmol). The mixture was stirred at room temperature for 18 h, diluted with CH_2Cl_2 (20 mL), and washed with saturated aqueous $NaHCO_3$ (2 × 20 mL). The separate aqueous layers were back-extracted with CH_2Cl_2 (20 mL), and the combined organic phase was washed with brine (30 mL), dried (Na_2SO_4), filtered, and concentrated by rotary evaporation to give 0.94 g of the desired product as a light brown semisolid. The crude product was combined with the products obtained from two earlier runs of this experiment (100 mg and 430 mg scale, respectively) and purified by LPC (eluting with 100% hexanes then 10% EtOAc in hexanes) to give 1.05 g (69%) of pure tetrahydroindene **8** as a white solid. Mp: 81−82 °C. IR (KBr press): 2256 (w), 1289 (s), 1271 (s), 1231 (s), 1221 (s), 1204 (s) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.78 (s, 3H, CH_3), 2.61, 2.66 (AB pattern, $J_{AB} = 19$ Hz, 2H, H6), 3.07, 3.23 (AB pattern, $J_{AB} = 20$ Hz, 2H, H1), 3.89 (s, 1H, H3a), 5.94−5.99 (m, 1H, H3), 6.23−6.28 (m, 1H, H2). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 18.81 (CH_3), 30.84 (C6), 36.58 (C1), 38.15 (C4), 51.41 (C3a), 56.83 (septet, $J = 25.7$ Hz, C5), 110.58 (*endo*-CN), 111.75 (*exo*-CN), 122.91 (q, $J = 288$ Hz, *exo*-CF_3), 123.23 (q, $J = 288$ Hz, *endo*-CF_3), 123.84 (C7 or C7a), 125.52 (C3), 131.25 (C7 or C7a), 136.27 (C2). ^{19}F NMR (377 MHz, $CDCl_3$) δ: −68.73 (q, $J = 11$ Hz, 3F), −66.21 (q, $J = 11$ Hz, 3F). MS (APCI, negative ion): *m/z* 320 (M^+), 291, 222, 214. Anal. Calcd for $C_{14}H_{10}N_2F_6$: C, 52.51; H, 3.15; N, 8.75; F, 35.60. Found: C, 52.56; H, 3.05; N, 8.78; F, 35.81.

A small sample of the product was crystallized from Et_2O/hexanes to give X-ray quality crystals. X-ray data for $C_{14}H_{10}N_2F_6$ (**8**) were collected at −100 °C using a colorless crystal with dimensions of ~0.23 × 0.24 × 0.28 mm. A total of 11050 reflections were collected and merged using Z^{41} ($R_m = 0.035$) to yield 4626 unique reflections with $I > \sigma 3(I)$. All of the observed data were used to calculate the triclinic cell parameters: $a = 12.842(1)$ Å, $b = 18.551(1)$ Å, $c = 9.302(1)$ Å, $\alpha = 98.26(1)°$, $\beta = 96.85(1)°$, and $\gamma = 71.46(1)°$. For $Z = 6$, the calculated density is 1.539 g/mL and μ(Mo) = 1.42 cm^{-1}. The full-matrix least squares refinement of 715 parameters in space group *P*-1 (no. 2) converged at R1 = 0.036, Rw = 0.039 with the goodness of fit = 1.90. The data/parameter ratio was 6.43. An ORTEP diagram is shown in Figure 1d with thermal ellipsoids drawn to the 50% probability level.

Treatment of **3** with acetic acid (200 mol %) in $CDCl_3$ did not produce any detectable amount of **8** after 9 d at room temperature. Treatment of **3** with trifluoroacetic acid (200 mol % or 40 mol %) in $CDCl_3$ for 16 h at room temperature gave a mixture of **8** and **6** in a ratio of 78:22, respectively.

3a,6-Dihydro-7-methyl-1*H*-indene-4,4,5,5-tetracarbonitrile (9).[14c] To a solution of bridged bicycle **5** (300 mg, 1.3 mmol) in $CDCl_3$ (15 mL) was added *p*-toluenesulfonic acid monohydrate (49 mg, 0.26 mmol). The mixture was heated at reflux for 1 h, diluted with CH_2Cl_2 (25 mL), and washed with saturated aqueous $NaHCO_3$ (2 × 20 mL). The combined organic phase was washed, dried (Na_2SO_4), filtered, and concentrated by rotary evaporation to give 0.27 g of the desired product as a brown oil. The crude product was purified by LPC (eluting with 100% hexanes then 10% EtOAc in hexanes) to give 170 mg (56%) of pure **9** as a white solid: mp 97−8 °C (lit.[14c] mp 92−3 °C). IR (KBr press): 2255 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.80 (s, 3H), 3.07, 3.30 (AB pattern, $J_{AB} = 18$ Hz, 2H, H1), 3.13−3.22 (m, 2H, H6), 4.08 (s, 1H, H3a), 5.98−6.02 (m, 1H, H3), 6.31−6.35 (m, 1H, H2). ^{13}C NMR (125 MHz, $CDCl_3$, APT pulse sequence with C and CH_2 indicated by (+) and CH and CH_3 by (−)) δ: 18.37 (CH_3), 36.67 (+), 38.00 (+), 38.74 (+), 41.55 (+), 50.52 (C3a), 108.38 (+), 110.92 (+), 111.03 (CN), 111.29(+), 121.39 (+), 124.57 (−), 129.89 (+), 136.66 (−). MS (APCI, negative ion): *m/z* (M^-). Anal. Calcd for $C_{14}H_{10}N_4$: C, 71.78; H, 4.30; N, 23.92. Found: C, 71.59; H, 4.30; N, 24.03.

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Supporting Information Available: Crystallographic structure determination of **3**, **5**, **6**, and **8** (CIF); calculated structures of the π-complexes of BTF and TCNE with **2**; photographs of the crystal-to-crystal conversion of **3**−**6**; numbering scheme for **3** and **5**−**9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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