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Remarkable Efficiency of the Aryne Chemistry of (Dehydro)octafluoro[2.2]paracyclophane When Using the Cadogan Method

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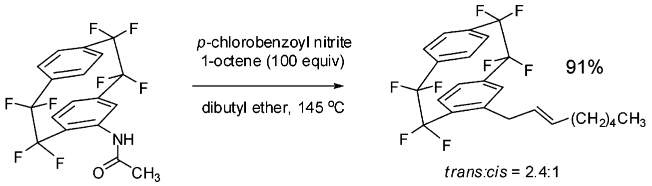

Generation of the aryne, (dehydro)octafluoro[2.2]paracyclophane, from its acetamide derivative utilizing the Cadogan method led to remarkable results with respect to Diels−Alder and ene reactivity. A comparison was made between this new and virtually unused method and our earlier reported results using Cram methodology (reaction of aryl iodide with potassium *tert*-butoxide). Surprisingly, no ene reactivity was observed with the Cram methodology. This mechanistic conundrum was examined extensively with no unambiguous explanation for the difference in reactivity being found.

Introduction

The behavior of acylarylnitrosamines in solution has evoked interest since Bamberger's discovery in 1897 that *N*-nitrosoacetanilide (**1**) decomposed easily in benzene at room temperature to give biphenyl and acetic acid.[1] The mechanistic complexity of this system, in which both free radical and ionic processes were clearly involved, was demonstrated by the efforts of a number of prominent groups.[2−6]

During the course of his extensive mechanistic studies of this reaction in the 1960−1970's, Cadogan discovered that under appropriate conditions **1** and other acylarylnitrosamines could also act as thermal precursors of benzynes, as evidenced by their trapping in Diels−Alder reactions (Scheme 1).[7,8] It was concluded that the addition of arynophiles, such as tetracyclone, to the reaction led to inhibition of the free radical chain process, thus allowing an alternative, benyzne-forming ionic process to dominate mechanistically.

The mechanism hypothesized by Cadogan for formation of benzyne by his method involves rearrangement of the *N*-nitrosoacetamide **1** to the azoacetate (**2**), which then is thought to dissociate to form the diazonium acetate, followed by deprotonation by acetate at the β-position and elimination of nitrogen to form benzyne (Scheme 2).

In the course of their studies, Cadogan and his co-workers found that a procedure involving in situ generation of the *N*-nitrosoacetanilide, by addition of 4-chlorobenzoyl nitrite to acetanilide in refluxing benzene in the presence of arenophiles, constituted a superior procedure for obtaining the benzyne chemistry.[9] Nevertheless, even under these optimal conditions, the yields of most Diels−Alder reactions deriving from Cadogan's benzyne method must be considered modest at best, with, for example, anthracene providing only a 16% yield of Diels−Alder product along with 24% of biphenyl (Scheme 3).

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(1) Bamberger, E. *Chem. Ber.* **1897**, *30*, 366−374.

(2) Hey, D. H.; Waters, W. A. *Chem. Rev.* **1937**, *21*, 169−208.

(3) Huisgen, R.; Horeld, G. *Justus Liebigs Ann. Chem.* **1949**, *1949*, 137−162.

(4) Barben, I. K.; Sushitzky, H. *J. Chem. Soc.* **1960**, 2735−2739.

(5) Ruchardt, C.; Freudenberg, B. *Tetrahedron Lett.* **1964**, *5*, 3623−3628.

(6) Cadogan, J. I. G. *Acc. Chem. Res.* **1971**, *4*, 186−192.

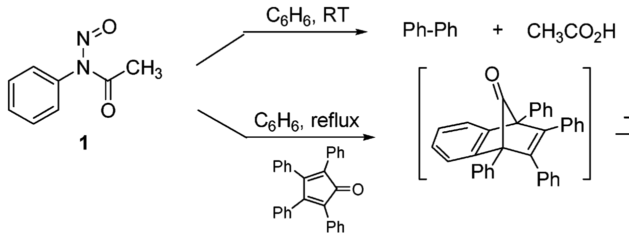
(7) Cadogan, J. I. G.; Hibbert, P. G. *Proc. Chem. Soc.* **1964**, 338−339.

(8) Cadogan, J. I. G.; Murray, C. D.; Sharp, J. T. *J. Chem. Soc., Perkin Trans. 2* **1976**, 583−587.

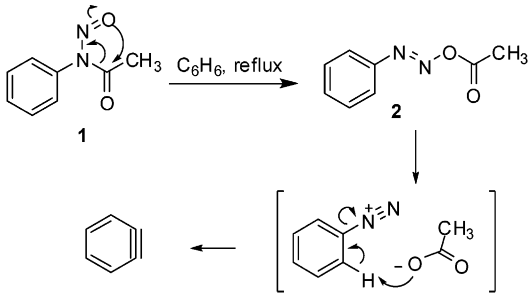
(9) Baigrie, B.; Cadogan, J. I. G.; Mitchell, J. R.; Robertson, A. K.; Sharp, J. T. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2563−2567.

10.1021/jo0620009 CCC: $37.00

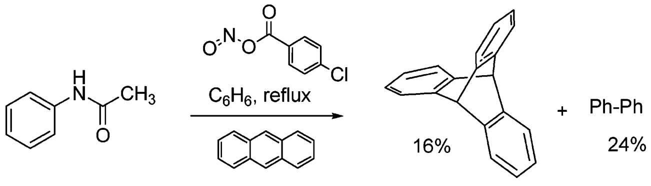
SCHEME 1. Thermal Decomposition of *N*-Nitrosoacetanilide



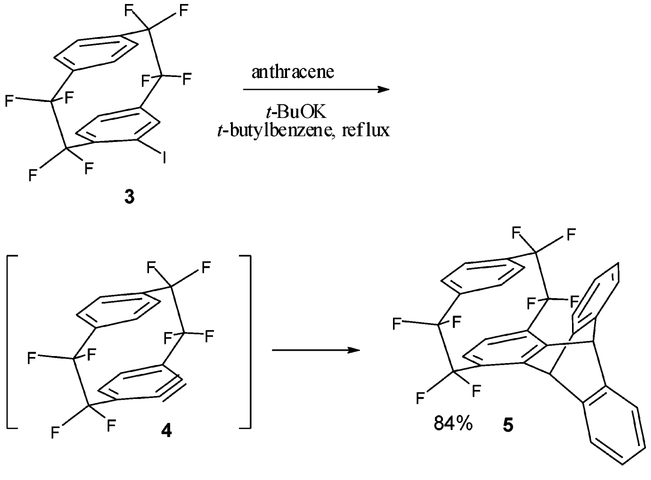
SCHEME 2. Proposed Mechanism for Aryne Formation in the Cadogan Process



SCHEME 3. Optimal Cadogan Benzyne Conditions



SCHEME 4. AF4-yne Chemistry under Classic Cram Conditions

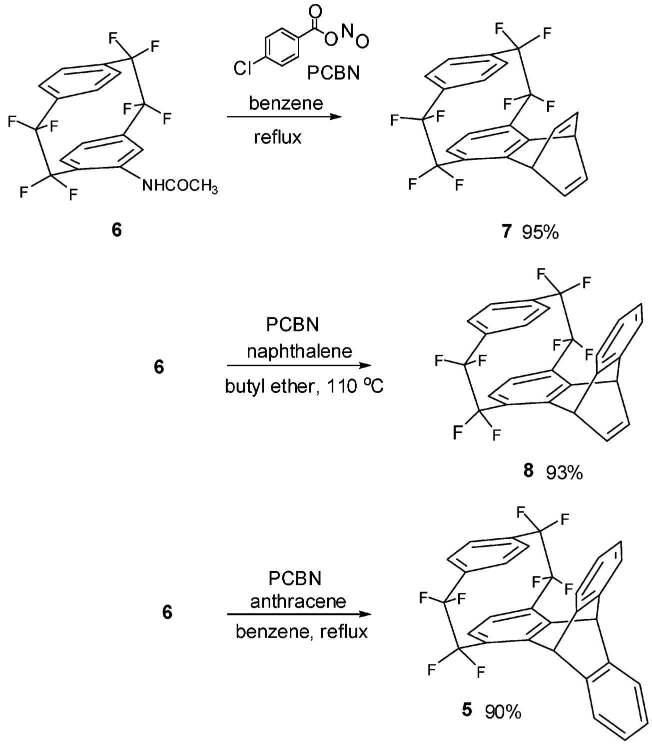


Probably for this reason, in the ensuing years since Cadogan's discovery of this chemistry, mention of it in the literature has been rare[10−12] and until the present work there appears not to have been a single occasion where this methodology has been successfully used for the purpose of carrying out synthetic aryne chemistry.

Results and Discussion

Aryne Chemistry of Octafluoro[2.2]paracyclophane. A few years ago, we discovered that AF4-iodide, **3**, undergoes facile elimination of HI under classic Cram conditions[13,14] using potassium *tert*-butoxide, and that the intermediate aryne (**4**) exhibits extraordinary Diels−Alder reactivity with a wide variety of arynophiles, including benzene (86%), naphthalene (86%), and anthracene (84%), as exemplified for anthracene in Scheme 4.[15] We were aware of Cadogan's early work with *N*-nitrosoacetanilide, and since the requisite AF4-amine precursor was already available to us as the precursor of iodide **3**, it was decided to take a look at Cadogan's procedure as a possible alternative source of the AF4 aryne.

SCHEME 5. Diels−Alder Chemistry



Diels−Alder Chemistry. The extraordinary success that has been encountered with this methodology in the AF4 system could never have been anticipated (Scheme 5). When the AF4-acetamide (**6**) was allowed to react with *p*-chlorobenzoyl nitrite (PCBN) in refluxing benzene, a yield of 90% of the Diels−Alder adduct was obtained. When only 1.2 equiv of anthracene were added, the anthracene adduct was obtained in 95% yield. Similarly the naphthalene adduct was obtained in 93% yield,

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(10) Gribble, G. W.; Keavy, D. J.; Branz, S. E.; Kelly, W. J.; Pals, M. A. *Tetrahedron Lett.* **1988**, *29*, 6227−6230.

(11) Cambie, R. C.; Higgs, P. I.; Rutledge, P. S.; Woodgate, P. D. *Aust. J. Chem.* **1994**, *47*, 1483−1508.

(12) Rüchardt, C.; Hassmann, V. *Liebigs Ann. Chem.* **1980**, 908−927.

(13) Cram, D. J.; Day, A. C. *J. Org. Chem.* **1966**, *31*, 1227−1232.

(14) Cadogan, J. I. G.; Hall, J. K. A.; Sharp, J. T. *J. Chem. Soc. C* **1967**, 1860−1862.

(15) Battiste, M. A.; Duan, J.-X.; Zhai, Y.-A.; Ghiviriga, I.; Abboud, K. A.; Dolbier, W. R., Jr. *J. Org. Chem.* **2003**, *68*, 3078−3083.

TABLE 1. Proton Affinities of Carbanions Derived from Diazonium Species (B3LYP/aug-cc-PVD//B3LYP/6-31G*)

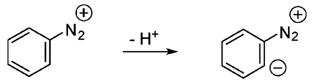
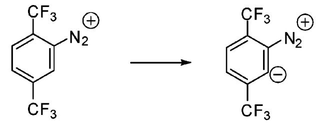
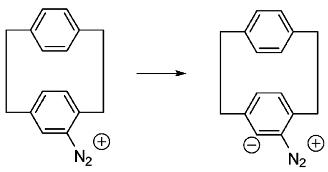
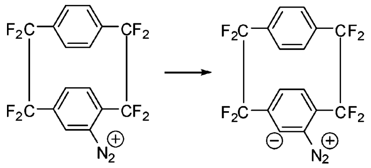
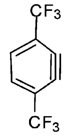
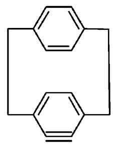
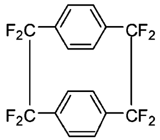
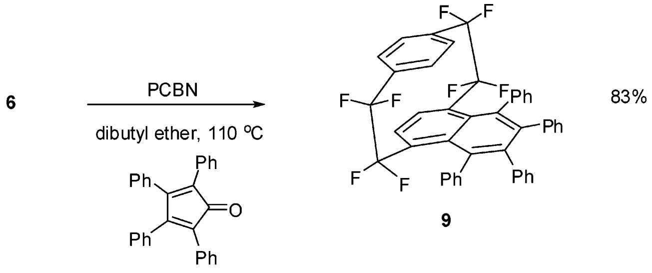
Species	Proton Affinities of carbanion (kcal/mol)	(relative)
	+ 266.8	(0.0)
	+ 248.5	(-18.3)
	+ 272.3	(+5.5)
	+ 248.3	(-18.5)

TABLE 2. Calculated Adiabatic Electron Affinities (B3LYP/aug-cc-PVDZ//B3LYP/6-31G*)

Aryne Species	EA (calc) (eV)	EA (calc) (kcal/mol)
	-0.93	-21.5
	-1.22	-49.6
	-0.98	-22.5
 **4**	-2.21	-50.9

SCHEME 6. DA Reaction with Tetracyclone



carrying out the reaction in butyl ether at 110 °C but with 1.2 equiv of naphthalene. These are remarkable results for any aryne reaction, much less one utilizing Cadogan methodology.

In retrospect, we attribute the relative ease of aryne formation in the AF4 system under Cadogan conditions to the probable enhancement of acidity of the β-hydrogens in this system due to the effect of the bridge fluorine substituents, which impart great electron deficiency to the benzene rings.

This same electron deficiency should also impart enhanced dienophilic reactivity to the aryne once it is formed. Arynes made more electrophilic by fluorine and chlorine substitution on the ring have previously been found to be among the most reactive.[16−18]

Computational results in support of both of these suppositions have been obtained. First, calculated proton affinities of a series of diazonium ions (Table 1) clearly indicate that the β-protons of the fluorine-containing diazonium ions are substantially more acidic than those of their nonfluorinated counterparts.

Second, the calculated adiabatic electron affinities of a series of arynes (Table 2) clearly indicate that the LUMOs of the fluorine-containing arynes are much lower in energy than those of their nonfluorinated counterparts. Thus they should be more reactive as electrophilic dienophiles.

Cadogan obtained his best yields when using tetracyclone as diene, obtaining yields as high as 78% when using *m*-chloroacetanilide as substrate.[9] Although the electron-deficient aryne, **4**, should not be a good electronic match for the inverse electron demand (electron-deficient) diene, tetracyclone, nevertheless, when tetracyclone was used as the diene in the reaction of **6** under Cadogan conditions, an 83% yield of decarbonylated adduct **9** was isolated (Scheme 6).

Ene Reactions. Arynes are known to also undergo ene reactions,[19] although there are few examples of high yields for such reactions.[20] Included among Cadogan's studies of benzyne as generated by treatment of acetanilide with PCBN was the reaction with methyl methacrylate, which led to a 31% yield of an ene product.[9]

When aryne precursor **6** was treated with PCBN in the presence of 100 equiv of 1-octene at 110 °C in butyl ether, an 86% yield of ene product **10** was obtained as a 2.4:1 ratio of trans to cis isomers. Likewise, reactions with cyclopentene and cyclohexene led to good yields of ene products (both giving mixtures of diastereomers) (Scheme 7).

When only 10 equiv of 1-octene was used, a 65% yield of products could be obtained comprised of 87% ene adduct **10** along with 13% of the product (AF4), where iodine has been reduced to H. When the reaction was run with 100 equiv at 145 °C, yields as high as 91% of **10** were obtained.

Thus aryne **4**, as generated from **6** under Cadogan conditions, exhibits excellent "ene" reactivity. In fact, when equivalent

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(16) Brewer, J. P. N.; Heaney, H. *Tetrahedron Lett.* **1965**, *6*, 4709−4712.

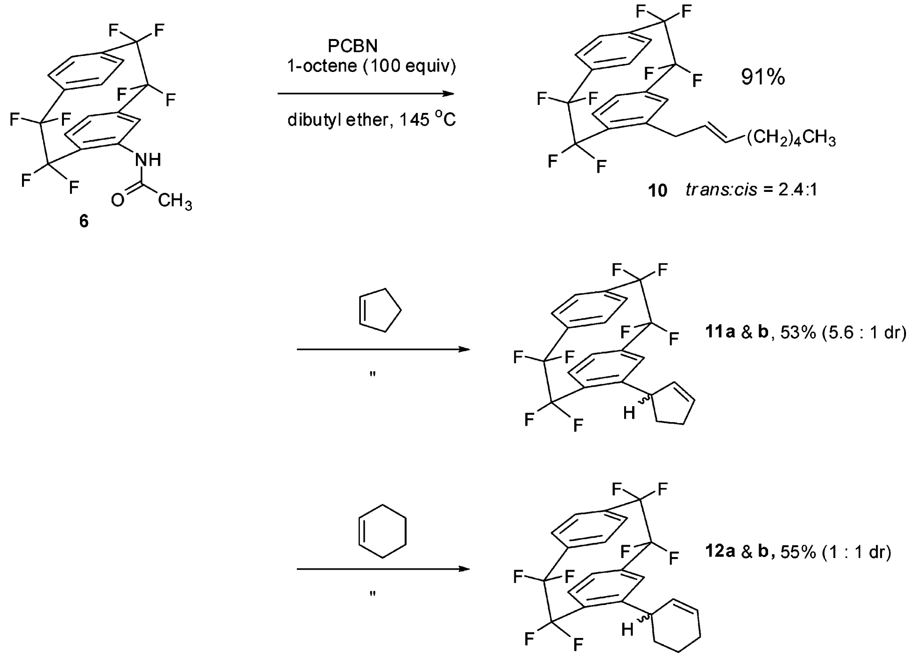
(17) Harrison, R.; Heaney, H. *J. Chem. Soc. C* **1968**, 889−892.

(18) Heaney, H.; Jablonski, J. M. *J. Chem. Soc. C* **1968**, 1895−1898.

(19) Simmons, H. E. *J. Am. Chem. Soc.* **1961**, *83*, 1657−58.

(20) Hoffmann, R. W. *Dehydrobenzene and Cycloalkynes*; Academic Press: New York, 1967; p 197.

SCHEME 7. Ene Reactions under Cadogan Conditions



SCHEME 8. Attempted Ene Chemistry under Cram Conditions

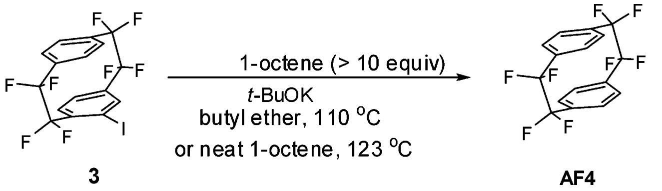


TABLE 3. Selectivity of Diels−Alder Reaction under Cram Conditions (5 h at 120 °C in *n*-Butyl Ether)

competition substrates[a]	ratio of substrates	DA adduct ratio	selectivity
A vs N	1:23.0	1.23:1	28.3:1
N vs B	1:56.8	5.46:1	310.1:1

[a] A = anthracene, N = naphthalene, B = benzene.

TABLE 4. Selectivity of Diels−Alder Reaction under Cadogan Conditions (3 h at 120 °C in Butyl Ether)

competition substrates[a]	ratio of substrates	DA adduct ratio	selectivity
B vs N	55.25:1	1:5.3	1:293
N vs A	20.3:1	1:1.9	1:40.5

[a] B = benzene, N = naphthalene, A = anthracene.

amounts of benzene and 1-octene are present when **4** is generated, only the ene product is formed, indicating that this ene reaction of **4** is significantly faster than its Diels−Alder reaction with benzene. A quantitative competition experiment led to determination of a reactivity ratio for 1-octene versus benzene of ~140.

It was therefore quite astounding to us when we found that no ene product from 1-octene could be detected when the aryne **4** was generated under Cram conditions from iodide **3** by our standard method of treatment with potassium *tert*-butoxide in butyl ether at 110 °C! Only the product of reduction (replacement of I with H) was observed. In fact, regardless of the choice of alkene, no ene reaction has yet to be observed, even as a minor process, when aryne **4** is generated under these conditions.

This presents a mechanistic conundrum, since one would naturally assume that a common intermediate, aryne **4**, is generated under both Cram and Cadogan conditions.

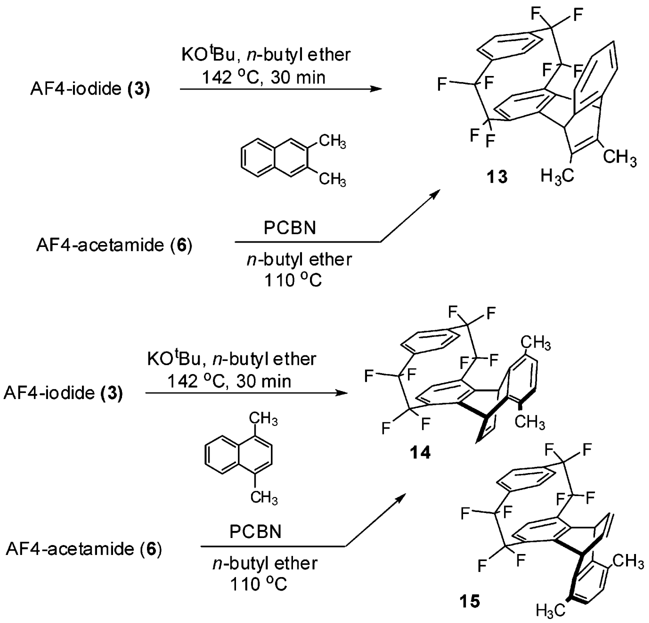
Competition Studies. With this in mind, competition experiments were carried out to test the common intermediacy of aryne **4**. Since both reactions exhibit high Diels−Alder reactivity, the relative reactivities of the aryne intermediates generated by each of the two methods were examined for their Diels−Alder reactions. Studies were carried out to determine the relative reactivities of anthracene, naphthalene, and benzene for both methods under (as much as possible) identical solvent and temperature conditions, in butyl ether at 110 °C.

The reactivities of the respective Diels−Alder substrates were compared directly under Cram conditions, with the results being given in Table 3. The observed relative reactivites for anthracene, naphthalene, and benzene under Cram conditions were thus determined to be 8780:310:1.

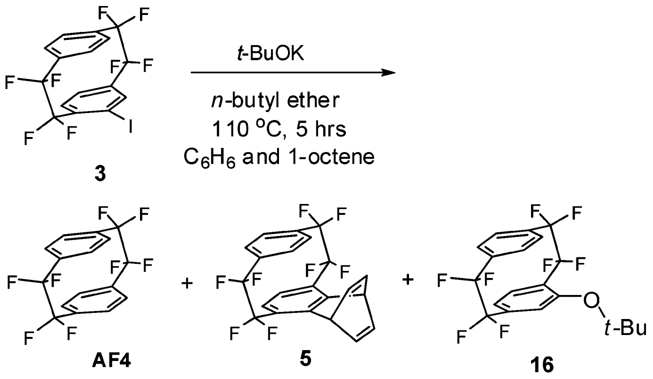
The competition experiments under Cadogan conditions were carried out similarly for the three Diels−Alder substrates, with the results being given in Table 4. Thus, the relative reactivities for anthracene, naphthalene, and benzene under Cadogan conditions are 11 800:293:1.

The observed Diels−Alder reactivities for the two methods of generation are thus somewhat different, but not significantly so. Although the competition experiments for the Cram and the Cadogan conditions were carried out under conditions as close to identical as possible, it must be remembered that the reactions are themselves quite different. For example, the reaction under Cadogan conditions is completely homogeneous, whereas that under Cram conditions is heterogeneous, with the KO^{t}Bu not being significantly soluble and solids being present throughout the reaction. Thus we do not believe that the small apparent differences in relative reactivities can be given much significance. That being the case, the fact that no ene reaction with 1-octene is observed under Cram conditions, when 1-octene is

SCHEME 9. Diels−Alder Reactions with Dimethylnaphthalenes



SCHEME 10. Impact of the Presence of 1-Octene under Cram Conditions



clearly more reactive than benzene under Cadogan conditions, is all the more incredible.

Similar reactivities were also observed for the two methods of generation in the reactions of AF4-yne with both 2,3- and 1,4-dimethylnaphthalene. The former compound underwent reaction exclusively with the more nucleophilic, dimethyl-substituted ring to give *endo*-product **13**, whereas steric hindrance due to the methyl substituents led to reaction exclusively with the nonsubstituted ring of 1,4-dimethylnaphthalene, giving a mixture of *endo*- and *exo*-products, **14** and **15**. The ratio of **14** to **15** under Cram conditions was 77:23, whereas under Cadogan conditions it was 65:35. Thus, in their Diels−Alder reactions, the AF4-yne species generated by the two different methods appear to have very similar reactivities.

Considerable effort has been made to elucidate the mechanistic differences between the two reaction conditions with respect to the ene reaction, but no satisfactory answer has emerged. It simply appears that the presence of 1-octene under Cram conditions introduces a new, alternative pathway for reaction of the iodide and/or the aryne, that of simple reduction of the iodine to form AF4, as seen in Schemes 8 and 10.

Thus, under reaction conditions where benzene would ordinarily be expected to undergo reaction with aryne **4**, the addition of significant amounts of 1-octene to the reaction mixture virtually inhibits the Diels−Alder process (Scheme 10 and Table 5 below). Another curious aspect of this study was the observed competitive formation of product **16** in some of these reactions. This product probably resulted from addition of *tert*-butoxide to aryne **4**. In our earlier studies of AF4 aryne chemistry using Cram conditions with more reactive naphthalene or anthracene substrates or a larger excess of benzene substrate, this product **16** had never been observed, even as a minor product. Nevertheless, it now appears that when insufficient amounts of a reactive substrate are present the *tert*-butoxide-trapped product can be formed. When the amount of 1-octene is increased to 58 equiv, however, this product disappears and reduction product, AF4, is the only one observed.

TABLE 5. Inhibition of Diels−Alder Reaction under Cram Conditions by the Presence of 1-Octene

substrate (equiv)		product yields (%)		
benzene	1-octene	AF4	Diels−Alder adduct **5**	*tert*-butoxide adduct **16**
1	0	45.8	3.5	35.0
1	1	61.0	4.9	34.1
11	11	79.4	trace	12.7
11	58	only		

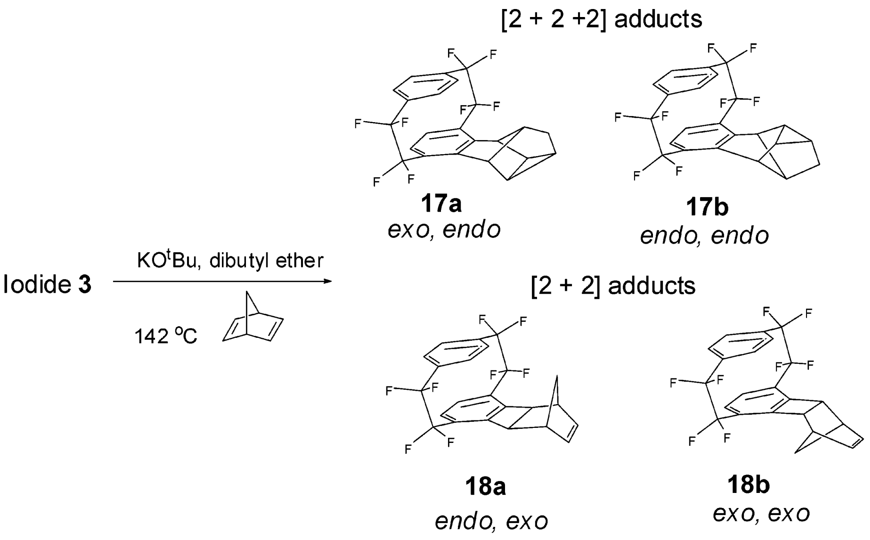
TABLE 6. Competition Reaction of Anthracene with 1-Octene in Butyl Ether for 5 h at 110 °C under Cram Condition

ratio (anthracene/ 1-octene)	results (DA product (**8**)/AF4)
1:1	only DA adduct obsd
1:10	82:18
1:40	55:45
1:100	30:70

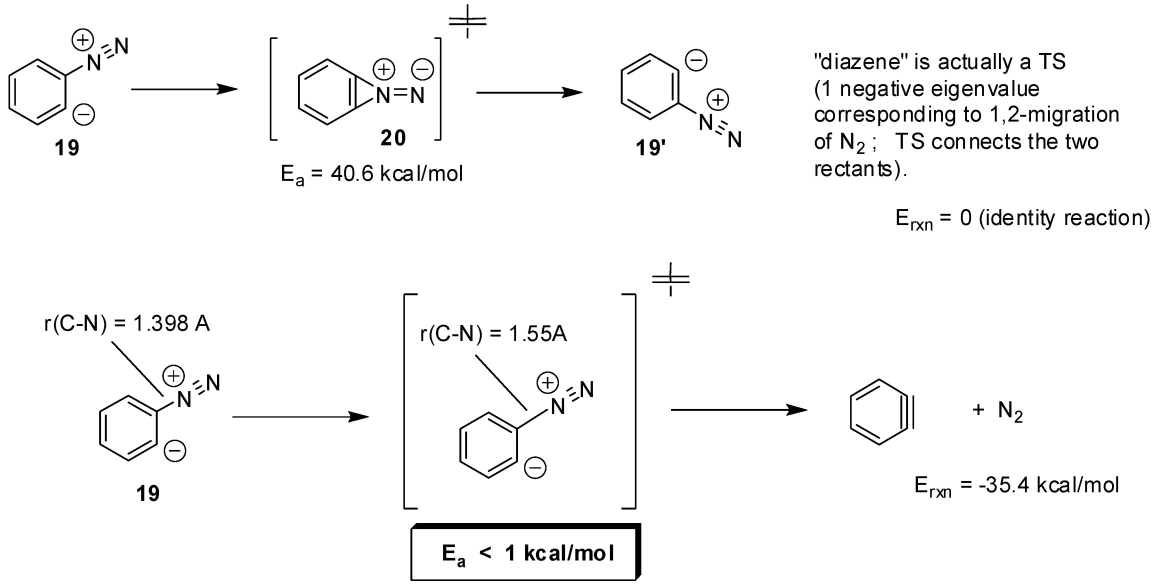
Substituting 1 equiv of anthracene for the benzene in the second experiment (anthracene and 1-octene each 1 equiv) leads to formation of the Diels−Alder adduct as the only product. Therefore, obviously, the presence of 1 equiv of 1-octene does not inhibit formation of the aryne. Instead, as indicated by the trend of the data given in Table 6, it must be involved in some concentration-dependent process that is competitive with either the formation of the aryne or the Diels−Alder chemistry of the aryne. We believe the former situation is more reasonable.

Initially we considered the possibility that, because of the extraordinary electron affinity of AF4 aryne **4**, 1-octene might act as a single electron donor to form the radical anion of **4**, which could then readily lead to the observed reduction product. However, it was found that norbornadiene, a much better electron donor than 1-octene, underwent reaction with **4** under Cram conditions to form a mixture of [2 + 2] and [2 + 2 + 2] cycloaddition products. The four products (Scheme 11), two [2 + 2+2] cycloaddition products **17a** (*exo* with respect to the paracyclophane and *endo* with respect to the norbornadiene) and **17b** (*endo*, *endo*) and two [2+2] cycloaddition products **18a** (*endo*, *exo*) and **18b** (*exo*, *exo*), were obtained in a total yield of 67%, with the ratios of products **17a**:**17b**:**18a**:**18b** being 62:27:3:8. Thus the [2 + 2+2] products (**17a**,**b**) were greatly predominant, which contrasts strongly with the selectivity of other arynes in their reactions with norbornadiene. For example, Heaney observed that the major product in the reaction of

SCHEME 11



SCHEME 12. Hypothetical Diazene Intermediate Mechanism



"diazene" is actually a TS (1 negative eigenvalue corresponding to 1,2-migration of N_2; TS connects the two rectants).

E_{rxn} = 0 (identity reaction)

E_{rxn} = -35.4 kcal/mol

tetrachlorobenzyne with norbornadiene was the [2 + 2] adduct (50%) with the [2 + 2 + 2] adduct being obtained in only 22% yield.[21]

The same four products were obtained under Cadogan conditions at 110 °C, but with less of a preference for the [2 + 2 + 2] adducts being observed (product ratios 39:21:21:19). In this case there appears to be a significant difference in the reactivity/selectivity exhibited by the arynes as generated by the two different methods.

There is still the possibility that the presence of 1-octene somehow facilitates a modification of the reactivity of *tert*-butoxide to make it act as an electron donor to AF4-iodide **3** instead of a base.

The results given in Table 6, indicating a competition between Diels−Alder reaction with anthracene and reduction (facilitated by 1-octene) could be explained by the competition occurring either at the iodide stage or the aryne stage. However, if the competition was at the aryne stage, one needs to explain why, in spite of 1-octene being more reactive than benzene toward the aryne, the results given in Scheme 10 indicate that benzene adduct can be formed in the presence of 1-octene under Cram conditions.

We considered the possibility that an aryne might not be involved in both cases. For the iodide/*tert*-butoxide reaction, an E_1cb mechanism involving formation of a carbanion which then eliminates iodide is generally invoked. We could not conceive of any species in this process, other than the aryne itself, which would be capable of undergoing Diels−Alder reactions. On the other hand, the Cadogan process involves a diazonium ion intermediate that is supposedly deprotonated followed by loss of N_2 to form the aryne. Could something else be happening here competitive with aryne formation? We hypothesized that, instead of the aryne leading to the ene reaction, the deprotonated diazonium ion, **19**, might cyclize to form diazene **20** (Scheme 12). In principle, diazene **20** could behave much like an aryne, but with different reactivity characteristics. However, that hypothesis was quickly dispelled when a computational examination of the energy surface of **19**

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(21) Heaney, H.; Jablonski, J. M.; Mason, K. G.; Sketchley, J. M. *J. Chem. Soc. C* **1971**, 3129−3131.

(Scheme 10) demonstrated clearly that loss of N_2 (E_a < 1 kcal/mol) will dominate any such hypothetical cyclization ($E_a = 40.6$ kcal/mol) to form diazene **20**, which was shown not to be an intermediate, but rather a transition state for the 1,2-shift of $(-N{\equiv}N)^+$.

Thus the mechanistic puzzle remains unsolved as this paper is written. Both computational and experimental efforts toward a resolution of this issue continue.

Experimental Section

General Information. ^1H and ^{13}C chemical shift data are directly indicated on the structures of the respective adducts provided either in the Results and Discussion Section or in the Experimental Section, whereas ^{19}F NMR data are provided in the Experimental Section below. When mixtures of products were analyzed, products were characterized by H1−C13 couplings as seen in the GHMQC and GHMBC spectra. A full description of such analyses can be found in the Supporting Information. Additional details regarding ^1H spectra, including coupling constants, may be found in the Supporting Information.

***p*-Chlorobenzoyl Nitrite (PCBN)**. Following the literature method,[9] to a sodium bicarbonate solution (9.0 g, 0.11mol) in water was added 4-chlorobenzoic acid (17 g, 0.12 mol). The solution was filtered hot and to the filtrate was added silver nitrate (19 g, 0.11mol) in water during stirring. The precipitated silver *p*-chlorobenzoate was filtered and washed with ethanol (twice) and dried over P_2O_5 under vacuum for 1 day.

To a stirred suspension of silver *p*-chlorobenzoate (20 g, 75 mmol) in 180 mL of dry CCl_4 at −10 °C was added nitrosyl chloride (NOCl) (8 g, 125mmol) during 30 min. The mixture was stirred for a further 20 min at −10 °C and 1 h at room temperature. The mixture was filtered rapidly after that and the residue was washed with CCl_4 twice. The filtrates were combined and evaporated under vacuum. The residue was distilled under vacuum (84−85 °C/2.5 mmHg) to give 12.1 g of a yellow-reddish solid (86%). The product (PCBN) was made into a 0.86 M solution in benzene or *n*-butyl ether for future use, and this solution was refrigerated until needed.

4-Acetamido-1,1,2,2,9,9,10,10-octafluoro[2.2]paracyclophane (6) (AF4-acetamide) was prepared as previously reported.[22]

Reaction of AF4-Acetamide 6 with Anthracene under Cadogan Conditions. A 50-mL three-necked round-bottom flask was charged with AF4-acetamide **6** (0.205 g, 0.500 mmol), 5 mL of *n*-butyl ether, and anthracene (0.18 g, 1.00 mmol, 2.00 equiv). This mixture was heated to 110 °C and PCBN (0.16 g, 0.85mmol) in 10 mL of *n*-butyl ether was added over a period of 30 min. The reaction mixture was maintained at this temperature overnight. Then the mixture was cooled and the solvent evaporated under vacuum. The residue was purified on a silica gel column, eluting with hexanes/ethyl acetate (100:1) to give the white crystalline Diels−Alder, 9,10-adduct **5** in yields that were consistently about 95%, with less than 3% of the 1,4 adduct being detected. ^1H, ^{13}C, and ^{19}F NMR spectra of **5** were consistent with those reported previously.[15]

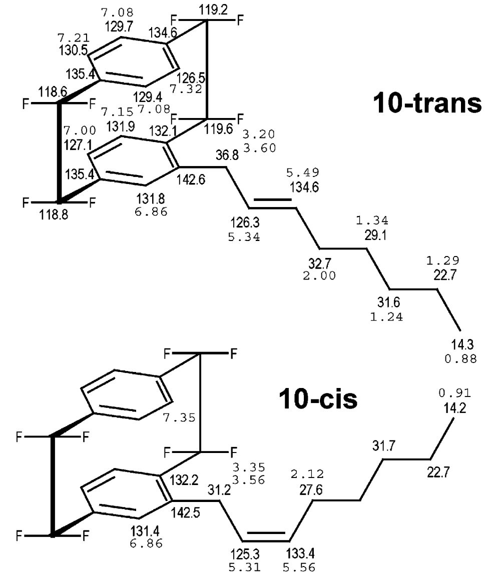
Reaction of AF4-Acetamide (6) with Naphthalene and Benzene under Cadogan Conditions. The analogous reaction with naphthalene proceeded similarly giving consistent total yields of *endo*- and *exo*-adducts in the range of 93%, the major product being *endo*-**8** along with 15−17% of the *exo*-product. When the reaction was carried out in refluxing benzene with no other substrate, the benzene adduct **7** was obtained in 90% yield. ^1H, ^{13}C, and ^{19}F NMR spectra of **7** and **8** were consistent with those reported previously.[15]

1-Octene Reaction with AF4-Acetamide under Cadogan Conditions. A 50-mL three-necked round-bottom flask was charged with AF4-acetamide (**6**) (0.205 g, 0.50 mmol), 5 mL of *n*-butyl ether, and 1-octene (7.85 mL, 50.0 mmol, 100 equiv). This mixture was heated to 110 °C and the PCBN (0.16 g, 0.85mmol) in 10 mL of *n*-butyl ether was added over a period of 30 min. The reaction mixture was then maintained at this temperature overnight, after which the mixture was cooled and solvent evaporated under vacuum. The residue was subjected to chromatography on a silica gel column, which was eluted with hexanes/ethyl acetate (100:1) to give 0.21 g of the oily ene product **10** (86%), as a 2.4:1 ratio of trans to cis isomers.

Trans isomer: ^{19}F NMR (eight equal intensity AB doublets) δ −110.6 (d, J = 243 Hz), −113.5 (d, J = 243 Hz), −114.8 (d, J = 239 Hz), −115.8 (d, J = 236 Hz), −117.5 (d, J = 242 Hz), −117.6 (d, J = 238 Hz), −118.8 (d, J = 239 Hz), −119.0 (d, J = 240 Hz).

Cis isomer: ^{19}F NMR (eight equal intensity AB doublets) δ −111.1 (d, J = 245 Hz), −113.5 (d, J = 245 Hz), −114.9 (d, J = 240 Hz), −115.8 (d, J = 236 Hz), −117.5 (d, J = 242 Hz), −117.6 (d, J = 238 Hz), −118.9 (d, J = 240 Hz), −119.1 (d, J = 239 Hz).

Cis,trans mixture: MS(EI) m/z 462(M^+)(15), 391(16), 365(17), 189(45), 215(19), 176(100); HRMS calcd for $C_{24}H_{22}F_8$ 462.1594, found 462.1593 (EI). Anal. Calcd for $C_{24}H_{22}F_8$: C, 62.34; H, 4.795. Found: C, 62.42; H, 5.01.



10-trans

10-cis

Reaction of Cyclopentene with AF4-Acetamide under Cadogan Conditions. The procedure was the same as above except that cyclopentene (10 equiv) was the reactant. The yield was 53% with two stereoisomers **11a** and **11b** in a ratio of 5.6:1.

Isomer 11a: ^{19}F NMR (eight AB doublets, although the signals at 116.90 and 116.94 are apparent broad singlets, with barely detectable AB sidebands) δ 109.8 (d, J = 245 Hz), 112.6 (d, J = 243 Hz), 116.9 (apparent br s, with detectable AB sideband with J_{AB} = 243), 116.94 (br s, J_{AB} obscured), 117.0 (d, J = 239 Hz), 117.6 (d, J = 241 Hz), 119.6 (d, J = 238 Hz), 119.7 (d, J = 242 Hz).

Isomer 11b: ^{19}F NMR (two AB doublets along with six apparent singlets) δ 107.8 (d, J_{AB} = 243 Hz), 112.8 (d, J_{AB} = 243 Hz), 115.6 (br s), 115.6 (br s), 117.7 (s), 117.8 (s), 118.3 (s), 118.4 (s).

Mixture of 11a and 11b: MS(EI) m/z 418 (M^+) (33), 242 (100), 176 (28). HRMS calcd for $C_{21}H_{14}F_8$ 418.0967, found 418.0942 (EI). Anal. Calcd for $C_{21}H_{14}F_8$: C, 60.29; H, 3.37. Found: C, 60.08; H, 3.38.

Reaction of Cyclohexene with AF4-Acetamide (6) under Cadogan Conditions. The procedure was the same as above except that cyclohexene (10 equiv) was the reactant. The product, which

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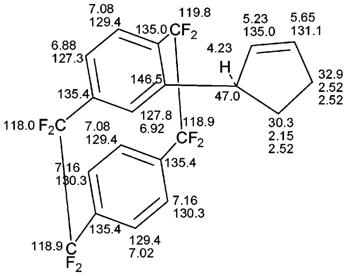
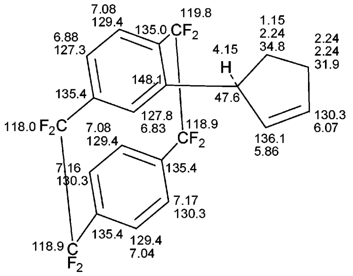
(22) Roche, A. J.; Dolbier, W. R., Jr. *J. Org. Chem.* **1999**, *64*, 9137−9143.

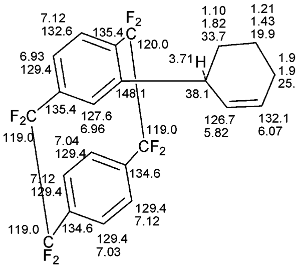


11a

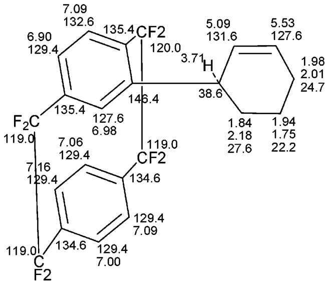


11b

was a mixture of diastereomers (**12a** and **12b**) in a 1:1 ratio, was obtained in 55% yield. ^{19}F NMR (for 1:1 mixture of both isomers)

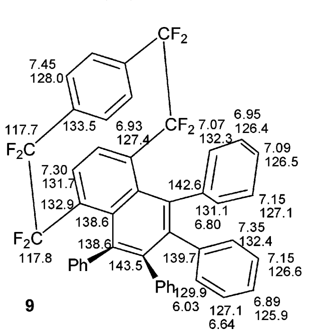


12a



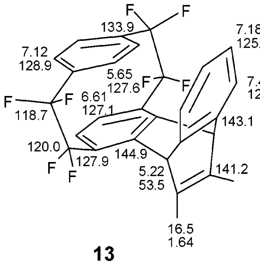
12b

δ −109.1 (d, J = 244 Hz), −109.8 (d, J = 244 Hz), −111.7 (d, J = 244 Hz), −112.9 (d, J = 244 Hz), −115.3 (d, J = 241 Hz), −116.6 (d, J = 241 Hz), −116.9 (d, J_{AB} = 241 Hz), −117.1 (d, J = 238 Hz), −117.5 (d, J = 241 Hz), −117.6 (d, J = 241 Hz), −119.0 (d, J = 238 Hz), −119.3 (d, J = 238 Hz), −119.3 (d, J = 241 Hz), −119.5 (d, J = 240 Hz); HRMS calcd for $C_{22}H_{16}F_8$ 432.1124, found 432.1104 (EI).



9

Reaction of Tetracyclone with AF4-Acetamide (6) under Cadogan Conditions. The procedure was the same as above except that 2,3,4,5-tetraphenylcyclopentadiene (1.5 equiv) was the substrate. The yield of product **9** was 83%. ^{19}F NMR (four equal intensity AB doublets) δ −107.7 (d, J = 253 Hz), −109.9 (d, J = 250 Hz), −116.3 (d, J = 241 Hz), −120.8 (d, J = 241 Hz); MS (EI) m/z 706 (M$^+$) (14), 526 (26), 352 (6), 176 (100); HRMS calcd for $C_{44}H_{26}$F8 706.1907, found 706.1933 (EI).



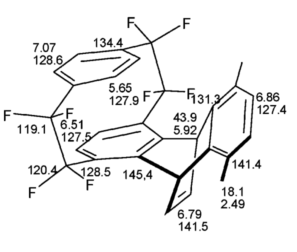
13

Reaction of 2,3-Dimethylnaphthalene with AF4-Iodide (3) under Cram Conditions. A 50-mL three-necked round-bottom flask was charged with IAF4 (0.30 g, 0.63 mmol), 10 mL of *n*-butyl ether, 2,3-dimethylnaphthalene (0.10 g, 0.6 mmol), and potassium *tert* -butoxide (0.40 g, 3.56 mmol). This mixture was heated to reflux at 142 °C and stirred at this temperature for 30 min. The residue was purified on a silica gel column, eluting with hexanes to give *endo*-adduct **13** (85 mg) in a yield of 67%. Solid starts to decompose at 168 °C: ^{19}F NMR δ −111.2, −114.9 (AB, J = 244 Hz, 4F), −116.4, −119.4 (AB, J = 238 Hz, 4F); MS(EI) m/z 506 (M$^+$) (77), 330 (100), 176 (14); HRMS calcd for $C_{28}H_{18}F_8$ 506.1280, found 506.1288 (EI).

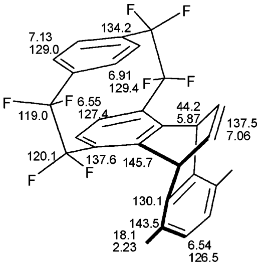
Reaction of 2,3-dimethylnaphthalene with AF4-acetamide (6) under Cadogan conditions. The reaction was carried out in the usual manner, as for naphthalene, and the same product (**13**) was obtained as that above.

Reaction of 1,4-Dimethylnaphthalene with AF4-Iodide (3) under Cram Conditions. The procedure was carried out as above except that 1,4-dimethylnaphthalene (0.10 g, 0.6mmol) was used as the substrate. A mixture of products (ratio 77:23) was obtained after refluxing for 30 min, which after chromatography in the usual manner gave major product *endo*-adduct **14** in a yield of 60%: ^{19}F NMR δ −108.9, −114.2 (AB, J = 244 Hz, 4F), −114.8, −118.5 (AB, J = 238 Hz, 4F). *Exo*-adduct (**15**): ^{19}F NMR δ −111.9, −115.2 (AB, J = 244 Hz, 4F), −117.7, −119.2 (AB, J = 241 Hz, 4F). HRMS of the cis,trans mixture: calcd for $C_{28}H_{18}F_8$ 506.1280, found 506.1293 (EI). The stereochemistry of each isomer was proven by the NOE's between 2.49 and 5.65 protons in the major and between 7.06 and 6.91 protons in the minor.

Reaction of 1,4-Dimethylnaphthalene with AF4-Iodide (3) under Cram Conditions. The reaction was carried out in the usual manner, as for naphthalene, and the same two products (**14** and **15**) were obtained but in a ratio of 65:35.



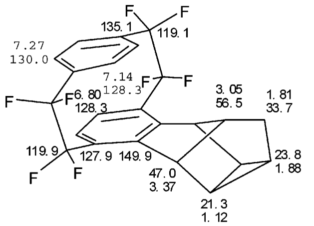
14



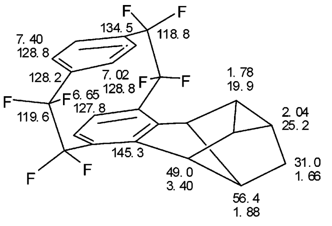
15

Reaction of AF4-Iodide (3) with Bicyclo[2.2.1]hepta-2,5-diene under Cram Conditions. The procedure was carried out as in the reactions above, except that bicyclo[2.2.1]hepta-2,5-diene (2 equiv) was used as the substrate. A product mixture of isomeric products (**17a**:**17b**:**18a**:**18b** ratio 62:27:3:8) was obtained in a total 67% yield after chromatography in the usual manner: two 1,4-addition products **17a**,**b**, and two 1,2-addition products **18a**,**b**. The mixture was analyzed and the four products characterized by H1−C13 couplings as seen in the GHMQC and GHMBC spectra. A full description of this analysis can be found in the Supporting Information. **17a-*exo,endo***: ^{19}F NMR, δ −110.5 (d, J = 241 Hz), −111.9 (d, J = 241 Hz), −112.8 (d, J = 241 Hz), −114.1 (d, J = 247 Hz), −115.0 (d, J = 238 Hz), −115.0 (d, J = 241 Hz), −115.2 (d, J = 238 Hz), −116.2 (d, J = 238 Hz), −116.3 (d, J = 241

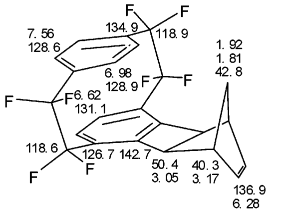
Hz), −117.0 (d, $J = 235$ Hz), −117.1 (d, $J = 241$ Hz), −117.2 (d, $J = 238$ Hz), −118.1 (d, $J = 238$ Hz), −117.4 (d, $J = 244$ Hz), −119.2 (d, $J = 238$ Hz), −119.7 (d, $J = 241$ Hz). **18a**: ^{1}H NMR, δ 7.56 (s, 2H), 6.98 (s, 2H), 6.62 (s, 2H), 6.28 (m, 2H), 3.17 (s, 2H), 1.92 (s, 1H), 1.81 (m, 1H); ^{13}C NMR δ 142.7, 136.9, 134.9, 131.1, 126.7, 128.6, 128.9, 126.7, 118.9, 118.6, 50.4, 42.8, 40.3. **18b**: ^{1}H NMR δ 7.31 (s, 2H), 7.23 (s, 2H), 6.92 (s, 2H), 6.31 (m, 2H), 2.88 (m, 2H), 2.86 (m, 2H), 1.21 (s, 1H), 0.73 (m, 1H); ^{13}C NMR δ 147.9, 137.1, 134.8, 129.8, 128.9, 128.5, 124.6, 118.4, 118.4, 46.6, 42.7, 41.4; ^{19}F NMR δ −111.4 (d, $J = 244$ Hz), −112.5 (d, $J = 244$ Hz), −115.3 (d, $J = 244$ Hz), −115.9 (d, $J = 244$ Hz), −117.2 (d, $J = 241$ Hz), −118.4 (d, $J = 241$ Hz), −119.4 (d, $J = 240$ Hz), −119.8 (d, $J = 241$ Hz); MS(EI) m/z 442 (M^+) (3), 191 (100), 176 (63), 126 (13). HRMS calcd for $C_{23}H_{14}F_8$ 442.0967, found 442.0974 (EI).



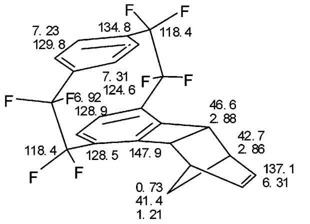
17a



17b



18a



18b

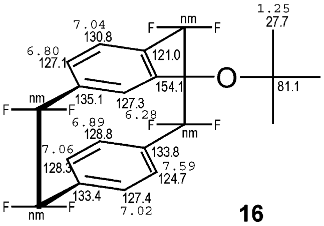
When pure bicyclo[2.2.1]hepta-2,5-diene was used as solvent and reactant, the ratio of **17a**:**17b**:**18a**:**18b** was 74:12:10:4. Isomer **17a** was separated from the others by chromatography and had a melting point of 233−235 °C.

Competition Experiments. Typical competition experiments are described below. Others, with variable amounts of reagents, were carried out in an analogous manner.

Reaction of Benzene with IAF4. A 50-mL three-necked round-bottom flask was charged with IAF4 (0.30 g, 0.63 mmol), 10 mL of *n*-butyl ether, benzene (66.0 μL, 0.73 mmol), and potassium *tert*-butoxide (0.40 g, 3.56 mmol). This mixture was heated to 110 °C and stirred at this temperature for 5 h. Then the mixture was cooled and the solvent was evaporated under vacuum. The residue was purified on a silica gel column and eluted with hexanes to give reduced AF4 (106 mg, 45.8%), *tert*-butoxide ion adduct **16** (85 mg, 35.0%), and benzene adduct (9 mg, 3.5%).

Reaction 1-Octene with AF4-Iodide under Cram Conditions. The procedure was identical to that above (0.12 g of **3**, 0.14 g of KO^{t}Bu with 2 or 10 equiv of 1-octene in 10 mL of *n*-butyl ether at 110 °C, or neat in refluxing 1-octene at 123 °C for 5 h). No ene product could be detected by NMR in any of these experiments. When 1-octene was used as solvent, the only product was AF4, where the iodine had been replaced by H. In the experiments where 2 and 10 equiv of 1-octene were used, AF4 and *tert*-butoxy-AF4 (**16**) (the product from addition of *tert*-butoxide to the AF4-aryne) were obtained in ratios of 26:74 and 64:36, respectively.

Benzene and 1-Octene with IAF4. A 50-mL three-necked round-bottom flask was charged with IAF4 (0.30 g, 0.63 mmol), 10 mL of *n*-butyl ether, benzene (64.0 μL, 0.72 mmol), 1-octene (112 μL, 0.71 mmol), and potassium *tert*-butoxide (0.40 g, 3.56 mmol). This mixture was heated to 110 °C and stirred at this temperature for 5 h. Then the mixture was cooled and solvent was evaporated under vacuum. The residue was purified on a silica gel column and eluted with hexanes to give reduced AF4 (146 mg, 61.0%), *tert*-butoxide ion adduct **16** (82 mg, 34.1%), and benzene adduct (12 mg, 4.9%). (Yields from ^{19}F NMR.) Subsequent reactions with 11 equiv each of both benzene and 1-octene resulted in reduced AF4 (181 mg, 79.4%), *tert*-butoxide ion adduct **16** (29 mg, 12.7%), and only a trace amount of benzene adduct. The reaction was run with 11 and 58 equiv of benzene and 1-octene, respectively, resulting in only the reduced AF4. All of these results are compiled in Table 5.



16

16: ^{19}F NMR δ −110.5 (d, $J = 243$ Hz), −114.1 (d, $J = 236$ Hz), −114.9 (d, $J = 236$ Hz), −115.1 (d, $J = 236$ Hz), −116.1 (d, $J = 237$ Hz,), −117.1 (d, $J = 238$ Hz), −118.1 (d, $J = 238$ Hz), −119.1 (d, $J = 237$ Hz).

Computational Experimental Details. The methodology used throughout was density functional theory (B3LYP/6-31G*) optimization/frequency analysis/ZPE determination for all relevant species and B3LYP and MP2 single point energies with large (Dunning's "correlation-consistent") aug-cc-PVDZ basis, performed upon optimized B3LYP/6-31G* structures.

Acknowledgment. Support of this research in part by the National Science Foundation is acknowledged with thanks. We also wish to thank Prof. Harry Heaney for providing his insights regarding the work.

Supporting Information Available: Characterization information including NMR spectra of product mixtures, with commentary. This material is available free of charge via the Internet at http://pubs.acs.org.

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