

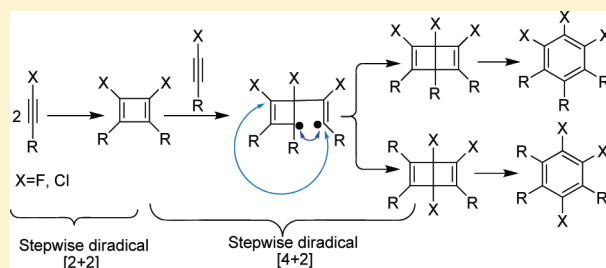
Mechanisms of the Thermal Cyclotrimerizations of Fluoro- and Chloroacetylenes: Density Functional Theory Investigation and Intermediate Trapping Experiments

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S Supporting Information

ABSTRACT: Theoretical studies of the mechanisms of the thermal cyclotrimerization of fluoro- and chloroacetylenes, which were reported by Viehe and Ballester, respectively, were conducted with the aid of density functional theory calculations of the (U)B3LYP functional, indicating that the thermal cyclotrimerizations of fluoro- and chloroacetylenes involve tandem processes of regioselectively stepwise [2+2] and stepwise [4+2] cycloadditions. These tandem processes generate 1,2,6-trihalo-Dewar benzenes and 1,2,4-trihalo-Dewar benzenes, which then isomerize to the corresponding benzenes when heated. The rate-determining step of the cyclotrimerizations of haloacetylenes is the dimerization step involving open-shell singlet diradical transition states and intermediates. The



substituent effects in the thermal cyclotrimerization of haloacetylenes have been rationalized using frontier molecular orbital theory. The higher reactivity of fluoroacetylenes compared to that of chloroacetylenes is due to the fact that fluoroacetylenes have lower singlet–triplet gaps than chloroacetylenes and more easily undergo dimerization and cyclotrimerization. In this report, additional experiments were performed to verify the theoretical prediction about the cyclotrimerization of chloroacetylene and to trap the proposed 1,4-dichlorocyclobutadiene intermediate. Experiments revealed that the thermal reaction of phenylchloroacetylene at 110 °C gave 1,2,3-triphenyltrichlorobenzene and 1,2,4-triphenyltrichlorobenzene together with a tetramer, *cis*-1,2,5,6-tetrachloro-3,4,7,8-tetraphenyltricyclo[4.2.0.0^{2,5}]octa-3,7-diene. The proposed 1,4-diphenyldichlorocyclobutadiene intermediate in the thermal cyclotrimerization of phenylchloroacetylene was successfully trapped using dienophiles of maleic anhydride and dimethyl acetylenedicarboxylate.

INTRODUCTION

Alkyne cyclotrimerization to form benzene derivatives is one of the most intensely studied reactions because of the ubiquitous presence of substituted benzenes in molecular sciences.¹ Alkyne cyclotrimerization reactions are typically performed in the presence of catalysts, which can be transition metals,² Lewis acids,³ amines,⁴ or disilanes.⁵ Uncatalyzed thermal cyclotrimerization of alkynes to give benzene derivatives was rarely reported,⁶ though the first uncatalyzed thermal cyclotrimerization of acetylene⁷ was discovered ~80 years before the first report of its catalytic version.^{2a} The process of uncatalyzed thermal cyclotrimerization of alkynes to benzene derivatives was usually conducted at a very high temperature to overcome the high reaction barrier. In 1866, Berthelot reported the first example of the thermal transformation of acetylene to benzene. The reaction was conducted at 400 °C, giving a complex mixture of products.⁷ A concerted pathway was proposed for the cyclotrimerization of acetylene, and the computed activation energy of the reaction was higher than 50 kcal/mol at different calculation levels.⁸ An interesting exception to all uncatalyzed and catalyzed alkyne cyclotrimerizations is the cyclotrimerization of *tert*-butylfluoroacetylene **1**,

reported by Viehe and co-workers.^{6a,b} This reaction was found to be spontaneous below 0 °C, yielding Dewar benzene **2**, benzvalene **3**, and an unidentified tetramer **4**. The trimers **2** and **3** were roughly equal in yield, and their total yield accounted for two-thirds of the entire reaction products. Tetramer **4** (its structure was not determined) accounted for 1–3% of the entire reaction products. When **2** and **3** were heated at a higher temperature (100 °C), they isomerized to 1,2,3-tri-*tert*-butyltrifluorobenzene **5** and 1,2,4-tri-*tert*-butyltrifluorobenzene **6**, respectively (Scheme 1).

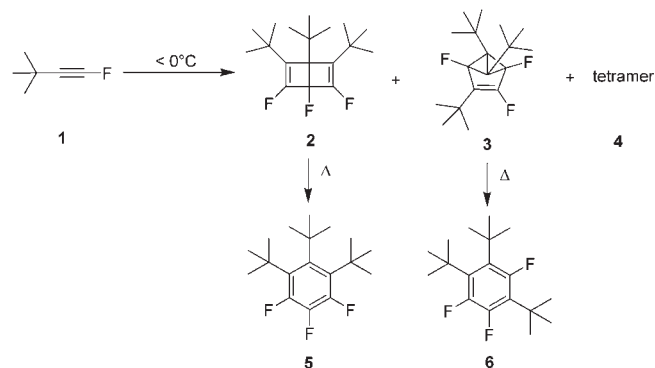
The proposed mechanism⁹ of the thermal cyclotrimerization described by Viehe is shown in Scheme 2. The cyclotrimerization was believed to start with the dimerization of two fluoroalkynes, giving rise to tetrahedrane **7a**, which was proposed to be in equilibrium with planar 1,4-difluorocyclobutadiene derivative **7b**, and 1,3-difluorocyclobutadiene derivative **7c**. Intermediate **7b/7c** could also exist in a diradical form of **7b'/7c'**. Then **7b** and **7c** reacted with the third fluoroalkyne to give trimers **2** and **3**,

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respectively. Finally, upon being heated, Dewar benzene derivative **2** and benzvalene derivative **3** isomerized to the aromatic 1,2,3-tri-*tert*-butyltrifluorobenzene **5** and 1,2,4-tri-*tert*-butyltrifluorobenzene **6**, respectively.

Scheme 1. Thermally Spontaneous Cyclotrimerization of *tert*-Butylfluoroacetylene



2+3=2/3 of the entire reaction product

2:3 ≈ 1:1

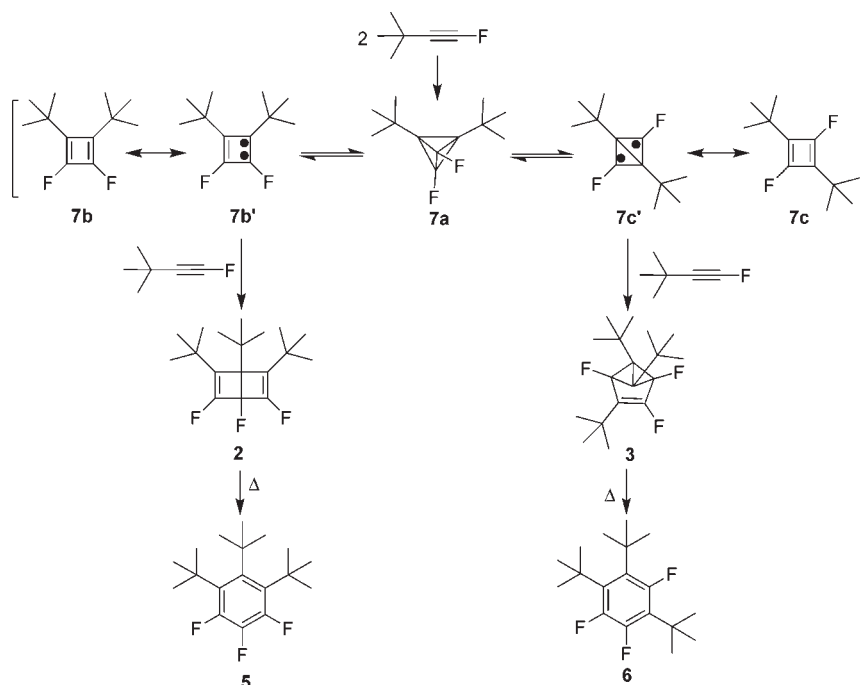
4=1~3% of the entire reaction product, unidentified tetramer

In 1986, Ballester and co-workers^{6c} found that perchlorophenylacetylene **8** can also undergo cyclotrimerization upon being heated in perchlorostyrene, giving perchloro-1,2,3-triphenylbenzene **9**, perchloro-1,2,4-triphenylbenzene **10**, and an unidentified isomeric $\text{C}_{24}\text{Cl}_{18}$ compound **11** (Scheme 3). Formation of **9** and **10** was also thought to proceed via a mechanism involving diradical cyclobutadiene and tetrahedrane intermediates, similar to the mechanism of fluoroacetylene cyclotrimerization proposed by Viehe.

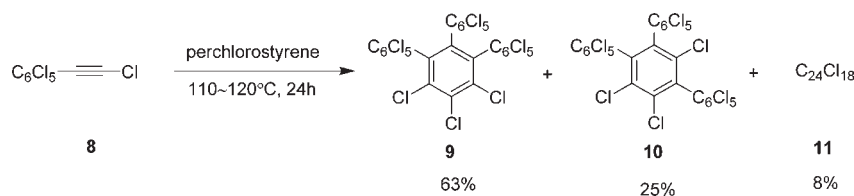
In 1993, Hopf and Witulski reported that 1,2,4- and 1,2,3-tricyanobenzenes were formed with other products when cyanoacetylene was heated at 160°C in a sealed tube.^{6d} Recently, they gave the energies of the products and the proposed intermediates, but no information about the transition states was given.¹⁰

The interesting phenomena of these uncatalyzed thermal cyclotrimerizations of alkynes have attracted some attention.^{8,10–12} However, several questions remain unanswered because of the scarce experimental and computational evidence. Why can these alkyne cyclotrimerization reactions occur under thermal reaction conditions? Why are fluoroacetylenes more reactive than chloroacetylenes? What factors control the regioselectivity in the thermal cyclotrimerization that gives different benzene derivatives (Schemes 1 and 3)? In particular, how does this process generate

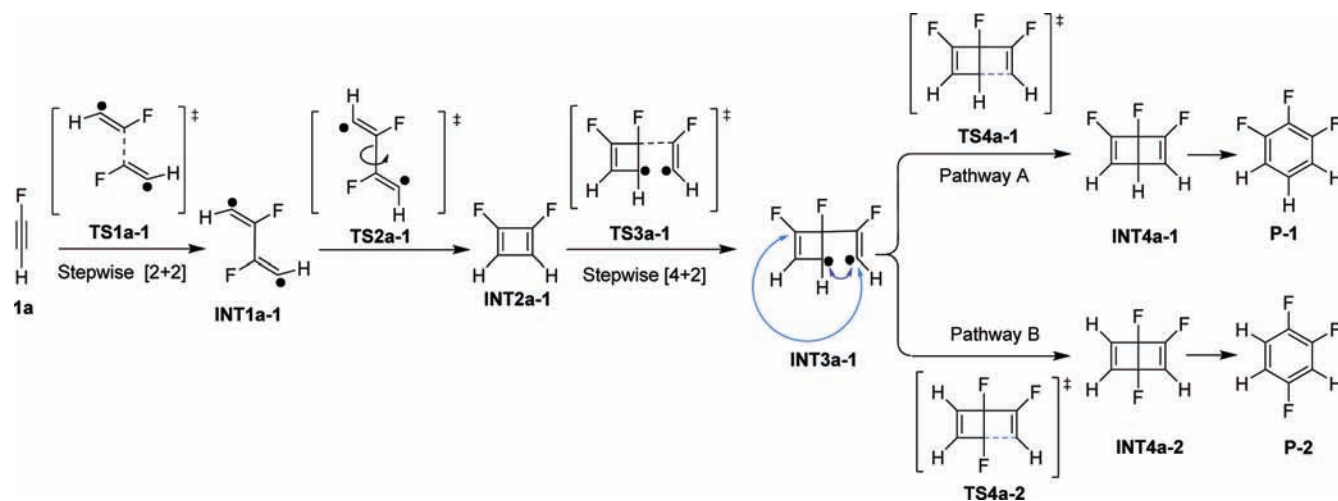
Scheme 2. Mechanism Proposed by Viehe for the Cyclotrimerization of *tert*-Butylfluoroacetylene



Scheme 3. Thermal Cyclotrimerization of Perchlorophenylacetylene



Scheme 4. Mechanism of the Cyclotrimerization of Fluoroacetylene Supported by DFT Calculations



the uncommon 1,2,3-trisubstituted benzene, which is difficult to produce by metal-catalyzed cyclotrimerizations of substituted alkynes? Another interesting question remained unanswered. What is the tetramer in Viehe's reaction?

Here we report the first computational study of the uncatalyzed cyclotrimerizations of haloacetylenes, aiming to answer the questions listed above. We believe that answering these questions is critical not only to our in-depth mechanistic understanding of these reactions but also to guiding the future design of other uncatalyzed cyclotrimerizations and studying the potential application of these reactions in material sciences and other disciplines. It is well-known that fluoroacetylene derivatives are highly reactive (sometimes explosive) and difficult to handle.¹³ Therefore, experimental investigation of fluoroacetylenes' reactions and reaction mechanisms and the experimental trapping of the proposed intermediates are very difficult. However, experimental studies of cyclotrimerizations of chloroacetylenes, if they can occur thermally, could be easily performed because chloroacetylenes are stable and can be easily prepared. Because of these facts, we investigated experimentally the thermal cyclotrimerization of arylchloroacetylene and trapped one of the proposed cyclobutadiene intermediates with the aim of further confirming or complementing our computational study. Furthermore, we expected that these new experiments could also serve to identify the possible tetramer in Viehe's reaction and provide information about the unidentified product in Ballester's reaction.

COMPUTATIONAL METHODS

All calculations were performed with Gaussian 03.¹⁴ The hybrid B3LYP functional¹⁵ in conjunction with the 6-31G(d) basis set¹⁶ was applied for the optimization of all the stationary points in the gas phase except for those singlet diradical transition states and intermediates, which were located at the UB3LYP/6-31G(d) level. This computational method has been successfully applied to study reactions involving singlet diradical intermediates and transition states.^{17–20} Frequency calculations were performed to confirm that each stationary point is either a minimum or a transition structure. Intrinsic reaction coordinate (IRC)²¹ calculations were used to confirm the connection among the reactants, products, and their transition states. For all singlet diradical transition

states and intermediates, the YJH spin-projection²² scheme has been used to reduce spin contamination. Orbital energies were computed using the HF/6-31G(d) method,²³ and the orbital coefficients listed are the 2p orbitals of carbons and fluorines and 3p orbitals of chlorines. ΔG , ΔH , and ΔE_0 are the calculated relative free energies, relative enthalpies, and zero-point energy (ZPE) corrected relative electronic energies in the gas phase, respectively. Unless otherwise specified, all discussed energies in what follows refer to ΔG values.

RESULTS AND DISCUSSION

Density Functional Theory (DFT) Study of the Cyclotrimerization of Fluoroacetylene. For the sake of calculation efficiency, we chose the fluoroacetylene reaction as the model reaction instead of the cyclotrimerization reaction of experimentally used *tert*-butylfluoroacetylene in the first attempt to understand the reaction mechanisms. Because the used fluoroacetylene is unsymmetric, there are several possible pathways for the cyclotrimerization of this fluoroacetylene, which had all been investigated by our DFT calculations. To present the results of our calculation clearly and concisely, we will first elucidate how the cyclotrimerization occurs in its most favored reaction pathway. Details of structures and energetics of the stationary points involved in this favored pathway will also be given. Then, we will present other competing but unfavored pathways, aiming to explain the regioselectivities of the cyclotrimerizations of haloacetylenes.

Favored Pathways for the Cyclotrimerization of Fluoroacetylene. The reaction pathways showing how the cyclotrimerization gives two benzene derivatives, P-1 and P-2, are summarized in Scheme 4. The computed energy surface for these processes is given in Figure 1. Structures of reactant, intermediate, and transition states are shown in Figure 2.

Our calculations suggest that cyclotrimerization starts with dimerization of fluoroacetylene **1a** to intermediate **INT2a-1**. The dimerization step occurs stepwise and involves the formation of a diradical intermediate **INT1a-1** (Scheme 4). Then the dimerization product **INT2a-1** reacts with the third fluoroacetylene to give a diradical intermediate **INT3a-1**, which undergoes ring closure via either pathway A or pathway B to give Dewar benzene **INT4a-1** or **INT4a-2**. Finally, isomerizations transform these

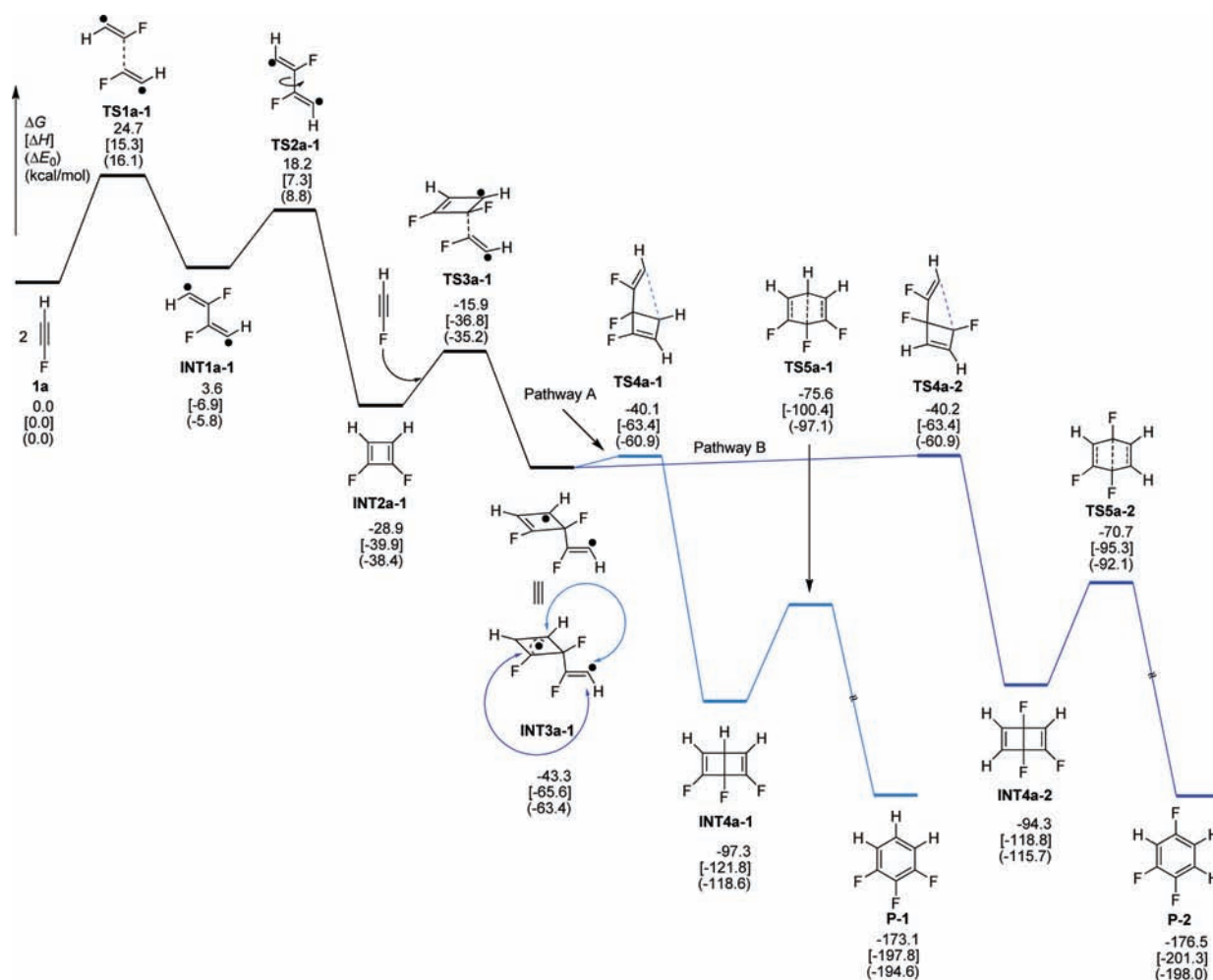


Figure 1. Energy surfaces of the favored pathways in the cyclotrimerization of fluoroacetylene. The steps from INT1a-1 to INT2a-1 and from INT2a-1 to INT3a-1 are not simple and involve a series of processes, and these are given in Figure 4.

Dewar benzenes to the corresponding benzene derivatives P-1 and P-2 upon heating.

The first step of the cyclotrimerization corresponds to the formation of the head-to-head diradical INT1a-1 (Figure 1). This step is easy with an activation energy of 16.1 kcal/mol and an activation free energy of 24.7 kcal/mol. In the C–C bond forming transition structure TS1a-1, the forming C–C bond is 1.89 Å long and has a *trans* conformation, as evidenced by the C3–C1–C2–C4 dihedral angle being 180° (Figure 2). The computed $\langle S^2 \rangle$ of TS1a-1 is 0.02, suggesting that the diradical character in the transition state has not been fully developed. In contrast, the formed intermediate INT1a-1 is a typical singlet diradical with a computed $\langle S^2 \rangle$ of 0.93. This is a σ -type diradical, as judged by its SOMO-1 orbitals. (Its SOMO orbitals are π -orbitals. The α - and β -radical spin orbitals of INT1a-1 and INT3a-1 are depicted in Figure 3.) INT1a-1 still adopts a *trans* conformation as TS1a-1 does, with the formed C–C bond being 1.48 Å long. Formation of this diradical intermediate INT1a-1 is exothermic by 6.9 kcal/mol, and this process is only slightly endogonic by 3.6 kcal/mol when considering the entropy penalty of this bimolecular process.

Calculations indicated that the ring closure from INT1a-1 to INT2a-1 is not simple and involves a series of processes (Figure 4). First, the *E,E*-isomer INT1a-1 isomerizes to the *E*,

Z-isomer INT1a-1EZ through a hydrogen switching transition state, TS1a-1EZ. Then another hydrogen switching through transition state TS1a-1ZZ gives the *Z,Z*-isomer INT1a-1ZZ. These two hydrogen switching processes are easy, with activation energies of only a few kilocalories per mole. Similar hydrogen switching is also involved in the course of formation of INT3a-1 from INT3a-1E. Intermediate INT1a-1ZZ is expected to give a *cis* diradical, which then undergoes ring closure to give INT2a-1, but the expected *cis* diradical is not a stationary point in the energy surface. Calculations showed that this hypothesized diradical directly undergoes ring closure to form the cyclobutadiene INT2a-1 under geometry optimization. This is similar to the process of dimerization of nitrile oxide studied by Houk and co-workers.^{17g} In TS2a-1, the forming C–C bond is 3.41 Å long, and it has a nearly perpendicular configuration with the C2–C3–C4–C1 dihedral angle being 101.3°. TS2a-1 has a diradical character with a computed $\langle S^2 \rangle$ of 1.01, indicating that TS2a-1 is a typical singlet diradical transition state. The ring closure process is easy with an activation energy of 14.6 kcal/mol with respect to INT1a-1 and is exothermic by 33.0 kcal/mol.

Once the 1,4-difluorocyclobutadiene is formed through the dimerization process, the next step in the cyclotrimerization is the [4+2] reaction between 1,4-difluorocyclobutadiene and the third fluoroacetylene. We found that the [4+2] reaction can

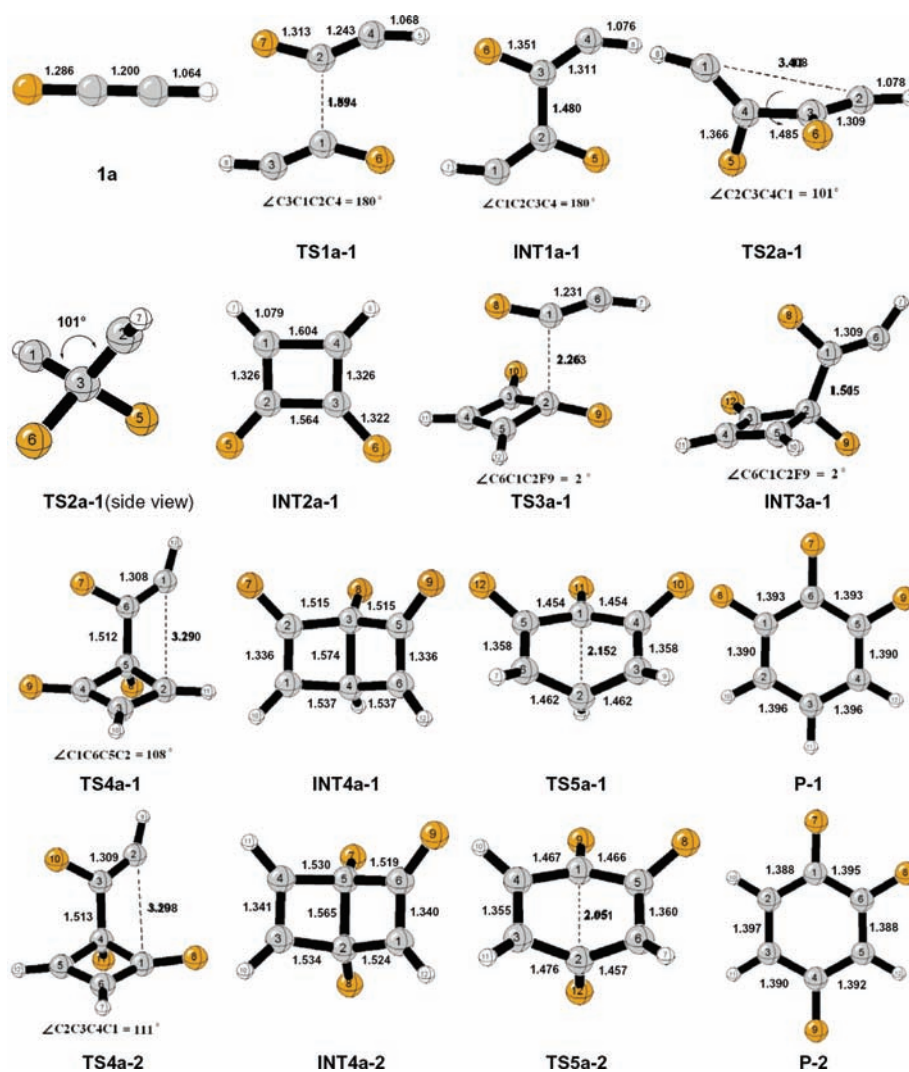


Figure 2. DFT-computed structures of the reactants, intermediates, transition states, and products.

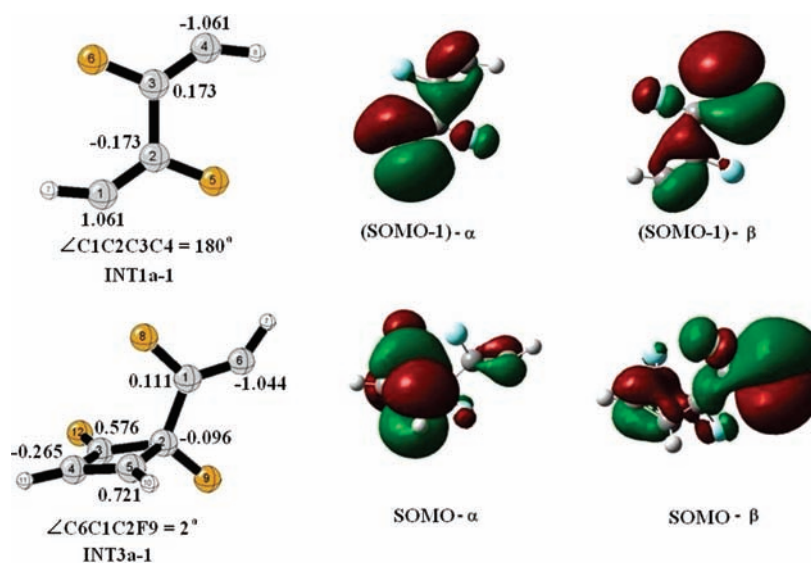


Figure 3. Spin densities and orbitals of INT1a-1 (SOMO-1) and INT3a-1 (SOMO).

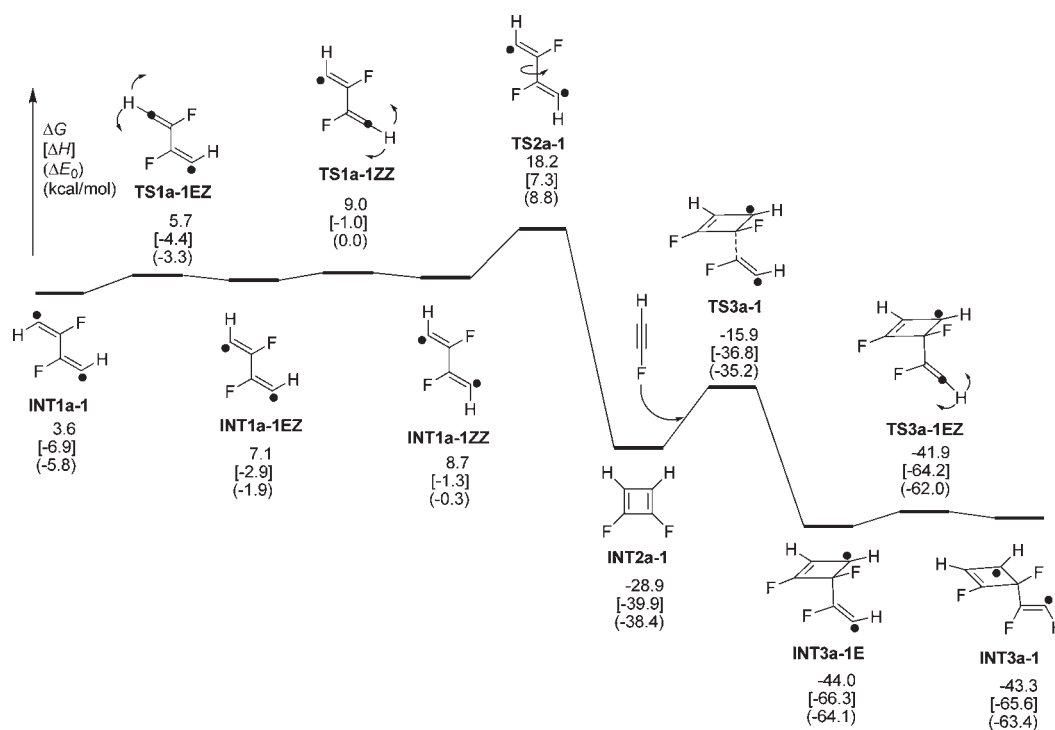


Figure 4. Hydrogen switching processes in the cyclotrimerization of fluoroacetylene.

occur with both concerted and diradical mechanisms. However, the concerted processes (see Table S5 of the Supporting Information) are not favored compared to the stepwise pathways. The stepwise [4+2] pathway starts from C–C bond formation via transition structure **TS3a-1**, generating a diradical intermediate, **INT3a-1**. (Hydrogen switching from another intermediate **IN3a-1E** to **INT3a-1** is also involved, and this step is easier. This is shown in Figure 4.) This step requires an activation energy of only 3.2 kcal/mol and an activation free energy of 13.0 kcal/mol. The forming C1–C2 bond in the transition state **TS3a-1** is 2.26 Å long. The $\langle S^2 \rangle$ in **TS3a-1** is 0.76, indicating that the diradical character in this transition state has already been formed. The formed C1–C2 bond in **INT3a-1** is 1.51 Å long. The $\langle S^2 \rangle$ in **INT3a-1** is 1.04, indicating that **INT3a-1** is a typical singlet diradical intermediate. The SOMO orbitals of **INT3a-1** show that the free radical on the four-membered ring is a delocalized allylic radical, which is characterized as a π -type radical. In contrast, the vinyl radical in **INT3a-1** is a σ -type radical composed of an sp^2 orbital, and this SOMO orbital is perpendicular to the plane of the double bond (see these orbitals in Figure 3). Calculations showed that formation of this diradical intermediate **INT3a-1** is exothermic by 25.7 kcal/mol and is exogonic by 14.4 kcal/mol. Then **INT3a-1** undergoes a ring closure reaction via two competing pathways, pathway A and pathway B, giving Dewar benzene derivatives **INT4a-1** and **INT4a-2**, respectively, with barriers of ~ 2.5 kcal/mol. This step is highly exothermic, which suggests that the formation of Dewar benzenes is irreversible and the regioselectivity of benzene derivative products is kinetically controlled. The two competing ring closures described above have similar activation energies, suggesting the ratio of **INT4a-1** to **INT4a-2** is 1:1. This agrees with the experimental results of Viehe, who showed the final benzene derivatives **5** and **6** were obtained in equal amounts (Scheme 1).

Finally, Dewar benzene **INT4a-1** isomerizes into the aromatic 1,2,3-trifluorobenzene **P-1** with an activation energy of 21.5 kcal/mol and an activation free energy of 21.7 kcal/mol.²⁴ Similarly, Dewar benzene derivative **INT4a-2** isomerizes into aromatic 1,2,4-trifluorobenzene **P-2** with an activation energy of 23.6 kcal/mol and an activation free energy of 23.6 kcal/mol. We can see that the activation energies of the isomerizations of Dewar benzenes to aromatic benzenes are higher than those of the cyclotrimerizations, suggesting that the thermal reaction of fluoroacetylene gives Dewar benzenes at lower temperatures, but it can produce benzenes if a higher temperature is used. This agrees with experimental findings, where Dewar benzenes were observed experimentally when cooler reaction conditions were used.^{6b}

From the computational results described above, we can see that the dimerization of two fluoroacetylenes to form cyclobutadiene is the rate-determining step and this step is irreversible. The overall activation energy is only 16.1 kcal/mol, and the activation free energy is 24.7 kcal/mol. The low activation energy of the rate-determining step explains why the cyclotrimerization of *tert*-butylfluoroacetylene can happen spontaneously below 0 °C. The overall reactions to form Dewar benzenes **INT4a-1** and **INT4a-2** are very exogonic by 97.3 and 94.3 kcal/mol, respectively. The low activation energy of 16.1 kcal/mol and the very high exothermicity of the cyclotrimerization of fluoroacetylenes are consistent with the fact that these reactions are prone to explosion under uncontrolled experimental conditions.^{6a,b,13}

Regioselectivity and Substituent Effects of the Dimerization of Fluoroacetylene. In the favored pathway described above, we have discussed only the formation of head-to-head **INT1a-1** via transition state **TS1a-1**. In theory, there are other possible competing pathways to give other cyclotrimerization products that were not observed experimentally. Therefore, we computed these possible pathways and analyzed why these pathways are not

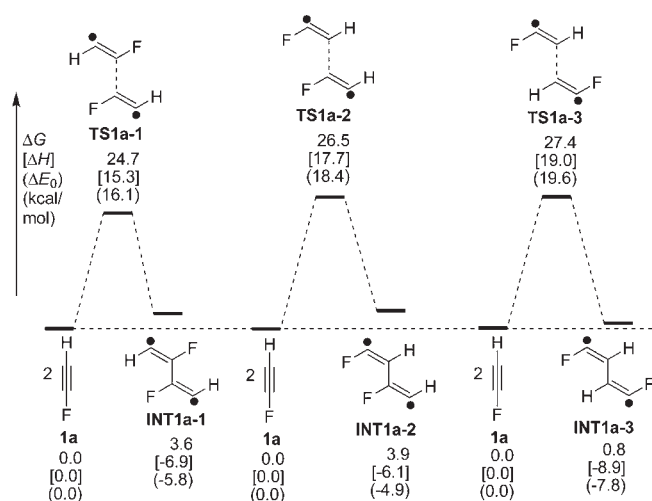


Figure 5. Energies of the competing transition states and diradical dimers.

Table 1. Activation Energies^a of the Competing Transition States

Entry	R	TS1a-1	TS1a-2	TS1a-3
1	R = H	16.1	18.4	19.6
2	R = Me	14.3	20.5	23.3
3	R = <i>t</i> Bu	12.9	22.6	27.8
4	R = Ph	8.4	19.4	25.3

^aThe energies of the transition states are relative to the energies of the corresponding separated fluoroacetylenes.

avored energetically. DFT calculation showed that the head-to-tail transition state **TS1a-2** and the tail-to-tail transition state **TS1a-3** are the other two competing transition states in the dimerization of fluoroacetylenes (Figure 5).

The relative activation energies of **TS1a-1**, **TS1a-2**, and **TS1a-3** are 16.1, 18.4, and 19.6 kcal/mol, respectively, indicating that the pathway for generating a C–C bond with fluorine substitution (head-to-head) is favored. Because both hydrogen and fluorine are not sterically demanding substituents, we can state that the significant preference of **TS1a-1** over **TS1a-2** or **TS1a-3** is not due to steric effects, but due to the stereoelectronic effects of the fluorine substituent.

Experimentally, *tert*-butylfluoroacetylene was used in the thermal cyclotrimerization reaction;^{6a,b} it is necessary to investigate the substituent effects of substituted fluoroacetylenes in this rate-determining step. To study both the stereoelectronic and steric effects, we chose methyl, *tert*-butyl, and phenyl as the substituents of fluoroacetylenes in the DFT calculations. The activation energies of the competing transition states in the dimerization of substituted fluoroacetylenes are listed in Table 1. Calculations also strongly suggest that head-to-head diradical dimers are formed exclusively, because the other competing pathways have activation energies higher than those in the head-to-head pathways by more than 6 kcal/mol.

The regioselectivity of the dimerization of fluoroacetylenes can be explained well with frontier molecular orbital (FMO) theory.²⁵ According to the FMO theory, the smaller the LUMO–HOMO energy gap, the easier the dimerization will be. In addition, FMO theory indicates that the larger molecular orbital coefficients in both LUMO and HOMO facilitate the overlap of molecular orbitals involved in the bond formation transition state. The calculated 2p molecular orbital coefficients of the acetylenic carbon attached to fluorine (we label this carbon as C_α) are larger than those of the other acetylenic carbon (we label this carbon as C_β) in both LUMO and HOMO (Table 2).²⁶ Therefore, the first forming C–C bond between two molecular fluoroacetylenes prefers to occur on the C_α atoms. This is why the head-to-head pathway is the favored pathway in the dimerization of fluoroacetylenes. It is interesting to see that substituting the hydrogen atom with an alkyl or aryl group in the fluoroacetylene increases the energies of the disfavored transition structures, making the head-to-head dimerization much more favored. On the other hand, alkyl and aryl substituents are more efficient than hydrogen in favoring the head-to-head dimerization of fluoroacetylenes (Table 1, entries 2–4), suggesting that the forming vinyl radical centers could be stabilized by the alkyl and aryl groups. We found that the *tert*-butyl group is more efficient than the methyl group in lowering the barrier of the head-to-head dimerization of alkylfluoroacetylenes. Interestingly, the phenyl group is the most efficient group in lowering the barrier of the head-to-head dimerization of substituted fluoroacetylenes (Table 1, entry 4). The activation energy of **TS1c-1** is 8.4 kcal/mol, lower than those of **TS1b-1** and **TS1-1** by 5.9 and 4.5 kcal/mol, respectively. This is consistent with the FMO theory in that the order of the LUMO–HOMO energy gaps is as follows: fluoroacetylene (17.6 eV) > methylfluoroacetylene (16.9 eV) > *tert*-butylfluoroacetylene (16.8 eV) > phenylfluoroacetylene (11.6 eV).

Possibility of the Existence of Tetrahedrane 7a in the Cyclotrimerization. Viehe and co-workers proposed that tetrahedrane **7a** (Scheme 2) could be formed in the reaction system. We found that formation of **7a** from *tert*-butylfluoroacetylene **1** is endothermic by 16.3 kcal/mol, much higher than the activation energy of dimerization to form **7b** (see Figure 6 and entry 3 of Table 1). This suggests direct formation of **7a** from **1** can be ruled out. Furthermore, this analysis indicates that head-to-head dimerization of **1** [through **TS1-1** (Table 1)] is favored versus head-to-tail dimerization [through **TS1-2** (Table 1)], meaning that the formation of **7c** from **1** through a stepwise [2+2] cycloaddition is impossible. Therefore, **7a** and **7c** cannot be involved in the cyclotrimerization of *tert*-butylfluoroacetylene. Actually, this can be further supported by experiments of Maier and co-workers,²⁷ who showed that formation of tetrahedrane can be achieved only by UV irradiation. A similar process of formation of tetrakis(trimethylsilyl)tetrahedrane could happen upon irradiation of tetrakis(trimethylsilyl)cyclobutadiene.²⁸ The four longer C–Si bonds and the four σ -donating silyl substituents were thought to be responsible for the high stability of tetrakis(trimethylsilyl)tetrahedrane. In the present system, such effects are absent, and therefore, tetrahedrane formation is not favored under thermal reaction conditions.

Regioselectivity of the Reaction of 1,4-Difluorocyclobutadiene with Fluoroacetylene. For the [4+2] reaction of 1,4-difluorocyclobutadiene with fluoroacetylene, there are also several possible pathways to give various [4+2] cycloadducts. Table 3 lists all four possible diradical pathways. Again, formation

Table 2. Molecular Orbital Coefficients and LUMO–HOMO Gaps of Haloacetylenes

Compound	H β α F 1a	Me β α F 1b	β α F 1	Ph β α F 1c	Me β α Cl 1f	Ph β α Cl 1d
LUMO						
Orbital Energy (eV)	6.5	6.4	6.5	3.0	5.7	2.7
HOMO						
Orbital Energy (eV)	-11.1	-10.5	-10.3	-8.6	-10.1	-8.5
Gap _{LUMO/HOMO} (eV)	17.6	16.9	16.8	11.6	15.8	11.2
Gap _{triplet/singlet} (eV) ^a	3.1	2.9	3.0	2.4	3.2	2.5

^a The energy gaps were calculated with optimized geometries in both triplet and singlet states.

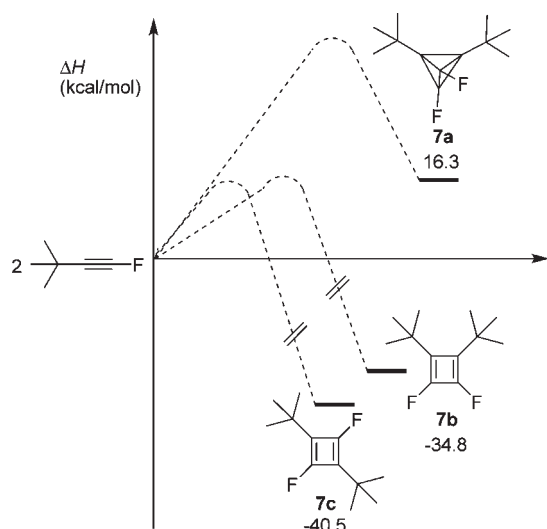


Figure 6. Energies of dimers of *tert*-butylfluoroacetylene 1.

of the first C–C bond in the reaction of 1,4-difluorocyclobutadiene and fluoroacetylene takes place on the C_{α} centers of the two molecules. Therefore, the head-to-head pathway via TS3a-1 is favored. This trend is observed for various substituted haloacetylenes (Table 3, entries 2–4).

The fact that the formation of a new C–C bond between the C_{α} centers is lower in activation energy than the competing pathways can also be rationalized by FMO theory (see the atom labeling in Table 4).

Calculations show that regardless of whether the substituent is a hydro, methyl, or phenyl group, the 2p coefficients of the frontier

molecular orbitals of the C_{α} atoms on the four-membered ring of 1,4-disubstituted difluoroacetylenes are larger than those of the C_{β} atoms in their LUMOs, whereas the molecular orbital coefficients of these atoms in their HOMOs are very close (Table 4).

Energetically, the energy gap between the HOMO of the hydro/methylfluoroacetylene and the LUMO of the 1,4-difluorobutadiene/1,4-dimethyldifluorobutadiene is smaller than the energy gap between the LUMO of the hydro/methylfluoroacetylene and the HOMO of the 1,4-difluorobutadiene/1,4-dimethyldifluorobutadiene. Therefore, the diradical reaction of the hydro/methylfluoroacetylene with the 1,4-difluorobutadiene/1,4-dimethyldifluorobutadiene will be mainly controlled by the orbital interaction between the HOMO of the hydro/methylfluoroacetylene and the LUMO of the 1,4-difluorobutadiene/1,4-dimethyldifluorobutadiene (Figure 7a,b). Therefore, the larger molecular orbital coefficients of the C_{α} atoms in HOMO of the hydro/methylfluoroacetylene (Table 2) and in the LUMO of the 1,4-difluorobutadiene/1,4-dimethyldifluorobutadiene (Table 4) facilitate the overlap of molecular orbitals involved in the bond formation process, leading to the first C–C bond in the reaction of hydro/methylfluoroacetylene and 1,4-difluorobutadiene/1,4-dimethyldifluorobutadiene forming between the C_{α} atom of the hydro/methylfluoroacetylene and the C_{α} atom of 1,4-difluorobutadiene/1,4-dimethyldifluorobutadiene. In contrast, the reaction between phenylfluoroacetylene and 1,4-diphenyldifluorobutadiene is dominated by the orbital interaction between the LUMO of the phenylfluoroacetylene and the HOMO of the 1,4-diphenyldifluorobutadiene (Figure 7c). Consequently, the first C–C bond in this reaction will also form between the C_{α} atom of the phenylfluoroacetylene and the C_{α} atom of 1,4-diphenyldifluorobutadiene, because larger molecular orbital coefficients in LUMO and HOMO facilitate the overlap of molecular orbitals involved in the bond formation transition state.

The [4+2] reaction could also occur via a concerted pathway, as demonstrated by Houk and Snapper.²⁹ However, this system is different from Houk and Snapper's system due to the presence of fluorine atoms. DFT calculations found that in our case, the concerted pathways are higher in energy than the diradical pathways shown in Table 3 (details can be seen in Table S5 of the Supporting Information). This can also be understood by invoking the mechanism of the reaction of tetrafluoroethylene and 1,3-butadiene studied by Borden and co-workers.³⁰ They found that tetrafluoroethylene and 1,3-butadiene prefer to form a 1,4-diradical intermediate instead of undergoing a concerted Diels–Alder reaction, because fluorine substituents have a profound stabilizing effect on diradical formation. Formation of the 1,4-diradical intermediate is also included in the stepwise [4+2] reaction of 1,4-difluorocyclobutadiene with fluoroacetylene. Therefore, it is not surprising that the concerted pathways are higher in energy than the diradical pathways for the [4+2] reactions shown in Table 3.

Cyclotrimerization of Chloroacetylenes. *Substituent Effects and Regioselectivity of the Dimerization of Chloroacetylenes in the Rate-Determining Step.* Experimentally, Viehe and co-workers

Table 3. Activation Energies^a of the Reactions of 1,4-Difluorocyclobutadiene and Fluoroacetylene

Entry	R	TS3a-1	TS3a-2	TS3a-3	TS3a-4
1	R = H	TS3a-1	TS3a-2	TS3a-3	TS3a-4
	ΔE_0 (kcal/mol)	3.2	5.7	4.4	4.8
2	R = Me	TS3b-1	TS3b-2	TS3b-3	TS3b-4
	ΔE_0 (kcal/mol)	3.5	10.1	7.4	8.0
3	R = ^t Bu	TS3-1	TS3-2	TS3-3	TS3-4
	ΔE_0 (kcal/mol)	3.3	20.9	13.5	12.6
4	R = Ph	TS3c-1	TS3c-2	TS3c-3	TS3c-4
	ΔE_0 (kcal/mol)	-0.5	12.1	4.2	7.0

^aThe energies of the transition states are relative to the energies of the corresponding difluorocyclobutadienes and fluoroacetylenes.

noticed that *tert*-butylchloroacetylene is thermally stable, suggesting that chloroacetylene is not reactive compared with its fluoro counterpart. Later, Ballester and co-workers reported the thermal cyclotrimerization of perchlorophenylacetylene at 110–120 °C, indicating that arylchloroacetylene is more reactive than alkylchloroacetylene. Therefore, we computed the dimerization processes of several chloroacetylenes to investigate their reactivities and regioselectivities (Table 5). Calculations show that arylchloroacetylenes (Table 5, entries 1 and 2) strongly favor the head-to-head dimerizations, whereas alkylchloroacetylenes (Table 5, entries 3–5) have a very weak or no preference for head-to-head dimerization. Again, this regioselectivity can be explained by FMO theory. For arylchloroacetylenes, the calculated molecular orbital coefficients of the C_α atoms are larger than those of the C_β atoms in both their LUMOs and HOMOs, while this difference is lost on methylchloroacetylenes (Table 2). That is why the formation of the head-to-head carbon–carbon bond is the favored pathway in the dimerization of arylchloroacetylenes, while alkylchloroacetylenes have a very weak or no preference for head-to-head dimerization.

Another conclusion drawn from the comparison of Tables 1 and 5 is that alkylchloroacetylenes are much more sluggish than their fluoro counterparts in undergoing dimerization by more than 12.8 kcal/mol in terms of the activation energy. Similar to the fluoroacetylenes, chloroacetylenes with aryl substituents are more reactive than alkyl chloroacetylenes during dimerization. For example, the activation energy for the dimerization of methylchloroacetylene is 27.1 kcal/mol, while those of phenylchloroacetylene and perchlorophenylacetylene are 21.8 and 22.1 kcal/mol, respectively. It is interesting to note that phenylchloroacetylene and perchlorophenylacetylene have the same dimerization reactivity. Experimentally, perchlorophenylacetylene gave cyclotrimerization products at high temperatures.^{6c} This implies that phenylchloroacetylene could also undergo cyclotrimerization under the same or similar reaction conditions. Our experimental proof of this will be given below.

To unveil the different reactivities of fluoroacetylene and chloroacetylene, we initially attempted to explain this difference with FMO theory. According to the FMO theory, the larger the

Table 4. Molecular Orbital Coefficients and LUMO–HOMO Gaps of 1,4-Difluorocyclobutadienes

Intermediate	INT2a-1	INT2b-1	INT2c-1
LUMO			
Orbital Energy (eV)	2.6	3.1	1.4
HOMO			
Orbital Energy (eV)	-8.0	-7.5	-6.8
Gap _{LUMO/HOMO} (eV)	10.6	10.6	8.2

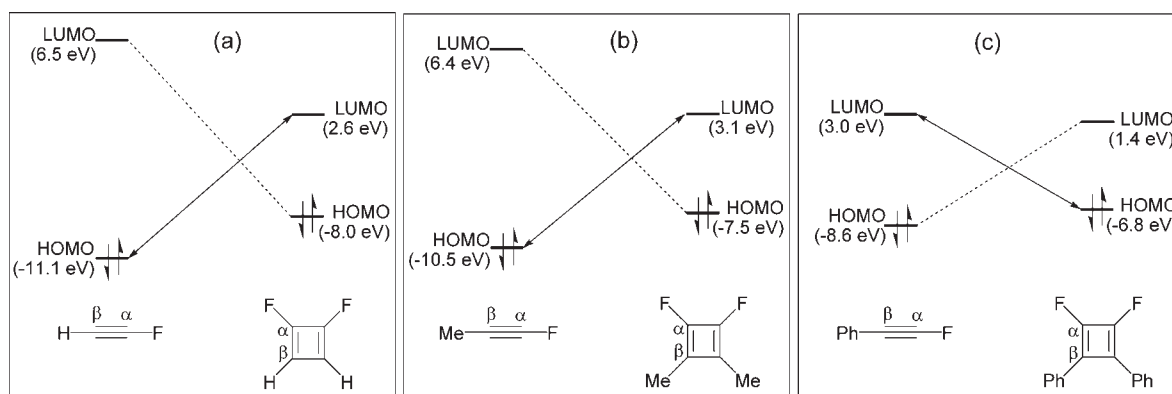


Figure 7. Orbital energies of fluoroacetylenes and 1,4-difluorobutadienes.

Table 5. Activation Energies^a of the Transition States in the Dimerization of Chloroacetylenes

Entry	R	TS1d-1	TS1d-2	TS1d-3	
1	R = Ph	TS1d-1	TS1d-2	TS1d-3	
		ΔE ₀ (kcal/mol)	21.8	26.4	29.5
2	R = C ₆ Cl ₅	TS1e-1	TS1e-2	TS1e-3	
		ΔE ₀ (kcal/mol)	22.1	27.9	34.8
3	R = Me	TS1f-1	TS1f-2	TS1f-3	
		ΔE ₀ (kcal/mol)	27.1	27.1	27.4
4	R = ^t Bu	TS1g-1	TS1g-2	TS1g-3	
		ΔE ₀ (kcal/mol)	28.6	30.5	34.8
5	R = Cy	TS1h-1	TS1h-2	TS1h-3	
		ΔE ₀ (kcal/mol)	27.4	27.7	27.3

^a The energies of the transition states are relative to the energies of the corresponding chloroacetylenes.

LUMO–HOMO energy gap, the higher the reaction barrier will be. As we have presented above, FMO theory can explain the substituent effects in both fluoro- and chloroacetylene systems but fails to explain why fluoroacetylene is more reactive than chloroacetylene. For example, the higher reaction barriers of chloroacetylenes have smaller LUMO–HOMO gaps, while the lower reaction barriers of fluoroacetylenes have larger LUMO–HOMO gaps (Table 2). This is in contradiction with FMO theory. We attributed the relative reactivity in dimerization of haloacetylenes to the energies required to convert haloacetylenes to their triplet diradical structures. In the dimerization transition states, the haloacetylenes adopt *trans* conformations, very similar to the interaction between two triplet diradicals. Therefore, the easier it is for a haloacetylene to form its triplet diradical, the more reactive this haloacetylene will be in dimerization. Our calculations found that the triplet–singlet gap of methylfluoroacetylene (2.9 eV) and phenylfluoroacetylene (2.4 eV) is smaller than that of methylchloroacetylene (3.2 eV) and phenylchloroacetylene (2.5 eV) (see Table 2). Therefore, fluoroacetylene more easily reaches the diradical transition state than chloroacetylene, making the former more reactive than the latter. Such an explanation is very similar to the valence bond theory for explaining reactivity.³¹

In addition, we can also attribute the high reactivity of fluoroacetylenes to the weakening of the π -bond of the fluoroacetylenes

and the preference of fluorine-substituted carbon centers for pyramidal geometries.^{11d,32} This is analogy to the explanation of the reactivity of tetrafluoroethylene by Borden and co-workers, showing that tetrafluoroethylene has a weak π -bond and prefers to generate fluorine-substituted radical centers with pyramidal geometries.³²

DFT Investigation of Cyclotrimerization of Phenylchloroacetylene. Figure 8 gives the DFT-computed energy surfaces of the cyclotrimerization of phenylchloroacetylene **1d** to yield 1,2,3-triphenyltrichlorobenzene **P-3** and 1,2,4-triphenyltrichlorobenzene **P-4**. The other competitive but disfavored pathways are given in the Supporting Information (Tables S6 and S8). DFT calculations show that the cyclotrimerization energy surfaces of phenylchloroacetylene are very similar to those of fluoroacetylene (Figure 1). The formation of **INT2d-1** is stepwise and involves diradical intermediate **INT1d-1** with an activation barrier of 21.8 kcal/mol, which is 13.4 kcal/mol higher than that for the dimerization of its fluoro counterpart (Table 1). This suggests that a higher temperature is required to achieve the cyclotrimerization of phenylchloroacetylene. This explains why Ballester had to conduct the reaction of perchlorophenylacetylene at 110–120 °C. The subsequent reaction between **INT2d-1** and **1d** to form **INT3d-1** with an activation barrier of 7.4 kcal/mol is also a regioselective process (Table S8 of the Supporting Information), followed by the formation of Dewar benzenes **INT4d-1** and **INT4d-2** via two competing pathways with very low activation barriers of 0.3 and 0.5 kcal/mol, respectively. Finally, the isomerization of **INT4d-1** and **INT4d-2** to benzenes **P-3** and **P-4** requires activation barriers of 17.4 and 28.7 kcal/mol, respectively. These isomerization barriers are close to the activation barrier of the dimerization process, suggesting that the cyclotrimerization of phenylchloroacetylene cannot stop at the Dewar benzenes but directly gives aromatic benzene derivatives 1,2,3-triphenyltrichlorobenzene **P-3** and 1,2,4-triphenyltrichlorobenzene **P-4**. This agrees with the results of Ballester's experiments.^{6c}

Experimental Test of the DFT Prediction and Trapping Experiments. To verify our prediction that unsubstituted arylchloroacetylene can undergo cyclotrimerization and to gain more information about this process, we embarked on the experimental studies of this reaction. In addition, we managed to trap the 1,4-disubstituted cyclobutadiene intermediate by two dienophiles. When phenylchloroacetylene **1d** was subjected to the thermal reaction conditions at 110 °C without using any solvent, three products of phenylchloroacetylene were isolated

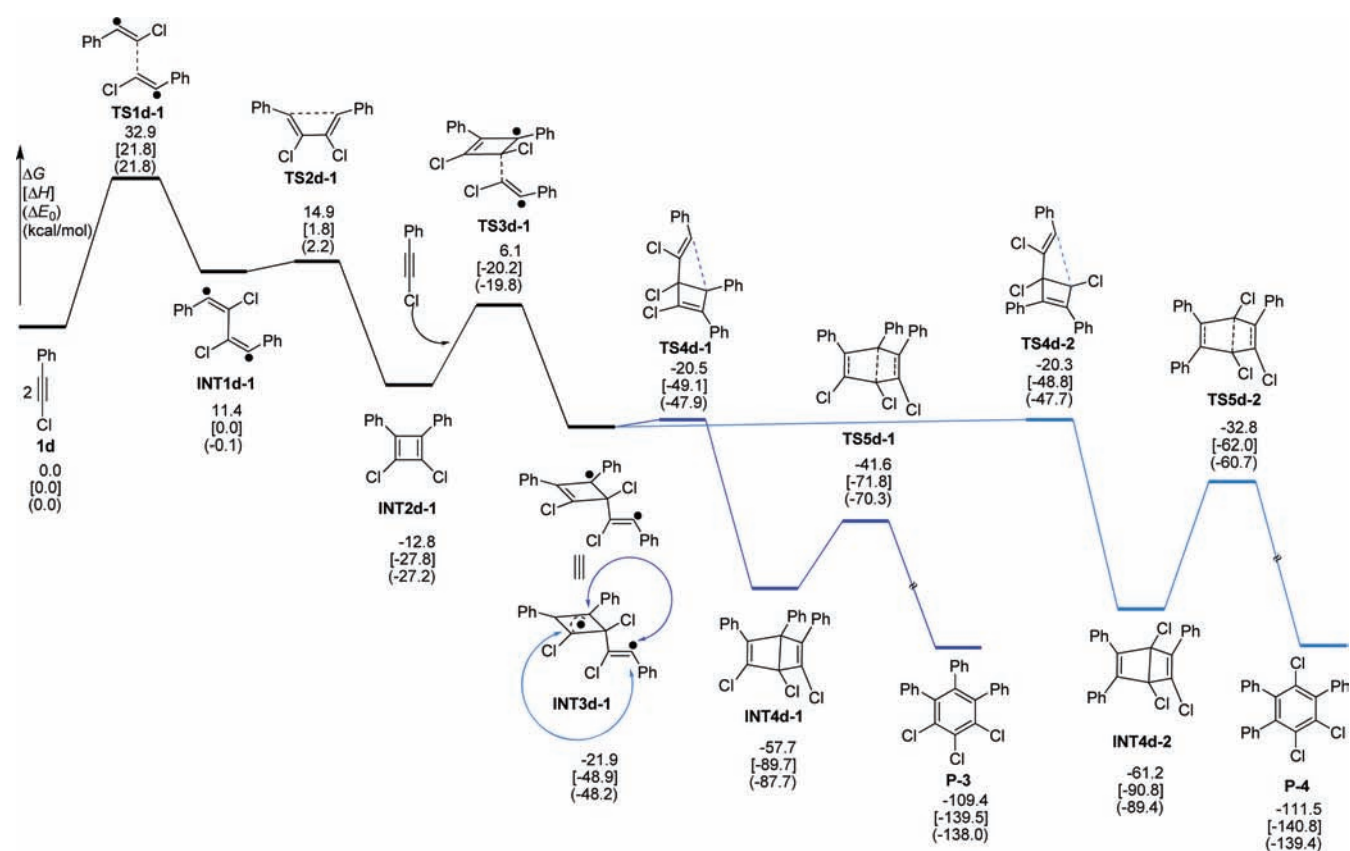


Figure 8. Calculated minimum energy pathway for the cyclotrimerization of phenylchloroacetylene.

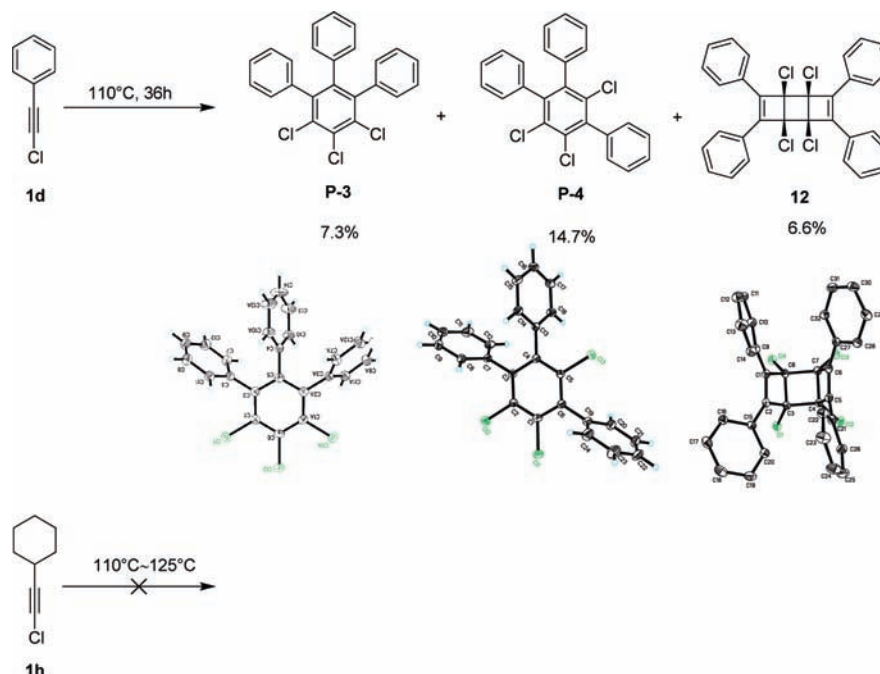
(Scheme 5). Two of them, 1,2,3-triphenyltrichlorobenzene **P-3** and 1,2,4-triphenyltrichlorobenzene **P-4** are trimers with yields of 7.3 and 14.7%, respectively. The third product is a ladderane,³³ *cis*-1,2,5,6-tetrachloro-3,4,7,8-tetraphenyltricyclo[4.2.0.0^{2,5}]octa-3,7-diene **12**, with a reaction yield of 6.6%. The structures of **P-3**, **P-4**, and **12** were confirmed by X-ray crystallographic analyses (Scheme 5). Trimers **P-3** and **P-4** are the expected products from the calculation study described above. Ladderane **12** is a dimer of 1,4-diphenyldichlorocyclobutadiene **INT2d-1**. From these experimental results, we propose that the unidentified tetramer in Viehe's experiment (Scheme 1) could be an analogue of ladderane **12**. The *cis* conformation of ladderane **12** is the result of the *syn* dimerization of **INT2d-1**. This process is similar to the *syn* dimerization of cyclobutadiene, which is thought to be a highly favored process.³⁴ In contrast, cyclohexylchloroacetylene **1h** is stable at 110 °C for 24 h and can polymerize slowly into unidentified dark polymers at 125 °C. This suggests that cyclohexylchloroacetylene is more sluggish than phenylchloroacetylene in cyclotrimerization, in good agreement with the results of our calculation (Table 5).

To further reveal the intermediary existence of antiaromatic **INT2d-1**, we conducted trapping experiments. Heating phenylchloroacetylene in the presence of maleic anhydride without solvent gives cycloadduct **13** in 20% yield (Scheme 6). In the presence of dimethyl acetylenedicarboxylate, cycloadduct **14** is obtained in 13% yield. The structure of **14** was confirmed by X-ray crystallographic analysis (Scheme 6). This experimental evidence clearly confirms the fact that **INT2d-1** is formed as an intermediate in the cyclotrimerization of phenylchloroacetylene.

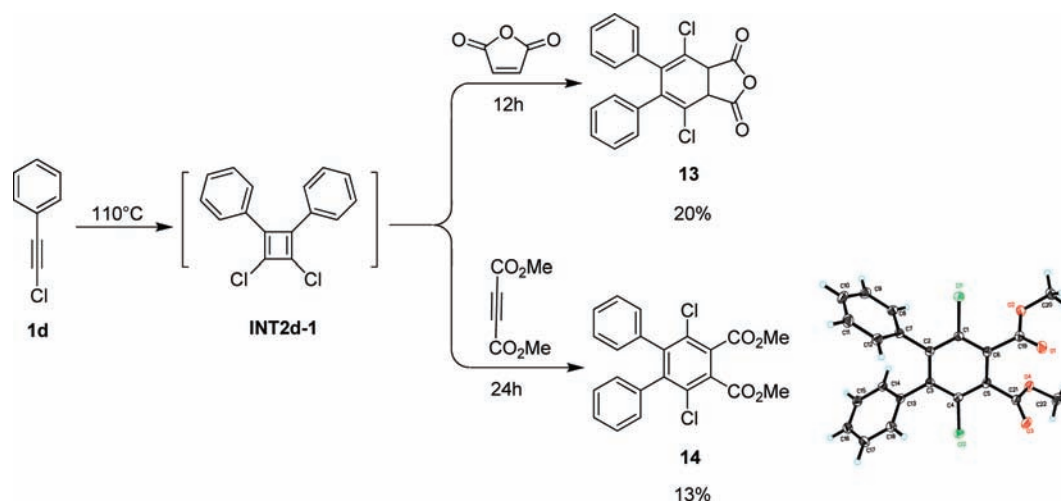
CONCLUSIONS

We theoretically scrutinized the thermal cyclotrimerizations of fluoro- and chloroacetylenes with computational and experimental studies. On the basis of these calculations, 1,4-dihalocyclobutadiene is regioselectively formed in a stepwise [2+2] cycloaddition of two haloacetylenes, which can be trapped regioselectively with another haloacetylene to generate a 1,4-diradical trimer intermediate. Finally, 1,2,6-trisubstituted Dewar benzene and 1,2,4-trisubstituted Dewar benzene are equally formed from the ring closure of the 1,4-diradical trimer intermediate in two competing pathways. The calculations suggest that the dimerization of the haloacetylene is the rate-determining step with an overall activation energy of 16.1 kcal/mol for fluoroacetylene and 21.8 kcal/mol for phenylchloroacetylene. That is why the fluoroacetylene cyclotrimerization can occur at low temperatures and the arylchloroacetylene cyclotrimerization can occur at 110 °C. The FMO theory was applied to explain the regioselective dimerization of haloacetylenes and the regioselective reaction of 1,4-dihalocyclobutadiene and haloacetylene. It predicted that formation of a bond on the halogenated carbon centers was always favored. It was found that the higher reactivity of fluoroacetylenes compared to that of chloroacetylenes is due to the fact that fluoroacetylenes have smaller singlet–triplet gaps than chloroacetylenes and more easily undergo dimerization and cyclotrimerization. In addition to the computational study, experiments were also conducted to identify the products of the cyclotrimerization and trap the proposed cyclobutadiene intermediate. The expected 1,2,3-trisubstituted and 1,2,4-trisubstituted benzenes were isolated from the thermal reaction of phenylchloroacetylene. In addition to these two expected trimers, a tetramer with a

Scheme 5. Thermal Cyclotrimerization of Phenylchloroacetylene and Cyclohexylchloroacetylene



Scheme 6. Trap INT2d-1 with Dienophiles



tricyclic skeleton was also isolated from the same reaction. In a trapping experiment, the proposed 1,4-disubstituted cyclobutadiene was successfully trapped with dienophiles of maleic anhydride and dimethyl acetylenedicarboxylate. These experimental findings gave concrete evidence to support the computational predictions.

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures, spectral data of all new compounds, and crystal structure data of **P-3**, **P-4**, **12**, and **14** in CIF format. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (19) Calculations using larger basis sets show that the activation energies of the dimerizations are higher by 4 kcal/mol than those using the 6-31G(d) basis set, but the conclusions using the 6-31G(d) basis set are the same as those obtained by using the 6-311++G(d,p) basis set. Therefore, we still prefer to use the results from the 6-31G(d) basis set. The computed energy surfaces for the cyclotrimerizations using the 6-311++G(d,p) basis set are given in the Supporting Information (Figures S1 and S2).
- (20) The basis set superposition errors (BSSE) are small using the 6-31G(d) basis set and can be completely neglected using the 6-311++G(d,p) basis set. See these results in the Supporting Information (Table S3).
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