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Concerted [4 + 2] and Stepwise (2 + 2) Cycloadditions of Tetrafluoroethylene with Butadiene: DFT and DLPNO-UCCSD(T) Explorations

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ABSTRACT: Tetrafluoroethylene and butadiene form the 2 + 2 cycloadduct under kinetic control, but the Diels−Alder cycloadduct is formed under thermodynamic control. Borden and Getty showed that the preference for 2 + 2 cycloaddition is due to the necessity for syn-pyramidalization of the two CF2 groups in the 4 + 2 transition state. We have explored the full potential energy surface for the concerted and stepwise reactions of tetrafluoroethylene and butadiene with density functional theory, DFT (B3LYP and M06-2X), DLPNO-UCCSD(T), and CASSCF-NEVPT2 methods and with the distortion/interaction−activation strain model to explain the energetics of different pathways. The 2 + 2 cycloadduct is formed by an anti-transition state followed by two rotations and a final bond formation transition state. Energetics are compared to the reaction of maleic anhydride and ethylene.

INTRODUCTION

Cycloadditions are versatile synthetic methods to make cyclic molecules through formation of two carbon−carbon or carbon−heteroatom bonds.1−4 The theoretical rationalizations and predictions of mechanisms of cycloadditions are significant achievements of Woodward and Hoffmann.5 While dienes and alkenes generally react in a [4 + 2] (Diels−Alder)6 fashion via a concerted pathway,7,8 halogenated dienes and alkenes often lead to (2 + 2) adducts by diradical mechanisms.

Bartlett and others found that dienes and halogenated ethylenes often give some, or all, 2 + 2 cycloadducts (Scheme 1).9−11 Figure 1 shows variable temperature studies performed by Weigert and Davis for the reaction of butadiene (2) and tetrafluoroethylene (TFE, 1).12 Up to 350 °C, only the 2 + 2 cycloaddition product, 2,2,3,3-tetrafluoro-1-vinylcyclobutane (3), was observed. In the range of 350−500 °C, the Diels−Alder product, 4,4,5,5-tetrafluorocyclohexene (4), was observed, but double elimination of HF from 4 produced the aromatic product, 1,2-difluorobenzene, above 500 °C.

The reaction of 1 and 2 was studied theoretically by Borden and Wang 30 years ago. They sought to quantify the π-bond strength of TFE.13 Calculations were performed at the HF/6-31G* level with an MP2 correction to account for electron correlation. It was determined that the origin of the weak π-
bond of 1 was due to the cost of planarizing the two CF₂ groups, highlighting the propensity of fluorine substituents to stabilize the sp³ geometry (Bent’s Rule).14

Later, but now 28 years ago, Borden and Getty calculated the energies of diradical intermediates and concluded that the Diels–Alder transition state is energetically unfavorable due to the necessity of syn-pyramidalization of the two CF₂ groups.15

While the results of Borden explain why the usually favored Diels–Alder reaction is disfavored here, there are many details of these reactions, as well as computational comparisons with systems that favor Diels–Alder additions, that attracted us to this reaction once again. We have studied cycloadditions involving concerted and 2 + 2 diradical pathways using contemporary theoretical methods. The details of mechanisms of 2 + 2 and Diels–Alder reactions and analysis of barriers by the distortion/interaction—activation strain model are reported here. The reactions of TFE were also compared to those of ethene and maleic anhydride.

### COMPUTATIONAL METHODS
All stationary points were fully optimized at both UB3LYP/6-311+ +G(d,p) and UM06-2X/6-311++G(d,p) levels of theory and verified as minima or first-order saddle points with frequency calculations using Gaussian 09.16 Diradicals were optimized as open-shell singlets. One should be aware of possible shortcomings of density functional theory (DFT) in this regard.17 Intrinsic reaction coordinate (IRC) calculations were also performed to link transition states to their respective minima. Calculations were performed in the gas phase at 1 atm and 635.15 K. Additionally, DLPNO-UCCSD(T)18 single-point energy calculations were performed using ORCA 4.0.19 and the cc-pVTZ20 basis set on UB3LYP/6-311+ +G(d,p) geometries. While UCCSD(T) calculations have been employed in investigations of diradicals,21 it has been noted that DLPNO-UCCSD(T) can lead to unphysical behavior in case of preceding broken symmetry self-consistent field (SCF) calculations.22 Therefore, the barriers of the rate-determining steps and the electronic nature of intermediate S were also investigated using a second-order perturbative treatment of CASSCF wave functions in the form of NEVPT2 calculations as implemented in ORCA. The (2,2) and (4,4) active space was chosen for reactants 1 and 2, respectively, while (6,6) was used for TS1–TS7 and S. Relative energies calculated at the NEVPT2 and DLPNO-UCCSD(T) level are in excellent agreement (Supporting Information, Figure S1). Detailed information about the computational methods is provided in the Supporting Information.

### RESULTS AND DISCUSSION
Stationary Points on the Potential Energy Surface.

Figure 2 shows the UB3LYP/6-311+ +G(d,p) optimized geometries of reactants (1, 2) and the products (3, 4) along with the six transition states (TS1–TS6) that lead to a diradical intermediate and one Diels–Alder transition state (TS7) leading to the concerted [4 + 2] product. Diradical formation arises from anti, gauche (+), or gauche (−) conformers about the newly forming C₂–C₃ bond. Butadiene may be s-cis (2c) or s-trans (2). Table 1 shows the computed UB3LYP/6-311+ +G(d,p), UM06-2X/6-311++G(d,p), and DLPNO-UCCSD(T)/cc-pVTZ single-point calculations, all of which predict that transition state TS1, which involves anti-attack on s-trans butadiene, has the lowest activation energy.

DLPNO-UCCSD(T) calculations predict that the three approaches involving s-trans-butadiene (TS1–TS3) are approximately 2.5 kcal/mol lower in energy than the corresponding approaches involving s-cis-butadiene (TS4–TS6), since butadiene prefers the s-trans conformation by 2.9 kcal/mol. The anti-transition states, TS1 and TS4, are more stable than their gauche (+) and gauche (−) counterparts by 1.6–2.2 kcal/mol.

At the UB3LYP/6-311+ +G(d,p) and DLPNO-UCCSD(T)/cc-pVTZ//UB3LYP/6-311+ +G(d,p) levels of theory, the concerted Diels–Alder transition state, TS7, is 3.9–4.2 kcal/mol lower in energy than the corresponding approaches involving s-cis and s-trans butadiene. The anti-transition states, TS6 and TS7, are approximately 2.5 kcal/mol lower in energy than the corresponding approaches involving s-cis and s-trans butadiene.

Figure 2. UB3LYP/6-311+ +G(d,p) optimized geometries and relative ΔE and ΔG₅₅ K energies of diradical-forming transition states (TS1–TS6) and the Diels–Alder transition state, TS7. Values shown are the forming bond length (C₂–C₃, in Å) and dihedral (C₁–C₂–C₃–C₄, indicating anti, gauche +, and gauche −) angle about the forming bond. Energies are relative to reactants 1 and 2 and are in kcal/mol. DLPNO-UCCSD(T)/cc-pVTZ//UB3LYP/6-311+ +G(d,p) and in case of transition states NEVPT2/def2-TZVP//UB3LYP/6-311+ +G(d,p), single-point electronic energies are also given. Numbering of carbon atoms in TS and intermediates is demonstrated in TS1.
mol higher in energy than the lowest diradical-forming transition state, TS6, while ΔΔG is 8.6 kcal/mol.

IRC calculations reveal that transition structures TS1, TS2, and TS3 lead directly to diradical intermediates 5, 8, and 6, respectively (Figure 3). Here, only the s-trans-butadiene reactant will be discussed, since the potential energy surface (PES) involving the s-cis-butadiene reactant is higher in energy by about 3 kcal/mol. The diradical intermediates 5 and 8 can be interconverted to 6 by transition states TS8 and TS11 (Figure 3) corresponding to rotation around the C2–C3 bond.

Once intermediate 6 is formed, inversion of the radical center at C1 is necessary to align the two radicals on C1 and C4, making ring closure facile.

This can be accomplished by inversion through a planar high-energy transition state TS12 or by rotation around the C1–C2 bond through TS9 (Figure 4). This rotation avoids the unfavorable planarization of the radical on C1. The rotational barrier for the conversion of 6 to 7 is 2.6 kcal/mol.

Table 1. Calculated Electronic Energies, Enthalpies, and Free Energies (in kcal/mol) at 623.15 K for 1–8 and TS1–TS12 at the Indicated Level of Theory

<table>
<thead>
<tr>
<th></th>
<th>UB3LYP/6-311+G(d,p)</th>
<th>UM06-2X/6-311+G(d,p)</th>
<th>DLPNO-UCCSD(T)/cc-pVTZ/UB3LYP/6-311+G(d,p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔE</td>
<td>ΔH</td>
<td>ΔG</td>
<td>ΔE</td>
</tr>
<tr>
<td>1 + 2</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>3</td>
<td>−33.9</td>
<td>−31.2</td>
<td>−5.1</td>
</tr>
<tr>
<td>4</td>
<td>−62.2</td>
<td>−59.1</td>
<td>−28.7</td>
</tr>
<tr>
<td>5</td>
<td>10.2</td>
<td>11.8</td>
<td>32.5</td>
</tr>
<tr>
<td>6</td>
<td>10.9</td>
<td>12.4</td>
<td>33.0</td>
</tr>
<tr>
<td>7</td>
<td>9.5</td>
<td>11.0</td>
<td>31.7</td>
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<tr>
<td>8</td>
<td>11.4</td>
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<td>33.8</td>
</tr>
<tr>
<td>TS1</td>
<td>23.2</td>
<td>23.5</td>
<td>44.8</td>
</tr>
<tr>
<td>TS2</td>
<td>24.8</td>
<td>15.0</td>
<td>46.1</td>
</tr>
<tr>
<td>TS3</td>
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<tr>
<td>TS12</td>
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<td>16.5</td>
<td>38.0</td>
</tr>
</tbody>
</table>

The minimum energy reaction paths (MERPs) for the formation of 3 and the concerted [4 + 2] cycloaddition pathway to form 4 are shown in Figure 5.

The MERP leading to the 2 + 2 adduct includes a flat, entropically controlled energy surface after the initial formation of a diradical. Similar energy surfaces have been described for other diradicals such as the tetratetramethylene species.28 The antiparadiral-forming transition state on s-trans-butadiene is the rate-limiting step for the formation of 3. For 5 to form 3, a vibrational mode corresponding to rotation around the C2–C3 bond must be activated in addition to the inversion of the radical at C1 by rotation through TS9 or inversion (TS12). The ring closure proceeds through a near barrierless reaction step (TS10). In accordance with experimental results, the concerted [4 + 2] pathway to form 4 is kinetically disfavored by 24 (E) kcal/mol over the diradical pathway forming the (2 + 2) product 3, but product 4 is thermodynamically favored over 3 by about 30 kcal/mol.

No direct pathway from s-cis- or s-trans-butadiene derived diradical species to the [4 + 2] product 4 could be found.

Distortion/Interaction–Activation Strain Analysis.

The preference for the kinetically controlled formation of 3 can be explained using the distortion/interaction–activation strain analysis,26–33 which was conducted using autoDIAS.34 In this analysis, the activation energy, ΔΔE, is divided into two components. The first component, ΔE_int, gives the energy required to distort the reactants to their transition state geometries without interactions. The second component, ΔE_int, is the interaction energy between distorted reactants, usually a stabilizing effect. The sum of ΔE_int and ΔE_int equals the energy of activation, ΔE. This analysis has been successfully applied to explain the reactivity in various
cycloaddition reactions.\(^{35-44}\) We compared the reactions of butadiene with ethylene \(^9\) and maleic anhydride \(^10\), which both yield exclusively Diels–Alder adducts, and butadiene with tetrafluoroethylene \(^1\), which gives the \(2 + 2\) adduct through diradical \(^5\). UB3LYP/6-311++G(d,p) structures were used for the distortion/interaction–activation strain analysis shown in Figure 6. The high distortion energy of the dienophile TFE (18.2 kcal/mol) in the Diels–Alder transition state \(TS7\) provides an explanation for the high energy of the concerted pathway in contrast to similar \(4 + 2\) cycloadditions. In the two prototypical Diels–Alder reactions with dienophiles \(9\) and \(10\), the dienophile distortion energy is much lower (8.6 and 10.2 kcal/mol, respectively). The high dienophile distortion energy in \(TS7\) is attributed to \(\text{syn}\)-pyramidalization, which distorts the relatively negative fluorine substituents into proximity. This is Getty and Borden’s conclusion.\(^{15}\)

By contrast, the stepwise \(2 + 2\) cycloaddition with tetrafluoroethylene has a low diene distortion energy (6.3 kcal/mol) in \(TS1\), thus leading to an overall decreased energy of activation and preference for this pathway. The distortion energy of tetrafluoroethylene in the diradical pathway, 17.9 kcal/mol, is similar to the value found for the concerted \([4 + 2]\) cycloaddition (18.2 kcal/mol). This can be explained by the fact that in \(TS7\), the out of plane bending of the fluorides in TFE is only \(15^\circ\) and the forming bond distance is 2.30 Å while in \(TS1\), the bending is much stronger with \(22^\circ\) and the forming bond distance is shorter with 1.97 Å. However, in \(TS1\), the second CF\(_2\) unit is free to adopt any conformation, which allows for better stabilization through anti-pyramidalization, while in \(TS7\), unfavorable \(\text{syn}\)-pyramidalization is enforced leading to similar distortion energy at lower geometric distortion. Figure 7 shows the TFE distortion energies along intrinsic reaction coordinates calculated for the \([4 + 2]\) cycloaddition proceeding through \(TS7\) and the diradical-forming reaction going through \(TS1\). As shown, for a given angle, the distortion energy is higher in the case of the \([2 + 4]\) reaction due to the forced \(\text{syn}\)-pyramidalization. The preference of alkenes and alkynes for \(\text{anti}\)-pyramidalization in both radical and ionic cases is well established.\(^{13,45-47}\)

Compared to the \(2 + 2\) diradical pathways of ethylene \((9)\) and maleic anhydride \((10)\), the forming C2–C3 bond length in \(TS1\) is significantly longer than those in \(TS15\) and \(TS16\).
Energy of Concert. The energy by which the activation energy of the concerted reaction is favored over stepwise reaction is the energy of concert.\(^4\)\(^8\) Figure 8 shows energy of concert analyses for the three reactions described earlier. The reaction of 2 with 1 has negative energy of concert. The stepwise reaction is preferred in this case by 4.2 kcal/mol. Reactions of 2 with 9 or 10 have positive energies of concert. The concerted mechanism is favored with similar energy of concert values, 9.6 and 9.5 kcal/mol, respectively. Previous calculations for butadiene and ethylene predicted energies of concert of 2–7 kcal/mol.\(^4\)\(^9\)

The stepwise reaction is preferred in the TFE case because the diradical intermediates and the transition states leading to them are stabilized. By contrast, the maleic anhydride dienophile stabilizes the concerted pathway to a large extent and the stepwise pathway less, although it does stabilize that also. The interaction energy in TS14 plays a large role in the stabilization of the \([4 + 2]\) cycloaddition pathway for maleic anhydride; this arises from the well-known charge transfer interactions resulting from the small highest occupied molecular orbital–lowest unoccupied molecular orbital (HOMO–LUMO) gap. The absence of energetically unfavorable syn-pyramidalization of \(\text{CF}_2\) centers in the dienophile of TS13 versus TS7 lowers the electronic energy of this transition state.

### CONCLUSIONS

The stepwise \((2 + 2)\) cycloaddition is kinetically preferred over the concerted Diels–Alder reaction for the butadiene–TFE reaction. The syn-pyramidalization penalty identified by Borden and Getty for the concerted reaction is consistent with this model. In addition, we identified the low diene distortion in the stepwise \((2 + 2)\) cycloaddition as an important factor for the preference of this pathway. Diradical transition structures TS1–TS6 are all lower in energy than the Diels–Alder transition state, TS7. These six transition states can all form the \((2 + 2)\) cycloaddition product. The MERP in Figure 5 shows that a preference for anti-diradical formation dominates, and subsequent rotation around the C2–C3 bond followed by radical inversion along a flat PES eventually affords the kinetic \((2 + 2)\) cycloaddition product.

### ASSOCIATED CONTENT

* Supporting Information

The Supporting Information is available free of charge at [https://pubs.acs.org/doi/10.1021/acs.joc.0c00222.](https://pubs.acs.org/doi/10.1021/acs.joc.0c00222)

UB3LYP and UM06-2X optimized geometries for all structures and detailed information on the computational methods; energies of UB3LYP/6-311++G(d,p) and UM06-2X/6-311++G(d,p) calculated structures; correlation between UCCSD(T) and NEVPT2 calculated relative energies; UCCSD(T) and NEVPT2 calculated energies (PDF)

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### Author Contributions

D.S. and R.P.P. contributed equally.

### Notes

The authors declare no competing financial interest.
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