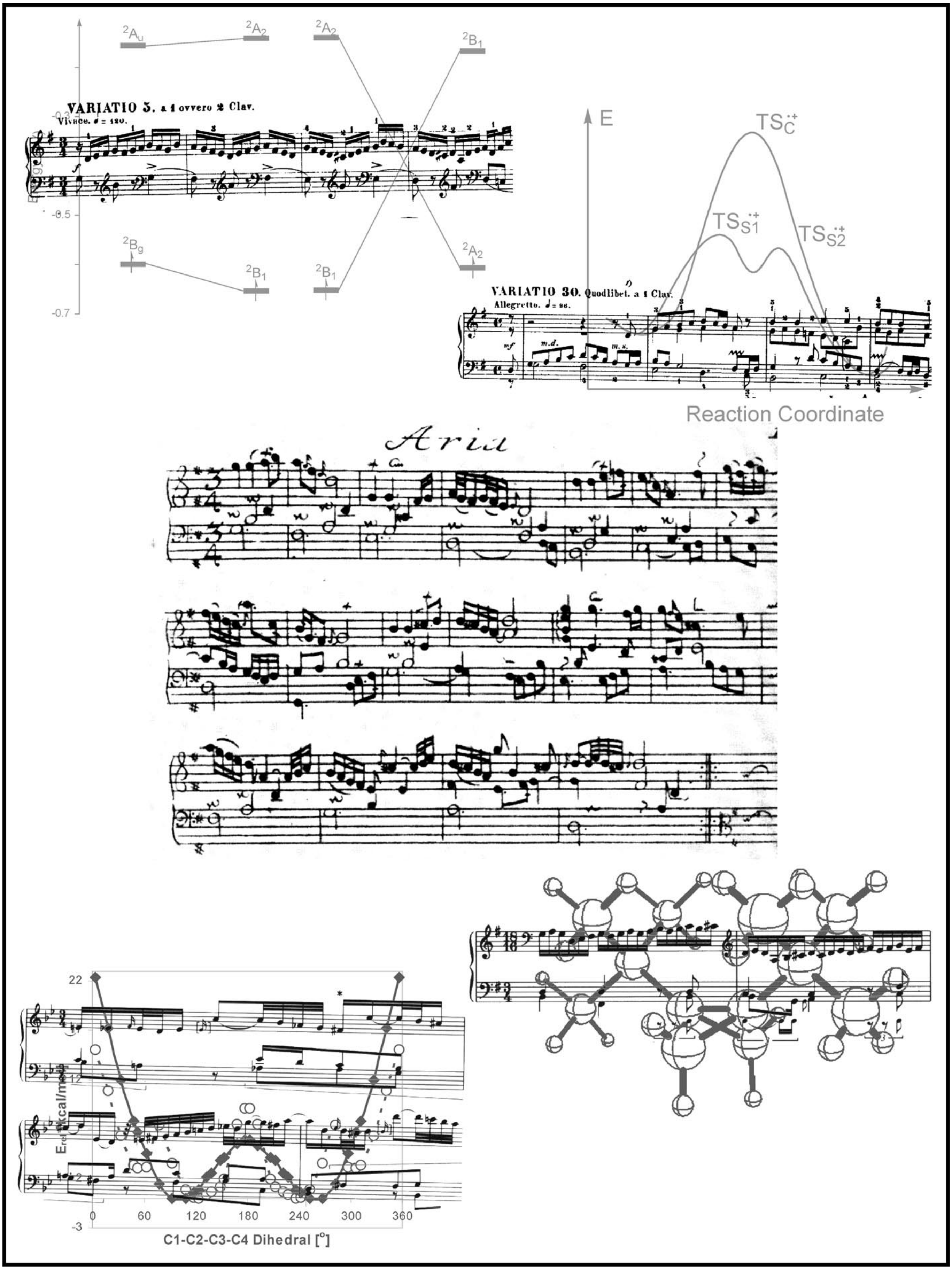
CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200600554


^2A_u
$^2A_2$
$^2A_2$
$^2B_1$
-0.3
VARIATIO 5. a 1 ovvero 2 Clav.
Vivace.
-0.5
^2B_g
$^2B_1$
$^2B_1$
$^2A_2$
-0.7
E
$TS_C^{\cdot+}$
$TS_{S1}^{\cdot+}$
$TS_{S2}^{\cdot+}$
VARIATIO 30. Quodlibet. a 1 Clav.
Allegretto.
Reaction Coordinate
Aria
22
E_{rel} [kcal/mol]
-3
0
60
120
180
240
300
360
C1-C2-C3-C4 Dihedral [°]

Structure and Reactivity of Radical Ions: New Twists on Old Concepts

Patrick J. Donoghue and Olaf Wiest*[a]

Abstract: Electron transfer is the simplest reaction possible, yet it has a profound impact on the structure and reactivity of organic compounds. These changes allow a new look at some of the fundamental concepts that are used to explain organic chemistry, such as symmetry, aromaticity, and bonding. The results from high-level electronic structure calculations are used to analyze the mechanistic differences in the pericyclic reactions of simple hydrocarbons and their radical cation counterparts. The importance of state symmetry correlation, Jahn–Teller distortions, delocalization, and fractional bonding for the reaction pathways of hydrocarbon radical cations is discussed.

Keywords: electron transfer • hydrocarbons • pericyclic reaction • radical ions • reaction mechanisms

Introduction

The chemistry of pure hydrocarbons has traditionally served as the training ground for the development of new concepts in organic chemistry. While the experimental demonstration of these concepts often posed significant challenges that resulted in a number of beautiful syntheses[1] and had numerous industrially important applications, much of this work was motivated by the abstract concepts of basic science. These could most easily be demonstrated without complicating interferences from functional groups for the simple, parent systems. It is therefore no coincidence that the areas of physical organic chemistry and hydrocarbon chemistry historically developed in tandem. A case in point are the current Gordon Conferences in Physical Organic Chemistry, which started in 1936 under the title of "Petroleum Chemistry" and continued through some of the most active periods in physical organic chemistry under the name of "Hydrocarbon Chemistry" before adopting their current name. Examples of the interplay of theoretical ideas and experimental work that flourished in the field of hydrocarbons include the concept of aromaticity and the work on annulenes,[2] the mechanistic analysis in an orbital framework and the study of pericyclic reactions or,[3] more recently, dynamic reaction control and the selectivity of biradical reactions.[4]

The formation of concepts, that is, the generalization of individual observations into abstract ideas as well as the expansion, modification, or even replacement of these concepts by qualitatively new and more comprehensive ones are relatively rare events in physical organic chemistry. The most common use of concepts to achieve scientific progress is the logical combination, application, and permutation of these abstract ideas. The most powerful concepts are thus those that are flexible enough to be applied to systems very different than the ones from which they were originally developed and that allow predictions than can be tested through experimental observation. In many cases, the true value of an abstract concept is not realized until much later when concepts are probed, expanded, and tested. The usefulness of an orbital description of chemical reactivity or the concept of aromaticity was not, for example, widely accepted until decades after the formulation.

The chemistry of hydrocarbon radical cations offers some unique opportunities to probe some of the most influential concepts in organic chemistry: the conservation of orbital symmetry (Woodward–Hoffmann rules), aromaticity (including the aromatic stabilization of transition states), and the concept of localization and delocalization of bonds. All of these concepts have inspired elegant experimental and theoretical studies that led to significant new insights over the last decades. For different reasons, the chemistry of simple hydrocarbon radical cations appears to defy or expand these fundamental concepts of organic chemistry. Nature exploits, for example, the chemistry of radical anions to achieve DNA repair through a symmetry-forbidden, but apparently concerted, mechanism.[5] In this contribution, we will discuss some examples of simple hydrocarbon radical

---

[a] P. J. Donoghue, Prof. Dr. O. Wiest
Department of Chemistry and Biochemistry
University of Notre Dame, Notre Dame, IN 46556–5670 (USA)
Fax: (+1) 574-631-6652
E-mail: owiest@nd.edu

cations that differ in their reactivity from their neutral counterparts and use electronic structure theory to analyze the origin of these differences. Special emphasis will be placed on the relationship of these results to some fundamental concepts of organic chemistry.

The Conservation of Orbital Symmetry

A classical example of an abstract concept that found widespread use in chemistry are the Woodward–Hoffmann rules,[3] which deduce the stereochemical course of pericyclic reactions from orbital symmetry considerations. The predictive power of the rules, together with the elegance of a simple argument based on symmetry, ensured that the principle of conservation of orbital symmetry continues to be one of the most influential principles in organic chemistry. A related concept that uses an orbital analysis to explain chemical reactivity is the frontier molecular orbital (FMO) concept. This approach, which is historically linked to the Woodward–Hoffmann rules through the joint 1981 Nobel Prize in Chemistry, allows for the semiquantitative prediction of relative rates and regiochemistry of many reactions, including pericyclic reactions. Considerations of the relative energies, coefficients, and node properties of the FMO are therefore standard tools for the organic chemist.

Pericyclic reactions are generally considered to be orbital controlled and to proceed via highly symmetric transition states.[6] The analysis of the orbital interactions within the FMO framework is fairly straightforward. As shown in Figure 1 on the left, two HOMO–LUMO interactions are possible. One of these interactions will be dominant because the interaction strength, according to Fermi's Golden Rule, depends inversely on the energy difference between the interacting orbitals. This analysis gave rise, for example, to the classification of the Diels–Alder reaction into normal and inverse electron-demand reactions. Analysis of the node properties and coefficients of the pair of orbitals involved in the dominant interaction then allows predictions of relative rates as well as stereo- and regiochemistry.

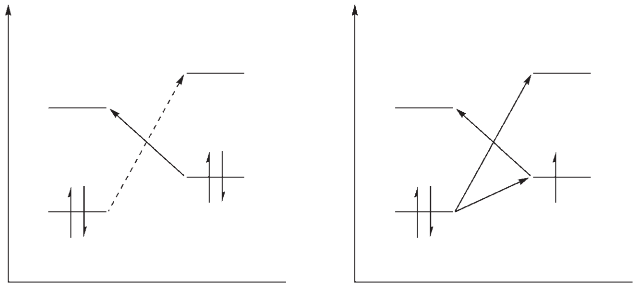
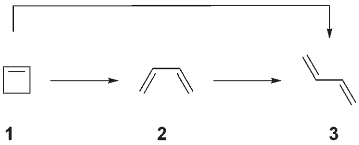


Figure 1. Orbital interactions in closed shell (left) and open shell molecule (right).

The removal or addition of an electron alters this scheme considerably, as shown in Figure 1 on the right. Even before considering any changes in the relative orbital energies, the possibility of additional interactions of the singly occupied molecular orbital (SOMO) of the radical ion with the HOMO or LUMO of its reaction partner can open new reaction pathways that are symmetry forbidden for the closed-shell molecules. As a result of these additional interactions, simple symmetry analysis of radical-ion reactions in analogy to their closed-shell counterparts is tempting,[7] but usually not correct. One example to illustrate this is the electron-transfer-catalyzed (ETC) reaction of a diene with a dienophile. For example, the symmetry analysis of the reaction in analogy to the Diels–Alder reaction predicts that the [3+2] cycloaddition, that is, the ionization of the diene, is found to be symmetry allowed. In contrast, the [4+1] reaction, that is, the one-electron oxidation of the dienophile, is symmetry forbidden.[8] However, experimental studies with electron-rich styrenes as dienophiles showed that this so-called "role selectivity" is not valid and that previous observations were due to the lower redox potential of dienes used in the original study.[9]

This does not imply that an orbital symmetry analysis of radical ion reactions cannot yield useful insights into formally pericyclic reactions of hydrocarbon radical cations. Two aspects of symmetry are important for radical ion reactions. First, in the reaction of a closed-shell molecule, all orbitals are doubly occupied and the electronic state is therefore A_1. The reaction is governed by symmetry to conserve the node topology of the orbitals involved in the reaction. In contrast, the electronic state of the radical cation is determined by the symmetry of the SOMO. Depending on the point group of the reactants and products, the electronic states of reactants and products may or may not correlate. Similar to the case of the Woodward–Hoffmann rules, which state that in a concerted reaction only orbitals of the same symmetry correlate, only electronic states of the same symmetry will correlate in a symmetry-preserving reaction of radical ions. Second, since the radical cation is an open-shell species, any orbital degeneracy caused by symmetry in the neutral counterpart is subject to a first- or second-order Jahn–Teller distortion,[10] which would remove the symmetry element that was preserved in the neutral reaction.

As was the case for the historical development of the Woodward–Hoffmann rules, the usefulness of an orbital and symmetry analysis can be illustrated using the case of the ring-opening reaction of cyclobutene (**1**) as a representative example. As shown in Scheme 1, neutral **1** ring opens to s-*cis*-1,3-butadiene (**2**), which then rapidly rotates around the central single bond to form the thermodynamically more stable s-*trans*-1,3-butadiene (**3**). The C_2 symmetry element is



Scheme 1. Ring opening of cyclobutene **1**.

preserved throughout the reaction, leading to a conrotatory motion of the ring opening.[3]

Matrix isolation studies showed that for the analogous ring opening of the cyclobutene radical cation $\mathbf{1}^{\cdot+}$, the reaction proceeds directly to the s-*trans*-1,3-butadiene $\mathbf{3}^{\cdot+}$, without forming the s-*cis* isomer first.[11] As shown in Figure 2, this is due to the lack of correlation between the electronic states of $\mathbf{1}^{\cdot+}$, which has a $^2B_1$ ground state, and $\mathbf{2}^{\cdot+}$, which has a $^2A_2$ ground state. Consequently, there is no symmetry-preserving pathway for the radical cation to form $\mathbf{2}^{\cdot+}$. On the other hand, the ^2B_g ground state of $\mathbf{3}^{\cdot+}$ does correlate with the $^2B_1$ ground state of $\mathbf{1}^{\cdot+}$ through a C_2 symmetric pathway. A symmetry-conserving pathway could therefore only form $\mathbf{3}^{\cdot+}$.[12] As is the case for the Woodward–Hoffman rules, this analysis is not strictly applicable to non-symmetry-conserving or stepwise pathways.

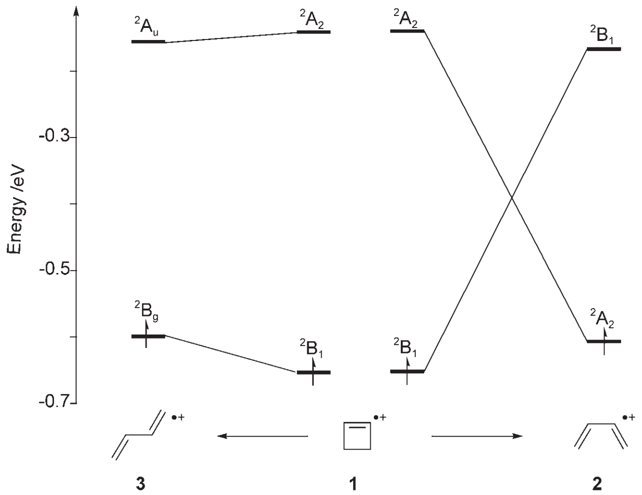


Figure 2. Orbital correlation for symmetry-preserving ring opening of the cyclobutene radical cation. Energies are from HF/6–31G*//B3LYP/6–31G* calculations.

Although this simple correlation analysis predicts that the symmetry-preserving ring opening to $\mathbf{3}^{\cdot+}$ is in principle possible, it does not make any statements about the character or energy of this transition state. As will be discussed in more detail later, because there are now an odd number of electrons in the system, no Hückel or Möbius aromatic system can be derived and the stabilization of the aromatic transition state is removed. Therefore, there is no energetic advantage to a symmetric transition state and other possible mechanisms must be considered, as they are energetically competitive. Three possible mechanisms can be considered for the reaction: a concerted C_2-symmetric pathway involving $\mathbf{4}^{\cdot+}$, a concerted C_1-symmetric pathway via $\mathbf{5}^{\cdot+}$, and a stepwise C_1-symmetric pathway involving the cyclopropyl carbinyl radical cation $\mathbf{5a}^{\cdot+}$ as shown in Figure 3.

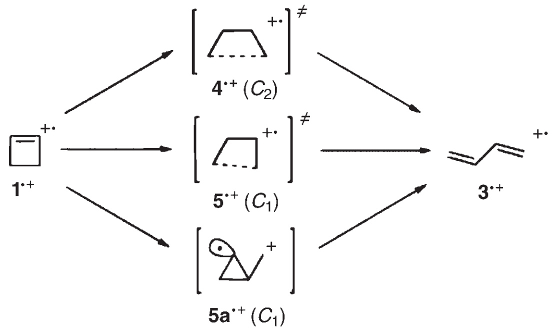

$\mathbf{4}^{\cdot+}$ (C_2)
$\mathbf{5}^{\cdot+}$ (C_1)
$\mathbf{5a}^{\cdot+}$ (C_1)
$\mathbf{1}^{\cdot+}$
$\mathbf{3}^{\cdot+}$
≠
≠
+·
+

Figure 3. Possible reaction pathways for the ring opening of $\mathbf{1}^{\cdot+}$.

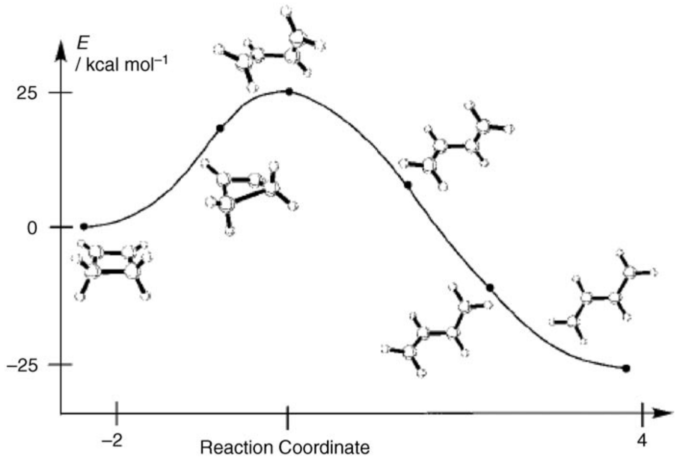


Figure 4. IRC for the ring opening of $\mathbf{1}^{\cdot+}$ via $\mathbf{4}^{\cdot+}$.

Interestingly, the transition structure $\mathbf{4}^{\cdot+}$ (shown in Figure 4) illustrates the second effect of symmetry that is not observed in closed-shell compounds. Harmonic frequency analysis of $\mathbf{4}^{\cdot+}$ shows that it is not a true transition state, but rather a second-order saddle point. The stronger of the negative frequencies corresponds to a Jahn–Teller type distortion of this saddle point, while the weaker corresponds to the expected carbon–carbon bond cleavage in the ring-opening reaction. A Jahn–Teller distortion can either occur if the unpaired electron is in an orbital that is degenerate due to symmetry, leading to a nuclear distortion to lift this degeneracy, or by vibronic coupling along an antisymmetric normal mode.[13] While the first type of Jahn–Teller effect (first-order Jahn–Teller effect) is common in open-shell inorganic complexes, the second type (second-order, vibronic, or pseudo-Jahn–Teller effect) has been described for a number of hydrocarbon radical cations.[14] Figure 4 shows the intrinsic reaction coordinate (IRC) calculation along the transition vector for carbon–carbon bond breakage in $\mathbf{4}^{\cdot+}$. It can be seen that the reaction pathway proceeds, as predicted by the symmetry analysis of the electronic states discussed earlier, smoothly from $\mathbf{1}^{\cdot+}$ to $\mathbf{3}^{\cdot+}$ via $\mathbf{4}^{\cdot+}$ without the involvement of $\mathbf{2}^{\cdot+}$.

The second negative frequency in $\mathbf{4}^{\cdot+}$ corresponds to the interchange between two enantiomeric transition structures, $\mathbf{5}^{\cdot+}$. Here, the symmetry of the molecule is lowered, and the first-order transition state $\mathbf{5}^{\cdot+}$ corresponds to a concerted C_1-symmetric pathway. The distortion occurs because the energy of the molecule is lowered by reducing the symmetry. Therefore, the activation energy of the concerted C_1-symmetric mechanism is less than that of the concerted C_2-symmetric pathway by ~5 kcal mol^{-1}, depending on the level of theory used. Figure 5 shows the computed IRC reaction pathway for the concerted C_1-symmetric mechanism. The lowered symmetry of $\mathbf{5}^{\cdot+}$ leads to a ^{2}A state that can correlate with either $\mathbf{2}^{\cdot+}$ or $\mathbf{3}^{\cdot+}$. Thus, the IRC can lead to $\mathbf{2}^{\cdot+}$ through a minimum-motion pathway, as shown in Figure 5.

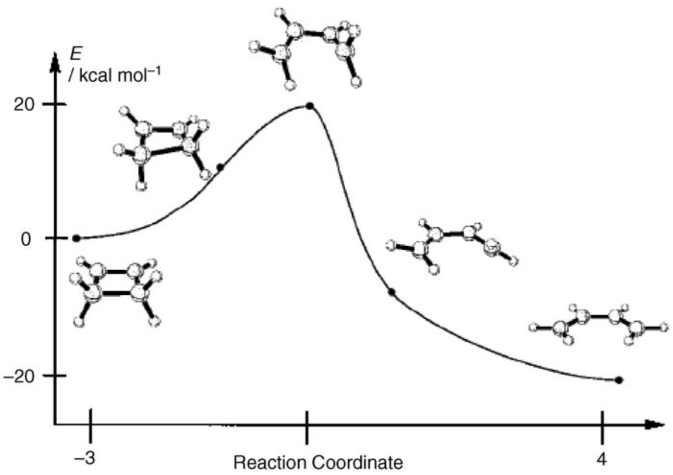
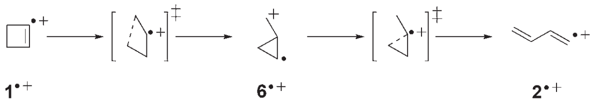


Figure 5. IRC for the ring opening of $\mathbf{1}^{\cdot+}$ via $\mathbf{5}^{\cdot+}$.

The third possible mechanistic pathway involves a stepwise mechanism that proceeds via a cyclopropylcarbinyl-type intermediate, $\mathbf{6}^{\cdot+}$ (Scheme 2). This mechanism was originally proposed by Bauld[15] and investigated in detail by Bally and co-workers.[16] They identified an intermediate in the reaction that has a very late transition state. The calculated first transition-state structure looks very intermediate-like, and this intermediate lies in a very shallow minimum. The computational method used to calculate this, MP2, is known to overestimate the stability of localized radicals, as it would be in the cyclopropyl intermediate $\mathbf{6}^{\cdot+}$, and attempts at locating this intermediate using other computational methods have not been successful.[12] The existence of a discreet intermediate in this reaction is therefore called into question and this mechanism appears to be unlikely. The finding that the PES is extremely flat and the presence or absence of intermediates depends on the computational method used is typical in the studies of hydrocarbon radical cations.



Scheme 2. Stepwise pathway for ring opening of $\mathbf{1}^{\cdot+}$.

Aromaticity of Transition States

Another concept widely used to explain the relatively low activation energy of pericyclic reactions is the notion that the transition structures of pericyclic reactions involving $4n+2$ electrons are stabilized through Hückel aromaticity, while systems with $4n$ electrons participating in the reaction are stabilized through Möbius aromaticity.[17] Thus, these pathways are thought to be favored over the corresponding biradical or zwitterionic pathways by aromatic stabilization. In comparison, any stepwise pathway would necessarily be initiated by a homolytic or heterolytic bond breaking, increasing the activation energy of this pathway. For many substituted systems, the exact balance between concerted and stepwise pathways involving intermediates that are stabilized by appropriate functional groups have long been the topic of passionate discussions.[6a] This is particularly true for the synthetically important class of cycloaddition reactions, including Diels–Alder reactions and 1,3-dipolar cycloadditions, for which a mechanistic switch from concerted to stepwise can have significant stereochemical consequences.

This scenario is again significantly altered for the case of the radical cationic reactions. First, the aromatic character of the concerted transition state is absent in the five-electron system. The transition state is not stabilized by aromaticity and therefore disfavored relative to the corresponding case of the six-electron reaction. It has been argued that such odd-electron systems are, at least in some cases, destabilized by antiaromaticity.[18] However, NICS calculations of the [2+2] cycloreversion of the cyclobutane radical cation show a non-aromatic character of the transition structure.[19] In addition, many concerted transition states of radical cations are also symmetric and subject to first- and second-order Jahn–Teller distortions as discussed above, which makes a symmetry-preserving pathway even more unfavorable. At the same time, the removal of an electron from the HOMO (or the addition of an electron to an antibonding orbital in the case of radical anions) leads to a weakening of the corresponding bond, which is now easier to break. The rate-determining transition state of the stepwise reaction pathway is therefore lowered in energy. As a result of these changes, the stepwise pathway is in many cases favored relative to the concerted one, as shown in Figure 6.

The mechanistic consequences of these conceptual changes have been studied in detail for the case of cycloadditions, in particular the Diels–Alder reaction. The neutral Diels–Alder reaction has been studied extensively,[6] and the Woodward–Hoffmann rules correctly predict the experimentally observed suprafacial stereochemistry of the addition. High-level computational studies in combination with kinetic isotope effect studies provide good evidence that for simple hydrocarbon systems, the aromatic stabilization of the transition states prevails in the neutral reaction.[20] The neutral reaction thus undergoes a concerted reaction that has an aromatic transition state.

The radical cation Diels–Alder reaction is also the most widely applied of all electron-transfer-catalyzed pericyclic

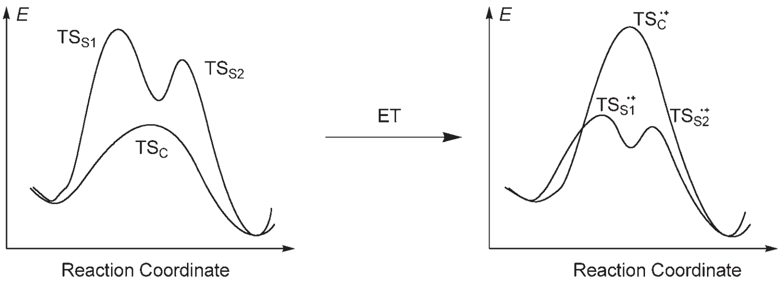


Figure 6. Relationship of concerted and stepwise mechanisms for neutral (left) and radical cation (right) Diels–Alder reaction.

reactions.[21–23] Extensive experimental[24,25] and computational[26] studies clearly established a stepwise pathway for this reaction. A comparison of the concerted and stepwise pathways for the parent reaction of ethylene with 1,3-butadiene and the 1,3-butadiene radical cation is of particular interest, because the comparison with the many other computational studies of this system illustrates the mechanistic changes caused by the electron transfer.

The key pathways and stationary points on the hypersurface and their energies relative to the product, the cyclohexene radical cation, are summarized in Figure 7. In agreement with the arguments made above, the C_s symmetric transition structure $\mathbf{7}^{\cdot+}$, corresponding to the concerted pathway, is the highest energy structure on this part of the $C_6H_{10}^{\cdot+}$ hypersurface. In addition, harmonic frequency analysis at the B3LYP/6–31G* level of theory identifies $\mathbf{7}^{\cdot+}$ as a second-order saddle point on the PES. This is due to a Jahn–Teller distortion similar as discussed earlier for the case of $\mathbf{4}^{\cdot+}$. As was the case for the electrocyclic ring opening of the cyclobutene radical cation, a symmetry-conserving mechanism can thus be ruled out for the radical cation Diels–Alder reaction.

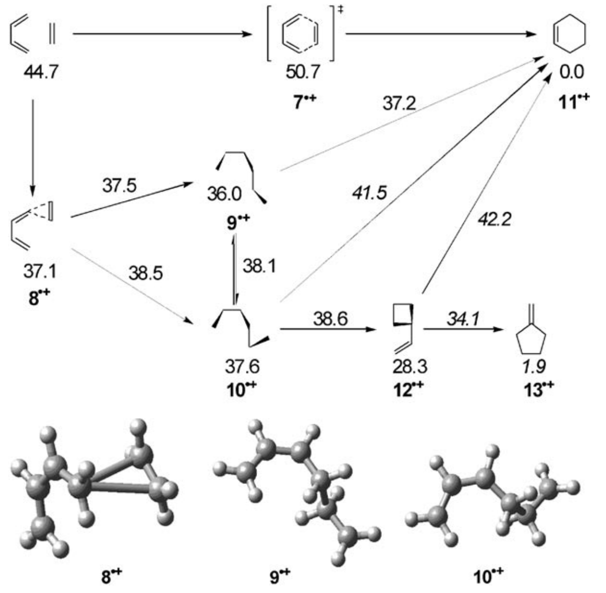


Figure 7. Reaction pathways for the parent radical cation Diels–Alder reaction. Values in plain text are from QCISD(T)//QCISD calculations, values in italics are from CCSD(T)//MP2 calculations.

Instead, the first step of the reaction is the formation of an ion-molecule complex $\mathbf{8}^{\cdot+}$ with a binding energy of ~7 kcal mol^{-1}. Depending on which carbon–carbon bond is formed, two different and rapidly interconverting acyclic intermediates $\mathbf{9}^{\cdot+}$ and $\mathbf{10}^{\cdot+}$ are generated. These intermediates correspond to the *anti* or *out-gauche* conformations, respectively, around the newly formed C_4–C_5 bond and differ in energy by 1.6 kcal mol^{-1}, more than the barrier for the cyclization of $\mathbf{9}^{\cdot+}$ to form the final product, the cyclohexene radical cation $\mathbf{11}^{\cdot+}$. The *out-gauche* conformer, $\mathbf{10}^{\cdot+}$, can either directly close to form the vinylcyclobutane radical cation $\mathbf{12}^{\cdot+}$ or, through another conformer, also close to $\mathbf{11}^{\cdot+}$. Schaefer and co-workers also investigated additional pathways leading from $\mathbf{12}^{\cdot+}$ to $\mathbf{11}^{\cdot+}$ (the so-called "indirect Diels–Alder reaction"[23,27]) and a series of Wagner–Meerwein-type 1,2-shifts that ultimately lead to $\mathbf{13}^{++}$.[26a,b]

Conceptually, two findings of these studies are noteworthy. First, the structures of the stepwise pathways for the radical cationic and the neutral, biradical reactions are quite similar. Comparison of the structures shown in Figure 7 with the ones obtained for the stepwise Diels–Alder reaction[28] or the vinyl cyclobutane rearrangement[29] reveal the close relationship of these pathways. This correspondence of the biradical and radical cationic structures is in agreement with the ideas outlined in Figure 6, in which the acyclic radical cation and the transition states leading to and from it correspond to the biradical species in the neutral reaction. Computational studies of other reactions, such as the 1,3-methylene shift in vinylcyclopropane,[30,31] also show the structural similarity of biradical and radical cationic structures, emphasizing the relationship of cations and radicals that is often discussed in elementary organic chemistry. Second, the activation energy of the radical cation Diels–Alder reaction is computed to be of 1.2 kcal mol^{-1}, as would be expected for a highly reactive intermediate such as a hydrocarbon radical cation. This is much smaller than the corresponding neutral reaction, which has an activation energy of 23.6 kcal mol^{-1}.[32] As discussed above, this is because the bond to be broken in the initial step is weakened by electron transfer. The first step thus corresponds to the attack of a radical cation on an olefin, which is essentially barrierless in the gas phase. Therefore, the rate-determining step is (and maybe somewhat unexpectedly) the rotation around the newly formed C_4–C_5 single bond to allow ring closure.

Bond Orders and Fractional Bonds

One role of concepts is to provide frameworks in which to think and a language to communicate ideas. The language of chemistry is arguably the chemical bond and its changes. The development of different ideas about bonding from the simple picture of single and double bonds to the fractional, delocalized bonds in nonclassical carbocations has been one of the most fruitful areas of physical organic chemistry. Finally, an intuitive understanding of the relative strengths of different types of bonds (e.g., single vs. double bonds, conjugation, or noncovalent interactions, such as hydrogen bonding) is basic material that every student of organic chemistry is expected to master. The removal of an electron out of a π or σ system completely changes the reactivity of the system. In a conjugated π system, the delocalization of spin and charge becomes a significant energetic factor that dominates the structure and reactivity of these radical cations, overriding other factors.

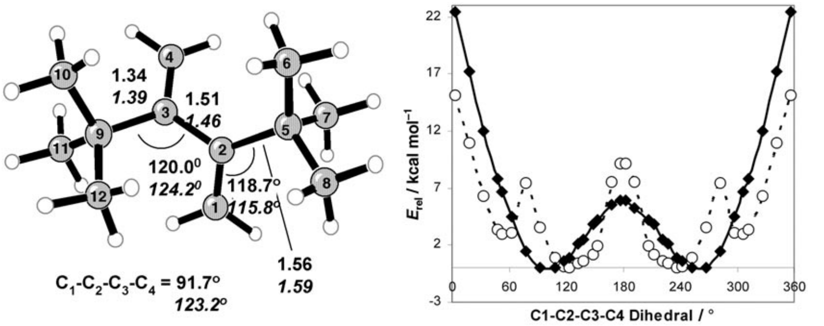


Figure 8. B3LYP/6–31G* Optimized structure and rotational profile for **14** (plain text, ◆) and **14**$^{\cdot+}$ (italics, ○).

The simplest conjugated π-system is 1,3-butadiene. It has been studied in considerable detail[33,34] and has been influential in the development of a number of concepts, such as conjugation, high-level electronic structure calculations of organic molecules,[35] or force field treatments of chemical bonding. The most stable conformation of 1,3-butadiene is the planar s-*trans* conformation (**3**), which is in equilibrium with gauche-like s-*cis* conformation (**2**), which is ~3 kcal mol^{-1} higher in energy. The activation energy for the rotation around the central single bond is 6–7 kcal mol^{-1} in the unsubstituted 1,3-diene and simple analogues.[36]

This situation is changed considerably for the s-*cis*- and s-*trans*-1,3-butadiene radical cations **2**$^{\cdot+}$ and **3**$^{\cdot+}$. Due to the presence of an unpaired electron and a positive charge, the stabilization obtained by delocalization is much higher and easily outweighs the steric repulsion of the hydrogen atoms. Consequently, **2**$^{\cdot+}$ is calculated to be planar, unlike **2** which is calculated to have a C-C-C-C dihedral angle of 13°. In fact, the delocalization of spin and charge causes the differences between formal C_2–C_3 single bond and the C_1=C_2 and C_3=C_4 double bonds to essentially disappear. As a result the bond lengths are very close, 1.39 and 1.42 Å respectively. This high degree of delocalization is also obtained in longer, iodine-doped conjugated polyenes and is thought to be responsible for their metal-like conductivity.[37] In addition, the electronic ground state of **2**$^{\cdot+}$ is $^2A_2$, whereas **3**$^{\cdot+}$ has a ^2B_g ground state, as shown in Figure 2.[38] This implies that there the rotation around the central double bond in **2**$^{\cdot+}$ not only has to overcome the double-bond character of the C_2–C_3 bond, but also has to localize spin and charge in order to break the symmetry and go from a $^2A_2$ to a ^2B_g state. Consequently, computational studies at the QCISD(T)/QCISD level of theory using a 6–31G* basis set gave a high barrier of 28.1 kcal mol^{-1} for this process.[39]

The rotational profile 2,3-*tert*-butyl-1,3-butadiene **14**, shown in Figure 8, exemplifies these concepts. The planar *cisoid* and *transoid* conformations are strongly destabilized by 22.4 and 16.0 kcal mol^{-1}, respectively, through repulsions of the *tert*-butyl groups with each other and with the methylene groups.[40] This leads to a perpendicular conformation of the diene unit, as was shown by Hopf and co-workers.[41] The *cisoid* conformation in **14**$^{\cdot+}$ is stabilized by 7.3 kcal mol^{-1} relative to the *cisoid* conformation of **14** through extended delocalization. The necessity to localize spin and charge and to break symmetry upon rotation around the C_2–C_3 bond leads to an additional energy maximum at 80°, although this barrier is much smaller than the one in **2**$^{\cdot+}$ due to the stabilizing effects of the substituents. Interestingly, the *transoid* conformation of **14**$^{\cdot+}$ is destabilized relative to the one of **14**, presumably because the shortened C_2–C_3 bond in the radical cation increases the steric repulsion.

A particularly interesting case of fractional bonding occurs in the bicyclobutane radical cations. In most hydrocarbon radical cations, the electron is removed from a π system owing to the extremely high redox potential of saturated hydrocarbons, which is difficult to realize experimentally.[42] [1.1.0]Bicyclobutane (**15**) is a rare case of a saturated hydrocarbon with a localized, high-energy HOMO due to the ring strain.[43] At the same time, the geometry of [1.1.0]bicyclobutane radical cation (**15**$^{\cdot+}$) does not allow for significant hyperconjugation or delocalization of spin and charge. As was pointed out by Bally, a planarization of **15**$^{\cdot+}$ is again not possible because **15**$^{\cdot+}$ and the planar cyclobutane-1,3-diyl radical cation have different electronic ground states.[44] The lack of state symmetry correlation cannot be overcome by steric repulsion that would be in analogy to known stable 1,3-diyls.[45] As shown in Figure 9, even the steric repulsion of the two *tert*-butyl groups in 1,3-di-*tert*-butyl[1.1.0]bicyclobutane does not break the central carbon–carbon bond in the radical cation, although it is lengthened

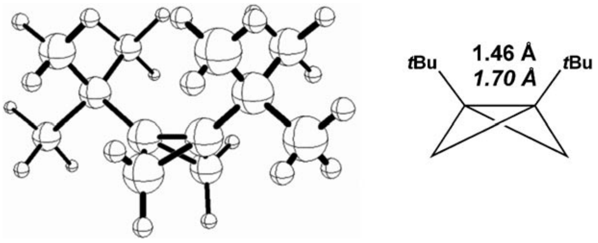


Figure 9. B3LYP/6–31G* structure of 1,3-di-*tert*-butyl-[1.1.0]bicyclobutane.

by 0.24 Å. Rather, the planarization of sterically crowded [1.1.0]bicyclobutanes leads to symmetry breaking and localization of spin and charge, which in turn leads to Wagner–Meerwein-type alkyl shifts to give the corresponding cyclobutenes.[46] These alkyl shifts are also observed experimentally upon irradiation of 1,3-di-*tert*-butyl-[1.1.0]bicyclobutane[47] and presumably occur through a biradical pathway, again re-emphasizing the relationship to the radical cationic pathway.

Conclusion

Even though the transfer of a single electron to or from a molecule is the simplest chemical transformation imaginable, it has profound implications on the concepts that provide the framework for thinking about the reactivity of that molecule. While for neutral, closed-shell molecules, there is a tendency of many reactions to proceed through symmetry conserving pathways, first- and second-order Jahn–Teller distortions lead to an equally strong tendency of open-shell molecules towards lower symmetry pathways. Similarly, the concept of aromatic transition-state stabilization, which biases many reactions towards a concerted mechanism, is replaced by a preference towards stepwise mechanisms. At the same time, the concept of orbital symmetry control is replaced with the symmetry of electronic states, which may not correlate and thus exclude certain pathways. The presence of a positive charge increases the energetic importance of resonance stabilization and delocalized, nonclassical single bonds. This leads not only to interesting questions of charge localization versus delocalization, but also poses formidable problems for electronic structure methods that are popular for the study of reaction mechanisms.

The findings outlined in this overview are of course not new concepts, but rather the result of the combination of the presence of an unpaired electron and a positive charge. In order to understand, classify, and predict radical cation reactivity, it is important to develop an intuitive understanding of the changed contributions of these fundamental concepts in ETC reactions[48] compared to the reactivity of neutral, closed-shell molecules organic chemists are more familiar with. It can be argued that the lack of such understanding is one reason for the rare application of radical ions as reactive intermediates in organic synthesis, despite the impressive enhancements in reactivity and selectivity that have been reported in the literature. On the other hand, the complexity added through these additional factors has the potential to expand existing concepts and lead to new discoveries. It is the hope of the authors that this general outline of the new twists that radical cationic reactivity can bring to old concepts can contribute to a wider application of these interesting reactive intermediates in organic chemistry.

Acknowledgements

We gratefully acknowledge the financial support of our work by the National Institutes of Health (CA73775), the National Science Foundation (CHE-9733050 and CHE-0415344), and the Volkswagen Foundation (I/72 647) as well as a Camille Dreyfus Teacher-Scholar Award to O.W. for financial support of different aspects of this work. We also appreciate many discussions with T. Bally (Fribourg), H. Hopf (Braunschweig), H. Schwarz, and D. Schroeder (Berlin), as well as D. A. Singleton (Texas A&M) that helped us refine the thoughts outlined in this contribution.

[1] For an overview of the most striking examples, compare: H. Hopf, *Classics in Hydrocarbon Synthesis*, Wiley-VCH, Weinheim, **1999**.

[2] For example: a) S. J. Cyvin, *Theory of Coronoid Hydrocarbons*, Springer, Berlin **1991**; b) P. von R. Schleyer, *Chem. Rev.* **2001**, *101*, 1115–1118 and other contributions in this special issue on aromaticity.

[3] a) R. B. Woodward, R. Hoffmann, *J. Am. Chem. Soc.* **1965**, *87*, 395–397.;b) H. C. Longuet-Higgins, E. W. Abrahamson, *J. Am. Chem. Soc.* **1965**, *87*, 2045–2046; c) R. B. Woodward, R. Hoffmann, *Angew. Chem.* **1969**, *81*, 797–869; *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 781–853.

[4] a) B. K. Carpenter, *Acc. Chem. Res.* **1992**, *25*, 520–528; b) B. K. Carpenter, *Angew. Chem.* **1998**, *110*, 3532–3543; *Angew. Chem. Int. Ed.* **1998**, *37*, 3341–3350.

[5] a) A. Sancar, *Chem. Rev.* **2003**, *103*, 2203–2238; b) C. B. Harrison, L. L. O'Neil, O. Wiest, *J. Phys. Chem. A* **2005** *109*, 7001–7012; c) N. J. Saettel, O. Wiest, *J. Am. Chem. Soc.* **2001**, *123*, 2693–2694.

[6] a) K. N. Houk, J. Gonzalez, Y. Li, *Acc. Chem. Res.* **1995**, *28*, 81–90; b) O. Wiest, K. N. Houk, *Top. Curr. Chem.* **1996**, *183*, 1–24; c) K. N. Houk, Y. Li, J. D. Evanseck, *Angew. Chem.* **1992**, *104*, 711–739; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 682–708.

[7] a) I. R. Dunkin, *Tetrahedron*, **1985**, *41*, 145–161; b) N. L. Bauld, J. Cessac, *J. Am. Chem. Soc.* **1977**, *99*, 23–26; c) M. J. Bishop, I. Fleming, *J. Chem. Soc. C* **1969**, 1712.

[8] D. J. Bellville, N. L. Bauld, R. Pabon, S. A. Gardner, *J. Am. Chem. Soc.* **1983**, *105*, 3584–3588.

[9] E. Steckhan, J. Mlcoch, *Tetrahedron Lett.* **1987**, *28*, 1081–1084.

[10] H. A. Jahn, E. Teller, *Proc. R. Soc. London Ser. A* **1937**, *161*, 220–235.

[11] J. N. Aebischer, T. Bally, K. Roth, E. Haselbach, F. Gerson, X.-Z. Qin, *J. Am. Chem. Soc.* **1989**, *111*, 7909–7914.

[12] O. Wiest, *J. Am. Chem. Soc.* **1997**, *119*, 5713–5719.

[13] I. B. Bersuker, *Chem. Rev.* **2001**, *101*, 1067–1114.

[14] a) P. Jungwirth, P. Čársky, T. Bally, *J. Am. Chem. Soc.* **1993**, *115*, 5776–5782; b) V. Hrouda, T. Bally, P. Čársky, P. Jungwirth, *J. Phys. Chem. A* **1997**, *101*, 3918–3924; c) F. Williams, *Radiat. Phys. Chem.* **2003**, *67*, 211–218; d) T. Bally, L. Truttam, S. Dai, F. Williams, *J. Am. Chem. Soc.* **1995**, *117*, 7916–7922.

[15] D. J. Bellville, R. Chelsky, N. L. Bauld, *J. Comput. Chem.* **1982**, *3*, 548–551.

[16] a) G. N. Sastry, T. Bally, V. Hrouda, P. Čársky, *J. Am. Chem. Soc.* **1998**, *120*, 9323–9334; b) V. Barone, N. Rega, T. Bally, G. N. Sastry, *J. Phys. Chem. A* **1999**, *103*, 217–219.

[17] a) H. E. Zimmerman, *Acc. Chem. Res.*, **1971**, *4*, 272–280; b) M. J. S. Dewar, *Angew. Chem.* **1971**, *83*, 859–875; *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 761–776.

[18] For an overview, see: A. D. Allen, T. T. Tidwell, *Chem. Rev.* **2001**, *101*, 1333–1348.

[19] O. Wiest, *J. Phys. Chem. A* **1999**, *103*, 7907–7911.

[20] B. R. Beno, K. N. Houk, D. A. Singleton, *J. Am. Chem. Soc.* **1996**, *118*, 9984–9985.

[21] a) S. Kadota, K. Tsubono, K. Makino, M. Takeshita, T. Kikuchi, *Tetrahedron Lett.* **1987**, *28*, 2857–2860; b) B. Harirchian, N. L. Bauld, *J. Am. Chem. Soc.* **1989**, *111*, 1826–1828; c) E. Marshall Wilson, J. G. Dietz, T. A. Shepherd, D. M. Ho, K. A. Schnapp, R. C. Elder, J. W. Watkins, L. S. Geraci, C. F. Campana, *J. Am. Chem. Soc.* **1989**, *111*, 1749–1754.

[22] a) J. Mattay, G. Trampe, J. Runsick, *Chem. Ber.* **1988**, *121*, 1991–2005; b) J. Mattay, J. Gersdorf, J. Mertes, *J. Chem. Soc. Chem. Commun.* **1985**, 1088–1090; c) J. Gersdorf, J. Mattay, *J. Photochem.* **1985**, *28*, 405–411; d) Y. Otsuji, *Kokagaku* **1997**, *11*, 20–24.

[23] a) H. Schmittel, H. von Seggern, *Angew. Chem.* **1991**, *103*, 981–983; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 999–1001; b) H. Schmittel, H. von Seggern, *J. Am. Chem. Soc.* **1993**, *115*, 2165–2177; c) M. Schmittel, C. Wöhrle, *Tetrahedron Lett.* **1993**, *34*, 8431–8434.

[24] a) N. L. Bauld, D. X. Gao, *J. Chem. Soc. Perkin Trans. 2* **2000**, 931–934; b) N. L. Bauld, J. K. Yang, *Tetrahedron Lett.* **1999**, *40*, 8519–8522.

[25] a) O. Wiest, E. Steckhan, *Tetrahedron Lett.* **1993**, *34*, 6391–6394; b) N. J. Saettel, O. Wiest, D. A. Singleton, M. P. Meyer, *J. Am. Chem. Soc.* **2002**, *124*, 11552–11559.

[26] a) M. Hofmann, H. F. Schaefer, *J. Am. Chem. Soc.* **1999**, *121*, 6719–6729; b) M. Hofmann, H. F. Schaefer, *J. Phys. Chem. A* **1999**, *103*, 8895–8905; c) U. Haberl, E. Steckhan, O. Wiest, *J. Am. Chem. Soc.* **1999**, *121*, 6730–6736; d) U. Haberl, E. Steckhan, O. Wiest, S. Blechert, *Chem. Eur. J.* **1999**, *5*, 2859–2865; e) H. Hu, P. G. Wenthold, *J. Phys. Chem. A* **2002**, *106*, 10550–10553; f) D. J. Goebbert, X. Liu, P. G. Wenthold, *J. Am. Soc. Mass Spectrom.* **2004**, *15*, 114–120; g) W. J. van der Hart, *Int. J. Mass Spectrom.* **2001**, *208*, 119–125; h) G. Bouchoux, J.-Y. Salpin, M. Yanez, *J. Phys. Chem. A* **2004**, *108*, 9853–9862; i) G. Bouchoux, M. T. Nguyen, J.-Y. Salpin, *J. Phys. Chem. A* **2000**, *104*, 5778–5786.

[27] a) D. W. Reynolds, B. Harirchian, H. S. Chiou, B. K. Marsh, N. L. Bauld, *J. Phys. Org. Chem.* **1989**, *2*, 57–88; b) N. L. Bauld, B. Harirchian, D. W. Reynolds, J. White, *J. Am. Chem. Soc.* **1988**, *110*, 8111–8117.

[28] E. Goldstein, B. Beno, K. N. Houk, *J. Am. Chem. Soc.* **1996**, *118*, 6036–6043.

[29] P. Caramella, P. Quadrelli, L. Toma, S. Romano, K. S. Khuong, B. Northrop, K. N. Houk, *J. Org. Chem.* **2005**, *70*, 2994–3008.

[30] For experimental studies, see: a) J. P. Dinnocenzo, D. A. Conlon, *J. Am. Chem. Soc.* **1988**, *110*, 2324–2325; b) J. P. Dinnocenzo, D. A. Conlon, *Tetrahedron Lett.* **1995**, *36*, 7415–7418; c) J. P. Dinnocenzo, M. Schmittel, *J. Am. Chem. Soc.* **1987**, *109*, 1561–1562; d) G. Bouchoux, J. Y. Salpin, M. Yanez, *J. Phys. Chem. A* **2004**, *108*, 9853–9862; e) S. Furmeier, J. O. Metzger, *J. Am. Chem. Soc.* **2004**, *126*, 14485–14492.

[31] For computational studies, see: a) J. Oxgaard, O. Wiest, *J. Am. Chem. Soc.* **1999**, *121*, 11531–11537; b) M. Hofmann, H. F. Schaefer, *J. Mol. Struct.* **2001**, *599*, 95–116; c) T. Herbertz, H. D. Roth, *J. Am. Chem. Soc.* **1998**, *120*, 11904–11911.

[32] M. Uchiyama, T. Tomioka, A. Amano, *J. Phys. Chem.* **1964**, *68*, 1878–1881.

[33] a) K. B. Wiberg, W. K. B. Rosenberg, P. R. Rablen, *J. Am. Chem. Soc.* **1991**, *113*, 2890–2898; b) A. Karpfen, C. H. Choi, M. Kertesz, *J. Phys. Chem. A* **1997**, *101*, 7426–7433.

[34] a) L. R. Pratt, C. S. Hsu, D. Chandler, *J. Chem. Phys.* **1978**, *68*, 4202–4212; b) M. E. Squillacote, R. S. Sheridan, O. L. Chapman, F. A. L. Anet, *J. Am. Chem. Soc.* **1979**, *101*, 3657–3659; c) W. A. Herrebout, B. J. van der Veken, A. Wang, J. R. Durig, *J. Phys. Chem.* **1995**, *99*, 578–585; d) M. A. Murcko, H. Castejon, K. B. Wiberg, *J. Phys. Chem.* **1996**, *100*, 16162–16168.

[35] S. Shih, R. J. Buenker, S. D. Peyerimhoff, *Chem. Phys. Lett.* **1972**, *16*, 244–251.

[36] M. E. Squillacote, F. Liang, *J. Org. Chem.* **2005**, *70*, 6564–6573.

[37] For reviews, see: a) A. D. Kachkovskii, *Theor. Exp. Chem.* **2005**, *41*, 139–164; b) P. Frere, P. J. Skabara, *Chem. Soc. Rev.* **2005**, *34*, 69–98; c) G. Wegner, *Contemp. Top. Polym. Sci.* **1984**, *5*, 281–319.

[38] a) J. Oxgaard, O. Wiest, *J. Phys. Chem. A* **2002**, *106*, 3967–3974; b) T. Bally, G. N. Sastry, *J. Phys. Chem. A* **1997**, *101*, 7923–7925; c) G. N. Sastry, T. Bally, V. Hrouda, P. Carsky, *J. Am. Chem. Soc.* **1998**, *120*, 9323–9334.

[39] J. Oxgaard, O. Wiest, *J. Phys. Chem. A* **2001**, *105*, 8236–8240.

[40] J. Oxgaard, O. Wiest, unpublished results

[41] a) M. Traetteberg, P. Bakken, H. Hopf, R. Haenel, *Chem. Ber.* **1994**, *127*, 1469–1478; b) M. Traetteberg, H. Hopf, H. Lipka, R. Haenel, *Chem. Ber.* **1994**, *127*, 1459–1467.

[42] In cases in which simple saturated hydrocarbons are oxidized, for example, by ionizing radiation, or if they are studied computationally, their structure resembles nonclassical carbocations. This can be rationalized by considering the similar energy level of the carbon–carbon single bonds that can lead to strong overlap of the unoccupied orbital with the occupied σ-orbitals of the carbon–carbon single bonds.

[43] a) S. C. Richtsmeier, P. G. Gassman, D. A. Dixon, *J. Org. Chem.* **1985**, *50*, 311–317; b) H. D. Roth, M. L. M. Schilling, P. G. Gassman, J. L. Smith, *J. Am. Chem. Soc.* **1984**, *106*, 2711–2712.

[44] T. Bally, *J. Mol. Struct.: THEOCHEM* **1991**, *227*, 249–264.

[45] D. Scheschkewitz, H. Amii, H. Gornitzka, W. W. Schoeller, D. Bourissou, G. Bertrand, *Science* **2002**, *295*, 1880–1881.

[46] N. J. Saettel, O. Wiest, *J. Org. Chem.* **2003**, *68*, 4549–4552.

[47] H. Hopf, H. Lipka, M. Traetteberg, *Angew. Chem.* **1994**, *106*, 232–233; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 204–205.

[48] For overviews of these attempts, see: a) T. Linker, M. Schmittel, *Radikale und Radikalionen in der Organischen Synthese*, Wiley-VCH, Weinheim, **1998**; b) M. Schmittel, A. Burghart, *Angew. Chem.* **1997**, *109*, 2658–2699; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2551–2589; c) N. L. Bauld, in *Advances in Electron Transfer Chemistry Vol.2* (Ed.: P. S. Mariano), JAI, New York **1992**, p. 1 d) M. Schmittel, M. K. Ghorai in: *Electron Transfer in Chemistry, Vol. 2: Organic and Metalorganic Systems* (Eds.: J. Mattay, D. Astruc), Wiley-VCH New York **2001** as well as other contributions in this volume.

Published online: July 28, 2006