Substituent Effects in the Vinylcyclopropane Radical Cation Rearrangement: A Computational Road to a New Synthetic Tool

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The effect of substituents on the rearrangement of vinylcyclopropane radical cation to cyclopentene was explored by density functional theory. Correlations have been established between the activation energy of the system and the nature, as well as the position, of the substituents. It was found that radical- or cation-stabilizing substituents in select positions reduce the activation energy for the rearrangement substantially, while activation energies for competing hydrogen shifts were largely left unchanged. We have identified positions in the vinylcyclopropane where substitution is necessary, and others that can be substituted less discriminately. The mechanism of the rearrangement changes from stepwise to concerted when a strongly cation-stabilizing substituent is used, because the first step in the stepwise reaction becomes a barrierless ring opening of a strained cyclopropane. Steric effects were also explored and have been found to be of crucial importance for the success of a rearrangement. Finally, a simple set of rules has been devised to predict the outcome of oxidation of a vinylcyclopropane without requiring detailed mechanistic investigations.

Introduction

The thermal [1,3] methylene shift of vinylcyclopropane to give cyclopentene is a synthetically useful rearrangement and that has been applied to a number of natural product syntheses (Figure 1).[1] The high activation energies, however, of these reactions − often larger than 50 kcal/mol − usually make pyrolytic conditions necessary, which severely limits the synthetic potential of the approach.[2] The origin of the high activation energy and the stereochemistry of the reaction, as well as mechanistic details, have been elucidated using computational methods.[3] A possible remedy to the problem of high activation energies is the use of electron transfer (ET) processes. The radical ions formed by ET show a much higher reactivity than their neutral counterparts, and thus they can be used for the acceleration of slow or symmetry-forbidden pericyclic reactions.[4]

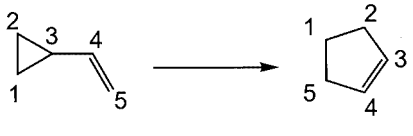

Figure 1. The vinylcyclopropane rearrangement

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The synthetic potential of ET catalysis was demonstrated by Dinnocenzo and co-workers who showed that upon one-electron oxidation, the rearrangement of a substituted vinylcyclopropane occurs in minutes at low temperatures,[5] an acceleration of the reaction by a factor of at least 10^{15}. The reaction is not stereospecific since one-electron oxidation of *cis*- and *trans*-1-anisyl-3,4-dimethyl-vinylcyclopropanes gave an 80% yield of a mixture of the corresponding cyclopentenes in the same diastereomeric ratio.

Substitution in the 3 and 4 positions was found to be essential for the reaction to occur, otherwise only isomerized reactant was isolated.[6] In contrast to these condensed-phase reactions of substituted vinylcyclopropanes, oxidation of the parent vinylcyclopropane **1** in the gas phase led exclusively to formation of 1,3-pentadiene and isoprene by ring opening of the cyclopropane followed by a hydrogen shift with a critical energy of ca.19.6 kcal/mol.[7] Similar hydrogen shifts have been observed in solution upon one-electron oxidation of bicyclic vinylcyclopropanes,[8] indicating that substitution of **1** at appropriate positions is a prerequisite for the formation of the cyclopentene rearrangement product.

Early studies at the INDO and UHF/STO-3G levels of theory investigated the structures of different conformers of the parent vinylcyclopropane radical cation $\mathbf{1}^{\cdot+}$ as well as several substituted derivatives.[9] A more recent study, of the electronic structures of *syn*-$\mathbf{1}^{\cdot+}$ and *anti*-$\mathbf{1}^{\cdot+}$ and their relationships to neutral **1** at the MP2/6-31G* level, was published by Herbertz et al.[10] The reactivity, however, of the vinylcyclopropane radical cation was not studied compu-

tationally until recently, when our group investigated the structure and reactivity of $\mathbf{1}^{\cdot+}$ at the B3LYP/6-31G* and QCISD(T)/6-31G*//QCISD/6-31G* levels of theory.[11] More recently, our study was duplicated by Hofmann and Schaefer, employing a different high-level ab initio method [CCSD(T)] for the final energy calculations.[12]

Five different reaction pathways for vinylcyclopropanes, summarized in Figure 2, have been studied previously: (i) the stereoisomerization via an acyclic intermediate, (ii) the [1,2] hydrogen shift leading to 1,4-pentadiene, (iii) the [1,2] hydrogen shift leading to 1,3-pentadiene, (iv) the interconversion of *syn*/*anti*-vinylcyclopropanes, and (v) the [1,3] methylene shift to form the cyclopentene radical cation. The activation energies for all these processes were found to be quite similar, making the different pathways competitive. With the exception of a small overestimation of the stabilization of the acyclic intermediates by homoconjugation,[12] the results from the B3LYP method were in good agreement with the highly correlated QCISD(T)/QCISD reference calculations, and the B3LYP method is consistently employed throughout this study. The [1,3] methylene shift is accessible only from the *syn*-vinylcyclopropane, as the C1 and C5 carbon atoms in *anti*-vinylcyclopropane are too far apart to create a new bond. Furthermore, *syn*-**1** is 3.0 kcal/mol higher in energy than *anti*-**1**, and the interconversion of *anti*- to *syn*-**1** has a higher activation energy than the [1,2] hydrogen shift leading to 1,3-pentadiene. Thus, in agreement with the experimental observations, oxidation of unsubstituted **1** is not expected to yield cyclopentene.

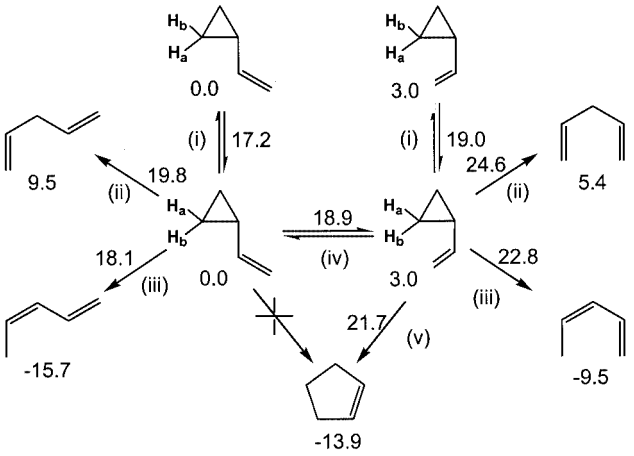

Figure 2. B3LYP/6-31G* PES of $\mathbf{1}^{\cdot+}$. Relative energies in kcal/mol

The key structures for the [1,3] sigmatropic shift of $\mathbf{1}^{\cdot+}$ are shown in Figure 3. The stepwise pathway involves formation of the acyclic intermediate $\mathbf{INT1-1}^{\cdot+}$, which is 15.6 kcal/mol less stable than *syn*-$\mathbf{1}^{\cdot+}$, via transition structure $\mathbf{TS1-1}^{\cdot+}$ with an activation energy of 18.7 kcal/mol. The electronic structure of $\mathbf{INT1-1}^{\cdot+}$ is best described as an allyl cation at C3−C4−C5, connected to a methylene radical at C1. With a dihedral angle C4−C3−C2−C1 of 15°, the carbon framework is essentially planar. $\mathbf{INT1-1}^{\cdot+}$ lies in a shallow groove on the potential energy hypersurface, and can close to form $\mathbf{CP\text{-}1}^{\cdot+}$ via transition structure $\mathbf{TS2-1}^{\cdot+}$ with an activation energy of 2.8 kcal/mol. The concerted [1,3] methylene shift involves the simultaneous bond breaking of C1−C3 and bond making of C1−C5, via transition structure $\mathbf{TS3-1}^{\cdot+}$ with an activation energy of 21.0 kcal/mol. As the concerted and stepwise pathways differ by only a few kcal/mol, it is not possible to make a definitive statement regarding the preferred pathway for the rearrangement of $\mathbf{1}^{\cdot+}$.

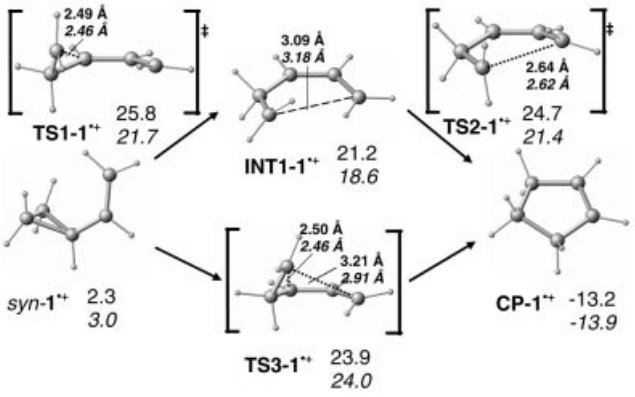

Figure 3. Stepwise (top) and concerted (bottom) pathways for the [1,3] methylene shift in $\mathbf{1}^{\cdot+}$. QCISD(T)//QCISD results are shown in plain text, B3LYP results are shown in italics. A dotted line indicates a forming/breaking bond

The synthetic use of the vinylcyclopropane radical cation rearrangement encounters three main obstacles: (i) the lower energy of the *anti* conformer, (ii) the competitive nature of [1,2] hydrogen shifts, and (iii) the activation energy of ca. 20 kcal/mol for the rearrangement, which is not competitive with the barrier for back electron transfer that has been estimated to be between 15 and 20 kcal/mol.[14]

Steric effects can alter the relative stabilities of the *syn* and *anti* conformers. It is well-known that the conformational preference of the vinylcyclopropane radical cation can be reversed by steric interactions.[3a,3d] This effect is demonstrated, for example, by the results of B3LYP calculations for the two conformations of 4-*tert*-butyl-vinylcyclopropane **2**. The repulsive interaction of the large substituent on C4′ with the *cis* hydrogen atoms at C1 and C2 leads to a reversal of the conformational preference. This observation is in analogy with the behavior of $\mathbf{2}^{\cdot+}$,[11] where slightly larger energy differences are calculated because of a smaller C3−C4 bond length. Since the barrier for rotation around the C3−C4 bond is relatively high at ca. 19 kcal/mol,[10] the *syn*/*anti* ratio in the radical cation will be determined by this ratio in the corresponding neutral vinylcyclopropane. The predominant conformation of substituted vinylcyclopropane radical cations can be estimated, therefore, by using much simpler methods, for example force-field calculations.

The activation energy for the desired [1,3] methylene shift should also be lowered, ideally below 18 kcal/mol, by radical or stabilizing substituents. Furthermore, the [1,3] methylene shift, where the spin and charge are localized in the carbon framework, can be stabilized by substituents to a

larger extent than the corresponding [1,2] hydrogen shifts, where spin and charge is localized mainly in the forming/breaking C−H bonds. If we can establish an understanding of the effect of substituents on the stationary points and reaction pathways of the vinylcyclopropane radical cation, then this reaction should be of more synthetic use. Here, we present a computational study of substituent effects on the different reaction pathways for the radical cation vinylcyclopropane rearrangement. The ultimate goal of this study is to formulate simple rules for the rearrangement that could make individual theoretical investigations unnecessary and allow simple predictions about the reaction pathways to be made based on the substitution pattern in the reactant.

Methodology

The problems associated with the calculation of hydrocarbon radical cations by different approaches, as well as the biases and accuracy of these methods, have been discussed in detail by our group[11,13a,13b,15] and others.[12,13c−13f,16] Here, we have adopted a computational strategy in which all structures were fully optimized and characterized at the B3LYP/6-31G* level of theory to ensure that all species have the correct number of negative eigenvalues. The one imaginary eigenfrequency of the transition structures was animated using MOLDEN[17] or verified using IRC calculations to ensure that the optimized stationary point corresponds to the transition structure of the desired reaction. All energies reported were corrected for zero-point vibrational energies from B3LYP calculations and were given in kcal/mol relative to the vinylcyclopropane radical cation at the same level of theory. This approach was found previously to be reasonably accurate as well as computationally efficient. All calculations were performed using the G98 series of programs.[18]

Results

Substituents at C4: Dinnocenzo and co-workers reported that a vinylcyclopropane without substituents in the 3 and 4 positions does not rearrange to the corresponding cyclopentene, while a methyl group at each position was sufficient to allow rearrangement to occur in high yield.[5] Since a methyl group is weakly electron donating with a σ^+ of −0.17, it is expected to have only a small effect on the energetics of the rearrangement. As will be shown below, all transition structures and intermediates involved in the rearrangement of the 4-methyl-vinylcyclopropane radical cation $\mathbf{3}^{\cdot+}$ have relative energies ca. 3 kcal/mol higher than their counterparts in $\mathbf{1}^{\cdot+}$, but the geometries are largely unchanged. The reason for the higher relative energies is most likely the selective stabilization of the starting material than any destabilizing effects on the intermediates of the reaction. Dinnocenzo's results are likely to have been caused by a change in the conformational preference of the vinyl group, in analogy to the case of **2** discussed earlier.[3a][3d,9] Indeed, our calculations for **3** showed that the *syn* isomer is only 0.2 kcal/mol higher in energy than the *anti* conformer.[11,15] While *syn*-**3** is still the less-favored conformer, the low energy difference corresponds to a 42:58 *syn*/*anti* ratio at room temperature. With more than 40% of **3** being in the *syn* conformer, this quantity is expected to be sufficient for the desired rearrangement to occur. Since the eventual goal of the studies presented here is a set of rules for the practical synthetic application of this reaction, all further investigations included a methyl group at C4 and comparisons will be made to $\mathbf{3}^{\cdot+}$ rather than $\mathbf{1}^{\cdot+}$ for reasons of consistency.

Substituents at C1: By examining the rearrangement of $\mathbf{1}^{\cdot+}$, it can be deduced that the most important position for substitution is C1, which is involved in both of the relevant steps of the rearrangement: the bond breaking of C1−C3 and the bond formation of C1−C5. Moreover, the relative energy of the acyclic intermediate is dependent on the stabilization of spin/charge at C1. While spin/charge on C3 and C5 are stabilized as allylic radicals or cations, the spin/charge on C1 can be stabilized only by a potential substituent. Recognizing that the intermediate $\mathbf{INT1-1}^{\cdot+}$ contains a primary radical at C1 explains the high-energy character of this species. Thus, substitution of C1 should stabilize the formerly primary radical in the intermediate and, according to the Hammond postulate, also the transition states to and from this intermediate. It is not clear, however, whether this substituent should be of cation- or radical-stabilizing character. Although C1 in $\mathbf{INT1-1}^{\cdot+}$ is a radical, substitu-

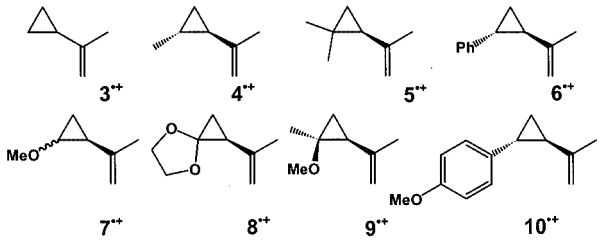

Figure 4. Vinylcyclopropanes $\mathbf{3}^{\cdot+}$ to $\mathbf{10}^{\cdot+}$

Table 1. Selected relative energies for the rearrangements of vinylcyclopropanes $\mathbf{1}^{\cdot+}$ to $\mathbf{10}^{\cdot+}$

	vcp		ts1	INT	ts2		cp
	ΔE	r(C1−C3)	ΔE	ΔE	ΔE	r(C1−C5)	ΔE
$\mathbf{1}^{\cdot+}$	0	1.63	18.7	15.6	18.4	3.00	−16.8
$\mathbf{3}^{\cdot+}$	0	1.60	22.9	19.7	22.4	2.70	−21.6
$\mathbf{4}^{\cdot+}$	0	1.74	18.8	16.4	18.4	2.93	−16.2
$\mathbf{5}^{\cdot+}$	0	1.96	11.9	8.7	13.1	3.08	−11.7
$\mathbf{6}^{\cdot+}$	0	1.87	12.6	12.5	12.7	2.59	−8.1
$\mathbf{t\text{-}7}^{\cdot+}$	0	2.11	−[a]	−[a]	7.1	2.51	−4.9
$\mathbf{s\text{-}7}^{\cdot+}$	0.4	2.14	−[a]	−[a]	6.8	2.68	−4.9
$\mathbf{8}^{\cdot+}$	0	2.36	−[a]	−[a]	11.5	1.98	8.9
$\mathbf{9}^{\cdot+}$	0	2.28	−[a]	−[a]	10.8	2.18	1.6
$\mathbf{10}^{\cdot+}$	0	1.74	−[a]	−[a]	12.0	2.44	−11.5

[a] Barrierless ring opening

ent effects observed for stabilization of cations are typically much larger than the ones obtained by radical-stabilizing groups. A cation-stabilizing substituent is thus more likely to change the electronic makeup of the intermediate. We studied a series of C1 substituted vinylcyclopropanes **4**−**8**, which are shown in Figure 4 together with the reference system **3**. All structures discussed in this paper will be specified using a number according to their substitution pattern as shown in Figure 4, and a prefix indicating their position on the hypersurface as follows: **TS1** for the transition structure for ring opening of the vinylcyclopropane radical cation, **INT** for the acyclic intermediate, and **TS2** for the transition structure for ring closure to the cyclopentene **CP**. **TS3** indicates the transition structure for the concerted rearrangement, while **TS4** and **TS5** denote the transition structures for the hydrogen shifts leading to the 1,4-pentadiene **PD14** and 2,4-pentadiene **PD24**, respectively. The results from these investigations are summarized in Table 1, and the corresponding σ^+ and $\sigma^\cdot$ values for substituents are presented in Table 2.[19]

The first and simplest C1 substituent included in this study is the methyl group. Optimization of *trans*-1,4-dimethyl-vinylcyclopropane (**4**$^{\cdot+}$) leads to a C_1 symmetric vinylcyclopropane in a gauche conformation, where (C2−C3−C4−C5) = 10.6° and (C1−C3−C4−C5) = 50.7° (Figure 5). There is also an elongation to 1.74 Å of the breaking bond C1−C3, while the C2−C3 bond is shortened to 1.53 Å. This structure is in contrast to the C_2 symmetric **3**$^{\cdot+}$, where both dihedral angles are 32.0° and the bond lengths C1−C3 and C2−C3 are 1.60 Å. The marked asymmetry of the bonds in **4**$^{\cdot+}$ indicates that the methyl substituent at C1 significantly changes the electronic nature of the vinylcyclopropane radical cation. Stabilizing spin/charge in C1 reduces electron density in the C1−C3 bond, and a lower electron density leads to a longer *r*(C1−C3). Where **3**$^{\cdot+}$ can be considered analogous to 1,3-butadiene radical cation, **4**$^{\cdot+}$ appears more like an allyl radical/cation with hyperconjugation to a secondary radical/cation. This analogy is further supported by the almost planar geometry of C3−C5, which is consistent with an allyl radical or cation.

The rearrangement proceeds via a transition structure **TS1**−**4**$^{\cdot+}$ with an activation energy of 18.6 kcal/mol relative to *syn*-**4**$^{\cdot+}$. This transition structure does not correspond to the breaking of the C1−C3 bond, but a rotation around the C1−C2 bond. Following the transition vectors by IRC calculations, the C1−C3 bond increases in length until it reaches ca. 2.6 Å, at which point the rotation occurs. The lack of a transition structure for the bond breaking indicates that there is still significant interaction, even at a C1−C3 bond length of 2.6 Å. The rotation leads to intermediate **INT-4**$^{\cdot+}$ with a relative energy of 16.4 kcal/mol. The electronic structure of this species is best described as an allyl cation/radical and a secondary radical/cation linked by a CH_2 unit. The electron distribution in **INT-4**$^{\cdot+}$ is more delocalized than for **1**$^{\cdot+}$, with a Mulliken charge of 0.21 electrons and a spin density of 0.60 electrons at C1. The remainder of the spin/charge is in the allyl moiety. The delocalization can be envisioned to occur through the σ framework, as the C1 p-orbital lacks significant overlap with the allyl π-orbitals. The rearrangement continues through the transition structure ts-**4**$^{\cdot+}$, which is only 2 kcal/mol higher in energy than the intermediate. As expected, the negative eigenfrequency in ts-**4**$^{\cdot+}$ corresponds to the forming bond C1−C5, with a bond length of 2.93 Å, and leads to the cyclopentene **CP-4**$^{\cdot+}$**.** The overall thermochemistry of the reaction is −16.2 kcal/mol, 5.4 kcal/mol less exothermic than the rearrangement of **3**$^{\cdot+}$. This observation is due to the selective stabilization of **4**$^{\cdot+}$ over **CP-4**$^{\cdot+}$. Conversely, the transition structures and intermediates of the rearrangement are 3−4 kcal/mol lower in energy than the corresponding structures for **3**$^{\cdot+}$**.** These numbers support the assumption that adding a stabilizing substituent to C1 lowers the activation energy of the reaction.

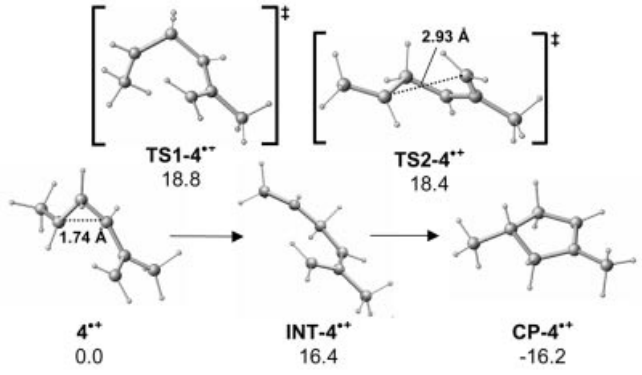

Figure 5. Rearrangement of **4**$^{\cdot+}$. Relative energies in kcal/mol

Optimization of 1,1,4-trimethyl-vinylcyclopropane **5**$^{\cdot+}$ yields a structure where *r*(C1−C3) = 1.96 Å and (C2−C3−C4−C5) = 5.0°. Breaking of the C1−C3 bond, followed by rotation around the C1−C2 bond, leads to the first transition structure **TS1**−**5**$^{\cdot+}$, which proceeds to **INT-5**$^{\cdot+}$, with relative energies of 11.9 kcal/mol and 8.7 kcal/mol, respectively. The population analysis of **INT-5**$^{\cdot+}$ indicates a charge of 0.56 electrons and a spin density of 0.28 electrons at C1, with the remaining spin/charge located in the allyl moiety. The rearrangement is completed through **TS2**−**5**$^{\cdot+}$ with a relative energy of 13.1 kcal/mol with an overall ther-

Table 2. Substituent σ^+ and $\sigma^\cdot$ values

	−H	$-CH_3$	$-C_6H_5$	$-OCH_3$	$-C_6H_4OCH_3$	$-C_3H_5$	−CN	$-CF_3$	−F
σ^+	0.0	−0.30	−0.18	−0.78	< -0.18[a]	−0.18	0.99	0.65	−0.07
$\sigma^\cdot$	0.0	0.11	0.46	0.24	> 0.39[a]	0.53	0.46	0.08	−0.08

[a] Estimated from $-C_6H_5$.

mochemistry of −11.7 kcal/mol. The C1−C5 distance in **TS2−5**$^{\cdot+}$ is 3.08 Å, slightly larger than in **TS2−3**$^{\cdot+}$ and **TS2−4**$^{\cdot+}$.

The C1−C3 bond length in *trans*-4-methyl-1-phenyl-vinylcyclopropane **6**$^{\cdot+}$, where the substituent could stabilize either a radical or a cation, is substantially elongated at 1.87 Å. The transition structure **TS1−6**$^{\cdot+}$, with a relative energy of 12.6 kcal/mol, is only 0.1 kcal/mol higher in energy than the acyclic intermediate **INT-6**$^{\cdot+}$. Similarly, the transition structure for ring closure, **TS2−6**$^{\cdot+}$, is only 0.2 kcal/mol higher in energy than **INT-6**$^{\cdot+}$. The intermediate, therefore, is in a very shallow well on the hypersurface, making it almost a concerted reaction. The overall thermochemistry of the rearrangement is −8.1 kcal/mol, with the spin and charge distributed evenly between the phenyl and olefin moieties in **CP-6**$^{\cdot+}$. The electronic structure of **INT-6**$^{\cdot+}$ can best be described as a cation at C1, delocalized into the phenyl moiety, connected to an allyl radical with a spin density of 0.78 distributed over C3−C5.

From the electronic structures of **INT-3**$^{\cdot+}$ to **INT-6**$^{\cdot+}$, it is clear that localization is preferred of the positive charge at C1 and of the radical in the allyl moiety. Adding a substituent at C1 with a pronounced radical-stabilizing effect, such as cyano group, is not expected to yield as much stabilization to the reaction as a cation stabilizing substituent, such as a methoxyl group. This hypothesis was tested by investigating the rearrangements of **7**$^{\cdot+}$ to **11**$^{\cdot+}$.

Calculation gave a structure of *trans*-1-methoxy-4-methyl-vinylcyclopropane *trans*-**7**$^{\cdot+}$ with a C1−C3 bond length of 2.11 Å and a dihedral angle (C2−C3−C4−C5) of 2.7°. Carbon atoms C1 and C3 are almost perfectly sp^2 hybridized, with deviations from planarity of less than 5°, indicating that the C1−C3 bond is essentially broken. To confirm that the bond breaking is indeed barrierless, we performed a scan of the C1−C3 bond length at the B3LYP/3−21G level of theory. No energy maximum could be located during this scan, indicating that the breaking of C1−C3 bond will be part of the electron transfer coordinate. This barrierless bond breaking is the continuation of a trend observed for the series **3**$^{\cdot+}$ to **6**$^{\cdot+}$, where *r*(C1−C3) increase steadily with more-stabilizing substituents. This follows the reasoning first presented in the discussion of **4**$^{\cdot+}$, where stabilization of spin/charge on C1 reduces electron density in the C1−C3 bond. Furthermore, reducing electron density from a strained bond eventually leads to bond breaking.

Elongating the bond also leads to a structure that closely resembles the acyclic intermediate. Comparing the relative energies of the first transition state and the intermediate in each of **3**$^{\cdot+}$ to **6**$^{\cdot+}$, it can be seen that the energy differences between the first **TS1** and **INT** are 3.2, 2.4, and 0.1 kcal/mol, for **3**$^{\cdot+}$, **4**$^{\cdot+}$, and **6**$^{\cdot+}$, respectively.[20] Thus, it is not surprising that no other intermediates could be located, while attempts to locate **TS1−7**$^{\cdot+}$ led to a transition structure 6.5 kcal/mol higher in energy than *trans*-**7**$^{\cdot+}$. IRC calculations revealed that this structure, labeled **TS$_{iso}$-7**$^{\cdot+}$, corresponds to the transition structure for the *cis*/*trans* isomerization of **7**$^{\cdot+}$. The transition structure for ring closure

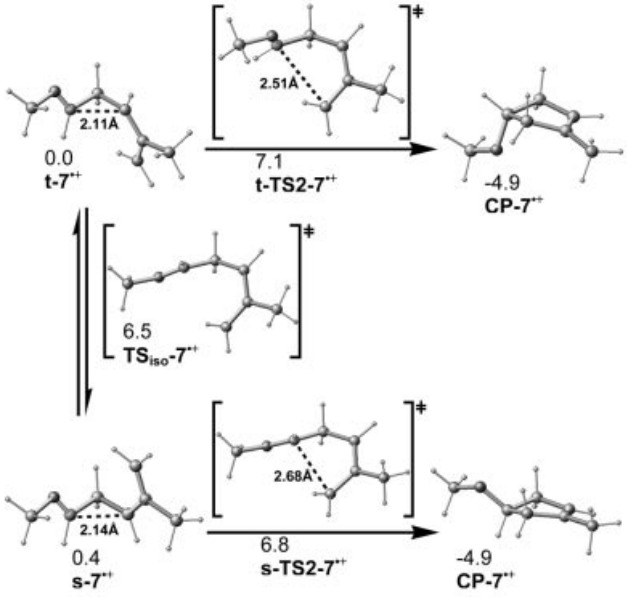

Figure 6. Rearrangement of **7**$^{\cdot+}$. Relative energies in kcal/mol

trans-**TS2−7**$^{\cdot+}$ is 7.1 kcal/mol higher in energy than *trans*-**7**$^{\cdot+}$. The C1−C5 distance is 2.68 Å, indicating a later transition state than in previous rearrangements. The product of the rearrangement, 1-methoxy-4-methylcyclopentene, (*trans*-**CP-7**$^{\cdot+}$), is 4.9 kcal/mol lower in energy than *trans*-**7**$^{\cdot+}$ and 12.0 kcal/mol lower in energy than *trans*-**TS2−7**$^{\cdot+}$. IRC calculations of *trans*-**TS2−7**$^{\cdot+}$ led to *trans*-**7**$^{\cdot+}$ and *trans*-**CP-7**$^{\cdot+}$, further confirming the absence of another intermediate (Figure 6).

The *cis* isomer of **7**$^{\cdot+}$ is only 0.4 kcal/mol higher in energy than *trans*-**7**$^{\cdot+}$**.** While *cis*-substituted cyclopropanes generally are significantly higher in energy than their *trans* isomers, because of steric repulsion of the eclipsed substituents, the large C1−C3 distance in **7**$^{\cdot+}$ reduces the steric repulsion substantially. The geometry of *cis*-**TS2−7**$^{\cdot+}$ is essentially identical to *trans*-**TS2−7**$^{\cdot+}$, with a C1−C5 distance of 2.68 Å and a relative energy 6.8 kcal/mol higher in energy than *trans*-**7**$^{\cdot+}$, well within the margin of error that can reasonably be expected from these calculations. The processes, which lead to two different stereoisomers of the same product, are thus competitive since the three relevant transition structures iso-**7**$^{\cdot+}$, *trans*-**TS2−7**$^{\cdot+}$ and *cis*-**TS2−7**$^{\cdot+}$ are all within 0.6 kcal/mol from each other. It is thus expected that, although the rearrangement of **7**$^{\cdot+}$ is formally a concerted process, both isomers of the product would be found because of rapid isomerization of the starting material. This process is similar to the thermal isomerization of neutral vinylcyclopropanes, which has been estimated to be ca. 20 times faster than the rearrangement.[21]

1-Isopropenyl-4,7-dioxaspiro[2.4]heptane (**8**$^{\cdot+}$) is electronically equivalent to a dimethoxy-substituted vinylcyclopropane, but with fewer degrees of conformational freedom. As a single methoxyl group is already highly cation stabilizing, it is not surprising that **8**$^{\cdot+}$ also undergoes barrierless ring opening, as is indicated by the computed C1−C3 distance of 2.36 Å. The majority of the charge, 0.70

electrons, resides on C1, while a spin density of 0.92 resides in the allyl moiety. Thus, much like $\mathbf{7}^{\cdot+}$, $\mathbf{8}^{\cdot+}$ can be considered a distonic radical cation.

In contrast to the previously discussed steady decrease in activation energy with more stabilizing substituents, the calculated activation energy for ring closure via **TS2−8**$^{\cdot+}$ is 11.5 kcal/mol. The break in the trend can be understood by examining the thermochemistry of the rearrangement, which is endothermic by 8.9 kcal/mol. In **CP-8**$^{\cdot+}$, the spin/charge is localized in the C3−C4 π-bond, and cannot take advantage of the cation-stabilizing effects of the dioxane. Thus, a distonic allyl radical and a dioxane-stabilized cation are significantly more stable than a radical cation localized in a π-bond, even though the latter compound has an additional σ bond. It should also be added that the main driving force for the thermal reaction, the release of ring strain, is all but negligible with a C1−C3 bond length of 2.36 Å in the starting material. The cause of the high activation energy is then apparent, as it must be higher than the energy of the product. **TS2−8**$^{\cdot+}$ is only 1.6 kcal/mol higher in energy than **CP-8**$^{\cdot+}$ and, thus, is a very late transition structure with r(C1−C5) = 1.98 Å, by far the shortest r(C1−C5) of any of the ring closure transition structures found in this study.

Adding a methyl group to C1 of $\mathbf{7}^{\cdot+}$ gives 1-methoxy-1,4-dimethyl-vinylcyclopropane ($\mathbf{9}^{\cdot+}$). The *cis*-methoxy isomer is the lower energy isomer of $\mathbf{9}^{\cdot+}$. Again, the ring opening occurs barrierlessly to a structure with a C1−C3 bond length of 2.28 Å, which leads to the final product via **TS2−9**$^{\cdot+}$ with a short r(C1−C5) of 2.18 Å and a relative energy of 10.8 kcal/mol. The rearrangement is endothermic by 1.6 kcal/mol. Compared to the rearrangement of $\mathbf{7}^{\cdot+}$, the activation energy is 4.0 kcal/mol higher and the overall reaction energy is endothermic by 5.6 kcal/mol. Compared to the rearrangement of $\mathbf{8}^{\cdot+}$, these values are 0.7 kcal/mol and 7.3 kcal/mol less exothermic, respectively. The reasoning presented for $\mathbf{8}^{\cdot+}$ is still valid for $\mathbf{9}^{\cdot+}$, with an added contribution from steric crowding of the transition structure.

The next compound studied was the *trans*-1-(4-methoxyphenyl)-4-methyl-vinylcyclopropane ($\mathbf{10}^{\cdot+}$), which is electronically similar to the compound used by Dinnocenzo.[5,6] Like the previously discussed derivatives, $\mathbf{10}^{\cdot+}$ opens without a barrier and undergoes *cis*/*trans* isomerization with a barrier of 7.1 kcal/mol. The transition structure for the ring closure, **TS2−10**$^{\cdot+}$, has an r(C1−C5) of 2.44 Å and a barrier of 12.0 kcal/mol. The overall thermochemistry of the reaction is −11.5 kcal/mol. The electron distribution in $\mathbf{10}^{\cdot+}$ is roughly the same as in $\mathbf{6}^{\cdot+}$, with the vast majority of the positive charge in the aromatic ring. These results are in good agreement with the experimental results. The lack of stereoselectivity of the rearrangement is accounted for by the lower energy of isomerization than of rearrangement, while the fact that the reaction is fast even at low temperatures is consistent with the calculated activation energy of 12 kcal/mol.[6]

Having shown that a cation-stabilizing substituent does indeed lower the activation energy of the rearrangement, attention was then turned to the effect of the radical-stabilizing cyano substituent. Optimization of *trans*-1-cyano-4-methyl-vinylcyclopropane ($\mathbf{11}^{\cdot+}$), shown in Figure 7, yielded a structure where the C1−C3 bond is elongated to 1.73 Å. Breaking of the C1−C3 bond, followed by rotation around the C1−C2 axis, yielded the transition structure **TS1−11**$^{\cdot+}$ with a relative energy of 10.1 kcal/mol. **TS1−11**$^{\cdot+}$ leads to the acyclic intermediate **INT-11**$^{\cdot+}$ with a relative energy of 8.8 kcal/mol (Table 3). From the population analysis of **INT-11**$^{\cdot+}$, with a charge of 0.10 electrons and a spin density of 0.89 electrons at C1, it is clear that the cyano substituent has the desired effect (i.e., localization of the unpaired electron on C1). **INT-11**$^{\cdot+}$ converts to the cyclopentene product via **TS2−11**$^{\cdot+}$ with a relative energy of 14.1 kcal/mol and a carbon−carbon distance r(C1−C5) = 2.60 Å. The overall thermochemistry of the reaction is −20.2 kcal/mol. Of note in this process is the difference in energy between **TS1−11**$^{\cdot+}$ and **TS2−11**$^{\cdot+}$: 4.0 kcal/mol. In the rearrangements of vinylcyclopropanes $\mathbf{1}^{\cdot+}$ to $\mathbf{7}^{\cdot+}$, the two transition structures are equally stabilized by the C1 substituent, differing by at most 1.2 kcal/mol in energy, whereas stabilization of **TS1** by the cyano substituent clearly dominates in the case of $\mathbf{11}^{\cdot+}$.

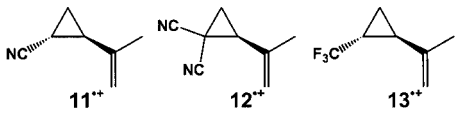

Figure 7. Substituted vinylcyclopropanes $\mathbf{11}^{\cdot+}$ to $\mathbf{13}^{\cdot+}$

Table 3. Selected relative energies for the rearrangements of vinylcyclopropanes $\mathbf{11}^{\cdot+}$ to $\mathbf{13}^{\cdot+}$

	vcp		ts1	INT	ts2		cp
	ΔE	r(C1−C3)	ΔE	ΔE	ΔE	r(C1−C5)	ΔE
$\mathbf{11}^{\cdot+}$	0	1.71	10.1	8.8	14.1	2.61	−20.2
$\mathbf{12}^{\cdot+}$	0	2.28	4.6	4.2	11.6	2.47	−14.4
$\mathbf{13}^{\cdot+}$	0	1.60	24.7	24.1	24.3	2.78	−20.7

Adding a second cyano group at C1 gives 1,1-dicyanovinylcyclopropane $\mathbf{12}^{\cdot+}$, shown in Figure 8. The first transition state, **TS1−12**$^{\cdot+}$, is slightly different from previously calculated structures with a relative energy of 4.6 kcal/mol. It is very close to C_2-symmetry, with a plane of symmetry through the C1−C2−C3−C4−C5 backbone. Converting $\mathbf{12}^{\cdot+}$ to **TS1−12**$^{\cdot+}$ necessitates not only a breaking of the C1−C3 bond, followed by a rotation around the C1−C2 bond, but also a rotation around the C2−C3 bond. Thus, it was somewhat surprising to see that the negative eigenfrequency in **TS1−12**$^{\cdot+}$ corresponds almost exclusively to a rotation around the C1−C2 bond. IRC calculations connected **TS1−12**$^{\cdot+}$ to $\mathbf{12}^{\cdot+}$ by closing of the C1−C3 bond, and to **INT-12**$^{\cdot+}$ by C1−C2 rotation followed by C2−C3 rotation. **INT-12**$^{\cdot+}$ is 4.2 kcal/mol higher in energy than $\mathbf{12}^{\cdot+}$. **TS2−12**$^{\cdot+}$, with a relative energy of 11.6 kcal/mol, has a C1−C5 distance of 2.47 Å and converts to **CP-12**$^{\cdot+}$ with an overall reaction energy of −14.4 kcal/mol. The en-

ergy difference between the two transition structures, 7.0 kcal/mol, is even more marked for $\mathbf{12}^{\cdot+}$ than it is for $\mathbf{11}^{\cdot+}$. The reason is most likely the electron distribution of the acyclic intermediate, which has a spin density of 0.89 at C1, thus reemphasizing the trend obtained for $\mathbf{11}^{\cdot+}$.

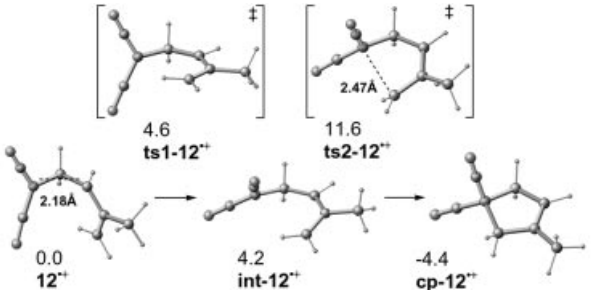

Figure 8. Rearrangement of $\mathbf{12}^{\cdot+}$. Relative energies in kcal/mol.

Conversely, cation-destabilizing substituents should increase the activation energy of the rearrangement. This concept is demonstrated for the case of 1-trifluoromethyl-4-methyl-vinylcyclopropane ($\mathbf{13}^{\cdot+}$). The trifluoromethyl group is strongly electron-withdrawing and, thus, disfavors charge development at C1. Thus, the breaking bond will be the C2−C3 bond. Indeed, calculations show that $\mathbf{13}^{\cdot+}$ has r(C1−C3) = 1.51 Å and r(C2−C3) = 1.60 Å. $\mathbf{TS1-13}^{\cdot+}$ is, as in previous rearrangements, a transition structure for rotation around the C2−C3 bond with an activation energy of 24.7 kcal/mol. $\mathbf{INT\text{-}13}^{\cdot+}$, with a relative energy of 24.1 kcal/mol, converts to $\mathbf{CP\text{-}13}^{\cdot+}$ via $\mathbf{TS2-13}^{\cdot+}$ with an activation energy of 24.3 kcal/mol. The overall thermochemistry is −20.7 kcal/mol. With an activation energy higher than the activation energy for unsubstituted vinylcyclopropane $\mathbf{1}^{\cdot+}$, the hypothesis introduced above appears to be justified.

Substituents at C5: The second position where substantial substituent effects can be expected is C5. Because of the electronic structure of the allyl moiety, substitution at C3 is expected to exhibit similar effects, while no significant effects are expected at C4. To test this hypothesis, we investigated a series of C5-substituted compounds (Figure 9). In Table 4, the results of these calculations are compared to the ones of the relevant C5-unsubstituted cases. The first C5-substituted compound studied is (*E*)-5-phenyl-4-methyl-vinylcyclopropane ($\mathbf{14}^{\cdot+}$). With a first transition structure with a relative energy of 19.5 kcal/mol, an acyclic intermediate with a relative energy of 18.5 kcal/mol and a second transition structure with a relative energy of 20.5 kcal/mol, the reaction pathway strongly resembles the one for $\mathbf{3}^{\cdot+}$. The energy difference between the two pathways is only ca. 2 kcal/mol, most likely a result of the shorter conjugated chain in the intermediate compared to the vinylcyclopropane. The thermochemistry of the rearrangement, however, is −4.4 kcal/mol, which is significantly lower than the value of −21.6 kcal/mol found for $\mathbf{3}^{\cdot+}$. The spin and charge in the cyclopentene cp-$\mathbf{14}^{\cdot+}$ are localized in the phenyl moiety, which is not conjugated to the C3−C4 π-bond, and, thus, the low exothermicity is caused by the loss of conjugation in the product.

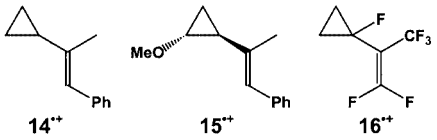

Figure 9. Substituted vinylcyclopropanes $\mathbf{14}^{\cdot+}$ to $\mathbf{16}^{\cdot+}$

Table 4. Selected relative energies for the rearrangements of vinylcyclopropanes $\mathbf{14}^{\cdot+}$ to $\mathbf{16}^{\cdot+}$

	vcp		ts1	INT	ts2		cp
	ΔE	r(C1−C3)	ΔE	ΔE	ΔE	r(C1−C5)	ΔE
$\mathbf{14}^{\cdot+}$	0	1.57	19.5	18.5	20.5	2.76	−4.4
$\mathbf{15}^{\cdot+}$	0	1.96	—[a]	—[a]	8.1	2.97	0.7
$\mathbf{16}^{\cdot+}$	0	1.79	—[a]	—[a]	10.6	2.62	−10.4

[a] Barrierless ring opening

Adding a phenyl unit to C5 of an already stabilized vinylcyclopropane such as $\mathbf{7}^{\cdot+}$ gives (*E*)-*trans*-1-methoxy-4-methyl-5-phenyl-vinylcyclopropane ($\mathbf{15}^{\cdot+}$). The value of r(C1−C3) = 1.96 Å, which is slightly shorter than that of 2.11 Å in $\mathbf{7}^{\cdot+}$, is consistent with the transfer of charge from C1 to the allyl moiety. The rearrangement is concerted with an activation energy of 8.1 kcal/mol, 1 kcal/mol higher than found in the rearrangement of $\mathbf{7}^{\cdot+}$. The overall thermochemistry of the rearrangement is 0.7 kcal/mol. The slightly higher activation energy and endothermicity is due to the loss of stabilization by the substituents of the radical cation in the product.

Finally, the rearrangement of 3,5,5-trifluoro-4-trifluoromethyl-vinylcyclopropane ($\mathbf{16}^{\cdot+}$), where the cation is destabilized by fluorine atoms in the C3, C4 and C5 positions,[22] was studied to elucidate the effect of σ-acceptors on the allyl moiety. This vinylcyclopropane radical cation has r(C1−C3) = 1.79 Å, r(C2−C3) = 1.51 Å and (C2−C3−C4−C5) = 10.2°. $\mathbf{16}^{\cdot+}$ is clearly not C2 symmetric like $\mathbf{1}^{\cdot+}$ and $\mathbf{3}^{\cdot+}$, but instead prefers to put the majority of the charge into the cyclopropyl moiety with the resulting bond elongation. $\mathbf{16}^{\cdot+}$ undergoes the rearrangement in a concerted fashion with an activation energy of 10.6 kcal/mol and an overall thermochemistry of −10.4 kcal/mol.

Substituent Effects on Hydrogen Shifts

It has been shown previously that the barrier for the [1,3] methylene shift in $\mathbf{1}^{\cdot+}$ is higher or equal in energy to the [1,2] hydrogen shifts leading to 1,4- and 1,3-pentadienes.[11] Thus, formation of pentadienes is the sole reaction observed in the gas phase.[7] The experimental findings of

Dinnocenzo and co-workers[6] could be explained by the hypothesis that transition structures of hydrogen shifts are not stabilized by substituents. To test this hypothesis, we carried out investigations of hydrogen shifts in the representative vinylcyclopropanes **t-7**$^{\cdot+}$, **11**$^{+}$ and **16**$^{\cdot+}$. The results of these studies are summarized in Figure 10.

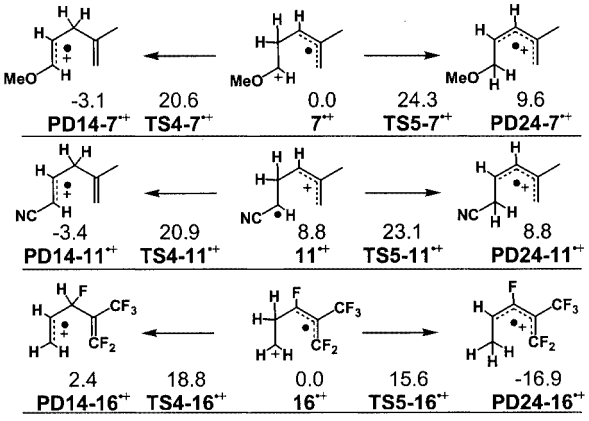

Figure 10. [1,2] Hydrogen shifts. Relative energies in kcal/mol

Starting from **7**$^{\cdot+}$, the activation energies for the transition structures for hydrogen shifts − **TS7−7**$^{\cdot+}$ leading to the 1,4-pentadiene **PD14−7**$^{\cdot+}$, and **TS8−7**$^{\cdot+}$ leading to the 2,4-pentadiene **PD24−7**$^{\cdot+}$ − are 20.6 and 24.3 kcal/mol, respectively. In contrast to earlier findings for **1**$^{\cdot+}$, **PD14−7**$^{\cdot+}$, with a relative energy of −3.1 kcal/mol, is more stable than **PD24−7**$^{\cdot+}$, which has a relative energy of 9.6 kcal/mol. The spin and charge in **PD14−7**$^{\cdot+}$ are stabilized by the methoxyl substituent, while **PD24−7**$^{\cdot+}$ is stabilized by conjugation. This situation is also reflected in the transition states leading to the respective products. Compound **11**$^{\cdot+}$, containing the radical-stabilizing cyano group at C1, undergoes hydrogen shifts with activation energies of 20.9 and 23.1 kcal/mol, leading to pentadienes with relative energies of −3.4 and 8.8 kcal/mol, respectively. Finally, the destabilized compound **16**$^{\cdot+}$ undergoes shifts with activation energies of 18.8 and 15.6 kcal/mol, leading to products with relative energies of 2.4 and −16.9 kcal/mol, respectively. It is clear that the hydrogen shifts explored here have activation energies on par with the hydrogen shifts in unsubstituted **1**$^{\cdot+}$ and, thus, are only moderately influenced by substitution. Since the activation energies of the desired [1,3] methylene shifts are significantly lowered by substituents, the hydrogen shift side reactions can be inhibited by radical- or cation-stabilizing substituents.

Conclusions

Appropriate substitutions are essential for controlling the rearrangements of vinylcyclopropane radical cations to cyclopentenes. The results described above can be summarized into a simple set of rules:

(i) A substantial amount of the neutral vinylcyclopropane must be in the syn-conformation.

This feature is because the *anti* conformer cannot rearrange to cyclopentene, as C1 and C5 are too far apart in space. The pathways originating from *anti*-**1**$^{\cdot+}$ and the corresponding ring-opened intermediate **INT2−1**$^{\cdot+}$ can be effectively suppressed by steric repulsion of substituents in the C4 position. The same effect can be achieved by a bulky group at C5, *cis* to the cyclopropane group at C4, or by locking the substituents about the π-bond in a *syn* conformation as part of a ring structure, providing the ring is not too strained.[8] Since rotation around the C3−C4 bond is slow in the radical cation, the *syn*/*anti* ratio is set in the neutral vinylcyclopropanes and can be evaluated by molecular mechanics calculations or by comparison with known systems.[3d] Preferentially, a substituent at C4 or C5 should not be spin/charge stabilizing, but even the effects of strongly stabilizing groups, such as phenyl units, are relatively small and raise the activation energy by 2 kcal/mol or less.

(ii) Substituents at C1 must be cation- or radical-stabilizing.

While both radical- or cation-stabilizing groups can lower the activation energy for the first step, radical-stabilizing groups do little to lower the energy of the bond-forming second step. The effect of cation-stabilizing groups at C1 is the more significant one and even weakly stabilizing groups are able to significantly lower the activation barrier and exclude hydrogen shift pathways. A radical-stabilizing substituent should be equally or more stabilizing than a cyano group. The effects were found to be roughly additive and can be qualitatively evaluated by σ^+ or $\sigma^{\cdot}$ values from the literature. To suppress the competing [1,2] hydrogen shifts, combined substituent constants of $\sigma^+ > 0.2$ or $\sigma^{\cdot} > 0.2$ are desirable.

(iii) The radical cation's rearrangement must be exothermic.

Although the opening of the strained cyclopropane ring will be exothermic in all cases, the ring closure to the final cyclopentene product can be rendered endothermic by strongly cation-stabilizing substituents on C1, as seen in **8**$^{\cdot+}$. This acyclic species can then undergo a variety of reactions, including reduction to a diradical species in a competing back-electron-transfer step, which could subsequently be converted into the thermodynamically favored neutral cyclopentene or back to the starting material, depending on the conformation. Dimerizations and other side reactions are also likely to occur, however. It should be noted that because of the influence of delocalization of spin and charge, the thermochemistry of a radical cation's reaction can be quite different from that of its neutral counterpart.

These guidelines derived from the computational results are in line with the experimental findings in the literature. The finding that the ET-induced rearrangement of 1-anisyl-3,4-dimethyl-vinylcyclopropane is successful,[5] while 1-anisyl-vinylcyclopropane gives the isomerized starting material,[6] is a demonstration of Rule (i). The exclusive hydrogen shift in α-thujene can be rationalized by the unfavorable thermochemistry of the rearrangement, as postulated by

Rule (iii). Preliminary studies in our laboratory on 4-methyl-5-phenyl-vinylcyclopropane also confirm the computational prediction derived from Rules (i) and (ii) that this compound does not rearrange. This result is most likely due to the activation energy of more than 15 kcal/mol making the rearrangement uncompetitive with back electron transfer. Finally, the rearrangement of acyclic vinylcyclopropanes will not be stereospecific. Similar to its thermal counterparts, the acyclic species involved in the reaction pathway can undergo rapid isomerization at C1. Potentially, stereochemistry can still be controlled, however, by steric or bonding interactions from other parts of the carbon chain. Further experimental attempts to verify these rules will be the subject of future studies.

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[22] The weakly donating effect of the fluorine substituent ($\sigma^+ = -0.07$) is more than offset by the strongly electron-withdrawing properties of the trifluoromethyl group ($\sigma^+ = -0.65$).

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