

# Substituent Effects in Pericyclic Reactions of Radical Cations: The Ring Opening of 3-Substituted Cyclobutene Radical Cations

David J. Swinarski and Olaf Wiest\*

Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556-5670

owiest@nd.edu

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The substituent effects on the ring-opening reaction of cyclobutene radical cations have been studied at the Becke3LYP/6-31G\* level of theory. The effect on the reaction energies and activation energies of the concerted and stepwise pathways of electron-donating substituents such as methyl and methoxy as well as electron-withdrawing substituents such as nitrile and carboxaldehyde in the 3-position of the cyclobutene is discussed. The exothermicity of the reaction correlates well with the ability of the substituent to stabilize the 1,3-butadiene radical cation by electron donation or conjugation. The relative stability of the (*E*) and (*Z*) isomers of the resulting 1,3-butadiene radical cations depends largely on steric effects. Similarly, steric effects are responsible for the relative energies of the different diastereomeric transition structures. The cyclopropyl carbinyl intermediate of the stepwise pathway resembles the nonclassical carbocation and is stabilized by electron-donating substituents. In the case of electron-donating substituents, this species becomes a minimum on the potential energy hypersurface, whereas unstabilized or destabilized cyclopropyl carbinyl radical cations are not minima on the hypersurface. The stabilization of the cyclopropyl carbinyl radical cation by substituents correlates qualitatively with the Brown–Okamoto substituent parameter  $\sigma^+$ . However, in all cases studied here, the concerted mechanism is the lowest energy pathway.

## Introduction

The acceleration of slow or symmetry-forbidden pericyclic reactions by electron transfer catalysis is one of the most simple applications of a redox umpolung possible, yet it can accelerate the rate by many orders of magnitude under mild conditions.<sup>1</sup> This, together with the very high selectivities observed in many of these reactions, makes the application of this method desirable in many areas of organic chemistry. To exploit the full potential of this reaction class, the mechanisms of these reactions need to be understood in more detail. Experimental studies of the mechanism using the traditional methods of mechanistic organic chemistry have proven to be difficult since the effects of solvents or substituents on the electron transfer and the chemical step are difficult to separate.<sup>2</sup> Consequently, the main tools for the investigation of these reactions have been mass spectroscopic studies and, more recently, the use of high-level ab initio calculations.

A class of pericyclic reactions of radical cations that is of particular interest is the electrocyclic ring opening of

cyclobutene radical cations. There are numerous reports on this reaction in the literature,<sup>3</sup> and the synthetic utility of the reaction has been demonstrated.<sup>4</sup> However, experimental studies of the reaction have not yielded conclusive evidence about the mechanism of the reaction.<sup>5</sup> For example, the activation energy was estimated to be  $\leq 7$  kcal/mol in mass spectroscopic studies,<sup>6</sup> while other studies indicated significantly higher activation energies of approximately 16.5 kcal/mol.<sup>7</sup> This situation is quite typical for many pericyclic reactions of radical cations in that a comprehensive understanding of the mechanistic details has yet to evolve.

In recent years, the use of highly correlated MO and hybrid DFT methods has contributed significantly to our understanding of these reactions as several studies of the

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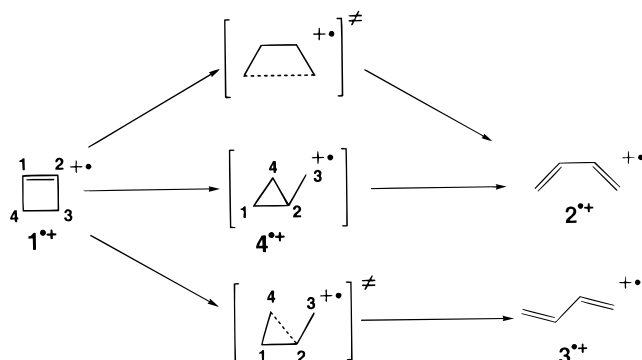
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**Figure 1.** Possible reaction pathways for the ring opening of the cyclobutene radical cation.

parent reactions of cycloadditions,<sup>8</sup> cycloreversions,<sup>9</sup> and sigmatropic shifts<sup>10</sup> appeared in the literature. The electrocyclic ring opening of the cyclobutene radical cation has been analyzed in detail.<sup>11</sup> A common feature of all of these reactions is that the corresponding potential energy hypersurfaces are extraordinarily flat, making several pathways simultaneously available for the reaction. For the case of the ring opening of the cyclobutene radical cation  $1^{+•}$ , the reaction pathways summarized in Figure 1 have been proposed.

There are two pathways leading from  $1^{+•}$  to  $2^{+•}$ : a concerted pathway through a nonsymmetric transition structure and a stepwise pathway involving a cyclopropyl carbinyl radical cation  $4^{+•}$  first proposed by Bauld.<sup>12</sup> A symmetry-conserving concerted pathway from  $1^{+•}$  to  $2^{+•}$  is not possible because there is no adiabatic connection between the two different electronic ground states of these molecules. Bally and co-workers also located a species connecting  $1^{+•}$  and  $3^{+•}$  which structurally resembles the cyclopropyl carbinyl intermediate. Depending on the level of theory used, this species represents either a shallow minimum on the hypersurface or a transition structure. Although the electronic states of  $1^{+•}$  and  $3^{+•}$  connect adiabatically through a  $C_2$ -symmetric structure, this structure was found to be a second-order saddle point due to vibronic Jahn–Teller interactions.<sup>11a</sup> The energy differences between these pathways are very small and the characteristics and geometries of the different species depend strongly on the computational method used. It is therefore likely that the relative energetics of the species on this so-called “Bauld-plateau” will be heavily influenced by dynamic, substituent, and solvent effects. Indeed, a recent computational investigation of this area of the  $C_4H_6^{+•}$  hypersurface using

continuum solvent models gave evidence for the specific stabilization of species that localize spin and charge.<sup>13</sup>

To understand the relationship between the experimental investigations on substituted cyclobutenes and the computational studies of parent  $1a^{+•}$  as well as to make pericyclic reactions of radical cations more predictable, and thus more synthetically useful, an understanding of the different possible reaction pathways and their influence on the different possible reaction pathways is highly desirable. This will also address several of the recently discussed<sup>8,11,13–15</sup> questions regarding concerted vs stepwise mechanisms for more realistic model compounds. Here, we present the first systematic computational study to address this problem. The paper is organized as follows: First, we will discuss the effect of representative substituents on the thermochemistry of the ring opening of 3-substituted cyclobutene radical cations. We will then investigate the effect of a typical substituent in the four diastereotopically different positions adjacent to the breaking bond in the concerted transition structure as well as for the stepwise pathway involving a cyclopropyl carbinyl-type radical cation. Finally, the effect of a larger number of different substituents on the relative energies of the concerted and stepwise reaction pathways is studied. To keep the number of different structures on these fairly complex hypersurfaces manageable, we decided to focus only on the lowest energy pathways for the two reaction mechanisms to form the corresponding *cis*-1,3-butadiene radical cations. The pathways leading to the *trans*-1,3-butadiene radical cation are therefore not considered, since the species involved are geometrically and electronically similar to the stepwise pathway leading to *cis*-1,3-butadiene radical cation. It can thus be expected that the substituent effects, the focus of this study, will be very similar.

## Computational Methodology

The question of which computational method is appropriate for the treatment of radical cations has been discussed at some length in the recent literature.<sup>8–14</sup> It is generally recognized that UHF and UMP2 wave functions are often severely spin contaminated. This can lead to significant errors in energies and geometries, rendering these methods unsuitable for the calculation of radical cations. The advantages and disadvantages of hybrid DFT methods for the calculation of radical cations have been a topic of recent studies. In particular the fact that Becke3LYP does not localize charge and spin densities as readily as other levels of theory led to a discussion of the bias of this method toward delocalized structures.<sup>15</sup> Many intermediates and transition states which have been located at lower levels of theory cannot not be located using Becke3LYP. Despite these concerns, we decided to use the computationally efficient Becke3LYP/6-31G\* method for all calculations described here. In previous studies by our group<sup>8a,b,9a,10a,11a</sup> and others<sup>10b,11b,13</sup> this method gave results which were generally in good agreement with those given by highly correlated MO methods such as the much more computationally expensive QCISD(T)//QCISD method. We therefore expect Becke3LYP/6-31G\* to yield adequate results, particularly since we will focus on energy differences due to substituent effects.

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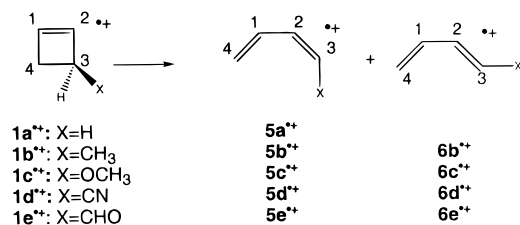
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**Figure 2.** Substituted cyclobutene radical cations studied.

**Table 1.** Reaction Energies and Selected Geometric Parameters for Substituted 1,3-Butadiene Radical Cations

compd	$\Delta E$ (kcal/mol)	$R_{C3-X}$ (Å)	$\varphi$ (deg)
<b>5a<sup>+</sup></b>	-20.2		
<b>5b<sup>+</sup></b>	-25.8	1.47	17.0
<b>6b<sup>+</sup></b>	-30.5	1.47	0.0
<b>5c<sup>+</sup></b>	-38.5	1.29	0.0
<b>6c<sup>+</sup></b>	-40.5	1.29	0.0
<b>5d<sup>+</sup></b>	-29.3	1.40	0.0
<b>6d<sup>+</sup></b>	-30.4	1.39	0.0
<b>5e<sup>+</sup></b>	-13.6	1.46	33.0
<b>6e<sup>+</sup></b>	-16.0	1.48	14.6

Calculations were performed with the G94 and G98 series of programs running on IBM SP1/SP2 and SGI Origin2000 computers at the High Performance Computing Complex at the University of Notre Dame and with G98 on the National Center for Supercomputing Applications' Origin2000.<sup>16</sup> All energies listed in this paper are relative to the corresponding cyclobutene radical cation reactant and are corrected for zero-point vibrational energies obtained at the same level of theory. All stationary points were characterized by harmonic frequency calculations. The one imaginary frequency of the transition structures was animated using MOLDEN<sup>17</sup> to ensure that the optimized stationary point corresponds to the transition structure of the desired reaction. In some cases, intrinsic reaction coordinate (IRC) calculations were used to confirm the identity of a given transition structure.

## Results and Discussion

**Thermochemistry.** We started our investigations by studying the overall thermochemistry of the ring opening of 3-substituted cyclobutene radical cations to *cis*-1,3-butadiene radical cations with the substituent in either the (*Z*) position, **5<sup>+</sup>**, or the (*E*) position, **6<sup>+</sup>**. Our results are summarized in Table 1 and Figure 2.

The nitrile, methoxy, and methyl substituents all lead to reactions more exothermic than the parent reaction. The reaction energy for the parent ring opening of **1a<sup>+</sup>** to **5a<sup>+</sup>** is -20.2 kcal/mol.<sup>11a</sup> Adding one methyl substituent in the 3-position in **1b<sup>+</sup>** changes the reaction energy to -25.8 kcal/mol to form the (*Z*)-isomer **5b<sup>+</sup>** and -30.5 kcal/mol to form the (*E*)-isomer **6b<sup>+</sup>**. The dihedral angle

of the carbon backbone is 17.1° in **5b<sup>+</sup>** as compared to 0.03° in **6b<sup>+</sup>**. We attribute the difference in reaction energies and geometry of the 1,3-butadiene radical cations to the steric repulsion of the methyl group with the *endo*-hydrogen at C<sub>4</sub> in **5b<sup>+</sup>**.

The methoxy substituent, a stronger electron donor, further increases the exothermicity of the reaction: the reaction energy to form **5c<sup>+</sup>** is -38.5 kcal/mol and the reaction energy to form **6c<sup>+</sup>** is -40.5 kcal/mol. The C<sub>3</sub>-O bond length is 1.29 Å in both isomers. This indicates that this bond has significant double bond character; that is, the oxygen atom exhibits some oxonium character in both isomers. In **5c<sup>+</sup>**, the lone pairs on oxygen point toward the carbon backbone, which is planarized to allow for maximum conjugation. The C<sub>4</sub>-O distance is 2.99 Å, suggesting that there could be a weak, stabilizing Coulomb interaction between the free electron pair on the oxygen and the delocalized positive charge in the 1,3-butadiene moiety.

The nitrile group was chosen for study due to its ability to stabilize radicals. Here, the reaction energy is -29.3 kcal/mol for the formation of **5d<sup>+</sup>** and -30.4 kcal/mol for the formation of **6d<sup>+</sup>**. The C<sub>3</sub>-C<sub>Nit</sub> bond length is 1.40 Å in both **5d<sup>+</sup>** and **6d<sup>+</sup>**, and the C-N bond length is 1.17 Å, indicating that the former has significant double bond character, while the nitrile bond is in the typical range for a triple bond. As is to be expected for a small substituent such as a nitrile, the energy difference between the (*E*) and (*Z*) configurations is fairly small, only 1.1 kcal/mol.

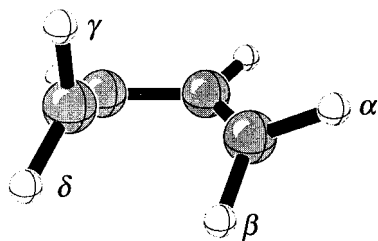
The aldehyde substituent is the only one leading to a reaction less exothermic than the parent reaction. The reaction is exothermic by -13.6 kcal/mol and -16.0 kcal/mol to form **5e<sup>+</sup>** and **6e<sup>+</sup>**, respectively. The electron-withdrawing character of the aldehyde substituent destabilizes the substituted 1,3-butadiene radical cation, thus making the reaction less exothermic than the parent reaction. The destabilization of the delocalized form of the radical cation is also apparent in the structure of the 1,3-butadiene moiety, which deviates considerably from planarity with C<sub>4</sub>-C<sub>1</sub>-C<sub>2</sub>-C<sub>3</sub> dihedral angles of 33.3° and 14.6° in **5e<sup>+</sup>** and **6e<sup>+</sup>**, respectively. Although a planar (*E*)-butadiene structure exists that does correspond to a local minimum on the potential energy surface, it is 7.5 kcal/mol higher in energy than **6e<sup>+</sup>**. The decreased stabilization of the radical cation is only partly recovered by the delocalization in the  $\alpha,\beta$ -unsaturated carbonyl functionality since the C<sub>2</sub>-C<sub>3</sub>-C-O bonds are not properly aligned; these dihedrals are 13.7° for **5e<sup>+</sup>** and 21.7° for **6e<sup>+</sup>**. Consequently, the C-O bond length is 1.22 Å for **5e<sup>+</sup>** and **6e<sup>+</sup>**, and the charges on the oxygen atom are -0.18 and -0.25, respectively, so there appears to be little oxonium ion character in these isomers.

In summary, the overall thermochemistry of the reaction is determined by the ability of the substituent to stabilize the 1,3-butadiene radical cation by electron donation or conjugation. The (*E*) isomer is 1-5 kcal/mol lower in energy than the (*Z*) isomer in all cases. The largest energy difference between isomers is in the methyl case, which is the largest substituent studied here, while the smallest energy difference is calculated for the smallest substituent, nitrile. We conclude that the difference in energy between the isomers is mostly due to steric interactions. If an isomerization is possible during the reaction and the product is thus determined

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**Figure 3.** Diastereotopic positions in the concerted transition structure  $7^{+\bullet}$ .

**Table 2. Selected Results for the Diastereomeric Transition Structures  $7^{+\bullet}$**

compd	$E_a$ (kcal/mol)	$R_{C1-C4}$ (Å)	$\phi_{C1-C2-C3-\alpha}$	$\nu^{imag}$ ( $\text{cm}^{-1}$ )
$7\alpha^{+\bullet}$	8.8	2.19	135	-318
$7\beta^{+\bullet}$	13.9	2.34	116	-436
$7\gamma^{+\bullet}$	10.1	2.23	141	-383
$7\delta^{+\bullet}$	10.2	2.09	137	-310

by thermodynamics, the predominant formation of the (*E*) isomers  $6^{+\bullet}$  would be expected.

**The Ring Opening of 3-Methylcyclobutene $^{+\bullet}$ .** We will now turn to the effect of a substituent on the activation energy. An unsymmetric pathway has been proposed for the concerted ring opening reaction of  $1\mathbf{a}^{+\bullet}$ .<sup>11a</sup> In this transition structure, shown in Figure 3, one methylene group is perpendicular to the carbon backbone while the other methylene group is at a 120° angle to the backbone. This results in four diastereotopic positions for the transition structure  $7^{+\bullet}$  at which a substituent could be placed. We studied the effect of a methyl substituent in each of the four positions labeled  $\alpha$ - $\delta$  as shown in Figure 3.

The effect on the geometry and relative energies of methyl substitution at these four positions leading to the diastereomeric transition structures  $7\alpha^{+\bullet}$ - $7\delta^{+\bullet}$  is compared in Table 2.  $7\alpha^{+\bullet}$ , the transition state with a methyl group at position  $\alpha$ , the least sterically hindered position, is the lowest in energy with a computed activation energy of 8.8 kcal/mol. Substitution at positions  $\gamma$  and  $\delta$  leads to transition states  $7\gamma^{+\bullet}$  and  $7\delta^{+\bullet}$ , which are with activation energies of 10.1 and 10.2 kcal/mol, respectively, very close in energy to each other and only 1.3 kcal/mol higher in energy than  $7\alpha^{+\bullet}$ . Finally, we found a transition state substituted at position  $\beta$ . However, steric factors force the breaking bond distance to be 0.1 Å greater than in  $7\alpha^{+\bullet}$ ,  $7\gamma^{+\bullet}$ , and  $7\delta^{+\bullet}$ , and both methylene groups in  $7\beta^{+\bullet}$  are nearly perpendicular to the carbon backbone. This hindrance is also reflected in the imaginary frequency, which is significantly higher than in the three other diastereomers; the more negative value indicates a stiffer potential in the transition state region of the potential energy surface. In summary, the relative energies of the four diastereomeric transition structures  $7^{+\bullet}$  are, at least in the case of the methyl substituent, dominated by steric interactions. This situation is comparable to the simpler case of the two diastereotopic positions in the thermal ring opening of  $1\mathbf{a}$ , which leads to different isotope effects for these positions.<sup>18</sup>

One of the key questions in earlier investigations of the ring opening of  $1\mathbf{a}^{+\bullet}$  was the existence and relative energy of a cyclopropyl carbinyl intermediate such as the

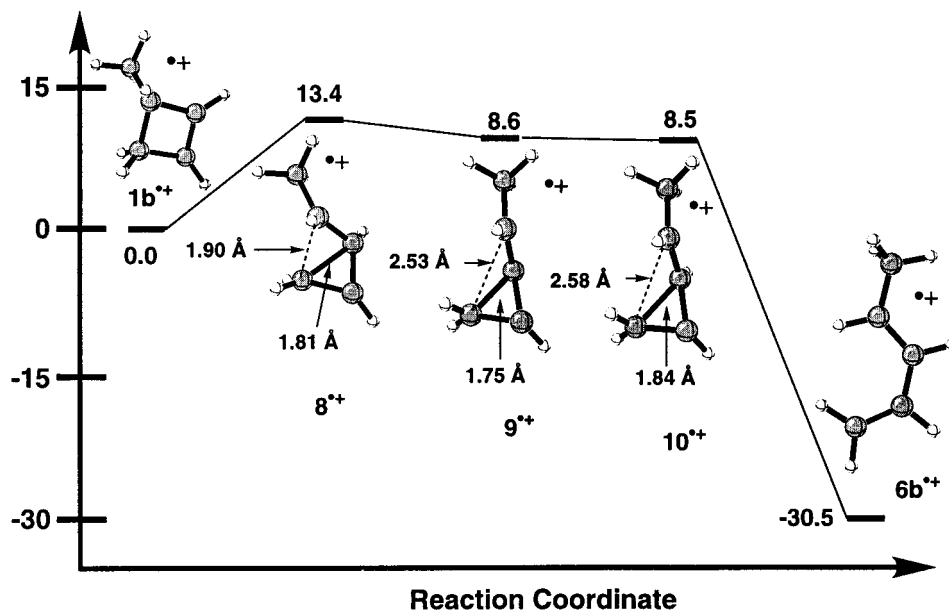
one proposed by Bauld et al.<sup>12</sup> For the unsubstituted case, such an intermediate has been found only at the MP2 level of theory; no minimum has been found using either Becke3LYP or QCISD methods. Single-point calculations on MP2 optimized structures using QCI and coupled cluster methods indicated, however, that the energy of such a structure would be very close to the energy of the concerted transition structure. It was speculated that substituent effects might stabilize this cyclopropyl carbinyl structure enough for it to become a local minimum.<sup>11</sup>

We therefore investigated the stepwise ring opening of the 3-methylcyclobutene radical cation  $1\mathbf{b}^{+\bullet}$  to form  $6\mathbf{b}^{+\bullet}$ . As can be seen from the results summarized in Figure 4, the methyl substituent does indeed stabilize the cyclopropyl carbinyl intermediate sufficiently to make this species a minimum on the Becke3LYP energy hypersurface. The problems of this method in localizing spin and charge in radical cations are therefore not observed in these unsymmetric structures. The activation energy of the first step involving transition structure  $8^{+\bullet}$  is 13.4 kcal/mol. The intermediate  $9^{+\bullet}$  is 8.6 kcal/mol higher in energy than  $1\mathbf{b}^{+\bullet}$ . In this structure, the  $C_4$ - $C_3$  distance has increased to 2.53 Å, indicating that the bond is completely broken, whereas there is a weak interaction with a bond length of 1.75 Å between  $C_2$  and  $C_4$ . The second transition structure  $10^{+\bullet}$  is 8.5 kcal/mol higher in energy than the cyclobutene; after zero-point energy correction this transition structure is actually lower in energy than the intermediate. We conclude that the minimum for the intermediate is extremely shallow, and the ring opening of the cyclopropyl carbinyl radical cation intermediate occurs barrierless. This is mostly due to the very exothermic reaction from  $9^{+\bullet}$  to  $6\mathbf{b}^{+\bullet}$ , making the very early transition structure for this step structurally and energetically similar to  $9^{+\bullet}$ . A structural feature shared by  $8^{+\bullet}$ - $10^{+\bullet}$  is that the exocyclic carbons are aligned with the  $C_2$ - $C_1$  bond; the  $C_2$ - $C_1$ - $C_3$ - $C_{Me}$  dihedral angle changes only slightly from 165° in the first transition structure to 173° in the second one.

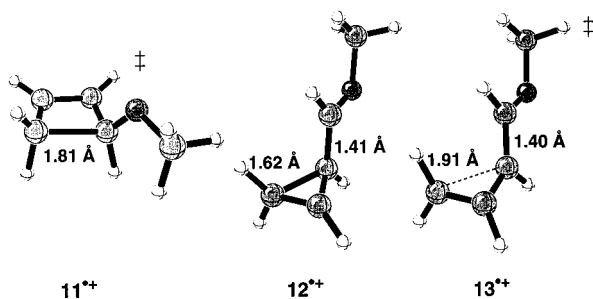
Because no intermediate for the unsubstituted case was found at the Becke3LYP level of theory, comparing the concerted and stepwise pathways previously required one of two evils: either comparing energies from high-level single calculations of structures obtained at a lower level of theory or comparing energies of fully optimized structures at a lower level of theory. In the case of the ring opening of  $1\mathbf{b}^{+\bullet}$ , we are able for the first time to directly compare the two pathways at a level of theory that has been shown to provide accurate results. The lowest energy concerted pathway via the transition structure  $7\alpha^{+\bullet}$  has an activation energy of 8.8 kcal/mol, whereas the first transition structure for the stepwise pathway,  $8^{+\bullet}$ , has an activation energy of 13.4 kcal/mol. This difference leads us to conclude that even though the methyl group stabilizes the cyclopropyl carbinyl intermediate sufficiently to make it a minimum on the potential energy surface, the concerted pathway will be preferred over the stepwise pathway. Second, we note that although an intermediate can be located, the ring opening of  $9^{+\bullet}$  to form  $6\mathbf{b}^{+\bullet}$  is effectively barrierless after zero-point correction.

**Effects of Other Substituents.** In the interest of simplicity, the effect of stronger electron-donating substituents such as the methoxy group and electron-withdrawing substituents such as the nitrile and aldehyde functionalities was only studied for the lowest

(18) (a) Wiest, O.; Houk, K. N.; Black, K. A.; Thomas, B., IV. *J. Am. Chem. Soc.* **1995**, *117*, 8594. (b) Baldwin, J. E.; Reddy, V. P.; Hess, B. A., Jr.; Schaad, L. *J. Am. Chem. Soc.* **1988**, *110*, 8555.



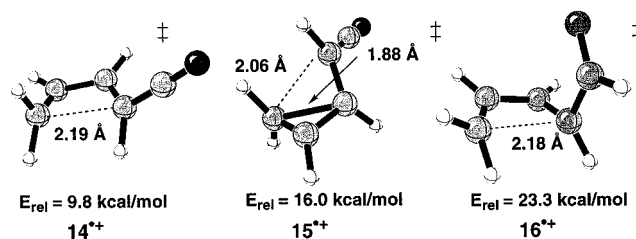
**Figure 4.** Stepwise pathway for the ring opening of  $1b^+$ .



**Figure 5.** Concerted transition structure  $11^+$  (left); stepwise intermediate  $12^+$  (middle), and second transition structure  $13^+$  (right) for the ring opening of  $1c^+$ .

energy pathways, i.e., for the positions  $\alpha$  and  $\gamma$  in the concerted transition structure and the stepwise reaction leading to the thermodynamically favored (*E*) isomers. Our results for the ring opening of the 3-methoxy cyclobutene radical cation  $1c^+$  are summarized in Figure 5.

The activation energy for the concerted pathway via transition structure  $11^+$  is only 0.4 kcal/mol after zero-point correction and thus the pathway is effectively barrierless. The reaction is highly exothermic, and in accordance with the Hammond postulate, this transition state closely resembles the reactant. With a  $C_3-C_4$  bond distance of 1.81 Å, it has the shortest breaking bond distance of all the concerted pathway transition structures we studied. For the stepwise pathway, intermediate  $12^+$  is actually 2.7 kcal/mol lower in energy than  $1c^+$ . Despite numerous attempts, we have not been able to locate a transition structure connecting  $1c^+$  and  $12^+$ , presumably because the reaction is barrierless. Unlike the methyl cyclopropyl carbinyl intermediate  $9^+$ ,  $12^+$  is in a relatively deep well on the potential energy hypersurface; the transition structure  $13^+$  for the formation of  $6c^+$  is 4.7 kcal/mol higher in energy than  $12^+$ . The relatively short  $C_2-C_4$  bond of 1.62 Å gives  $12^+$  the geometric structure of a cyclopropyl carbinyl intermediate. The positive charge is borne almost entirely by  $C_3$  and the methoxy carbon, and the carbinyl moiety bisects the cyclopropyl ring to allow for maximum interaction



**Figure 6.** Concerted transition structures  $14^+$  and  $15^+$  for the ring opening of  $1d^+$ , and concerted transition structures  $16^+$  for the ring opening of  $1e^+$ .

of this positive charge with the Walsh orbitals of the cyclopropyl ring. The  $C_3-C_2$  bond in  $12^+$  has significant double bond character, as shown by its length of 1.41 Å, and this does not change greatly in the transition structure  $13^+$  connecting  $12^+$  to  $6c^+$ . The main geometric features of transition structure  $13^+$  are the lengthening of the  $C_2-C_4$  bond to 1.91 Å and an alignment of the methoxy group with  $C_3-C_2-C_1$ .

For the nitrile case, the concerted transition structure  $14^+$  connects  $1d^+$  to  $6d^+$  with an activation energy of 9.8 kcal/mol. The geometry of  $14^+$  is analogous to that of  $7a^+$  in that the substituent occupies the sterically least crowded position. The bond length of the breaking  $C_3-C_4$  bond is virtually identical to the one in  $7a^+$ . A second transition structure  $15^+$  (Figure 6, middle) with an activation of 16.0 kcal/mol was also located. Even though this structure resembles the cyclopropyl carbinyl intermediate and the transition structure for the formation of the *trans*-1,3-butadiene radical cation,<sup>11b</sup> normal-mode analysis and IRC calculations show that  $15^+$  is a transition structure that connects  $1d^+$  to  $6d^+$ .  $15^+$  appears to be unique in that transition structures similar to this geometry were not found for any other substituent. The higher activation energy associated with  $15^+$  suggests that the pathway through  $14^+$  will dominate. Extensive searches for a cyclopropyl carbinyl intermediate located several stationary points on the potential energy surface. However, normal-mode analysis showed that all these structures had one negative frequency, and intrinsic reaction coordinate (IRC) calculations suggested that

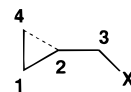
these points are transition structures for the interconversion of two isomers of the cyano bicyclobutane radical cation rather than intermediates for the ring opening of **1d**<sup>+</sup>. This is comparable to earlier findings that on the "Bauld Plateau", the transition structures for the formation of bicyclobutane and 1,3-butadiene radical cations are closely related.<sup>11b</sup>

Given the geometric and energetic similarities between the concerted transition structures **7α**<sup>+</sup> and **14**<sup>+</sup>, we were surprised that no stepwise pathway could be located for the case of the nitrile substituent. The stabilization of the radical cation in **15**<sup>+</sup> appears not to be sufficient to make that structure a minimum on the potential energy hypersurface. It can therefore be deduced that the better stabilization of the cationic character by the methyl group<sup>19</sup> has a more significant effect on whether the cyclopropyl carbinyl intermediate is a minimum on the hypersurface than the better stabilization of the radical character by the nitrile group.<sup>20</sup> We also investigated whether a nitrile substituted at C<sub>1</sub> would sufficiently stabilize the radical center to create a minimum on the hypersurface. However, an extensive search yielded no cyclopropyl carbinyl-type minimum with the substituent at this position.

As noted previously, the aldehyde group is the only substituent studied for which the ring-opening reaction is less exothermic than the parent reaction. The concerted pathway transition structure **16**<sup>+</sup> (Figure 6, right) resembles the concerted transition structures discussed earlier in that the cyclobutene moiety is essentially planar. The length of the breaking bond, 2.18 Å, is close to the values obtained for the methyl, methoxy, and nitrile substituents. However, the activation energy for this pathway is 23.3 kcal/mol, 5.2 kcal/mol higher than that calculated for the parent reaction.<sup>11</sup> Furthermore, the substituent is at position γ; the corresponding transition structure with the aldehyde functionality in position α is actually 0.4 kcal/mol higher in energy than **16**<sup>+</sup>.<sup>21</sup>

It is noteworthy that while no cyclopropyl carbinyl intermediate could be located for the parent system, such an intermediate exists in a very shallow well on the hypersurface for the 3-methyl derivative and is actually 2.7 kcal/mol more stable than the cyclobutene reactant in the case of the 3-methoxy derivative. A similar trend is obtained for the lengths of the breaking C<sub>2</sub>–C<sub>4</sub> bond, which varies from 1.62 Å in **12**<sup>+</sup> to 1.75 Å in **9**<sup>+</sup>. In the parent case, no stable bond is formed. The length of this bond and the relative stability of the cyclopropyl carbinyl intermediate appear to be correlated with the electron-donating ability of the substituent. This can be explained by considering a stabilization of the cation at C<sub>3</sub> through an interaction with the electrons in the C<sub>2</sub>–C<sub>4</sub> bond, similar to the situation in the nonclassical cyclopropyl carbinyl cation and the related cyclobutyl and allyl carbinyl cation structures.<sup>22</sup> Such a nonclassical cyclopropyl carbinyl radical cation has recently been proposed in reactions of the norbornene radical cation.<sup>23</sup> In the unstabilized and destabilized radical cations **1a**<sup>+</sup>, **1d**<sup>+</sup>

**Table 3. Selected Bond Lengths, Relative Energies, and LFER Parameters for Substituted Cyclopropyl Carbinyl Radical Cations**



X =	$R_{C2-C4}$	$E_{rel}$	$\sigma_p^{+a}$	$\sigma_p^{*a}$
CHO			0.47	<i>b</i>
CN			0.66	0.24–0.7
H			0.0	0.0
CH <sub>3</sub>	1.750	8.6	–0.31	0.03
F	1.733	5.9	–0.07	–0.07
OCN	1.707	10.3	<i>b</i>	<i>b</i>
NCO	1.669	0.8	–0.19	<i>b</i>
OCOCH <sub>3</sub>	1.626	–0.4	–0.19	–0.05
OCH <sub>3</sub>	1.615	–2.7	–0.79	0.11

<sup>a</sup> Recommended value from ref 21. <sup>b</sup> No value given.

and **1e**<sup>+</sup>, the stabilization of the cation by electron density from the C<sub>2</sub>–C<sub>4</sub> bond leads to a barrierless cleavage of that bond. If the cation at C<sub>3</sub> is sufficiently stabilized by electron-donating substituents, the cyclopropyl carbinyl radical cation intermediate becomes a minimum on the potential energy hypersurface.

To further investigate this apparent relationship between the donor capabilities of the substituent and the structure and energy of the cyclopropyl carbinyl intermediate, we performed calculations on the cyclopropyl carbinyl intermediate for the fluoride, acetoxy, cyanate, and isocyanate substituents. These substituents were chosen based on the hypothesis that, even though no substituent parameters are available for radical cations, the stabilization of the positive charge is more important for the characteristics and relative energies of a cyclopropyl carbinyl intermediate. Therefore, these features should qualitatively correlate with a parameter such as the Brown–Okamoto  $\sigma^+$  parameter. Our results for all substituted cyclopropyl carbinyl intermediates are summarized in Table 3.<sup>24</sup>

The results in Table 3 clearly show that the original hypothesis is correct. The C<sub>2</sub>–C<sub>4</sub> bond length, which can be viewed as a measure of the degree of stabilization of the positive charge via a nonclassical carbocation, is a function of the electron-donating ability of the substituent as measured by the Brown–Okamoto  $\sigma_p^+$  value. The  $\sigma_p^+$  value appears to have a smaller but not insignificant influence as can be seen from the relatively long C<sub>2</sub>–C<sub>4</sub> bond length in the case of the methyl-substituted **9**<sup>+</sup>. This sequence implies that the C<sub>2</sub>–C<sub>4</sub> bond lengths in the unsubstituted, nitrile, and aldehyde cases would have to be so long (perhaps 1.8 Å or more) that these structures could not exist as minima on the hypersurface. With the exception of the fluoro-substituted compound, for which the cyclobutene radical cation reactant is distorted and destabilized by the strong electron-withdrawing inductive effect of the fluorine substituent, the relative energies of the cyclopropyl carbinyl follow the same trend.

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(20) (a) Packer, J. E.; Heighway, C. J.; Miller, H. M.; Dobson, B. C. *Austr. J. Chem.* **1980**, *33*, 965. (b) Creary, X.; *J. Org. Chem.* **1980**, *45*, 280. (c) Creary, X.; Mehrsheikh-Mohammadi, M. E.; McDonald, S. J. *Org. Chem.* **1987**, *52*, 3254.

(21) We also located another transition structure resembling the cyclopropyl carbinyl structure **15**<sup>+</sup>. However, IRC calculations showed that it does not connect to the *cis*-1,3-butadiene radical cations **5e**<sup>+</sup> or **6e**<sup>+</sup> and it is therefore not discussed here.

(22) For an in-depth discussion of the C<sub>4</sub>H<sub>8</sub><sup>+</sup> manifold, compare, e.g.: (a) Wiberg, K. B.; Hess, B. A., Jr.; Ashe, A. J., III. In *Carbonium Ions*; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley-Interscience: New York, 1972; Vol. 3, p 1295. (b) Olah, G. A.; Reddy, P.; Prakash, G. K. S. *Chem. Rev.* **1992**, *92*, 69.

(23) Ramsden, C. A.; Smith, R. G. *Org. Lett.* **1999**, *1*, 1591.

(24) Hansch, C.; Leo, A.; Hoekman, D. *Exploring QSAR*; ACS: Washington, DC, 1995; Vol. 2.

### Summary and Conclusions

Here we report what is to the best of our knowledge the first systematic study of substituent effects in radical cation pericyclic reactions. The thermochemistry of the reactions is largely controlled by the electron-donating ability of the substituent in the 3-position of the cyclobutene radical cation. The relative energies of the products and the different diastereomeric transition structures are dominated by steric interactions.

For all substituents studied here, the concerted mechanism is the lowest energy pathway. However, the stepwise pathway is only a few kcal/mol higher in energy. The characteristics of the cyclopropyl carbinyl structure, in particular whether it represents a minimum or a transition state on the potential energy hypersurface, are again dominated by the electron-donating abilities of the substituent. The stabilization of the cyclopropyl carbinyl structure is continuous and correlates approximately with the Brown–Okamoto  $\sigma^+$  values. In the results presented here, the transition from a minimum to a saddle point occurs between the donating abilities of a methyl and a hydrogen substituent, although this will depend somewhat on the computational method used. Furthermore, solvent effects have been shown to provide additional stabilization for the intermediate of a stepwise pathway. In comparison to the electron donating ability of the substituent, the radical stabilizing properties of the substituent in the 3-position are less important, as exemplified by the nitrile substituent. It can therefore be deduced that of the two possible distonic structures of the cyclopropyl carbinyl intermediate, the one with the positive charge at C<sub>3</sub> and the radical at C<sub>1</sub> is dominant due to the stabilization of this structure as a nonclassical cyclopropyl carbinyl cation.

In agreement with the available experimental results,<sup>6</sup> the calculated activation energies for 3-substituted cyclobutene radical cations are lower than the ones calculated for the parent system. However, the activation energies presented here are still significantly higher than the ones obtained in the gas phase by CID experiments, casting further doubts on the validity of the absolute values for the activation energies obtained there.<sup>11b,13</sup>

The results discussed in this manuscript represent the first step in obtaining a more thorough understanding of the mechanistic changes in radical cation chemistry that are induced by different substituents. Future studies will have to show if the findings presented here are transferable to other pericyclic reactions of radical cations. This will allow the prediction of these synthetically useful reactions based on well-understood parent reactions.

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**Supporting Information Available:** Cartesian coordinates, total energies,  $S^2$  values, and zero-point corrected energies of all structures as well as negative frequencies where applicable are available in ASCII format. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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