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Theoretical Characterization of Cycloaddition Reactions of the Cyclopropylcarbinyl Cation

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Summary: The gas-phase cycloaddition reactions of ethylene and 1,3-butadiene with the cyclopropylcarbinyl cation to produce the cyclohexyl and cycloocten-5-yl cation, respectively, have been computationally characterized. At levels of theory up to MP2/cc-pVDZ the reactions are quite asynchronous but are concerted (i.e., there is only one transition state prior to formation of the product carbocycles).

Cationic variants of the classical Diels−Alder [4 + 2] cycloaddition are well known. The allyl cation reacts with both alkenes[1] and dienes[2,3] to create 5- and 7-membered rings as the products of [3 + 2] and [3 + 4] cycloadditions, respectively. In addition, when standard Diels−Alder chemistry proceeds sluggishly because of a lack of reactivity in either or both of the components, conversion of one or the other to its corresponding cation[4,5] or radical cation[6−9] has been shown to lower the corresponding activation barrier tremendously. We present here theoretical studies for a different variation on this theme making use of the cyclopropylcarbinyl cation.

The cyclopropylcarbinyl cation has been the subject of intensive experimental[10−14] and theoretical[15−18] scrutiny. High levels of gas-phase theory[16−18] and low-temperature nuclear magnetic resonance studies in superacid solvent[11] and amorphous SbF$_5$[12] agree that the cation is best described as a rapidly equilibrating mixture of cyclopropylmethyl (**1**) and nonclassical bicyclobutonium (**2**) cations. Although product mixtures obtained from nucleophilic trapping of the cation typically include homoallylic products,[19−22] the homoallyl cation (**3**) lies roughly 30 kcal/mol higher in energy than **1** and **2** and is thus not a significant contributor to the cation equilibrium population at moderate temperatures.[18] This situation is summarized in Figure 1. Prior synthetic work making use of the cyclopropylcarbinyl cation has included selectively draining the equilibrium of **2** to create neutral 4-membered rings,[23] including β-lactams,[24] by substitution of electrofuges at appropriate positions in cation precursors.

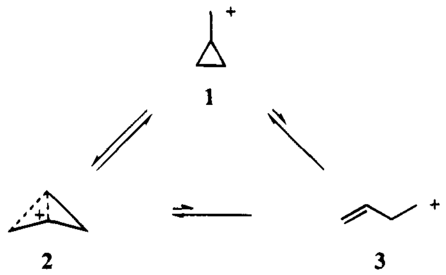

Figure 1. Cyclopropylcarbinyl cation equilibrium.

We have performed[25] Hartree−Fock (HF) and second-order many-body perturbation theory (MP2) calculations which illustrate **1** to be an efficient partner in cycloaddition reactions with both ethylene and 1,3-butadiene that produce the cyclohexyl and cycloocten-5-yl cations, respectively. These processes are depicted schematically in Scheme 1. We emphasize that these reactions are not classical pericyclic cycloadditions in the sense defined by Woodward and Hoffmann;[26] i.e., they do not involve a continuous overlap of π orbitals. Rather, these are reactions that generate [4 + *n*] carbocycles from separate components via a single transition state.

Energies of activation may be found in Tables 1 and 2, and selected geometric data for the transition state structures **4** and **5** are provided in Figure 2 as calculated at the HF/cc-pVDZ and MP2/cc-pVDZ levels of theory (139 and 177 contracted basis functions for **1** + ethylene and **1** + 1,3-butadiene, respectively). Extensive theoretical studies on typical Diels−Alder reactions have established that such moderate levels of theory are consistent

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Scheme 1

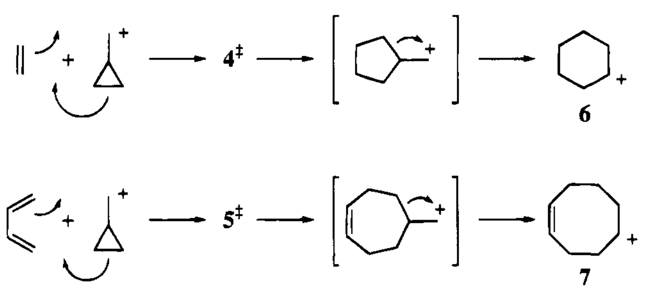

Table 1. Absolute Energies (au) and Activation Energies (kcal/mol) Relative to Separated Reactants for Reaction of 1 with Ethylene[a]

level of theory	**1**	ethylene	**4**	$\Delta E^‡$
HF/3-21G	−154.356 28	−77.600 99	−231.961 13	−2.4
HF/6-31G*	−155.227 25	−78.031 72	−233.263 40	−2.8
HF/cc-pVDZ	−155.237 66	−78.040 17	−233.278 46	−0.4
MP2/3-21G	−154.705 08	−77.781 31	−232.488 09	−1.1
MP2/6-31G*	−155.725 26	−78.285 03	−234.020 87	−6.6
MP2/cc-pVDZ	−155.768 20	−78.315 30	−234.093 86	−6.5
ΔG^o_{298}(trv)[b]	0.072 03	0.030 28	0.127 01	15.5
composite G^o_{298}[c]	−155.696 17	−78.345 58	−234.220 87	**9.0**[d]

[a] All structures were fully optimized at the given level of theory. [b] Thermal translational, rotational, and vibrational corrections at 298 K derived from MP2/6-31G* harmonic frequency calculations. [c] Sum of MP2/cc-pVDZ energies and thermal free energy corrections (preceding two rows). [d] Free energy of activation in the gas phase.

Table 2. Absolute Energies (au) and Activation Energies (kcal/mol) Relative to Separated Reactants for Reaction of 1 with 1,3-Butadiene[a]

level of theory	**1**	*s-cis*-1,3-butadiene	**5**	$\Delta E^‡$
HF/3-21G	−154.356 28	−154.053 94	−308.439 19	−18.2
HF/6-31G*	−155.227 25	−154.913 46	−310.162 82	−13.9
HF/cc-pVDZ	−155.237 66	−154.928 42	−310.18293	−10.6
MP2/3-21G	−154.705 08	−154.407 98	−309.154 72	−26.1
MP2/6-31G*	−155.725 26	−155.416 97	−311.191 65	−31.0
MP2/cc-pVDZ	−155.768 20	−155.463 93	−311.281 01	−30.7
ΔG^o_{298}(trv)[b]	0.072 03	0.059 76	0.161 43	18.6
composite G^o_{298}[c]	−155.696 17	−155.404 17	−311.119 58	**−12.1**[d]

[a] All structures were fully optimized at the given level of theory. [b] Thermal translational, rotational, and vibrational corrections at 298 K derived from MP2/6-31G* harmonic frequency calculations. [c] Sum of MP2/cc-pVDZ energies and thermal free energy corrections (preceding two rows). [d] Free energy of activation in the gas phase.

with higher levels as regards geometrical aspects of the transition state structures.[27-30]

Bond making to the cyclopropylmethyl position is clearly far ahead of bond making/breaking at the reacting 3-membered ring carbon, i.e., the reaction is highly asynchronous. Nevertheless, when the intrinsic reaction coordinate (IRC)[31,32] is followed forward from either **4** or **5**, no stable intermediates intervene prior to formation of the product 6- and 8-membered rings. As illustrated in Scheme 1, however, it is an *exo*cyclic 3-membered ring bond that breaks, not the endocyclic one, as a result of improved overlap of the bond orbital for the former with the π^* orbital of the approaching electrophile. However, the resulting incipient cyclopentylmethyl and 4-cycloheptenylmethyl cations are not stationary, but instead undergo spontaneous ring expansion to generate products **6** and **7**.

Following the IRC's in the reverse direction reveals that it is somewhat ambiguous to describe these cycloadditions as concerted, since, because of the relatively high energy of **1** in the gas phase, the separated reactants do not represent minima on the hypersurface, per se. Rather, their approaches to form ion dipole complexes are barrierless. In the intermediate complexes the C−C bond lengths for the forming bonds at the cyclopropylmethyl carbon are 2.053 Å and 1.582 Å for **1** + ethylene and **1** + 1,3-butadiene, respectively, at the HF/3-21G level. Clearly, the latter includes significant allyl cation character—this stabilization is also apparent in the TS structures; inspection of C−C bond lengths illustrates **5** to be a later transition state structure than **4**.

In the gas phase at our highest level of theory, the free energies of activation (i.e., thermal vibrational corrections to the potential energies have been added using the harmonic approximation and standard statistical mechanical formulas[25g]) relative to separated reactants are 9.0 and −12.1 kcal/mol for the reactions proceeding through **4** and **5**, respectively. The effects of solvation have been estimated for aqueous solvent using the quantum statistical AM1−SM2 continuum model.[33,34] Including differential free energies of solvation,[35] aqueous activation free energies through **4** and **5** are predicted to be 9.9 and −5.1 kcal/mol, respectively. Although the reactive intermediates would obviously not be stable in aqueous solution, these hypothetical activation barriers may be viewed as qualitatively representative of the facility of the corresponding reactions in unreactive polar solvents. The higher barrier for the [4 + 2] reaction relative to the [4 + 4] *in the gas phase* reflects the cationic characters of **4** and **5**; the former structure resembles a primary carbocation while the latter resembles a more stable allyl cation. For the same reason, i.e., charge being more dispersed in the latter transition state structure, *solvation* increases the barrier relative to the gas phase for the latter reaction by about 8 kcal/mol more than it does for the former.

While theory indicates that the subject reactions should proceed readily, other issues remaining to be addressed include stereoselection for substituted reactants, detailed analyses of temperature and solvent effects, and the degree to which the various intermediates and products are subject to nonproductive side reactions, e.g., polymerization, 1,2-hydride shifts, carbocyclic rearrangements, etc.[36] Such concerns are, of course, usually far more efficiently addressed via experiment than theory. In any case, we consider the potential of simple reactions like the one in Scheme 2 for the creation of highly functionalized 8-membered rings from commercially available starting materials to be intriguing. The calculations suggest that there is no a priori energetic

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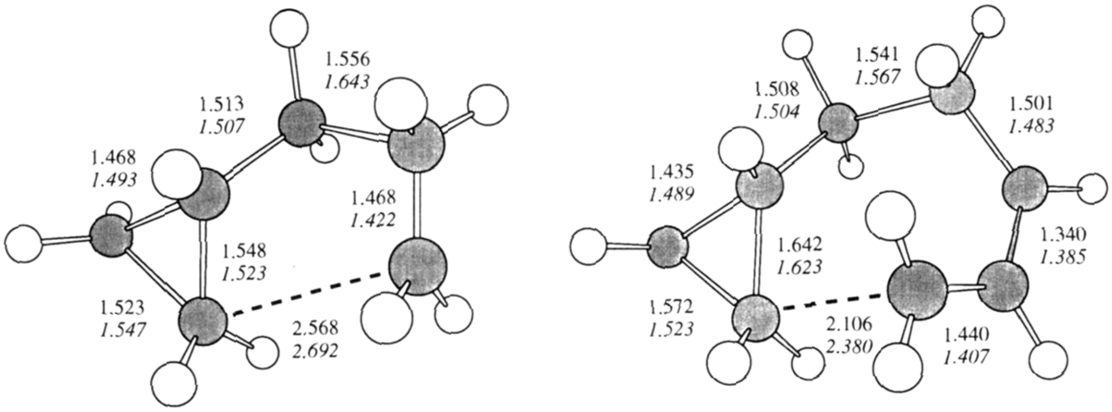
(35) Absolute AM1−SM2 free energies of aqueous solvation (kcal/mol) are as follows: ethylene, 0.8 (expt 1.3); 1,3-butadiene, 0.6 (expt 0.6); **1**, −50.5; **4**, −48.7; **5**, −42.9.

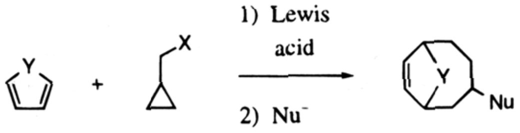
(36) We have also examined 1,3-butadiene reacting as a 2π instead of a 4π component and found $\Delta G^‡$ to be lower by slightly less than 5 kcal/mol at the MP2/cc-pVDZ level. Taken at face value, this would imply little [4 + 4] product should be expected. However, it is a small enough free energy difference that changes in substitution pattern, solvation, etc. might well favor the [4 + 4] pathway.



4 **5**

Figure 2. C−C bond lengths (Å) for the cycloaddition transition state structures of **1** + ethylene and **1** + 1,3-butadiene at the HF/cc-pVDZ and MP2/cc-pVDZ (italics) levels of theory.

Scheme 2



impediment given a suitable experimental design. We conclude by noting that it is the *classical* cation **1** that participates in the cycloaddition reactions, not its nonclassical equilibrium partner **2**—the failure of substituted cyclopropylcarbinyl cations to adopt nonclassical structures[13] should not thus be an impediment to their use as reactants in this process.

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Supplementary Material Available: Cartesian coordinates for **4** and **5** and graphical representations of the cycloaddition IRC's (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.