

# A Becke3LYP/6-31G\* Study of the Cope Rearrangements of Substituted 1,5-Hexadienes Provides Computational Evidence for a Chameleonic Transition State

David A. Hrovat,<sup>†</sup> Brett R. Beno,<sup>‡,§</sup> Holger Lange,<sup>‡</sup> Hi-Young Yoo,<sup>‡,||</sup> K. N. Houk,<sup>\*,‡</sup> and Weston Thatcher Borden<sup>\*,†</sup>

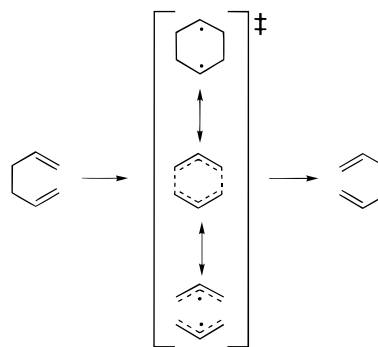
Contribution from the Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90095-1569 and the Department of Chemistry, Box 351700, University of Washington, Seattle, Washington 98195-1700

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**Abstract:** B3LYP/6-31G\* calculations have been performed on the chair Cope rearrangements of a wide variety of 1,5-hexadienes, substituted with cyano or with vinyl groups. In agreement with experimental data from the study of phenyl substituent effects, cyano and vinyl groups at C(2) and C(5) are found to provide cooperative lowering of the activation enthalpy, as are substituents at C(1), C(3), C(4), and C(6). In contrast, the stabilization of the transition structure by substituents at C(2) and C(4) or at C(1), C(3), and C(5) is predicted to be competitive, rather than cooperative. These findings are consistent with what Doering has termed a chameleonic transition state for the Cope rearrangement, one in which the relative importance of the cyclohexane-1,4-diyl and bis-allyl radical resonance contributors can be altered by substituents, depending on the carbons to which the substituents are attached. The computed bond lengths in the transition structures and the calculated and experimentally observed kinetic isotope effects are all consistent with a chameleonic transition state for the Cope rearrangement.

## Introduction

The Cope rearrangement is an unusual pericyclic reaction in that this rearrangement could, in principle, occur by two different diradical pathways.<sup>1</sup> Breaking the C(3)–C(4) bond in 1,5-hexadiene leads to a pair of allyl radicals, whereas making a bond between C(1) and C(6) leads to cyclohexane-1,4-diyl. However, the heat of formation of two allyl radicals<sup>2</sup> and that estimated for cyclohexane-1,4-diyl, assuming no interaction between the radical centers,<sup>3</sup> are, respectively, 26 and 11 kcal/mol higher than the experimental heat of formation of the transition state for the Cope rearrangement of 1,5-hexadiene.<sup>4</sup> These energy differences represent the effect that concerted bond breaking and bond making has on lowering the enthalpy of the transition state, relative to each of the two diradical alternatives.



**Figure 1.** The Cope rearrangement and the three different resonance contributors to the transition state.

As shown in Figure 1, the delocalized bonding in the transition structure for the Cope rearrangement can be represented schematically as a resonance hybrid, containing contributions from the two diradical extremes.<sup>1</sup> This representation has the virtue of predicting that radical-stabilizing groups at C(2) and C(5), as well as at C(1), C(3), C(4), and C(6) should lower the activation enthalpy for the Cope rearrangements of substituted 1,5-hexadienes, as has been found to be the case experimentally. The rate-accelerating effects of phenyl substituents have been the most extensively studied,<sup>5</sup> but the effects of cyano<sup>6</sup> and vinyl<sup>7</sup> have also been investigated.

<sup>†</sup> University of Washington.

<sup>‡</sup> University of California.

<sup>§</sup> Current address: Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT 06492.

<sup>||</sup> Current address: Air Force Research Laboratory/PRS, Edwards Air Force Base, CA 93524.

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The positioning of radical-stabilizing substituents on 1,5-hexadiene is likely to affect not only the degree to which they lower the activation enthalpy but also the geometry of the transition structure. For example, a transition structure resembling two weakly interacting allyl radicals might be favored by substituents at C(1), C(3), C(4), and C(6), whereas a transition structure that resembles cyclohexane-1,4-diyl could be favored by substituents at C(2) and C(5). The secondary deuterium kinetic isotope effects (SKIEs) measured by Conrad and Gajewski for the Cope rearrangements of substituted 1,5-hexadienes provide strong experimental evidence that the transition structure does, in fact, change in response to the positioning of substituents.<sup>8</sup> Doering has suggested the term “chameleonic” to describe such a variable transition structure.<sup>9</sup>

Although SKIEs provide evidence for a chameleonic Cope transition state, the experiments on the Cope rearrangements of substituted 1,5-hexadienes leave a number of questions unanswered. Among them are the following: How much are the bond lengths in the transition structure for the Cope rearrangement of the parent 1,5-hexadiene altered by substituents at different carbons? Are the effects on the geometry and the stabilization energy strictly additive when two substituents are attached to the carbons in 1,5-hexadiene [e.g., C(1) and C(4) or C(2) and C(5)] that allow both substituents to stabilize the same diradical contributor to the transition structure? In such a case is the geometry of highest symmetry a transition state or an energy minimum on the potential-energy surface? What is the effect on the geometry and energy of the transition structure in the Cope rearrangement of a 2,4-disubstituted 1,5-hexadiene, where each substituent stabilizes a different diradical contributor to the transition structure?

Although some information about a few of these questions can be gleaned from the available experimental data, the uncertainties in the experimental activation enthalpies make answers to detailed questions about additivity of substituent effects uncertain. Moreover, if a diradical intermediate is formed in the Cope rearrangement of a disubstituted 1,5-hexadiene, no information about the energy of this intermediate is available from the measurement of the activation parameters for the transition state leading to it. Similarly, although secondary isotope effects can provide qualitative information about the extent of bond making and bond breaking in the transition structure, its precise geometry is not accessible experimentally. For these reasons, we have turned to electronic structure calculations to answer the questions posed in the previous paragraph.<sup>10</sup>

Convergence on a consistent transition structure for even the parent Cope rearrangement has proven unexpectedly challenging for ab initio calculations.<sup>1b–d</sup> It has been found that inclusion of dynamic electron correlation<sup>11</sup> is necessary to obtain not only satisfactory activation enthalpies but also the geometries of

transition structures.<sup>12</sup> Since analytical gradients are not yet available for methods that use second-order perturbation theory to supply electron correlation for CASSCF wave functions, complete geometry optimizations at the CASPT2<sup>13a</sup> or CASMP2<sup>13b</sup> levels of theory are not currently feasible.

Calculations on the Cope rearrangement that use density functional theory (DFT) provide an attractive alternative to ab initio calculations. DFT calculations at the B3LYP/6-31G\* level give activation enthalpies for the Cope rearrangements of 1,5-hexadiene,<sup>14</sup> more highly unsaturated derivatives,<sup>15</sup> and semi-bullvalene<sup>16</sup> that are in nearly exact agreement with the experimental values. The fact that DFT also gives calculated secondary kinetic isotope effects (SKIEs) for the Cope rearrangement of 1,5-hexadiene that are in very good agreement with those that have been measured<sup>14a</sup> provides permissive evidence that the geometries of transition structures are also accurately calculated by this method.

In this paper we describe the results of B3LYP/6-31G\* calculations on the Cope rearrangements of derivatives of 1,5-hexadiene. Since, as already noted, more experimental information is available for phenyl than for any other substituent,<sup>5</sup> phenyl was our substituent of choice. However, a complete B3LYP/6-31G\* study of phenyl substituent effects on the Cope rearrangement proved too time-consuming for the computational resources currently available to us,<sup>17</sup> so we elected to use vinyl in place of phenyl.

Vinyl provides only slightly more radical stabilization than phenyl; the difference amounts to about 2 kcal/mol.<sup>18</sup> Unfortunately, very little experimental information is available concerning the effects of vinyl substituents on the Cope rearrangement.<sup>7</sup> Therefore, we also carried out calculations on the effects of cyano substituents, for which somewhat more experimental data has been published.<sup>6</sup> Since cyano has higher symmetry and fewer atoms than vinyl, we performed a larger number of calculations with cyano than with vinyl groups as substituents.

**Computational Methodology.** DFT calculations were performed with the 6-31G\* basis set,<sup>19</sup> using the hybrid, three-parameter, exchange functional of Becke<sup>20a</sup> and the nonlocal correlation functional of Lee, Yang, and Parr.<sup>20b</sup> Restricted

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(17) For example, a complete B3LYP/6-31G\* vibrational analysis on the optimized  $C_{2h}$  structure in the chair Cope rearrangement of 2,5-diphenyl-1,5-hexadiene required over 7.5 days on a Digital Personal Workstation 433au. Small imaginary frequencies were found for the two possible combinations of phenyl torsions but not for asymmetric distortion of the C–C bonds in the cyclohexane-1,4-diyl ring. These results suggest the existence of  $C_2$ ,  $C_i$ , and probably  $C_1$  conformers of a diradical intermediate, thus necessitating transition state searches and subsequent vibrational analyses of much longer duration than the calculations in  $C_{2h}$  symmetry.

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B3LYP/6-31G\* calculations were performed on the reactants and most of the transition states, but unrestricted (U)B3LYP/6-31G\* calculations were carried out to check for the intermediacy of diradicals and diradical character in the transition states leading to them. Stationary points were located, and vibrational analyses were performed at either the B3LYP or the UB3LYP level, using Gaussian 94.<sup>21</sup> Corrections for differences in both zero-point vibrational energies (ZPE) and heat capacities were calculated from unscaled vibrational frequencies. SKIEs were also computed without scaling, using the program Quiver.<sup>22</sup>

We arbitrarily chose a common temperature of 298 K at which to compute the heat capacity corrections and the SKIEs, even though, in practice, the temperatures at which the Cope rearrangement kinetics were measured would vary widely with the number and positions of the substituents. The choice of temperature has little effect on the heat capacity corrections. They differ by less than one kilocalorie per mole between reactants and transition states, and their variations with substituents amount to only a few tenths of a kilocalorie per mole.

In contrast, the size of SKIEs is highly temperature dependent, and the virtue of computing all of them at a common temperature is that their sizes can then be compared. However, for molecules for which experimental SKIEs are available for the Cope rearrangements of closely related derivatives of 1,5-hexadiene, we have also computed the SKIEs at the temperature at which the experiments were performed.

## Results and Discussion

For each cyano-substituted 1,5-hexadiene, the relative enthalpies of the reactant, the Cope transition state, and any intermediate in the Cope rearrangement are given in Table 1. The C—C bond lengths in each transition structure and intermediate are shown in Figure 2. The same information for the vinyl-substituted 1,5-hexadienes is provided in Table 2 and Figure 3. Comparisons of calculated SKIEs with those that have been measured for closely related derivatives of 1,5-hexadiene are given in Table 3. A complete tabulation of all the SKIEs that have been computed is available as Supporting Information.

**Cyano Substituents. (A) Effects of Cyano Substituents on Enthalpies.** An *E*-1-cyano group raises the activation enthalpy for the Cope rearrangement of 1,5-hexadiene by 2.3 kcal/mol, but a 3-cyano substituent lowers the activation enthalpy by 3.9 kcal/mol. The difference of 6.2 kcal/mol between the enthalpy of *E*-1-cyano-1,5-hexadiene and its 3-cyano isomer reflects the strong preference for conjugation of the cyano group with the double bond. This thermodynamic factor causes  $\Delta H^\ddagger$  for the Cope rearrangement of *E*-1-cyano-1,5-hexadiene to be higher than that for the unsubstituted hydrocarbon. Such thermodynamic effects on the activation barriers for 3,3-sigmatropic shifts have been discussed extensively for the Claisen rearrangement.<sup>23</sup>

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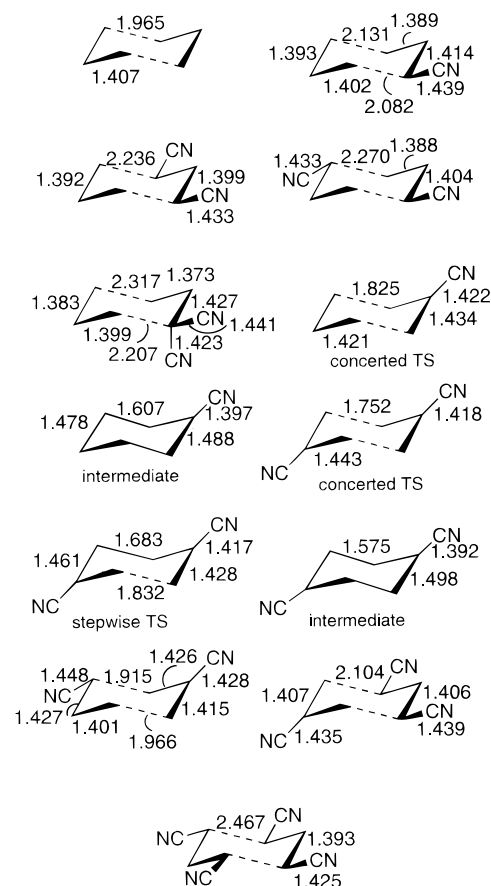
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**Table 1.** Absolute Energies and Zero Point Energies and Enthalpies at 298 K, Relative to the Reactants, for the Stationary Points on the Potential Surface for Cope Rearrangement of Cyano-Substituted 1,5-Hexadienes, Computed at the Becke3LYP/6-31G\* Level

substitution pattern	energy (hartrees)		$\Delta ZPE$ (kcal/mol)	$\Delta H_{298}$ (kcal/mol)
	1,5-hexadiene	chair cope TS or intermediate		
H	-234.61171	-234.55687	-0.30	33.2
1-CN	-326.85789	-326.79996	-0.87	35.5
3-CN	-326.84799	-326.79996	-0.64	29.3
1,3-diCN	-419.09054	-419.04082	-0.99	29.7
1,4-diCN	-419.09139	-419.04120	-1.06	29.9
3,3-diCN	-419.07186	-419.03267	-0.71	23.3
1,1-diCN	-419.09148	-419.03267	-1.45	34.9
2-CN	-326.85568	-326.80976	0.07	28.0
2-CN <sup>a</sup>	-326.85568	-326.81059	0.21	27.8
2,5-diCN	-419.09911	-419.05914	0.19	24.4
2,5-diCN <sup>b</sup>	-419.09911	-419.05918	-0.33	23.9
2,5-diCN <sup>c</sup>	-419.09911	-419.06606	0.76	20.2
2,4-diCN	-419.09004	-419.04621	-0.29	26.5
1,3,5-triCN	-511.33018	-511.28142	-0.94	29.1
1,3,4,6-tetraCN	-603.55598	-603.51370	-1.60	24.7

<sup>a</sup> UB3LYP/6-31G\* optimized C<sub>3</sub> intermediate ( $S^2 = 0.80$ ). <sup>b</sup> UB3LYP/6-31G\* optimized C<sub>2</sub> transition state ( $S^2 = 0.08$ ). <sup>c</sup> UB3LYP/6-31G\* optimized C<sub>2h</sub> intermediate ( $S^2 = 0.94$ ).



**Figure 2.** Bond lengths of the transition structures and intermediates of the Cope rearrangements of 1,5-hexadiene and cyano-substituted derivatives.

Were attachment of a cyano group to C(1) or C(3) to affect only the energies of the *E*-1- and 3-cyano-1,5-hexadiene isomers relative to each other, the average of the two activation enthalpies would remain at 33.2 kcal/mol. Instead, the average is 0.8 kcal/mol lower, indicating that the cyano group lowers the enthalpy of the transition state by this amount, relative to its effect on the average enthalpy of the reactant and product.



**Table 2.** Absolute Energies and Zero Point Energies and Enthalpies at 298 K, Relative to the Reactants, for the Stationary Points on the Potential Surface for Cope Rearrangement of Vinyl-Substituted 1,5-Hexadienes, Computed at the Becke3LYP/6-31G\* Level

substitution pattern	energy (hartrees)			
	1,5-hexadiene	chair cope TS or intermediate	$\Delta ZPE$ (kcal/mol)	$\Delta H_{298}$ (kcal/mol)
1-vinyl	-312.01650	-311.95466	-1.06	37.1
2-vinyl	-312.01301	-311.96276	-0.30	30.4
2-vinyl <sup>a</sup>	-312.01301	-311.96271	-0.81	30.0
2-vinyl <sup>b</sup>	-312.01301	-311.97011	-0.31	26.0
3-vinyl	-312.00149	-311.95466	-0.64	28.1
1,3-divinyl	-389.40558	-389.35501	-1.36	29.9
1,4-divinyl	-389.40538	-389.35597	-1.16	29.3
2,5-divinyl <sup>c</sup>	-389.41418	-389.37327	-0.77	24.2
2,5-divinyl <sup>d</sup>	-389.41418	-389.39066	-0.36	13.8
2,4-divinyl	-389.40207	-389.35768	-0.53	27.3
2,4-divinyl <sup>e</sup>	-389.40207	-389.35840	-0.65	26.7
2,4-divinyl <sup>f</sup>	-389.40207	-389.36178	-0.38	24.9
1,3,5-trivinyl	-466.80668	-466.75551	-1.30	30.4
1,3,5-trivinyl <sup>g</sup>	-466.80668	-466.75323	-0.87	32.2

<sup>a</sup> UB3LYP/6-31G\* optimized transition state ( $S^2 = 0.14$ ). A second transition structure with slightly lower enthalpy ( $\Delta H_{298} = 29.6$  kcal/mol) also connects to the UB3LYP intermediate. <sup>b</sup> UB3LYP/6-31G\* optimized intermediate ( $S^2 = 0.94$ ). <sup>c</sup> UB3LYP/6-31G\* optimized transition state ( $S^2 = 0.10$ ). <sup>d</sup> UB3LYP/6-31G\* optimized intermediate ( $S^2 = 1.01$ ). <sup>e</sup> UB3LYP/6-31G\* optimized transition state ( $S^2 = 0.47$ ). We were unable to find the higher energy of the two UB3LYP transition structures that connect to the UB3LYP intermediate, but its enthalpy should be less than the value of  $\Delta H_{298} = 27.3$  kcal/mol found for the RB3LYP transition structure. <sup>f</sup> UB3LYP/6-31G\* optimized intermediate ( $S^2 = 0.93$ ). <sup>g</sup> UB3LYP/6-31G\* optimized intermediate ( $S^2 = 0.93$ ).

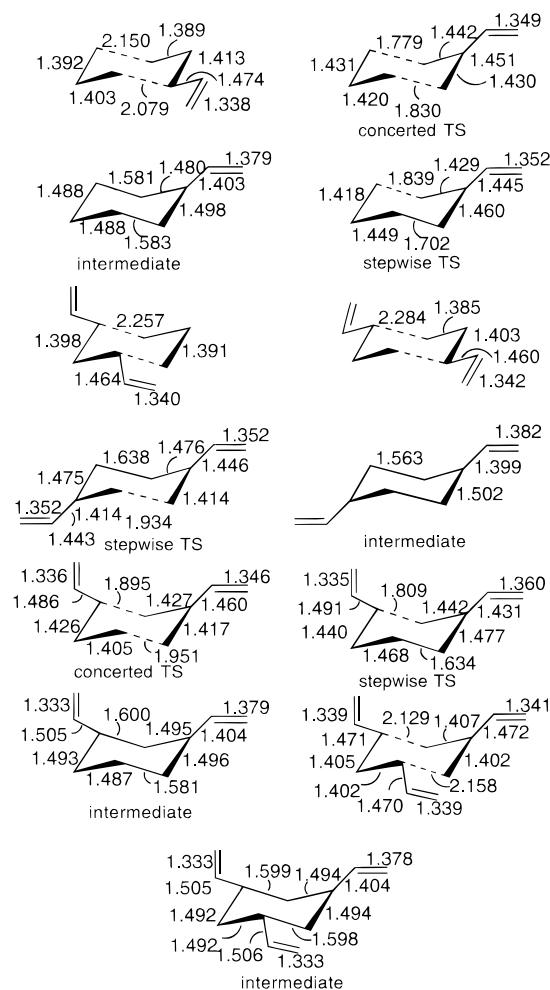
Since the Cope rearrangement of 1,4-dicyano-1,5-hexadiene is degenerate, the activation enthalpy for this reaction can be compared directly with that for the parent. Table 1 shows that the activation enthalpy for 1,4-dicyano is lower by 3.3 kcal/mol, which is slightly more than four times the average lowering of  $\Delta H^\ddagger$  (0.8 kcal/mol), caused by a single cyano group at one of these two carbons.

The Cope rearrangement of 1,3-dicyano-1,5-hexadiene is also degenerate, but in this case, both cyano groups are attached to the same allylic fragment in the transition structure. However, as shown in Table 1, the effect on the activation enthalpy of having both cyano groups on the same allylic fragment, rather than on different allylic fragments, is negligible.

The Cope rearrangement of 3,3-dicyano-1,5-hexadiene to its 1,1-dicyano isomer is computed to be exothermic by 11.6 kcal/mol. This is only slightly less than twice the exothermicity of 6.2 kcal/mol that is computed for moving one cyano group into conjugation with the double bond. The average enthalpy of activation for the Cope rearrangements that equilibrate 3,3- and 1,1-dicyano-1,5-hexadiene is 4.1 kcal/mol lower than that for the parent Cope rearrangement. Thus, two cyano groups on the same carbon have a slightly larger effect on stabilizing the transition structure than when one is attached to C(1) and the other to C(3) or C(4).

The activation enthalpy for the rearrangement of a 1,2-dialkyl derivative of 3,3-dicyano-1,5-hexadiene was found by Cope and co-workers to be  $\Delta H^\ddagger = 25.2$  kcal/mol.<sup>6a</sup> This experimental value is in good agreement with the value of  $\Delta H^\ddagger = 23.3$  kcal/mol that we have computed for the Cope rearrangement of the compound without the alkyl groups. At least for this compound, the energetic effects of the two cyano substituents appear to be satisfactorily computed at the B3LYP/6-31G\* level of theory.

As shown in Table 3, we have also calculated the SKIEs at 90 °C for the Cope rearrangements of 3,3-dicyano-1,5-hexadiene-6,6-d<sub>2</sub> and 4,4-d<sub>2</sub>. These isotope effects have been measured

**Figure 3.** Bond lengths of the transition structures and intermediates of the Cope rearrangements of vinyl-substituted 1,5-hexadienes.**Table 3.** Comparison of the Experimental (Exp)<sup>8</sup> and Calculated (Calcd, B3LYP/6-31G\*) Secondary Kinetic Isotope Effects ( $k_H/k_D$ ) for the Cope Rearrangement of Substituted 1,5-hexadienes

substitution pattern		$T$ (°C)	$k_H/k_D$	H $\rightleftharpoons$ D	$k_H/k_D$	H $\rightleftharpoons$ D
3-methyl-2-phenyl	exp	174.6	1.09	(3,4,4)	0.772	(1,1,6,6)
2-vinyl	calcd		1.01	(3,3,4,4)	0.784	(1,1,6,6)
2,5-diphenyl	exp	55.5	1.07	(3,3,4,4)	0.636	(1,1,6,6)
2,5-divinyl	calcd <sup>a</sup>		1.03	(3,3,4,4)	0.637	(1,1,6,6)
3,3-dicyano-1,2-diethyl	exp	90.0	1.19	(4,4)	0.943	(6,6)
3,3-dicyano	calcd		1.14	(4,4)	0.927	(6,6)

<sup>a</sup> Using the steady-state approximation for the intermediate.

at this temperature by Sunko and co-workers for dialkyl derivatives of these two compounds.<sup>24</sup> Our calculated bond-making and bond-breaking SKIEs of, respectively,  $k_H/k_{D2} = 0.927$  and  $k_H/k_{D2} = 1.14$  are in reasonable agreement with the experimental values of  $k_H/k_{D2} = 0.943$  and  $k_H/k_{D2} = 1.19$ , although B3LYP seems to underestimate slightly the amount of bond breaking in and, hence, the diradical character of the transition structure. This might reflect the fact that the transition structure is actually a maximum in  $\Delta G$ , not  $\Delta H$ , along the reaction coordinate; the experimental geometry could be influenced by the more favorable  $\Delta S$  for a looser transition structure that resembles more closely two allyl radicals.<sup>10</sup>

(24) Humski, K.; Malojcic, Borcic, S.; Sunko, D. E. *J. Am. Chem. Soc.* 1970, 92, 6534.

A cyano substituent at C(2) is computed to lower the activation enthalpy for the Cope rearrangement ( $\Delta\Delta H^\ddagger = 5.2$  kcal/mol), much more than the average effect of 1-cyano and 3-cyano groups ( $\Delta\Delta H^\ddagger = 0.8$  kcal/mol). It might be argued that there is only half as much radical character at each of the four equivalent carbons in the resonance contributor that depicts the transition structure as two weakly interacting allyl radicals than there is at the two equivalent carbons in the cyclohexane-1,4-diyl resonance contributor. However, the two cyano substituents in 1,3- and 1,4-dicyano-1,5-hexadiene reduce the activation enthalpy by just 3.5 and 3.3 kcal/mol, respectively, which is only about two-thirds of the reduction due to the single cyano group in 2-cyano-1,5-hexadiene.

The same observation can be made for phenyl substituents from the experimental data of Dewar and Doering. A substituent at C(2)<sup>5a,c</sup> has a larger effect than substituents at both C(1) and C(4)<sup>5d,e</sup> on reducing the activation enthalpy for the Cope rearrangement.

Analyzed in terms of the two resonance contributors in Figure 1, the calculations of the cyano substituent effects and the experimental data on the effects of phenyl groups both indicate that the bonding in the Cope transition structure resembles that in cyclohexane-1,4-diyl more than in two weakly interacting allyl radicals. This is consistent with the 15 kcal/mol lower heat of formation of cyclohexane-1,4-diyl<sup>3</sup> than of two allyl radicals.<sup>2</sup> The lower-energy resonance structure makes the greater contribution to the electronic structure of the transition state.

In fact, a UB3LYP optimized diradical intermediate is computed to be 0.2 kcal/mol lower in energy than the concerted transition structure. As shown in Figure 2, the geometry of the intermediate resembles cyclohexane-1,4-diyl, while the nearly isoenergetic concerted transition structure has stretched C—C bonds, characteristic of a delocalized aromatic species. Both are nearly the same in energy; the potential surface is very flat in this region.

With cyano substituents at both C(2) and C(5), B3LYP predicts a net lowering of the activation enthalpy of  $\Delta\Delta H^\ddagger = 8.8$  kcal/mol, which is less than twice the value of  $\Delta\Delta H^\ddagger = 5.2$  kcal/mol for a single cyano substituent at C(2). However, a UB3LYP calculation finds a  $C_{2h}$  energy minimum, which has a calculated enthalpy that is 4.2 kcal/mol lower than the  $C_{2h}$  B3LYP transition structure.<sup>25,26</sup>

Because  $S^2 = 0.94$  for this UB3LYP reaction intermediate, it is a mixture of 53% pure singlet ( $S^2 = 0$ ) and 47% pure triplet ( $S^2 = 2.00$ ) states; the computed energy is a weighted average of these two states. At the optimized geometry of the intermediate, the triplet UB3LYP energy ( $S^2 = 2.03$ ) is 2.6 kcal/mol higher than that of the mixed ( $S^2 = 0.94$ ) spin state. Therefore, the energy of the UB3LYP diradical with  $S^2 = 0$  should be

(25) For the Cope rearrangements of 1,5-hexadiene and 2-cyano-1,5-hexadiene, UB3LYP intermediates with  $S^2 = 0.63$  and 0.80, respectively, were also found.<sup>26</sup> However, the UB3LYP energy of the former  $C_{2h}$  intermediate was computed to be 3.2 kcal/mol higher than that of the B3LYP  $C_{2h}$  transition structure, and the UB3LYP energy of the latter  $C_s$  intermediate was computed to be just 0.2 kcal/mol below the B3LYP  $C_s$  transition structure. In the latter case the asymmetric UB3LYP transition structure was not located, but it is almost certainly higher in energy than the B3LYP transition structure.

(26) The instability toward the breaking of spin symmetry of B3LYP has been discussed by Davidson for rearrangement of 1,5-hexadiene. (Davidson, E. R. *Chem. Phys. Lett.* **1998**, *284*, 301 and Davidson, E. R. *Int. J. Quant. Chem.* **1998**, *69*, 241). Unlike some other computational methods that are based on restricted wave functions, B3LYP at least gives a lower-energy  $C_{2h}$  structure than the corresponding unrestricted calculation (i.e., UB3LYP) for the parent Cope rearrangement. A more detailed analysis of the diradical and aromatic character of the variable Cope transition state has been performed by V. N. Staroverov and E. R. Davidson, submitted for publication.

$\sim 2.2$  kcal/mol lower than that of this mixed spin state, or  $20.2 - 2.2 = 18.0$  kcal/mol.<sup>27</sup> Thus, from our UB3LYP calculations, the energy of the singlet ( $S^2 = 0$ ) diradical intermediate is estimated to be only 18.0 kcal/mol above that of 2,5-dicyano-1,5-hexadiene.

The calculated net stabilization of 15.2 kcal/mol that is provided by the two cyano groups in this diradical intermediate is  $\sim 5$  kcal/mol greater than twice the 5.4 kcal/mol net stabilization computed for a single cyano substituent. Consequently, it would appear that the effects of the two cyano groups on stabilizing this diradical intermediate, relative to the reactant, are not merely additive but are actually cooperative.

Interestingly, the enthalpies of the B3LYP  $C_{2h}$  transition structure for the concerted reaction and the UB3LYP  $C_2$  transition structure ( $S^2 = 0.08$ ), which connects the reactant to the UB3LYP  $C_{2h}$  diradical intermediate, are nearly identical. Both give enthalpies of activation that are very close to the experimental value of  $\Delta H^\ddagger = 23.3$  kcal/mol, measured by Schmid and co-workers for a methyl derivative of 2,5-dicyano-1,5-hexadiene.<sup>6b</sup> This agreement with experiment provides additional evidence that the cyano substituent effects on the Cope rearrangement are accurately calculated at the (U)B3LYP/6-31G\* level of theory.

The experimental activation enthalpies for the Cope rearrangements of 2-phenyl- and 2,5-diphenyl-1,5-hexadiene also reveal a cooperative effect between the two phenyl groups in stabilizing the transition structure.<sup>5a</sup> The first phenyl group lowers the activation enthalpy by 4.2 kcal/mol, while each phenyl group in the disubstituted case lowers the activation enthalpy by 6.1 kcal/mol.

Both substituents in 2,5-dicyano- and in 2,5-diphenyl-1,5-hexadiene are on carbons where they can stabilize the cyclohexane-1,4-diyl resonance contributor to the electronic structure of the  $C_{2h}$  species, formed in the Cope rearrangement of each of these two compounds. As a result, the  $C_{2h}$  species acquires more of the character of this diradical than when only a single substituent is present at C(2) in the reactant. This allows the radical-stabilizing substituents attached to C(2) and C(5) in the reactant each to provide more stabilization for the  $C_{2h}$  species than a single substituent at just one of these carbons.<sup>28</sup>

The calculated value of  $\Delta H^\ddagger = 24.7$  kcal/mol for the Cope rearrangement of 1,3,4,6-tetracyano-1,5-hexadiene reveals the existence of a cooperative substituent effect for this reaction, too, in which all four cyano groups are positioned to stabilize the bis-allylic resonance contributor to the transition structure. The value of  $\Delta\Delta H^\ddagger = 8.6$  kcal/mol for the four cyano groups in this compound is  $\sim 2.0$  kcal/mol larger than twice the value of  $\Delta\Delta H^\ddagger = 3.3$ – $3.5$  kcal/mol for the two cyano substituents in both 1,3- and 1,4-dicyano-1,5-hexadiene.

The enthalpy of activation for the Cope rearrangement of 1,3,4,6-tetraphenyl-1,5-hexadiene<sup>5e</sup> provides experimental evidence for the same type of cooperative substituent effect. The two phenyl substituents in 1,4-diphenyl-1,5-hexadiene lower the enthalpy of activation from that for the Cope rearrangement of 1,5-hexadiene by  $\Delta\Delta H^\ddagger = 3.6$  kcal/mol.<sup>5d</sup> However, the four phenyl substituents in 1,3,4,6-tetraphenyl-1,5-hexadiene provide an enthalpy of activation lowering of  $\Delta\Delta H^\ddagger = 12.2$  kcal/mol,

(27) Goldstein, E.; Beno, B.; Houk, K. N. *J. Am. Chem. Soc.* **1996**, *118*, 6036. (b) Yamaguchi, K.; Jensen, F.; Dorigo, A.; Houk, K. N. *Chem. Phys. Lett.* **1988**, *149*, 537.

(28) However, a necessary condition for a cooperative effect to occur between two identical substituents is merely that attachment of the first must cause a change, usually in geometry, that allows attachment of the second substituent to provide even more stabilization than that furnished by the first alone. Coolidge, M. B.; Borden, W. T. *J. Am. Chem. Soc.* **1990**, *112*, 1751.

a transition state stabilization energy which is not twice, but more than three times greater than that in the diphenyl compound.

In contrast to the cooperative effects of simultaneous substitution at C(2) and C(5), or at C(1), C(3), C(4), and C(6), substitution of cyano at C(2) and C(4) gives an effect that B3LYP predicts to be clearly competitive.<sup>29</sup> Whereas a cyano group at C(2) is calculated to lower the activation enthalpy for the Cope rearrangement of 1,5-hexadiene by 5.2 kcal/mol, the cyano group at C(2) of 2,4-dicyano-1,5-hexadiene lowers the activation enthalpy for the Cope rearrangement of 3-cyano-1,5-hexadiene by only 2.8 kcal/mol.

Even more striking is the B3LYP prediction that addition of a cyano substituent to C(5) of 1,3-dicyano-1,5-hexadiene lowers the activation enthalpy for Cope rearrangement by just 0.6 kcal/mol. This is only about 10% of the calculated effect of the addition of a C(2) cyano substituent on the Cope rearrangement of 1,5-hexadiene. If the activation enthalpies of 1,3,5-tricyano- and 2-cyano-1,5-hexadiene are compared, B3LYP predicts that the pair of cyano substituents at C(1) and C(3) actually raise the activation enthalpy by 1.1 kcal/mol.

The competitive effect that is predicted for 2,4-dicyano-1,5-hexadiene arises because the C(4) cyano group stabilizes the resonance contributor representing two weakly interacting allyl radicals and thus enhances its contribution to the Cope transition structure. Since the cyclohexane-1,4-diyl resonance contributor becomes less important, addition of the C(2) cyano group is less effective at stabilizing the transition structure in the Cope rearrangement of 2,4-dicyano-1,5-hexadiene than of 2-cyano-1,5-hexadiene.

This explanation for the competitive effect of the cyano substituents in 2,4-dicyano-1,5-hexadiene is supported by the computational results for the Cope rearrangement of 1,3,5-tricyano-1,5-hexadiene. The cyano groups at C(1) and C(3) in the latter diene both stabilize the resonance contributor representing two weakly interacting allyl radicals. Thus, this contributor is more important in the transition structure for the Cope rearrangement of 1,3,5-tricyano-1,5-hexadiene than of 2,4-dicyano-1,5-hexadiene. Consequently, the C(5) cyano group in 1,3,5-tricyano-1,5-hexadiene is predicted to have almost no effect on lowering the Cope activation enthalpy, relative to that for 1,3-dicyano-1,5-hexadiene, and the C(1) and C(3) cyano groups are actually predicted to make the activation enthalpy for the tricyano compound higher than that for 2-cyano-1,5-hexadiene.

**(B) Effects of Cyano Substituents on Chair Transition Structures.** Support for these explanations of the cooperative and competitive cyano substituent effects on the enthalpies of the chair transition structures and intermediates in Cope rearrangements comes from the predicted C–C bond lengths at these chair geometries. Figure 2 shows that even a single cyano group at C(3) of 1,5-hexadiene has a major effect on the bond lengths in the transition structure for the chair Cope rearrangement of this compound.

Although the calculated activation enthalpy for the Cope rearrangement of 1,4-dicyano-1,5-hexadiene is only 3.3 kcal/

mol lower than for the parent hydrocarbon, the cyano groups at C(1) and C(4) lengthen the interallylic distance in the transition structure by 0.305 Å. In the transition structure the intraallylic bonds to the carbons to which the cyano groups are attached are 0.016 Å longer than the intraallylic bonds to the unsubstituted carbons. This is indicative of some degree of localization of one electron at each of the cyano-substituted carbons in the transition structure.

The four cyano substituents in 1,3,4,6-tetracyano-1,5-hexadiene result in the interallylic bonds in the  $C_{2h}$  transition structure for its Cope rearrangement being 2.467 Å long. The stabilization of the bis-allylic resonance contributor to the transition structure by all four cyano groups makes the interallylic C–C bonds >0.5 Å longer than those in the  $C_{2h}$  transition structure for the Cope rearrangement of unsubstituted 1,5-hexadiene.

Addition of cyano substituents to C(2) and C(5) of 1,5-hexadiene also results in large changes in the bond lengths of the transition structure for the chair Cope rearrangement. A single cyano group at C(2) in the reactant shortens the interallylic bond lengths in the  $C_s$  transition structure by 0.140 Å. A second cyano group at C(5) in the reactant shortens these C–C bonds by an additional 0.073 Å in the  $C_{2h}$  B3LYP transition structure and by 0.142 Å in the  $C_{2h}$  UB3LYP diradical intermediate.<sup>30</sup>

It has been noted previously that, because the Cope transition structure is a resonance hybrid, the potential surface for the parent Cope rearrangement is pathologically flat along a coordinate that shortens and lengthens the interallylic bonds, while preserving  $C_{2h}$  symmetry.<sup>12</sup> It is clearly this flatness that allows radical-stabilizing substituents to have such large effects on the geometries of the transition structures and intermediates in Cope rearrangements.

For example, we find that distorting the  $C_{2h}$  geometry of the transition structure for the Cope rearrangement of 1,5-hexadiene to the  $C_i$  geometry of the transition structure for the 1,4-dicyano derivative requires only 2.5 kcal/mol, despite the 0.26 Å change in the lengths of the interallylic bonds. The analogous distortions of the 1,5-hexadiene Cope transition structure to the B3LYP and UB3LYP optimized  $C_{2h}$  geometries for the 2,5-dicyano derivative require, respectively, 3.4 kcal/mol (B3LYP) and 4.8 kcal/mol (UB3LYP).<sup>31</sup>

The driving force for these geometry changes is that cyano substituents provide more stabilization at geometries with more diradical character than at the geometry of the transition structure for the Cope rearrangement of unsubstituted 1,5-hexadiene. For example, at the transition state geometry for the Cope rearrangement of 1,4-dicyano-1,5-hexadiene, the cyano substituents furnish 5.3 kcal/mol more stabilization energy than at the transition state geometry for the parent Cope rearrangement. For the rearrangement of 2,5-dicyano-1,5-hexadiene, the corresponding increases in substituent stabilization energy were calculated to be 6.9 and 12.7 kcal/mol, respectively, at the B3LYP and UB3LYP levels of theory.<sup>32</sup>

(30) The restricted B3LYP calculation almost certainly underestimates this change in bond lengths. However, because the UB3LYP calculation gives a mixed state ( $S^2 = 0.94$ ) that is nearly an equal mixture of singlet and triplet, UB3LYP almost certainly overestimates this bond length change. Through-bond interaction between the radical centers in the singlet should result in it having longer interallylic C–C bonds than the triplet.

(31) At the UB3LYP geometry for the diradical intermediate formed from 2,5-dicyano-1,5-hexadiene, a UB3LYP calculation for singlet cyclohexane-1,4-diyl gives  $S^2 = 0.92$ , and the UB3LYP energy is lower than the B3LYP energy for this species by 16.3 kcal/mol. Since the B3LYP energy of the triplet state ( $S^2 = 2.00$ ) at this geometry is 3.1 kcal/mol above the mixed state with  $S^2 = 0.92$ , a true ( $S^2 = 0$ ) UB3LYP singlet cyclohexane-1,4-diyl would be lower in energy than the mixed state by an additional 2.6 kcal/mol at this geometry.

(29) Dewar and Wade found that the substituents in 2,4-diphenyl-1,5-hexadiene lower the enthalpy of activation from that for the parent hydrocarbon by  $\Delta\Delta H^\ddagger = 8.9$  kcal/mol, which is 0.7 kcal/mol less than the sum of the substituent effects in 2-phenyl-1,5-hexadiene ( $\Delta\Delta H = 4.2$  kcal/mol) and 3-phenyl-1,5-hexadiene ( $\Delta\Delta H^\ddagger = 5.4$  kcal/mol).<sup>5a</sup> However, experimental uncertainties in the activation enthalpies, combined with the fact that the kinetics for the phenyl-substituted derivatives were measured in *o*-dichlorobenzene,<sup>5a</sup> whereas  $\Delta H^\ddagger = 33.5$  kcal/mol for 1,5-hexadiene is a gas-phase value,<sup>4</sup> caution against attaching any significance to this small deviation from additivity.



Returning to the comparison of the chair geometries for the Cope rearrangements of 2-cyano- and 2,5-dicyano-1,5-hexadiene, the intrallylic C–C bond lengths are longer and the C–CN bond lengths shorter in the latter than in the former chair geometry. This difference is especially striking when the comparison is made using the UB3LYP geometry for the dicyano diradical intermediate.<sup>30</sup> Addition of the second cyano substituent causes the UB3LYP geometry for the dicyano intermediate to resemble a cyclohexane-1,4-diyl more closely than the monocyano transition structure does.

The effects on the geometry of the transition structure of the competitive interaction between the substituents in 2,4-dicyano-1,5-hexadiene are also apparent in Figure 2. The interallylic bond lengths in the transition structure do not resemble those in the transition structures for the Cope rearrangements of either of the monosubstituted compounds. In fact, the bond lengths in the 2,4-dicyano transition structure are closest to those in the transition structure for the parent Cope rearrangement. Because each of the two cyano groups stabilizes a different resonance contributor to the transition structure, neither group is successful in distorting the C–C bond lengths toward a geometry where either of the cyano groups could, by itself, provide the greatest stabilization.

As shown by the results in Table 1, the C(2) and C(4) cyano groups in the disubstituted transition structure each provide less stabilization than they do in the corresponding monosubstituted transition structure. Consequently, each of the C–CN bond lengths in the disubstituted transition structure is longer than the C–CN bond length in the corresponding monosubstituted transition structure. However, consistent with the greater transition structure stabilization provided by a cyano group at C(2) than at C(3), the former C–CN bond length is shorter than the latter in both the mono- and disubstituted transition structures.

In the transition structure for the Cope rearrangement of 1,3,5-tricyano-1,5-hexadiene, the interallylic C–C bond lengths are about the same as the average of those in the transition structure for the Cope rearrangement of 3-cyano-1,5-hexadiene. As indicated by the interallylic bond lengths in the 2-cyano-, 3-cyano-, and 2,4-dicyano-1,5-hexadiene transition structures, it appears that the effects of C(2) and C(3)/C(4) cyano groups on distorting these interallylic bond lengths from those in the transition structure for the parent hydrocarbon are about the same. This near cancellation results in the average interallylic bond lengths in the transition structures for the Cope rearrangements of 3-cyano- and 1,3,5-tricyano-1,5-hexadiene being very similar.

Because the C(5) cyano group provides only a 0.7 kcal/mol additional lowering of the enthalpy of activation for the Cope rearrangement of 1,3,5-tricyano-1,5-hexadiene, one would expect the C(5)–CN bond length in the transition structure for this reaction to be longer than the C(2)–CN bond lengths in the transition structures for the Cope rearrangements of any of the 2-cyano-1,5-hexadienes. Figure 2 shows that this is, in fact, the case. Consistent with the calculated effect of the pair of cyano groups at C(1) and C(3) on increasing the enthalpy of activation for the Cope rearrangement of 1,3,5-tricyano-1,5-hexadiene from that for 2-cyano-1,5-hexadiene, the C(5)–CN bond length in the transition structure for the former reaction is 0.013 Å longer than the C(2)–CN bond in the transition structure for the latter.

**Vinyl Substituents.** A comparison of Table 1 with Table 2 shows that the effects of a single vinyl substituent are very

similar to the effects caused by a single cyano group. In the 1-vinyl case, the activation enthalpy for Cope rearrangement is increased by 3.9 kcal/mol; in the 3-vinyl case it is decreased by 5.1 kcal/mol. The average value for the activation enthalpy is 32.6 kcal/mol, which is only 0.6 kcal/mol lower than  $\Delta H^\ddagger$  for the parent reaction. This very small reduction is comparable to that for cyano groups attached at the same two carbons ( $\Delta\Delta H^\ddagger = 0.8$  kcal/mol).

When substituted at C(2), one vinyl group leads to a decrease in the activation enthalpy to  $\Delta H^\ddagger = 30.4$  kcal/mol, which is about 2 kcal/mol smaller than the reduction in  $\Delta H^\ddagger$  for 2-cyano ( $\Delta H^\ddagger = 28.0$  kcal/mol). This result is somewhat surprising because a vinyl substituent would be expected to provide more stabilization than cyano for a radical center at C(2).

In fact, as shown in Table 2, UB3LYP calculations do find a diradicaloid intermediate for the Cope rearrangement of 2-vinyl-1,5-hexadiene with  $S^2 = 0.94$  and at an enthalpy 26.0 kcal/mol above the reactant. The comparable values in Table 1 for the UB3LYP intermediate in the Cope rearrangement of 2-cyano-1,5-hexadiene are  $S^2 = 0.80$  and  $\Delta H^\ddagger = 27.8$  kcal/mol. Thus, at the UB3LYP level of theory, vinyl does, indeed, provide more stabilization for a radical center at C-2.

Because of the orientation of the C(2) vinyl substituent, both the B3LYP transition structure and the UB3LYP intermediate are asymmetric. Therefore, two different transition structures connect the UB3LYP intermediate to the reactant and product, which also differ by whether the C(2) vinyl group is *s-cis* or *s-trans* to the double bond between C(1) and C(2). The higher-energy UB3LYP transition structure ( $\Delta H^\ddagger = 30.0$  kcal/mol) connects to *s-cis*-2-vinyl-1,5-hexadiene; the lower-energy structure ( $\Delta H^\ddagger = 29.6$  kcal/mol) connects to the *s-trans* conformer. The two UB3LYP transition structures have much lower values of  $S^2$  (0.14 and 0.25, respectively) than the UB3LYP intermediate, and both of their energies are less than 1 kcal/mol below that of the B3LYP transition structure.

For the degenerate Cope rearrangement of 1,4-divinyl-1,5-hexadiene, the activation enthalpy is 3.9 kcal/mol below that for the parent reaction and 3.3 kcal/mol below the average  $\Delta H^\ddagger$  for 1- and 3-vinyl substitution. As is the case for 1,4-dicyano-1,5-hexadiene, the effect of the 1,4-divinyl substituents on the geometry of the transition structure is large; the interallylic distance is 0.3 Å longer than in the parent reaction, even though their influence on the activation energy is rather small.

Not unexpectedly, the degenerate Cope rearrangement of 1,3-divinyl-1,5-hexadiene is calculated to have a value for  $\Delta H^\ddagger$  very close to that of the 1,4 isomer. The values of, respectively,  $\Delta H^\ddagger = 29.9$  and 29.3 kcal/mol in Table 2 for these two degenerate Cope rearrangements are very close to the values of  $\Delta H^\ddagger = 29.7$  and 29.9 kcal/mol in Table 1 for the same reactions with cyano substituents at C(1) and C(3) and at C(1) and C(4).

The strongest stabilization by two vinyl substituents is predicted for the Cope rearrangement of 2,5-divinyl-1,5-hexadiene. The UB3LYP barrier height is lowered by 9.0 kcal/mol to  $\Delta H^\ddagger = 24.2$  kcal/mol, due to the cooperative effect of the two radical-stabilizing substituents on the nearly closed-shell (UB3LYP gives  $S^2 = 0.10$  at this geometry) transition structure. However, much lower in energy than this UB3LYP transition structure is the UB3LYP intermediate with  $C_i$  symmetry. As shown in Table 2, its UB3LYP energy is computed to be 10.4 kcal/mol below the UB3LYP energy of the transition structure.

The UB3LYP intermediate has  $S^2 = 1.01$ , so it is truly a diradical but a mixture of a pure triplet ( $S^2 = 2.0$ ) and a pure singlet ( $S^2 = 0.0$ ) state. Since the former is computed to be 1.2

(32) At the B3LYP geometry of the transition structure for the Cope rearrangement of 1,5-hexadiene, even with one cyano group at C(2) and one at C(5), a "singlet" UB3LYP calculation gives  $S^2 = 0$  and the same energy as a restricted B3LYP calculation.

kcal/mol higher in energy than the mixed state, the pure singlet diradical is predicted to be only 12.6 kcal/mol above the reactant.

Even if the enthalpy of the mixed ( $S^2 = 1.01$ ) spin state is used, the stabilization energy per vinyl substituent of the UB3LYP intermediate, relative to the B3LYP transition structure for the Cope rearrangement of unsubstituted 1,5-hexadiene, is computed to be  $(33.2 - 13.8)/2 = 9.7$  kcal/mol.<sup>33</sup> Comparison of this value with the UB3LYP stabilization energy of 7.2 kcal/mol, calculated for the Cope rearrangement of 2-vinyl-1,5-hexadiene, indicates a strong cooperative effect between the vinyl substituents in stabilizing the diradical intermediate. As shown by comparison of both the geometries of the mono- and divinyl intermediates in Figure 2 and the associated values of, respectively,  $S^2 = 0.94$  and 1.01, addition of the second vinyl substituent gives an intermediate with more cyclohexane-1,4-diyl diradical character. This allows each of the vinyl groups to provide greater stabilization for this intermediate than the single vinyl group furnishes for the monosubstituted intermediate.<sup>28</sup>

The geometries of the transition states, which lead to the diradical intermediates in the Cope rearrangements of 2,5-divinyl- and 2,5-dicyano-1,5-hexadiene, are similar. However, in the divinyl case the bond breaking/bond making process is not as advanced [ $C(3)-C(4) = 1.638$  Å and  $C(1)-C(6) = 1.934$  Å] as in the dicyano species [ $C(3)-C(4) = 1.683$  Å,  $C(1)-C(6) = 1.832$  Å]. Thus, the divinyl transition state is the earlier of the two, in accord with the lower energy of the diradical intermediate to which it leads.

We calculated the secondary kinetic isotope effects (SKIEs) for the Cope rearrangement of 1-vinyl-, 2-vinyl-, 1,4-divinyl-, and 2,5-divinyl-1,5-hexadiene. Experimental data are available for 2-phenyl-3-methyl- and 2,5-diphenyl-1,5-hexadiene. The computational and experimental results are summarized in Table 3. If a vinyl group is assumed to provide a good model for a phenyl substituent, then the calculated values for the SKIEs are in reasonable agreement with the experimental data. The largest deviation from experiment, for 3-methyl-2-phenyl, may be due to the lack of the 2-methyl group in the calculations.

We also performed calculations on the Cope rearrangements of 2,4-divinyl-1,5-hexadiene and 1,3,5-trivinyl-1,5-hexadiene. In these reactions the stabilizing effects of the vinyl groups at C(2) and C(5) are anticipated to be competitive with those at C(1), C(3), and C(4), rather than cooperative, since substitution of vinyl groups at these two different types of carbons each stabilizes a different diradical resonance contributor to the Cope transition structure (Figure 1).

Comparing the B3LYP values of  $\Delta H^\ddagger = 28.1$  kcal/mol for 3-vinyl with  $\Delta H^\ddagger = 27.3$  kcal/mol for 2,4-divinyl, the C(2) vinyl group is found to lower the activation enthalpy by only 0.8 kcal/mol. This lowering of  $\Delta H^\ddagger$  is considerably less than the 2.8 kcal/mol by which addition of a 2-vinyl group lowers the

B3LYP value of  $\Delta H^\ddagger$  for the Cope rearrangement of 1,5-hexadiene.

If, instead, comparison is made for the enthalpies of the UB3LYP intermediates in the Cope rearrangements of 2-vinyl- and 2,4-divinyl-1,5-hexadiene, relative to the reactants, Table 2 shows that the C(4) vinyl group in the reactant lowers the relative enthalpy of the latter intermediate by only 1.1 kcal/mol. This is also considerably less than the 5.1 kcal/mol lowering of  $\Delta H^\ddagger$  computed for Cope rearrangement of 1,5-hexadiene by addition of a vinyl group to C(3).

As shown in Table 2, the addition of a vinyl group at C(5) is predicted actually to raise by 0.5 kcal/mol the B3LYP value of  $\Delta H^\ddagger$  for the Cope rearrangement of 1,3-divinyl-1,5-hexadiene. B3LYP thus predicts that conjugation of the C(5) vinyl group with the double bond at this carbon in the reactant provides slightly more energy lowering than any radical-stabilizing effect that the C(5) vinyl group has in the transition structure.

An alternative comparison, the effect of vinyl substitution at C(1) and C(3) on the UB3LYP relative energy of the diradical stabilized by a C(5) vinyl group [i.e., the diradical formed from 2-vinyl-1,5-hexadiene] shows that the two additional vinyl groups substantially raise the energy of this diradical, relative to the reactant. The UB3LYP calculation on the trivinyl intermediate finds a diradicaloid ( $S^2 = 0.93$ ) local minimum, with an enthalpy that is 1.8 kcal/mol higher than the B3LYP transition structure. The diradicaloid intermediate resembles a cyclohexane-1,4-diyl, for which vinyl groups at C(1) and C(3) in the reactant can provide no allylic stabilization.

In contrast, since the C(1) vinyl group in the reactant is conjugated with the double bond at this carbon, it does stabilize the reactant. Addition of vinyl groups at C(1) and C(3) of "5"-vinyl-1,5-hexadiene is actually computed by UB3LYP to provide 6.2 kcal/mol more stabilization for the reactant than for the cyclohexane-1,4-diyl formed from it.

Addition of vinyl substituents at C(1) and C(3) is predicted to have a negligible effect on the relative energy of the B3LYP transition structure for the Cope rearrangement of "5"-vinyl-1,5-hexadiene. Table 2 shows that the B3LYP values of  $\Delta H^\ddagger$  for the Cope rearrangements of 2-vinyl and 1,3,5-trivinyl-1,5-hexadiene are computed to be essentially the same. If the energies of either of the transition structures that leads to the UB3LYP intermediate in the Cope rearrangement of 2-vinyl-1,5-hexadiene are used, addition of the two vinyl substituents is actually computed to raise  $\Delta H^\ddagger$  slightly.

## Conclusions

As shown in Figure 1, there are two very different diradical resonance contributors to the transition state for the Cope rearrangement of 1,5-hexadiene. Substituents at C(1), C(3), C(4), and C(6) in the reactant can stabilize one of these structures, and substituents at C(2) and C(5) can stabilize the other. Both the present calculations and previous experiments<sup>5-8</sup> confirm that radical-stabilizing substituents at either one or the other of the two different types of carbons in Figure 1 do lower the energy of the transition structure, relative to the reactant. Substituents at C(2) and C(5) have a much larger stabilizing effect than substituents at the other four carbons of 1,5-hexadiene, suggesting that the transition state for the parent Cope rearrangement resembles cyclohexane-1,4-diyl more than it resembles two weakly interacting allyl radicals. This inference is consistent with estimates of the relative energies of these two diradicals.

A fundamental question about the transition structure for the Cope rearrangement is whether it retains the same size contribu-

(33) Another, perhaps more meaningful comparison, would be of the stabilization per vinyl substituent of cyclohexane-1,4-diyls, lacking any through-bond interactions between the two radical centers, relative to 1,5-hexadiene. If such species are modeled by the triplet states of the diradicals, then the relevant energies are the 41.0 kcal/mol higher energy of triplet cyclohexane-1,4-diyl, relative to 1,5-hexadiene, and the 15.0 kcal/mol higher energy of triplet 1,4-divinylcyclohexane-1,4-diyl, relative to 2,5-divinyl-1,5-hexadiene. The resulting net stabilization energy of 13.0 kcal/mol provided by each vinyl group is comprised of the stabilization of triplet cyclohexane-1,4-diyl upon converting the secondary radical centers into tertiary, allylic radical centers, minus the stabilization of 1,5-hexadiene by addition of *s-trans* vinyl groups at C(2) and C(5), where they are in conjugation with the double bonds at these two carbons. By using experimental heats of formation, Doering and Wang estimate a net stabilization per vinyl group of 12.0 kcal/mol.<sup>9b</sup>



tions from these two diradicals, regardless of substituents, or whether the sizes of these contributions can be altered by substituents. In the former type of transition state, which Doering has termed centaurial,<sup>9</sup> substituent effects would be additive; in the latter, which Doering has termed chameleonic, substituent effects could be either cooperative or competitive, depending on the carbons to which radical-stabilizing substituents were attached.

A number of different types of evidence indicate that the transition structure for the Cope rearrangement is chameleonic, capable of responding in different ways to the substitution of radical-stabilizing substituents at the two different types of carbons. This evidence includes the following: (a) the cooperativity, calculated for substituents at C(2) and C(5) and at C(1), C(3), C(4), and C(6), and found experimentally for phenyl groups at these two sets of carbons,<sup>5a,5c</sup> (b) the competition between substituents at C(2) and C(4) and at C(1), C(3), and C(5), (c) the large changes in geometry with substituents that we compute for the transition structures, and (d) the variations, both calculated and found,<sup>8</sup> in the secondary kinetic isotope effects for bond making and bond breaking with substituents. In particular, the geometries computed here provide strong support to the conclusions made by Gajewski on the basis of KIEs,<sup>8</sup> that the transition state is variable and altered by substitution.

In the 2,4-disubstituted-1,5-hexadienes, the stabilization of a different type of diradical resonance contributor by each of the substituents clearly creates a confused chameleon. Unable to adapt by the conflicting demands of the two substituents to become more like two allyl radicals and, simultaneously, also more like cyclohexane-1,4-diyl, the transition structure winds up remaining very much like that for the parent Cope rearrangement. Consequently, the net stabilization of the transition structure for the Cope rearrangement of a 2,4-disubstituted 1,5-hexadiene is expected to be somewhat less than the stabilization provided by each of the substituents individually.<sup>29</sup> This expectation is confirmed by the results of our B3LYP calculations.

In the 1,3,5-trisubstituted-1,5-hexadienes, the substituents at C(1) and C(3) both stabilize the bis-allyl resonance contributor. The single substituent at C(5) is insufficient to induce the transition structure to have much resemblance to cyclohexane-1,4-diyl. Consequently, addition of a C(5) substituent to a 1,3-disubstituted 1,5-hexadiene provides a small fraction of the stabilization that the same substituent provides for the Cope rearrangement of the unsubstituted parent. B3LYP calculations on 1,3,5-tricyano- and 1,3,5-trivinyl-1,5-hexadienes predict that

substituents at C(1) and C(3) can actually raise the activation enthalpy for Cope rearrangement of the trisubstituted diene slightly above that for the diene with a single radical-stabilizing substituent at C(2).

Recent experiments on the Cope rearrangements of 1,3,5-triphenyl<sup>9b</sup> and 1,3-dicyano-5-phenyl-1,5-hexadiene<sup>34</sup> find that the effects of the substituents at C(1) and C(3) and the phenyl group at C(5) deviate from additivity in the direction predicted by our B3LYP calculations. However, although the substituent effects measured by them are clearly competitive in both compounds, the substituents at C(1) and C(3) do effect some lowering of  $\Delta H^\ddagger$ , albeit by only about half as much as when these these groups are substituted at C(1) and C(3) of 1,5-hexadiene. Calculations on the compounds actually studied by Doering and Wang will answer the question of whether this small difference between their experimental and our computational results is due to a difference between the phenyl substituents in the 1,5-hexadienes on which they made their kinetic measurements and the cyano and vinyl substituents in the 1,5-hexadienes on which we performed our calculations.

Both theoretical and experimental studies show that substituents not only stabilize the Cope rearrangement transition state but also alter the geometry to maximize this stabilization. Multiple substituents may work together to alter the nature of the transition state or may compete and give a compromise structure. The results are closest to a chameleon adapting as a single organism to the environment represented by the substituents.

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**Supporting Information Available:** Energies and Cartesian coordinates of stationary points. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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