

A Simple Mathematical Model for the Cooperative and Competitive Substituent Effects Found in the Cope Rearrangements of Phenyl-Substituted 1,5-Hexadienes

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Abstract: A simple mathematical model is derived for the dependence of the substituent effects in the Cope rearrangements of substituted 1,5-hexadienes on the interallylic bond lengths in the transition structures. The model qualitatively reproduces the cooperative substituent effects that have been found in the Cope rearrangements of 2,5-diphenyl- and 1,3,4,6-tetraphenyl-1,5-hexadiene and the competitive substituent effects that have been found in the Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene. B3LYP/6-31G* calculations have been performed in order to assess more quantitatively the performance of the model, and the results of these calculations are discussed.

The effects of substituents on ΔH^\ddagger for the Cope rearrangement¹ can be either cooperative or competitive.² For example, as shown in Table 1, a single phenyl substituent at C2 lowers ΔH^\ddagger for the Cope rearrangement of 1,5-hexadiene³ by 4.2 kcal/mol,⁴ but a second phenyl group, attached to C5, lowers the experimental enthalpy of activation by 8.0 kcal/mol, nearly twice as much.^{4,5} Clearly, there is a strong cooperative effect between phenyl substituents at C2 and C5 on lowering the barrier height.

Phenyl groups at C1, C3, C4, and C6 of 1,5-hexadiene also give rise to a strongly cooperative substituent effect. When one phenyl group is attached to C1 and another to C3, the barrier to the Cope rearrangement is decreased by 3.0 kcal/mol from that for the unsubstituted molecule.⁶ If the phenyl substituent effects on the Cope rearrangement were additive, augmentation of the phenyl groups at C1 and C3 by another pair at C4 and C6 would be anticipated to lower ΔH^\ddagger by another 3.0 kcal/mol. However, the measured effect of the additional pair of phenyl groups is three times larger, lowering ΔH^\ddagger for the Cope rearrangement by an additional 9.2 kcal/mol.⁷ As in the case of phenyl substituents at C2 and C5, the effect of phenyl substituents at C1, C3, C4, and C6 of 1,5-hexadiene is obviously cooperative.

In contrast to the cooperative substituent effects described above, placement of phenyl groups at C1, C3, and C5 of 1,5-hexadiene results in a competitive substituent effect.⁶ As already noted, a single phenyl group at C2(C5) lowers ΔH^\ddagger by 4.2 kcal/mol, and phenyl groups at C1 and C3 lower ΔH^\ddagger by 3.0 kcal/mol. However, the simultaneous presence of phenyl groups at C1, C3, and C5 lowers ΔH^\ddagger by 5.7 kcal/mol, 1.5 kcal/mol *less* than the 7.2 kcal/mol expected on the basis of substituent effect additivity.

Table 1 shows that B3LYP/6-31G* calculations give activation enthalpies for the Cope rearrangement of 1,5-hexadiene⁸ and of phenyl-substituted derivatives^{2b} that are in very good agreement with experiment. This agreement lends credibility to the calculated dependence in Table 1 of the interallylic distance, R , in Cope transition structures (TSs) on the number and placement of radical stabilizing, phenyl substituents. Phenyl groups at C2 and C5, which can stabilize diradical structure **A** in Figure 1, are predicted to shorten R , whereas phenyls at C1, C3, C4, and C6, which stabilize diradical structure **C**, are predicted to lengthen R .

Direct experimental evidence that the Cope rearrangement has a variable TS, in which the bond lengths change with the presence and placement of radical-stabilizing substituents, comes from the secondary kinetic isotope effects, measured by Gajewski and Conrad.⁹ Doering has coined the term “chameleonic” to describe the Cope TS and the ability of

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Table 1. Effect of Phenyl Substituents on the Calculated and Experimental Activation Enthalpies (kcal/mol) for the Cope Rearrangements of Phenyl Substituted 1,5-Hexadienes and on the Differences (Å) between the Calculated Interallylic Distance, R , in Each TS and R_0 in the TS for Unsubstituted 1,5-Hexadiene

substituents	method ^a	$\Delta\Delta H^\ddagger$ (calc.)	$\Delta\Delta H^\ddagger$ (exp.)	$R - R_0^b$
none	B3LYP	0 ^c	0 ^d	0 ^e
2-phenyl	B3LYP	-2.8		-0.128, -0.144
2-phenyl	UB3LYP	-2.9		-0.188, -0.265
2-phenyl	UB3LYP	-4.0 ^f	-4.2 ^g	-0.366
1,3-diphenyl	B3LYP	-3.0	-3.0 ^h	0.253
2,5-diphenyl	B3LYP	-8.1		-0.171, -0.285
2,5-diphenyl	UB3LYP	-8.4		-0.126, -0.298
2,5-diphenyl	UB3LYP	-11.9 ^f	-12.2 ^{g,i}	-0.389
1,3,5-triphenyl	B3LYP	-4.0	-5.7 ^h	0.148, 0.141
1,3,4,6-tetraphenyl	B3LYP	-14.1	-12.2 ^j	0.684

^a The 6-31G* basis set was used for all of the calculations in this table. ^b Difference for, respectively, the forming bond in the TS and the breaking bond, in the TS. Just one difference between the interallylic bond lengths R and R_0 is given for those TSs that have a plane of symmetry. ^c Enthalpy relative to $\Delta H^\ddagger = 33.2$ kcal/mol. ^d Enthalpy relative to the value of $\Delta H^\ddagger = 33.5$ kcal/mol, reported in ref 3. ^e $R_0 = 1.965$ Å. ^f Enthalpy, relative to the reactant, of the diradicaloid intermediate. ^g Reference 4. ^h Reference 6. ⁱ Reference 5. ^j Reference 7.

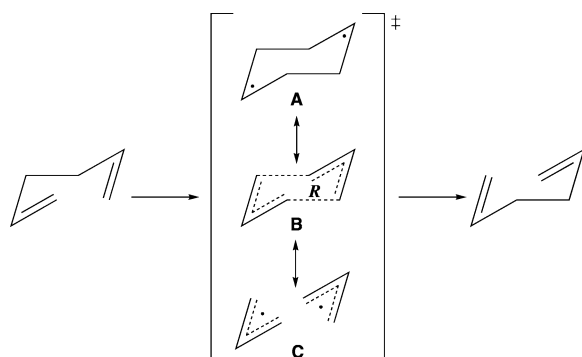


Figure 1. Depiction of possible TSs for the Cope rearrangement. In the two diradical extremes bond making either precedes (A) or lags behind (C) bond breaking, while in TS B bond making and bond breaking occur synchronously. The interallylic distance (R) is expected to increase in going from TS A to TS C.

the bond lengths in it to alter in response to radical stabilizing substituents.⁵

In this paper we present a simple mathematical model for the dependence of the energy of the Cope TS on the presence and placement of radical stabilizing substituents. This model is helpful for analyzing how the chameleonic character of the Cope TS gives rise to the cooperative and competitive substituent effects that are evident in the values of $\Delta\Delta H^\ddagger$ in Table 1.

A Simple Mathematical Model for the Effects of Substituents

The optimal value of R , the interallylic distance in the TS for the Cope rearrangement of a substituted 1,5-hexadiene, can be viewed as a compromise between maximizing the

magnitude of the substituent stabilization energy of the TS (ΔE_{subst})¹⁰ and minimizing the energetic cost (ΔE_{dist}) of distorting the interallylic bond lengths in the TS from the optimal value of R_0 ($= 1.965$ Å at the B3LYP/6-31G* level)⁸ for the Cope rearrangement of unsubstituted 1,5-hexadiene. Thus, the optimal value of R maximizes the magnitude of the net TS stabilization energy (ΔE_{stab}),¹⁰ which is the sum of ΔE_{dist} and ΔE_{subst} .

$$\Delta E_{\text{stab}} = \Delta E_{\text{dist}} + \Delta E_{\text{subst}} \quad (1)$$

The simplest possible mathematical model for finding this value of R assumes that the energy of the C_{2h} structure in the chair Cope rearrangement of unsubstituted 1,5-hexadiene increases quadratically with the difference between R and R_0 . The energy required to distort the interallylic distance from R_0 is then given by

$$\Delta E_{\text{dist}} = k_{\text{dist}}(R - R_0)^2/2 \quad (2)$$

A mathematical expression for ΔE_{subst} can be derived by considering the effect of phenyl substituents at, for instance, C1 and C3 on the energy of the high-symmetry chair structure. Since radical stabilizing groups at C1 and C3 lower the energy of structure C in Figure 1, they will have their greatest effect at values of $R > R_0$, where the wave function becomes increasingly like that for two allyl radicals. Conversely, the energy lowering provided by the phenyl substituents at C1 and C3 will decrease in size with decreasing values of R . Therefore, the leading term in the expression for the effect of the interallylic distance on the stabilization of the high-symmetry chair structure by phenyl groups at C1 and C3 must be linear in R

$$\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0 = -k_{\text{subst}}(R - R_0) \quad (3)$$

where $\Delta E_{\text{subst}}^0$ is the stabilization provided by the phenyl substituents at R_0 , and k_{subst} is positive.

Thus, at least for values of R around R_0 , the dependence on R of the energy of the high-symmetry species in the chair Cope rearrangement of 1,3-diphenyl-1,5-hexadiene can be written as

$$\begin{aligned} \Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0 &= \Delta E_{\text{dist}} + \Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0 \\ &= k_{\text{dist}}(R - R_0)^2/2 - k_{\text{subst}}(R - R_0) \end{aligned} \quad (4)$$

where $\Delta E_{\text{stab}}^0 = \Delta E_{\text{subst}}^0$ is the substituent stabilization energy at R_0 .

Differentiating eq 4 with respect to R , the high-symmetry chair structure of minimum energy (i.e. the TS) for the Cope rearrangement of 1,3-diphenyl-1,5-hexadiene is predicted to occur at

$$R - R_0 = k_{\text{subst}}/k_{\text{dist}} \quad (5)$$

Substituting the expression for $R - R_0$ in eq 5 back into eq 4, the energy difference between the TS and the chair

geometry at $R = R_0$ is given by

$$\begin{aligned}\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0 &= \Delta E_{\text{dist}} + \Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0 \\ &= k_{\text{dist}}(k_{\text{subst}}/k_{\text{dist}})^2/2 - k_{\text{subst}}(k_{\text{subst}}/k_{\text{dist}}) \\ &= k_{\text{subst}}^2/2k_{\text{dist}} - k_{\text{subst}}^2/k_{\text{dist}} \\ &= -k_{\text{subst}}^2/2k_{\text{dist}}\end{aligned}\quad (6)$$

Eq 6 predicts that at the optimal value of R

$$\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0 = -\Delta E_{\text{dist}} = (\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0)/2 \quad (7)$$

This relationship between ΔE_{dist} and $(\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0)/2$ is analogous to that in the virial theorem,^{11a} with ΔE_{dist} and $(\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0)$ in eq 7 corresponding, respectively, to kinetic and potential energy.

If a second pair of phenyl substituents is added to 1,3-diphenyl-1,5-hexadiene at C4 and C6, the second term in eq 4 is multiplied by a factor of 2. The TS for the Cope rearrangement is then predicted to have an interallylic distance, R , such that

$$R - R_0 = 2k_{\text{subst}}/k_{\text{dist}} \quad (8)$$

Upon increasing R from R_0 to $R_0 + 2k_{\text{subst}}/k_{\text{dist}}$, the energy of the C_{2h} structure for the Cope rearrangement of 1,3,4,6-tetraphenyl-1,5-hexadiene is predicted to decrease by

$$\begin{aligned}\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0 &= k_{\text{dist}}(2k_{\text{subst}}/k_{\text{dist}})^2/2 - 2k_{\text{subst}}(2k_{\text{subst}}/k_{\text{dist}}) \\ &= -2k_{\text{subst}}^2/k_{\text{dist}}\end{aligned}\quad (9)$$

The net stabilization energy in eq 9 is four times larger in magnitude than that in eq 6 for the chair TS for the Cope rearrangement of 1,3-diphenyl-1,5-hexadiene. Thus, if ΔE_{stab}^0 in eqs 6 and 9 is small, the simple mathematical model in eq 4 correctly predicts the existence of the cooperative substituent effect in 1,3,4,6-tetraphenyl-1,5-hexadiene, whereby the four phenyl substituents lower ΔH^\ddagger for the Cope rearrangement by four times more than the pair of phenyl substituents in 1,3-diphenyl-1,5-hexadiene.⁷

The origin of the cooperative effect, predicted by the model, can be easily seen in eq 9. Doubling the number of phenyl substituents doubles the number of radical stabilizing groups that are positioned to stabilize structure **C** in Figure 1. In addition, doubling the number of phenyl substituents is predicted by eq 8 to make the difference between R and R_0 in the TS twice as large for 1,3,4,6-tetraphenyl-1,5-hexadiene (eq 8) as for 1,3-diphenyl-1,5-hexadiene (eq 5), thus doubling the stabilization of the TS that is provided by each phenyl group. Consequently, adding phenyl substituents to C4 and C6 of 1,3-diphenyl-1,5-hexadiene is predicted to quadruple $\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0$.

The doubling of $R - R_0$ in the TS for the Cope rearrangement of 1,3,4,6-tetraphenyl-1,5-hexadiene is also predicted to quadruple ΔE_{dist} , which depends quadratically on $R - R_0$. Since doubling the number of phenyl substituents quadruples both $\Delta E_{\text{subst}}^R - \Delta E_{\text{subst}}^0$ and ΔE_{dist} , $\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0$ in eq 9 for the Cope rearrangement of 1,3,4,6-

tetraphenyl-1,5-hexadiene is four times larger than $\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0$ in eq 6 for the Cope rearrangement of 1,3-diphenyl-1,5-hexadiene.

Although the simple mathematical model, embodied in eq 4, apparently predicts the size of the cooperative substituent effect in the Cope rearrangement of 1,3,4,6-tetraphenyl-1,5-hexadiene^{2b,7} the model fails to predict correctly the calculated value of R in the TS for this reaction. The model predicts that $R - R_0$ in the TS for the Cope rearrangement of 1,3,4,6-tetraphenyl-1,5-hexadiene (eq 8) should be twice as large as $R - R_0$ in the TS for the Cope rearrangement of 1,3-diphenyl-1,5-hexadiene (eq 5). However, Table 1 shows the B3LYP/6-31G* ratio of $R - R_0$ values actually is 0.684/0.253 = 2.70, 35% higher than expected.

This failure of the model could reside in the assumption that ΔE_{dist} is quadratic over the difference of nearly 0.7 Å between R_0 and R in the TS for the Cope rearrangement of 1,3,4,6-tetraphenyl-1,5-hexadiene. However, another possibility is that relief of steric repulsion between the pairs of phenyl groups at C1–C6 and C3–C4 in the C_{2h} chair TS geometry has the effect of making k_{subst} for 1,3,4,6-tetraphenyl-1,5-hexadiene more than a factor of 2 larger than k_{subst} for 1,3-diphenyl-1,5-hexadiene. Results of calculations, described in the next section, indicate that both effects contribute to the ratio of $R - R_0$ values in the TSs for the Cope rearrangements of these two dienes being 35% higher than expected.

The simple model in eq 4 also fails to predict correctly the ratio of $R - R_0$ values in the TSs for the Cope rearrangements of 2-phenyl- and 2,5-diphenyl-1,5-hexadiene. Phenyl groups at C2 and C5 provide stabilization for structure **A** in Figure 1. Consequently, they have their greatest stabilizing effect at values of $R < R_0$, where the wave function in the TS becomes increasingly like that for cyclohexane-1,4-diyl. As a result, the sign of the right-hand side of eq 3 is positive for 2-phenyl- and 2,5-diphenyl-1,5-hexadiene. Therefore, for the Cope rearrangement of 2-phenyl-1,5-hexadiene, eq 3 must be replaced by

$$\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0 = k'_{\text{subst}}(R - R_0) \quad (10)$$

where, like k_{subst} , $k'_{\text{subst}} > 0$.

The second phenyl group in 2,5-diphenyl-1,5-hexadiene makes the expression for $\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0$ a factor of 2 greater than the expression in eq 10 for 2-phenyl-1,5-hexadiene. Thus, replacing k_{subst} in eqs 4 and 8 by k'_{subst} , the model again predicts a ratio of 2.0 for $R - R_0$ in the Cope TS for these two dienes. However, the UB3LYP/6-31G* ratio is only $-0.389/-0.366 = 1.06$.

The problem here is certainly the assumption in eq 2 that ΔE_{dist} is quadratic. If the ratio of $R - R_0$ values really were 2.0, the UB3LYP value of $R = 1.599$ Å in the TS for the Cope rearrangement of 2-phenyl-1,5-hexadiene would give $R = 1.233$ Å in the TS for the Cope rearrangement of 2,5-diphenyl-1,5-hexadiene. This predicted bond length is about 0.3 Å shorter than the typical length of a C–C single bond.

If a Morse, rather than a quadratic potential is used, the energy for compressing a C–C single bond to a length substantially below 1.54 Å increases exponentially with

decreasing R .^{11b} Consequently, the assumption of a quadratic potential for ΔE_{dist} in eq 2 greatly underestimates the energetic cost of decreasing R in the TS for the Cope rearrangement of 2,5-diphenyl-1,5-hexadiene below the value of $R = 1.599 \text{ \AA}$ in the TS for the Cope rearrangement of 2-phenyl-1,5-hexadiene.

Despite the failure of the simple model in eq 4 to predict the size of R in the TS for the Cope rearrangement of 2,5-diphenyl-1,5-hexadiene, the model does predict the existence of the cooperative effect of the pair of phenyl groups on the enthalpy of activation.^{4,5} Assuming for 2-phenyl-1,5-hexadiene that

$$R - R_0 = -k'_{\text{subst}}/k_{\text{dist}} \quad (11)$$

then

$$\begin{aligned} \Delta E_{\text{stab}} - \Delta E^0_{\text{stab}} &= k_{\text{dist}}(-k'_{\text{subst}}/k_{\text{dist}})^2/2 + k'_{\text{subst}}(-k'_{\text{subst}}/k_{\text{dist}}) \\ &= -k'_{\text{subst}}{}^2/2k_{\text{dist}} \end{aligned} \quad (12)$$

Since UB3LYP/6-31G* calculations find that R is nearly the same in the TSs for the Cope rearrangements of 2-phenyl- and 2,5-diphenyl-1,5-hexadiene, ΔE_{dist} is approximately the same for both TSs. However, due to the presence of two phenyl groups in 2,5-diphenyl-1,5-hexadiene, the term for $\Delta E_{\text{subst}} - \Delta E^0_{\text{subst}}$ is a factor of 2 larger in the TS for the latter reaction than in the TS for the former. Therefore, the expression for $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}}$ in the latter reaction is

$$\begin{aligned} \Delta E_{\text{stab}} - \Delta E^0_{\text{stab}} &= k_{\text{dist}}(-k'_{\text{subst}}/k_{\text{dist}})^2/2 \\ &\quad + 2k'_{\text{subst}}(-k'_{\text{subst}}/k_{\text{dist}}) \\ &= -3k'_{\text{subst}}{}^2/2k_{\text{dist}} \end{aligned} \quad (13)$$

Comparison of eq 13 with eq 12 results in the prediction that $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}}$ should be a factor of 3 larger for the Cope rearrangement of 2,5-diphenyl-1,5-hexadiene than for the Cope rearrangement of 2-phenyl-1,5-hexadiene. Assuming again that ΔE^0_{stab} is small, this prediction is consistent with both the experimental and UB3LYP values of $\Delta\Delta H^\ddagger$ in Table 1.

The mathematical reason for the prediction, that $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}}$ should be a factor of 3 larger for the Cope rearrangement of 2,5-diphenyl-1,5-hexadiene than for the Cope rearrangement of 2-phenyl-1,5-hexadiene, is that in eq 12 the first term, which gives ΔE_{dist} , cancels half of the second term, which gives $\Delta E_{\text{subst}} - \Delta E^0_{\text{subst}}$. In eq 13 the term for ΔE_{dist} is the same as in eq 12; but the term for $\Delta E_{\text{subst}} - \Delta E^0_{\text{subst}}$ is twice as large, which makes the difference between these two terms three times larger in eq 13 than in eq 12.

In physical terms, the second phenyl group in 2,5-diphenyl-1,5-hexadiene provides the same amount of TS stabilization as the lone phenyl group in 2-phenyl-1,5-hexadiene. However, because the interallylic distances, R , in the two TSs are nearly the same, the stabilization of the TS by the second phenyl group comes without the energetic cost of $(\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}})/2$, paid by the first phenyl group, for distorting R from R_0 in the TS for the Cope rearrangement of unsubstituted 1,5-hexadiene.

The simple mathematical model in eq 4 also accounts for the competitive phenyl substituent effects, computed for^{2b} and found in⁵ the Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene. Combining eqs 3 and 10 gives the expression for $\Delta E_{\text{subst}} - \Delta E^0_{\text{subst}}$ in the TS for the Cope rearrangement of this compound as

$$\Delta E_{\text{subst}} - \Delta E^0_{\text{subst}} = (k'_{\text{subst}} - k_{\text{subst}})(R - R_0) \quad (14)$$

Substituting this expression for $\Delta E_{\text{subst}} - \Delta E^0_{\text{subst}}$ into eq 4 and maximizing the magnitude of ΔE_{stab} gives

$$\begin{aligned} R - R_0 &= (k_{\text{subst}} - k'_{\text{subst}})/k_{\text{dist}} \\ &= k_{\text{subst}}/k_{\text{dist}} - k'_{\text{subst}}/k_{\text{dist}} \end{aligned} \quad (15)$$

According to eq 15, $R - R_0$ in the TS for the Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene should be equal to the algebraic sum of $R - R_0$ in the TS for 1,3-diphenyl-1,5-hexadiene in eq 5 and $R - R_0$ in the TS for 2-phenyl-1,5-hexadiene in eq 11. Using the B3LYP results in Table 1,¹² $R - R_0 = 2.110 - 1.965 = 0.145 \text{ \AA}$ is, indeed, reasonably close to the sum of $0.253 - 0.136 = 0.117 \text{ \AA}$.

Upon increasing the interallylic distance from $R_0 = 1.965 \text{ \AA}$ to $R = R_0 + (k_{\text{subst}} - k'_{\text{subst}})k_{\text{dist}}$, the net stabilization of the TS for the Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene is given by

$$\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}} = -(k_{\text{subst}} - k'_{\text{subst}})^2/2k_{\text{dist}} \quad (16)$$

$\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}}$ in eq 16 is smaller in size than the sum of the net stabilization energies of the TSs for the Cope rearrangements of 1,3-diphenyl-1,5-hexadiene (eq 6) and 2-phenyl-1,5-hexadiene (eq 12) by

$$\begin{aligned} -(k_{\text{subst}} - k'_{\text{subst}})^2/2k_{\text{dist}} + k'_{\text{subst}}{}^2/2k_{\text{dist}} \\ + k_{\text{subst}}{}^2/2k_{\text{dist}} = k_{\text{subst}}k'_{\text{subst}}/k_{\text{dist}} \end{aligned} \quad (17)$$

Thus, eq 17 predicts the existence of the competitive substituent effect that is computed for and found in the Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene.

In physical terms the existence of this effect is due to the fact that phenyls at C1 and C3 provide the most stabilization of the high-symmetry chair structure for the Cope rearrangement at $R > R_0$, whereas a phenyl group at C5 provides the most stabilization at $R < R_0$. At the compromise value of R in the TS for the Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene, the phenyl groups at C1 and C3 provide less stabilization than they do in the TS for the Cope rearrangement of 1,3-diphenyl-1,5-hexadiene, and the phenyl group at C5 provides less stabilization than it does in the TS for the Cope rearrangement of 2-phenyl-1,5-hexadiene. This is the origin of the competitive substituent effect in the Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene.

Additional Computational Tests of the Mathematical Model

The simple mathematical model in eq 4 predicts successfully the existence of the cooperative and competitive phenyl substituent effects, seen in Table 1, but only if the differences between $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}}$ values, derived from the model, can

Table 2. Dissection of the Effects of Phenyl Substituents on Lowering the Energy of the TS for the Chair Cope Rearrangement of 1,5-Hexadiene^a

substituents	$R - R_0$ (Å)	ΔE_{dist}	$\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0$	$\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0$	ΔE_{stab}^0	ΔE_{stab}
2-phenyl ^c	-0.366	3.3	-6.2	-2.9	-1.7	-4.6
2-phenyl ^d	0.145	0.7	1.4	2.1	-1.7	0.4
2,5-diphenyl ^c	-0.389	3.7	-12.9	-9.2	-3.7	-12.9
1,3-diphenyl	0.253	2.0	-4.0	-2.0	-0.7	-2.7
1,3-diphenyl ^d	0.145	0.7	-2.4	-1.7	-0.7	-2.4
1,3,5-triphenyl	0.145	0.7	-1.1	-0.4	-2.8	-3.2
1,3,4,6-tetraphenyl	0.684	12.0	-23.7	-11.7	-1.4	-13.1
1,3,4,6-tetraphenyl ^e	0.253	2.0	-9.3	-7.3	-1.4	-8.7

^a Energies (kcal/mol) were obtained from B3LYP/6-31G* calculations in the manner described in the text. ^b $\Delta E_{\text{subst}}^0 = \Delta E_{\text{stab}}^0$. ^c Values are from UB3LYP calculations. ^d Calculations performed at, $R = 2.110$ Å, the interallylic bond distance in the TS for Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene. ^e Calculations performed at $R = 2.218$, the interallylic bond distance in the TS for Cope rearrangement of 1,3-diphenyl-1,5-hexadiene.

be equated with the $\Delta\Delta H^\ddagger$ values in Table 1. The apparent success of the model thus suggests that substituent-induced lengthening or shortening of the interallylic bond lengths must be the dominant mode by which phenyl substituents stabilize the Cope TS and thus lower the enthalpy of activation for the Cope rearrangement.

$\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0 \approx \Delta E_{\text{stab}}$ in eqs 6, 9, 12, 13, and 16 requires that, at least for phenyl substituents, $\Delta E_{\text{stab}} \gg \Delta E_{\text{stab}}^0$. This means that the net substituent stabilization energies must be much larger at the TS geometries than at R_0 , the interallylic bond length in the TS for the Cope rearrangement of unsubstituted 1,5-hexadiene.

To test whether ΔE_{stab} is, in fact, much larger than ΔE_{stab}^0 , we carried out electronic structure calculations. We also computed ΔE_{dist} , the difference between the energy of the Cope TS for unsubstituted 1,5-hexadiene at R and at R_0 . From the difference between $(\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0)$ and ΔE_{dist} we were able, using eq 4, to obtain $(\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0)$. We were thus able to test the predicted virial-theorem-like relationship in eq 7 between $\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0$, ΔE_{dist} , and $\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0$.

As in our previous studies of Cope substituent effects,² the electronic structure calculations utilized Becke's 3-parameter functional,¹³ in conjunction with the correlation functional of Lee, Yang, and Parr¹⁴ and the 6-31G* basis set.¹⁵ The B3LYP/6-31G* calculations were performed with the Gaussian 98 suite of programs.¹⁶

The B3LYP values of ΔE_{dist} , $\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0$, $\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0$, $\Delta E_{\text{stab}}^0 (= \Delta E_{\text{subst}}^0)$, and ΔE_{stab} are given in Table 2 for the Cope rearrangements of 2-phenyl, 1,3- and 2,5-diphenyl-, 1,3,5-triphenyl-, and 1,3,4,6-tetraphenyl-1,5-hexadiene. Because the values of ΔE_{stab} in Table 2 are uncorrected for differences in zero-point energies or integrated heat capacities, these values are similar to but not exactly the same as the corresponding B3LYP values of $\Delta\Delta H^\ddagger$ in Table 1.

A number of observations can be made from inspection of Table 2. First, at R_0 , the interallylic bond length in the TS for the parent Cope rearrangement, a phenyl group at C2 provides $\Delta E_{\text{stab}}^0 = 1.7$ kcal/mol of stabilization, which is slightly more than twice the stabilization furnished by a pair of phenyl groups at C1 and C3. The larger amount of stabilization provided by a single phenyl group at C2 supports the conjecture, based on the relative enthalpies of the two diradical extremes in Figure 1,^{2a} that the TS for the Cope rearrangement of unsubstituted 1,5-hexadiene resembles cyclohexane-1,4-diyl (A) more than two allyl radicals (C).^{1,3}

The values of ΔE_{stab}^0 for 2,5-diphenyl, 1,3,5-triphenyl, and 1,3,4,6-tetraphenyl substituents are each close to being the sum of the appropriate ΔE_{stab}^0 values for 2-phenyl and 1,3-diphenyl substituents. It is noteworthy that, even for the phenyl substituents in 2-phenyl- and 2,5-diphenyl-1,5-hexadiene, ΔE_{stab}^0 is only about one-third to one-quarter, respectively, of ΔE_{stab} , the total net lowering by the substituents of the energy of the Cope TS, relative to the energy of the reactants.

The fact that substituents provide a comparatively small amount of stabilization at $R_0 = 1.965$ Å was first found for cyano, rather than for phenyl substituents.^{2a} This finding is consistent with the results of Staroverov and Davidson. They used local spin analysis to show that not only does the TS for the parent Cope rearrangement have little diradical character^{17a} but also that, at the geometry of this TS, radical stabilizing substituents do little to enhance the diradical character of the wave function.^{17b}

Another observation, which can be made from the results in Table 2, is that at the optimal values of R for the intermediate in the Cope rearrangement of 2-phenyl-1,5-hexadiene and for the TSs in the Cope rearrangements of 1,3-diphenyl- and 1,3,4,6-tetraphenyl-1,5-hexadiene, $\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0 \approx -\Delta E_{\text{dist}} \approx (\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0)/2$. These are the relationships predicted by eq 6 under the assumption that ΔE_{dist} is quadratic in $R - R_0$. The least-squares plot in Figure 2 shows how well the equality between $\Delta E_{\text{stab}} - \Delta E_{\text{stab}}^0$ and $-\Delta E_{\text{dist}}$ holds for the Cope rearrangements of these three dienes.

As discussed in the previous section, at small values of R , ΔE_{dist} is not quadratic in $R - R_0$, and the intermediates in the Cope rearrangements of 2-phenyl- and 2,5-diphenyl-1,5-hexadiene have UB3LYP values of R that differ by only 0.023 Å. Because the value of R in the two intermediates is nearly the same, the value of $\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0 = -12.9$ kcal/mol for the UB3LYP diradical intermediate in the Cope rearrangement of 2,5-diphenyl-1,5-hexadiene is only about a factor of 2 larger than $\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0 = -6.2$ kcal/mol for the UB3LYP diradical intermediate in the Cope rearrangement of 2-phenyl-1,5-hexadiene.

The fact that R is nearly the same in the two diradical intermediates has another consequence—upon adding a second phenyl group to C5 of the diene, the approximate doubling of $\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0$ occurs with an increase in ΔE_{dist} of only 0.4 kcal/mol. Therefore, upon addition of a

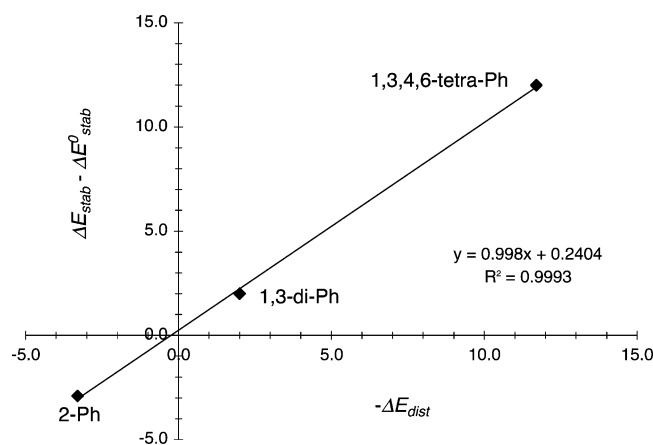


Figure 2. Linear least-squares plot of $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}}$ vs $-\Delta E_{\text{dist}}$ for 2-phenyl-, 1,3-diphenyl-, and 1,3,4,6-tetraphenyl-1,5-hexadiene.

second phenyl group at C5, the 6.3 kcal/mol increase in the size of the net stabilization energy, $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}}$, is only 0.4 kcal/mol less than the 6.7 kcal/mol increase in the size of $\Delta E_{\text{subst}} - \Delta E^0_{\text{subst}}$.

Because addition of a phenyl group to C5 of 2-phenyl-1,5-hexadiene increases the magnitude of $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}}$ in the diradical intermediate by 6.3 kcal/mol, $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}} = -9.2$ kcal/mol for 2,5-diphenyl-1,5-hexadiene is more than a factor of 3 larger in magnitude than $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}} = -2.9$ kcal/mol for 2-phenyl-1,5-hexadiene. However, as expected, the ratio of ΔE^0_{stab} values for the two dienes is only about two. Therefore, the ratios of their ΔE_{stab} values in Table 2 and their $\Delta\Delta H^\ddagger$ values in Table 1 are each a little less than a factor of 3.

When a pair of phenyl substituents is added to C1 and C3 of 1,5-hexadiene, the value of R in the TS increases by 0.253 Å. However, when a second pair of phenyls is added to C4 and C6 of 1,3-diphenyl-1,5-hexadiene, the value of R in the TS increases by 0.431 Å, a 70% larger increase than for addition of the first pair of phenyl groups. Consequently, in the TS for the Cope rearrangement of 1,3,4,6-tetraphenyl-1,5-hexadiene the substituent stabilization energy, $\Delta E_{\text{subst}} - \Delta E^0_{\text{subst}} = -23.7$ kcal/mol, is not a factor of 4, but a factor of about 6 larger in size than $\Delta E_{\text{subst}} - \Delta E^0_{\text{subst}} = -4.0$ kcal/mol in the TS for the Cope rearrangement of 1,3-diphenyl-1,5-hexadiene.

When a second pair of phenyl groups is added to C4 and C6 of 1,3-diphenyl-1,5-hexadiene, but the interallylic distance is frozen at the value of $R = 2.218$ Å in the TS for the Cope rearrangement of the disubstituted diene, Table 2 shows that $\Delta E_{\text{subst}} - \Delta E^0_{\text{subst}} = -9.3$ kcal/mol. This increase in the magnitude of $\Delta E_{\text{subst}} - \Delta E^0_{\text{subst}}$ is 30% more than the factor of 2 that is expected for doubling the number of phenyl substituents at a fixed value of R . It seems likely that the 1.3 kcal/mol of extra stabilization comes from a reduction in the steric repulsion between the pairs of phenyl groups at C1–C6 and C3–C4 upon increasing R by 0.253 Å from $R_0 = 1.965$ Å in the TS for the parent Cope rearrangement to $R = 2.218$ Å in the TS for the Cope rearrangement of 1,3-diphenyl-1,5-hexadiene.

The hypothesis, that steric repulsion between phenyl groups is relieved by lengthening R in the TS for the Cope

rearrangement of 1,3,4,6-tetraphenyl-1,5-hexadiene, is also consistent with the fact that $R - R_0 = 0.684$ Å in the TS for this reaction. As already noted, this change in interallylic bond lengths is a factor of 2.7 greater than $R - R_0 = 0.253$ Å in the TS for the Cope rearrangement of 1,3-diphenyl-1,5-hexadiene, rather than the expected factor of 2.0.

However, the fact that ΔE_{dist} is not quadratic out to $R = 2.649$ Å also contributes to the ratio of the changes in interallylic bond lengths being larger than the ratio of 2.0 expected from eq 8. Table 2 shows that $\Delta E_{\text{dist}} = 2.0$ kcal/mol for lengthening R by 0.253 Å from $R_0 = 1.965$ in the TS for the Cope rearrangement of unsubstituted 1,5-hexadiene to $R = 2.218$ Å in the TS for the Cope rearrangement of 1,3-diphenyl-1,5-hexadiene. If ΔE_{dist} were quadratic in $R - R_0$, $\Delta E_{\text{dist}} = 14.6$ kcal/mol would be expected for lengthening R by 0.684 Å from $R_0 = 1.965$ to $R = 2.649$ Å in the TS for the Cope rearrangement of 1,3,4,6-tetraphenyl-1,5-hexadiene. However, as Table 2 shows, the actual value of $\Delta E_{\text{dist}} = 12.0$ kcal/mol in the latter TS.

Upon increasing the interallylic distance from $R = 2.218$ Å to $R = 2.649$ Å, ΔE_{dist} increases by 10.0 kcal/mol, and this energy increase cancels all but 4.4 kcal/mol of the increase of 14.4 kcal/mol in the magnitude of ΔE_{subst} , the substituent stabilization energy. Therefore, of the 9.7 kcal/mol increase in the magnitude of $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}}$ that results from adding a pair of phenyl groups to C4 and C6 of the TS for the Cope rearrangement of 1,3-diphenyl-1,5-hexadiene, 5.3 kcal/mol (55%) comes from the two additional phenyl groups increasing the magnitude of ΔE_{subst} at $R = 2.218$ Å, and the remainder comes from the 4.4 kcal/mol increase in the size of the difference between ΔE_{subst} and ΔE_{dist} as R increases from 2.218 Å to 2.649 Å.

The data in Table 2 are useful for a detailed understanding of not only the cooperative substituent effects, which have been both observed in and computed for the Cope rearrangements of 2,5-diphenyl- and 1,3,4,6-tetraphenyl-1,5-hexadiene (Table 1), but also of the competitive substituent effect in the Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene.⁵ Table 2 shows that at $R - R_0 = -0.366$ Å the C2 phenyl group in 2-phenyl-1,5-hexadiene provides a net stabilization of $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}} = -2.9$ kcal/mol, and at $R - R_0 = 0.253$ Å the C1 and C3 phenyl groups in 1,3-diphenyl-1,5-pentadiene provide a net stabilization of $\Delta E_{\text{stab}} - \Delta E^0_{\text{stab}} = -2.0$ kcal/mol. However, as discussed in the previous section, the Cope rearrangement of 1,3,5-triphenyl-1,5-pentadiene occurs at a compromise TS geometry with $R - R_0 = 0.145$ Å. At this TS geometry, neither the phenyl groups at C1 and C3 nor the phenyl group at C5 provide as much net stabilization as these phenyl groups furnish in the TSs for the Cope rearrangements of, respectively, 1,3-diphenyl-1,5-pentadiene at $R - R_0 = 0.253$ Å and 2-phenyl-1,5-hexadiene at $R - R_0 = -0.366$ Å.

Table 2 reveals that at $R - R_0 = 0.145$ Å the C2 phenyl group in 2-phenyl-1,5-hexadiene provides 2.1 kcal/mol less net stabilization than at $R_0 = 1.965$ Å and 5.0 kcal/mol less net stabilization than at $R - R_0 = -0.366$ Å. At $R = 2.110$ Å the C1 and C3 phenyl groups in 1,3-diphenyl-1,5-pentadiene provide 1.7 kcal/mol more stabilization than at

$R_0 = 1.965 \text{ \AA}$ but 0.3 kcal/mol less stabilization than at $R - R_0 = 0.253 \text{ \AA}$.

Thus, assuming additivity, one might expect the three phenyl groups in 1,3,5-triphenyl-1,5-pentadiene would provide 5.3 kcal/mol less net TS stabilization than the total amount they furnish in the Cope rearrangements of 1,3-diphenyl-1,5-pentadiene and 2-phenyl-1,5-hexadiene. In fact, Table 2 shows that $\Delta E_{\text{stab}} = 3.2 \text{ kcal/mol}$ for the Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene, a value that is 4.1 kcal/mol smaller in magnitude than the sum of the ΔE_{stab} values for the Cope rearrangements of 2-phenyl-1,5-pentadiene and 1,3-diphenyl-1,5-pentadiene.

This difference between the ΔE_{stab} values in Table 2 is 1.1 kcal/mol larger than the difference of $4.0 + 3.0 - 4.0 = 3.0 \text{ kcal/mol}$ between the calculated $\Delta\Delta H^\ddagger$ values in Table 1 and 2.6 kcal/mol larger than the difference of $4.2 + 3.0 - 5.7 = 1.5 \text{ kcal/mol}$ between the experimental $\Delta\Delta H^\ddagger$ values.

The biggest contributor to making the difference of 3.0 kcal/mol between the calculated $\Delta\Delta H^\ddagger$ values 1.5 kcal/mol larger than the difference between the experimental $\Delta\Delta H^\ddagger$ values is the fact that the calculated value of $\Delta\Delta H^\ddagger$ for the Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene is 1.7 kcal/mol smaller in size than the experimental value. Nevertheless, the calculated and experimental $\Delta\Delta H^\ddagger$ values in Table 1 both show that the substituent effects in the Cope rearrangement of this compound are competitive.

Summary and Conclusions

The simple mathematical model in eq 4 assumes that radical stabilizing substituents attached to 1,5-hexadiene prefer interallylic bond lengths, R , in the TS for the Cope rearrangement that allow the substituents to provide the greatest amount of stabilization energy (ΔE_{subst}) for the TS and that the leading term in ΔE_{subst} is linear in R . The model also assumes that lengthening or shortening these bonds from the preferred value, R_0 , in the TS for the Cope rearrangement of unsubstituted 1,5-hexadiene results in an energy increase (ΔE_{dist}) that is quadratic in the difference between R and R_0 . Minimization of the net stabilization energy, $\Delta E_{\text{stab}} = \Delta E_{\text{dist}} + \Delta E_{\text{subst}}$, gives the expression in eq 5 for the optimal value of R in the TS for the Cope rearrangement of a substituted 1,5-hexadiene.

At this value of R , eq 6 predicts a relationship between $\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0$, the difference between the substituent stabilization energies at R and R_0 , and ΔE_{dist} that is reminiscent of the relationship between potential and kinetic energy in the virial theorem. The results of B3LYP/6-31G* calculations show that the predicted relationship between $\Delta E_{\text{subst}} - \Delta E_{\text{subst}}^0$ and ΔE_{dist} does, in fact, hold in the TSs for the Cope rearrangement of several phenyl-substituted 1,5-hexadienes.

B3LYP calculations also show that the effect of phenyl substituents on stabilizing the Cope TS is much smaller at R_0 than at the optimal value of R . Therefore, the major mechanism by which phenyl substituents lower ΔH^\ddagger for the Cope rearrangement is to increase the magnitude of ΔE_{subst} by distorting the interallylic bond lengths in the TS from R_0 to R . The dependence of ΔE_{subst} on R is what gives rise to

the cooperative substituent effects, both calculated and observed, in the Cope rearrangements of 2,5-diphenyl- and 1,3,4,6-tetraphenyl-1,5-hexadiene and to the competitive substituent effect, both calculated and observed, in the Cope rearrangement of 1,3,5-triphenyl-1,5-hexadiene.

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