Origin of the Preference for the Chair Conformation in the Cope Rearrangement. Effect of Phenyl Substituents on the Chair and Boat Transition States

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Abstract: *d,l*- and *meso*-2,2'-bis[1-methylene-1,2,3,4-tetrahydronaphthalenes] **8** and **9** were synthesized, and the activation energy parameters for their unimolecular [3,3] sigmatropic rearrangement to 1,2-bis(3,4-dihydro-1-naphthalenyl)ethane (**13**) were determined. The *d,l* diastereomer is constrained to undergo Cope rearrangement in the chair conformation while the meso diastereomer is constrained to the boat. At 150 °C $k_{d,l}/k_{meso} = 7 \times 10^6$. A comparison of activation energy parameters allows quantification of the effect of 2,5-diphenyl substituents on the chair-boat energy difference. Comparison with suitable bis(methylenecycloalkane) models reveals that the enthalpy of activation for the chair and boat transition states is lowered the same amount (7.5-8.5 kcal/mol). This result relegates secondary orbital interactions to a relatively minor role as a cause of the chair-boat energy difference. These results do not support the notion that the chair and boat topologies proceed by different mechanisms. The anomalous entropies of activation of the chair and boat transition states can be understood in terms of a resonance hybrid model comprised of two extreme forms (loose and tight), with substituents altering their relative contributions. A simple force field model is used to account for the major differences in energy between the chair and boat transition states.

Introduction

The mechanistic details of the Cope rearrangement continue to stimulate debate.[1] The issues have focused on the timing of bond-making and bond-breaking steps,[2] the possible intervention of discrete 1,4-diyl intermediates,[3-5] and the influence of substituents on the rate of rearrangement.[6,7] However, despite any remaining uncertainty regarding the mechanism of reaction, the synthetic utility of the Cope (and Claisen) rearrangement remains undiminished.

This utility is due, in large part, to the strong conformational bias that the reaction exhibits. The four-center or chairlike transition state is found to be lower in energy than the six-center or boatlike transition state.[8-12] Substituents orient themselves so that the bulkiest prefer to occupy the less congested quasi-equatorial positions (Figure 1). This working model allows for product formation with predictable stereochemistry.[13]

In simple aliphatic systems, the chair-boat energy difference is typically 5-10 kcal/mol.[3,10-12] The origin of this preference is often attributed to an unfavorable through-space *secondary orbital interaction* present in the six-center boatlike transition state, but absent in the four-center transition state.[14-16] Despite the continued attention that secondary orbital interactions receive in providing the basis of the Cope and Claisen diastereoselectivity, little experimental verification of its importance has been forthcoming. In pericyclic reactions such as the Diels-Alder cycloaddition, both experimental[17] and theoretical[18] estimates of the magnitude of secondary orbital interactions have revealed stabilizing interactions in the endo transition state in the range of 0.8-1.3 kcal/mol. The magnitude of this small, but sometimes important, effect is such so as to be easily outweighed by nonbonded repulsive interactions arising from other interactions in the molecule.

This study was undertaken to probe the two transition states of the Cope rearrangement. It provides a chance to test the response of the chair and boat pathways to substituents at positions 2 and 5, thus affording the opportunity to reveal any fundamental differences between the two reaction pathways and develop an understanding of the origin of the chair-boat energy difference in the Cope rearrangement. The system chosen for study is the [3.3] sigmatropic rearrangement of bis(methylenecycloalkanes) (Figure 2).[11] Bis(methylenecycloalkanes) exist as a pair of diastereomers, both of which can undergo Cope rearrangement to a common product. The interesting feature of these molecules is the conformation that each diastereomer must adopt in order to undergo rearrangement (Figure 2). The terminal carbon of the exocyclic methylene groups must gain a proximate relationship in order to undergo rearrangement. The meso diastereomer accomplishes this in a six-center or boatlike conformation (local C_{2v} symmetry). Although other conformations are readily accessible, the boatlike conformation is the only one from which a [3.3] sigmatropic rearrangement can occur. In the case of the *d,l* diastereomer, the four-center or chairlike conformation (local C_{2h} symmetry) is the only one accessible for rearrangement. The

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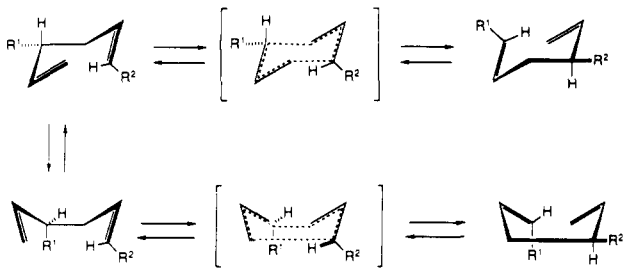

Figure 1.

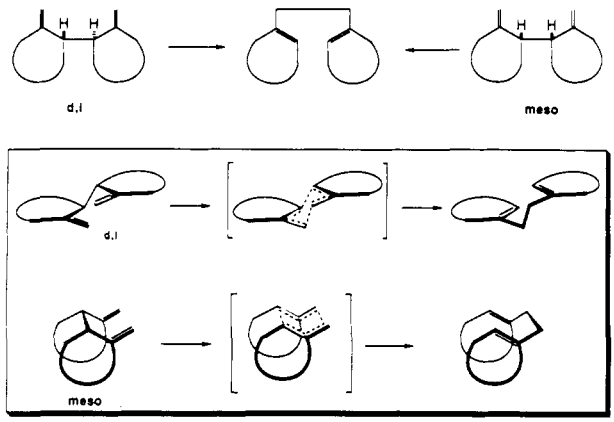

Figure 2.

stereoisomeric bis(methylenecycloalkanes), therefore, provide an opportunity to probe both chair and boat transition states in a closely related family of dienes. Specifically, we are interested in examining the influence of substituents placed at the 2- and 5-positions of the diene on both the chair and boat transition states. These studies were intended (1) to reveal if the chair and boat transition states respond differently to these perturbations, a finding that would establish if the two transition states (or intermediates) are fundamentally different, and (2) to observe if the chair–boat energy *difference* is diminished by placing conjugating substituents at positions C-2 and C-5 of the diene. The secondary orbital interaction, which is proposed to produce an unfavorable, destabilizing interaction between the C-2,5-positions in the six-center boat transition state, is expected to be diminished as a result of decreased coefficients that arise by a conjugating substituent at these positions.

Analysis of the influence of substituents on [3,3] sigmatropic rearrangements requires recourse to a theoretical framework. This is the area that has proven to be most controversial, and pointed disagreement exists whether substituents at positions 2 and 5 should exert an effect on the rate of a Cope rearrangement that proceeds via a pericyclic transition state.[6,7,16]

Although analysis of our results will unavoidably involve recourse to a mechanistic framework, it is not likely to provide for an unambiguous resolution between alternative mechanisms. However, the probable origins of the chair–boat energy differences or at least the relative importance of various contributors, can be established.

The bis(methylenecycloalkanes) that were chosen for study were the *d,l*- and *meso*-2,2′-bis[1-methylene-1,2,3,4-tetrahydronaphthalenes] **8** and **9**. Their choices represent an opportunity to substitute a phenyl ring at both C-2 and C-5 of the 1,5-diene. Benzannulation ensures that the aromatic ring will not be forced out of conjugation during the reaction; thus, a uniform phenyl effect on both *d,l* and meso isomers is secured.

Results

Synthesis of 2,2′-Bis[1-methylene-1,2,3,4-tetrahydronaphthalenes] and Related Derivatives. A considerable effort was expended exploring what appeared to be straightforward routes to the desired target via β,β′-bis(α-tetralone) derivatives. This chemistry included oxidative coupling and nucleophilic substitution

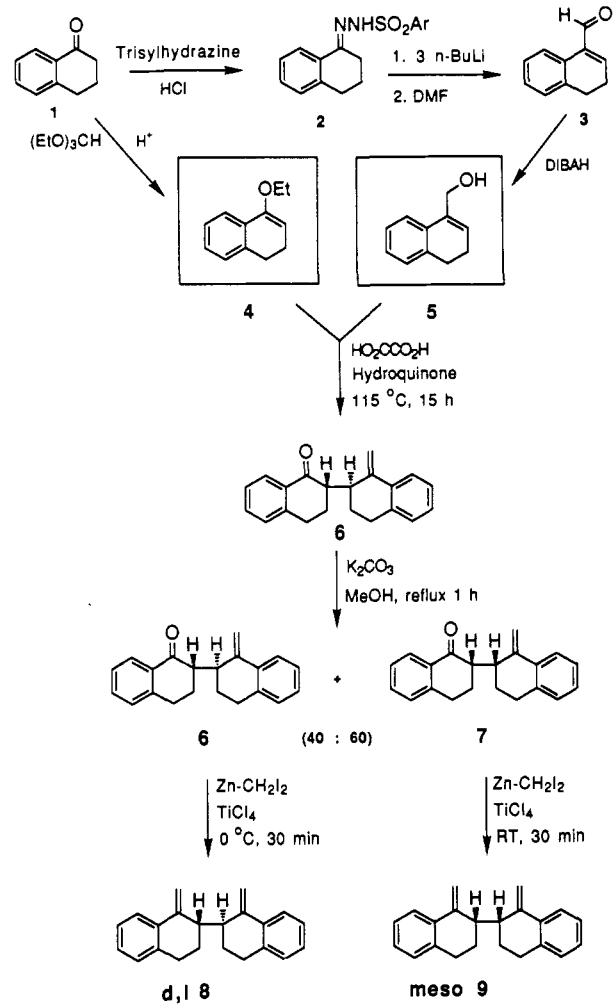

Figure 3.

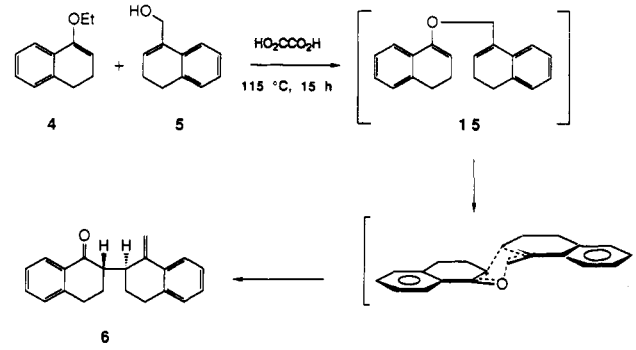

Figure 4.

of α-tetralone and its β-substituted derivatives.[19] This effort was unsuccessful, all reactions resulting in either very low yield or none of the desired diketone product. The problem was resolved by employing a Claisen strategy to gain entry into monomethylene ketone **6** (Figure 3). The route provided a stereospecific synthesis of ± *R,R* monomethylene ketone **6** which could be converted directly to the *d,l*-bis(methylenetetrahydronaphthalene) **8**. Epimerization of **6** to a mixture of ± *S,R* and ± *R,R* isomers followed by chromatographic separation afforded the ± *S,R* monomethylene ketone **7** which in turn is converted to the meso diastereomer **9**. The synthesis is outlined in Figure 3.

Methylene ketone **6** is the expected Claisen rearrangement product from allylic alcohol **5** and vinyl ether **4** (Figure 4). Thus,

(19) We are grateful to Dr. Philip Beauchamp for his contributions to the early stages of this research.

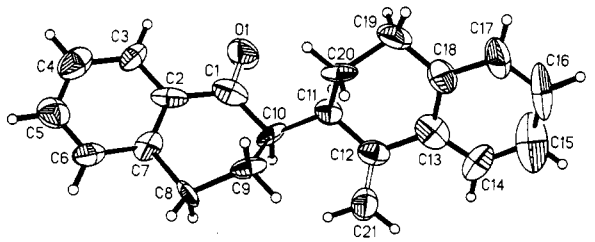

Figure 5. ORTEP plot of ketone **6**.

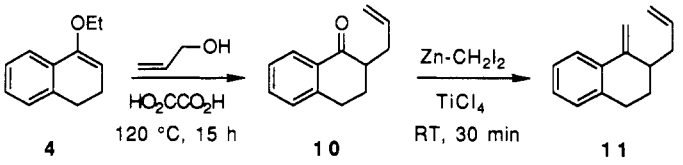

Figure 6.

treatment of 1-tetralone (**1**) with triethyl orthoformate and a catalytic amount of concentrated HCl gave the ethyl vinyl ether **4** in 78% yield.[20] Conversion of **1** to the trisylhydrazone **2** followed by a Shapiro reaction[21] using DMF as the electrophile afforded the α,β-unsaturated aldehyde **3** (65%). DIBALH reduction of aldehyde **3** gave the allylic alcohol **5**.[22] The Claisen rearrangement was achieved by heating a 2:1 ratio of enol ether **4** and **5** (neat, 115 °C, 15 h) with oxalic acid and a trace of hydroquinone inhibitor.[23] Rearrangement resulted in a single isomeric (>98%) product. On the basis of the lower energy chair conformation for the Claisen rearrangement[24] and stereochemical results of related rearrangements,[25] the methylene ketone **6** is expected to be the ± *R,R* diastereomer (Figure 4). The structure of **6** was unambiguously established by a single-crystal X-ray analysis.[26] The ORTEP is given in Figure 5.

The *d,l* bismethylene **8** is prepared from ketone **6** using the method of Takai.[27] Since this procedure does not result in ketone epimerization, pure *d,l*-bismethylene **8** is expected to be formed. This expectation is consistent with the kinetic behavior of **8** (vide infra) since the Cope rearrangement product **13** was a contaminant when **8** was exposed to temperatures only slightly above 25 °C.

Preparation of the ± *S,R* diastereomer **7** required epimerization (K_2CO_3, MeOH, reflux, 1 h) which produced a 60:40 mixture of the stereoisomers. The pure ± *S,R* isomer **7** could be isolated by chromatotron chromatography. Methylenation as before proceeded to give *meso*-2,2′-bis[1-methylene-1,2,3,4-tetrahydronaphthalene] **9**. The stereochemical assignment is consistent with the kinetic behavior (vide infra).

Analysis of the phenyl substituent effect also required tetrahydronaphthalene derivative **11**. Its synthesis was also achieved by a related Claisen strategy as outlined in Figure 6.

Kinetic Results. The rate of rearrangement of tetrahydronaphthalene derivative **11** in benzene was studied between 138 and 180 °C in sealed ampules (Figure 8). Reactions were monitored by gas chromatography. Kinetic studies of *d,l*-bismethylene **8** were conducted in benzene-d_6 at temperatures between 40 and 70 °C. The reactions were monitored by NMR spectroscopy for both appearance of product and disappearance of starting material. The rearrangement exhibited first-order kinetics, and 1,2-bis(3,4-dihydro-1-naphthalenyl)ethane (**13**) was the sole reaction product. The rate constants are given in the Experimental Section; the derived activation energy parameters are summarized in Table I.

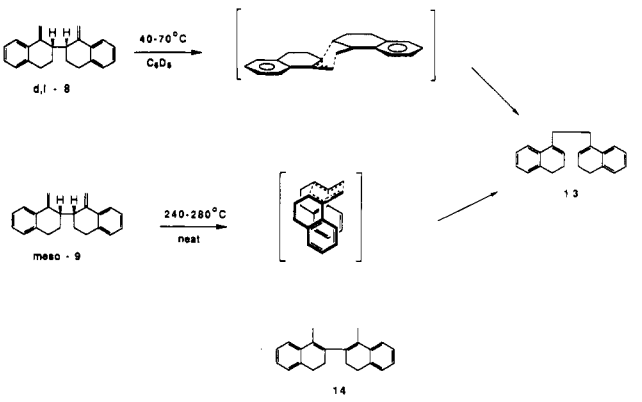

Figure 7.

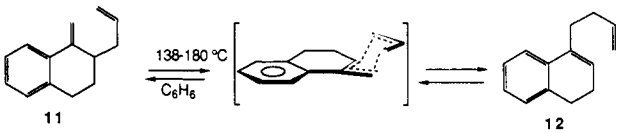

Figure 8.

The meso isomer **9**, on the other hand, required temperatures between 240 and 280 °C for the rearrangement to proceed at a convenient rate. In preliminary studies, the isomerization of **9** to **14** was found to compete favorably with the Cope rearrangement. It was not until a rigorous protocol of cleaning the glass reaction surfaces *and* inclusion of small quantities of Proton Sponge was this side reaction completely suppressed. Under these conditions, the thermal rearrangement, as monitored by GC, exhibited clean first-order kinetics. The derived activation energy parameters are given in Table I.

Discussion

The synthesis and unambiguous stereochemical assignment of the *d,l* and meso diastereomers **8** and **9** was achieved by the route outlined in Figure 3. The key step in this synthesis, a Claisen rearrangement of bis(dihydronaphthalene) enol ether **15**, produces a single stereoisomer that arises from the *chair* transition state of the Claisen rearrangement (Figure 4).[24] The structure of **6** is unambiguously established as ± *R,R* by a single-crystal X-ray structure.[26] ± *R,R* ketone **6** is epimerized in methanolic potassium carbonate at reflux to produce a 60:40 mixture of stereoisomers. The calculated free energy difference is $\Delta\Delta G^{338}_{6\text{-}7} = 0.24$ kcal/mol. The difference in steric energy of the ground states of the two isomers as calculated by MM2 is 0.10 kcal/mol.[28]

Olefins **8** and **9** are not readily interconverted, so experimental determination of their relative free energies of formation cannot be obtained directly. However, the similarity of the free energies of the isomeric ketones ($\Delta\Delta G^{338}_{6\text{-}7} = 0.24$ kcal/mol) and the calculated (MM2) difference in steric energy of **8**–**9** of 1.3 kcal/mol support the conclusion that the two isomers have heats of formation that are within 1 kcal/mol. This value is within the current limits of estimation. For our purposes, we will consider the energies of these two isomers as equivalent. Under the conditions of both isomerizations, the rearrangements are essentially irreversible (>99%), and since both *d,l* and meso isomers rearrange to a

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(26) X-ray diffraction data for compound **6**, $C_{21}H_{20}O$. The crystal belongs to the orthorhombic system with unit cell parameters at 296 K: $a = 7.312$ (2) Å, $b = 15.488$ (6) Å, $c = 27.586$ (6) Å, and $V = 3.160$ (16) Å^3. The space group is *Pcab* with $Z = 8$ formula units/unit cell and $D_{calcd} = 1.23$ mg/m^3.
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Table I. Experimental Activation Energy Parameters for the Cope Rearrangement

structure	no.	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}_{523}$[a]	$\Delta G^{\ddagger}_{523}$[a]
→ low → high	**16**[10] **16**[10]	33.5 ± 0.5 44.7 ± 2.0	−13.8 ± 1.0 −3.0 ± 3.6	40.5 ± 1.0 46.3 ± 3.8
	17[11]	31.4 ± 0.5	10.6 ± 1.0	36.9 ± 1.0
	18[6]	29.6	−9.7	34.7
	19[6]	21.3	−19.1	31.3
	11[b]	26.8 ± 0.1	−13.5 ± 0.2	33.9 ± 0.2
	20[11]	29.2 ± 0.5	−8.3 ± 1.2	33.8 ± 1.1
	21[11]	45.3 ± 1.0	5.0 ± 2.0	42.7 ± 1.0
	8[b]	21.8 ± 3.1	−6.5 ± 3.1	25.2 ± 2.9
	9[b]	36.7 ± 2.1	−2.7 ± 3.1	38.1 ± 3.7

[a] Errors are standard deviations. [b] This work.

common product (**13**), the overall thermodynamics of the rearrangements are, within the limits of uncertainty, the same (±1 kcal/mol). The difference in rates and activation energies, therefore, reflect the difference in transition state energies for the two reactions (Figure 7).

Consistent with their stereochemical assignment, the two stereoisomers exhibit striking differences in chemical reactivity. *d,l*-**8** undergoes [3,3] sigmatropic rearrangement at a measurable rate *at room temperature*. A single product, the α,α'-ethano-bridged bis(dihydronaphthalene) **13** is formed in quantitative yield. The meso diastereomer **9**, on the other hand, requires temperatures *greater than 200 °C* to effect rearrangement to the same Cope product **13**. The relative rate of rearrangement at an intermediate temperature (150 °C) is computed to be $k_{d,l}/k_{meso} = 7 \times 10^6$!

Since both isomers rearrange to a common product, the net change in free energy for both reactions is the same. The seven million fold rate difference arises exclusively from the difference in energy between the chair and boat transition states of *d,l*-**8** and *meso*-**9**. The rates of Cope rearrangement of **8** and **9**, together with a model compound **11**, were examined as a function of temperature to permit evaluation of the activation parameters. These results are summarized in Table I.

The present study relies upon a comparison of activation energy parameters to probe transition-state structure. We have chosen the enthalpy of activation ($\Delta H^{\ddagger}$) as the basis of comparison for several reasons. First, the reactions being compared proceed at comparable rates at temperatures that differ by more than 200 °C! The choice of an appropriate temperature at which to compute the $\Delta G^{\ddagger}$ is not clear. Second, since the entropies of activation ($\Delta S^{\ddagger}$) can differ substantially depending upon the reactant structure and transition-state topology, the choice of temperature used to compute the $\Delta G^{\ddagger}$ results in significant differences in $\Delta\Delta G^{\ddagger}$ ($(T\Delta\Delta S) \neq 0$). In view of these complications, $\Delta H^{\ddagger}$ is used to compare these reactions. A discussion of the entropies of activation of the rearrangements is postponed to a later section.

The Chair Cope Transition State: Phenyl Substituent Effects. Phenyl substituents at the 2,5- and 3,4-positions of 1,5-dienes are known to produce dramatic rate increases in the Cope rearrangement.[6,29] Systems previously studied involve freely rotating

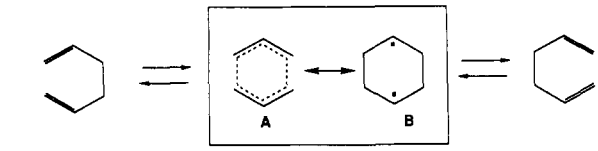

Figure 9.

Figure 10.

phenyl sp^2 or phenyl sp^3 carbon–carbon bonds. Assuming the phenyl substituent effect involves a stereoelectronic component (coplanarity of the phenyl and 1,5-diene π systems), it is informative to compare the magnitudes of these effects with those in the current investigation since, in the latter examples, benzannulation enforces coplanarity of the aromatic ring and the 1,5-diene π system. The comparisons are found in Table I.

The substitution of phenyl groups at positions 2 and 5 of 1,5-hexadiene results in a lowering of the enthalpy of activation by 12.2 kcal/mol (**16** → **18** → **19**).[6] In the chair TS‡ of the related benzannulated methylenecyclohexane **8**, the phenyl substituents reduce the activation enthalpy by 7.4 kcal/mol. The corresponding reductions in free energy of activation are $\Delta\Delta G^{\ddagger}$ = 9.2 and 8.6 kcal/mol, respectively. Although exact quantitative comparisons between the two systems are not warranted, two phenyl groups produce a 7–12-kcal stabilization of the chair Cope transition state. Since the *greatest* stabilization is found in the conformationally mobile 1,5-hexadiene **19**, it seems reasonable that, in this transition state, the aromatic ring is coplanar with the 1,5-diene π system. This analysis is consistent with the recent finding of Doering and co-workers.[30]

The incremental phenyl effects resulting from substitution at positions 2 and 5 in the acyclic series are 3.9 and 8.3 kcal/mol, respectively (entries **16** → **18** → **19**). With the reasonable assumption that **11** undergoes rearrangement exclusively via the chair (Figure 8), a more uniform effect (4.6, 5.0 kcal/mol) is observed in the benzannulated series **17** → **11** → **8**. No explanation has been proposed for the substantial variations in the phenyl substituent effect in the aliphatic series.

Phenyl Substituent Effect on the Chair–Boat Energy Difference: Importance of Secondary Orbital Interactions. The success of the Cope rearrangement derives from the strong conformational bias for the chair transition state and the resulting predictable product stereochemistry. What is the origin of this preference? Despite continuing debate regarding the timing of bond breaking and bond making and the possible involvement of biradicaloid intermediates, there has been little attention given to this matter or to discussions of factors that can influence the energy gap. Since the original analysis by Woodward and Hoffmann,[14] the chair–boat energy difference has been attributed in part or entirely to secondary orbital interactions.[15] These arise from antibonding interactions between the two interacting allyl fragments that are used to model the Cope transition state. In this model, the difference between the chair and boat forms arises from a through-space antibonding interaction. Specifically, the overlap between the C-2 and C-5 atomic orbitals is greater in the boat than in the chair. Consequently, the negative bond order between them serves to destabilize the boat with respect to the chair transition state. For our purposes, the analysis of Bordon[16] and Gajewski[2] is particularly useful. The transition state of the Cope rearrangement is viewed as a

(29) (a) Lutz, R. P.; Berg, H. A. J. *J. Org. Chem.* **1980**, *45*, 3915. (b) Lutz, R. P.; Bernal, S.; Boggio, R. J.; Harris, R. O.; McMicholas, M. W. *J. Am. Chem. Soc.* **1971**, *93*, 3985.

(30) Roth, W. R.; Lennartz, H.-W.; Doering, W. v. E.; Birladeauv, L.; Gulor, C. A.; Kitagawa, T. *J. Am. Chem. Soc.* **1990**, *112*, 1722.

resonance hybrid of the two extreme resonance forms (Figure 9). The analysis can account for the observed effect of substituents at positions 2 and 5; that is, conjugating groups at positions 2 and 5 of the 1,5-diene are expected to accelerate the reaction. In addition, the through-space destabilizing secondary orbital interaction at C-2 and C-2′ differentiates the chair and boat topologies (Figure 10).

Dienes **8** and **9** provide an opportunity for evaluating the importance of this secondary effect. Placement of conjugating substituents, such as phenyl, at positions C-2 and C-5 will diminish the coefficients at these atoms. The chair and boat transition states should respond differently to this perturbation since the proposal is the through-space antibonding interactions at these positions give rise to the chair–boat energy difference. The magnitude of this differential effect will reflect the importance of the secondary orbital interaction.

The response of the chair and boat transition states to phenyl substituents at the 2- and 5-positions is summarized in Table I. The data may be analyzed in several ways, but the comparisons lead to essentially the same conclusions. The enthalpy of activation differences for the *d,l* (chair) and meso (boat) transition states for bis(methylenecyclohexanes) **20** and **21** is 16.1 kcal/mol. For the isomeric bis(methylenetetrahydronaphthalenes) **8** and **9**, this difference is 14.9 kcal/mol. Using a somewhat different comparison, the phenyl substituent effect on the chair transition states (**20–8**) is 7.4 kcal/mol while the phenyl effect on the boat transition states (**21–9**) is 8.6 kcal/mol. *These differences in activation enthalpy are well within experimental uncertainty and reveal that the transition-state enthalpy of the boat and chair forms respond in an identical manner to conjugating substituents at positions 2 and 5.*

Two important conclusions can be drawn from these results. First, the failure to detect a sizable differential substituent effect on the chair and boat transition states argues against secondary orbital interactions making an *important* contribution to the energy difference between these transition states of the Cope rearrangement. Second, these results offer *no* support for the conclusions drawn by Dewar and co-workers that the chair and boat transition states of the Cope rearrangement proceed by fundamentally different mechanisms.[31,32] Their conclusions, drawn from a combination of experimental results and theoretical calculations, propose that the chair transition state proceeds via a biradicaloid mechanism while the boat proceeds by an aromatic-like transition state. According to Dewar, biradicaloid transition states are expected to respond to 2,5-diphenyl substituents by an increased rate of reaction (consistent with previous experimental observations); the aromatic-like transition state, however, is predicted to be *unresponsive* to substituents at the 2,5-positions.[6b] This is clearly not the case since the enthalpic response of both chair and boat transition states is the same; thus, there does not appear to be a need to complicate this rearrangement with unnecessary multiple mechanisms.

Entropy of Activation of the Cope Rearrangement. The entropies of activation for the chair and boat transition states remain one of the most perplexing aspects of this reaction. The chair transition state is often characterized by a large negative entropy of activation. Indeed, this is often cited as a characteristic of highly organized pericyclic transition states that involve simultaneous loss of a number of rotational degrees of freedom.[33] It was suggested that the magnitude of the entropy of activation in stereochemically uncertain Cope rearrangements may be used as a mechanistic guide since the boat was thought to be less negative.[11]

However, with the accumulation of additional experimental data, it is clear that the magnitude of $\Delta S^{\ddagger}$ is quite "system dependent" and cannot, at present, be used as a guide for distinguishing the chair and boat topologies.[34,35] Indeed, accounting for activation entropy in the chair and boat transition states remains a significant problem at the very highest levels of theory.[36,37]

In consideration of the structural effects on the activation entropy of the Cope rearrangement, it is perhaps safe to analyze trends only within a limited family of compounds. Our analysis, therefore, is confined to the $\Delta S^{\ddagger}$ for the series of bis(methylenecyclohexanes) that are summarized in Table I. The difference in entropy of activation for *d,l* and meso **20** and **21** reflect a gap typical for the chair and boat transition states in the acyclic Cope rearrangement (−13 eu). Phenyl substituents at positions 2 and 5 result in a marked reduction of the gap—significantly the entropy of the boat transition state is now small (but negative!). The chair–boat entropy difference is only −4 eu. Thus, the entropy of activation for the chair and boat transition state exhibits a different response to phenyl substitution: *the boat transition state is more responsive.* What might be the origin of this effect? There is agreement that the boat transition state is "looser" in comparison with the chair. This is noted at both ab initio[38] and AM1 levels of calculation.[37] For example, the *C-1,6 and C-3,4 bond distances* are calculated to be 2.086 Å for the chair and 2.316 Å for the boat.[38,39] Analysis of kinetic secondary isotope effects for the Cope rearrangement is also consistent with this interpretation.[34] The "looser" transition state for the boat implies a species with lower frequency vibrations (higher density of states), consistent with the entropy of the boat being considerably larger (more positive) than the chair. Although current state of the art calculations are still not able to reproduce the magnitude of this effect, there seems to be agreement regarding this likely representation. Why then should phenyl substituents at positions 2 and 5 diminish the entropy gap? Phenyl substituents are expected to increase the importance of the 1,4-biradicaloid resonance contribution to the transition state (Figure 9, structure B). This effectively leads to more highly developed bond formation at C-1,6 and C-3,4. The increased contribution of B is expected to result in a "tighter" transition state of the Cope rearrangement. Recent computational studies support this view.[39] The introduction of cyano substituents at positions 2 and 5 result in a *chair* transition state that is lower in energy than the parent diene by 6–8 kcal/mol. Furthermore, the interallylic bond distance (C-1,6 and C-3,4) is shortened by 4–8%; thus, conjugating substituents at positions 2 and 5 can alter the structure of the chair Cope transition state in the direction of diradical structure B. *We would predict that similar substituents will have an even more pronounced effect on the boat transition state.* This is simply a consequence of the fact that the boat transition state is significantly "looser" to begin with; thus, 2,5-diphenyl substituents can produce a more significant tightening of the boat over the chair. Admittedly, the relationship between our definition of the transition state "looseness" and the experimentally determined entropy of activation is far from secure; certain aspects of our proposal are subject to computational analysis. It is important to note that Doering has explicitly pointed out that the phenyl substituent effect should "tighten up" the transition state, resulting in a lower (more negative) $\Delta S^{\ddagger}$.[30]

MM2 Analysis. The failure to detect a significant difference in the phenyl substituent effect for the chair and boat transition states leaves secondary orbital interactions relegated to minor importance. The question remains: To what can the significant energy difference between the chair and boat transition states be attributed? The most obvious answer must focus on differences

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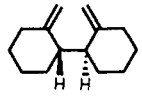
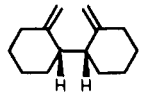
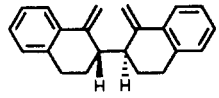
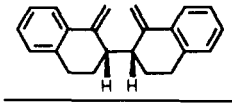
(37) Dewar, M. J. S.; Jie, C. *J. Am. Chem. Soc.* **1987**, *109*, 5893.
(38) Morokuma, K.; Borden, W. T.; Hrovat, D. A. *J. Am. Chem. Soc.* **1988**, *110*, 4474.
(39) Hrovat, D. A.; Borden, W. T.; Vance, R. L.; Rondan, N. G.; Houk, K. N.; Morokuma, K. *J. Am. Chem. Soc.* **1990**, *112*, 2018.
(40) Bearpark, M.; Bernardi, F.; Olivucci, M.; Robb, M. A. *J. Am. Chem. Soc.* **1990**, *112*, 1732.
(41) For a recent effort to detect a metastable intermediate in a [3,3] sigmatropic rearrangement, see: Owens, K. A.; Berson, J. A. *J. Am. Chem. Soc.* **1988**, *110*, 627.

Table II. Calculated Differences of Steric Energy of the Chair and Boat Transition-State Models

structure	no.	steric energy (kcal/mol)	steric energy difference of chair–boat (kcal/mol)
 (chair)	**16**	28.3	8.1
 (boat)	**16**	36.4	
	**20**	43.9	14.1
	**21**	58.0	
	**8**	44.9	9.4
	**9**	54.3	

in energy between chair and boat conformations of six-membered rings.

In order to evaluate differences in conformational energy, we have estimated the energy of the chair and boat transition states in selected systems. Employing the MM2 force field,[28] the 1,5-diene was fixed in local C_{2v} and C_{2h} symmetry. The C-1,6 bond distance was set at 2.0 Å, a value selected on the basis of the bond distance calculated by ab initio methods for the chair transition state, and the 3,4-bond was left unchanged. No effort was made to pyramidalize the carbon at positions 2 and 5,[35] nor was there any effort to adjust the hybridization at either of the terminal olefin atoms. The MM2 steric energies calculated are summarized in Table II. The calculated difference in steric energy for *d,l* and meso **20** and **21** gives a reasonable approximation of the experimentally determined activation energy difference. The phenyl-substituted derivatives **8** and **9** are approximated less well by this approach (9.4 kcal/mol calculated vs 14.9 kcal/mol found). The steric energy difference of the parent 1,5-hexadiene (chair vs boat) is also lower than the experimentally determined value (8.1 vs 11 kcal/mol).

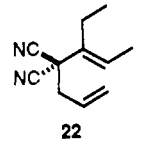
It is clear, however, that this very crude approximation gives a reasonable accounting for the energy differences between the chair and boat transition states. The model could be improved by adjusting the interallylic bond distances; for example, the phenyl substituted derivatives are expected to be modeled by a shorter interallylic bond distance (1.866 vs 2.00 Å) which would increase the calculated value. *The important point is that the chair–boat energy differences are approximated by a simple force field model that only accounts for differences in nonbonded steric interactions between the chair and boat conformations.*

Solvent Effects. The Cope and Claisen rearrangements as well as many other pericyclic reactions show a *slight* response to variation in solvent polarity in accordance with an isopolar activated complex.[42] Dewar has proposed that the 4-fold increase in rate of Cope rearrangement of 3-phenyl-1,5-hexadiene on going from the gas phase to *o*-dichlorobenzene (ODCB) is due to a highly polarizable transition state. This data is then used to support the contention that the Cope transition state is biradicaloid.

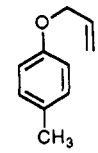
(42) *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; Reichardt, C., Ed.; VCH: Weinheim, 1988.

We have also observed modest solvent effects in the Cope rearrangement of **11**; the rate increases 72% over a series of solvents that range from octane to ODCB (150 °C).

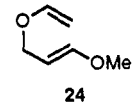
Examination of the literature reveals that solvent effects of this magnitude are common for pericyclic reactions.[42] For example, a 17-fold increase in rate is observed for **22** (cyclohexane → $EtOH/H_2O$, 1:1),[43] a 36-fold increase for **23** (*n*-tetradecane → $EtOH/H_2O$),[44] and a 22-fold increase for **24** (benzene → MeOH).[45]



22



23



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These results should be compared with solvent effects in bonafide free-radical-forming reactions. In a typical example, the rate of decomposition of AIBN in 36 solvents varied by a factor of 2–4.[46] In general, there is a lack of any *marked* solvent effects in most free-radical-forming reactions.[42]

Both pericyclic reactions and free-radical-forming reactions are quite *insensitive* to solvent effects. We may conclude that (1) all pericyclic reactions proceed by free-radical (or biradicaloid) intermediates or (2) the solvent effects observed for both types of reactions offer no support for the notion that these modest effects can be used as a mechanistic guide to distinguish between pericyclic and free-radical reaction mechanisms. We prefer the latter interpretation.

Mechanism of the Cope Rearrangement. Roth and Doering concluded that the [3,3] sigmatropic rearrangement of 2,5-diphenyl-1,5-hexadiene is not concerted but proceeds via a 1,4-cyclohexadiyl intermediate.[30] Semiempirical calculations support this view.[4] The conclusion was drawn from thermochemical arguments; specifically the experimentally observed activation energy places the transition state *above* estimates of the heat of formation of the 1,4-diphenyl-1,4-cyclohexadiyl and *below* the energy computed for the putative concerted transition state. These arguments are seductive but not persuasive since they contain assumptions which presuppose the behavior of the putative intermediates or transitions states.[36,38–40] A key assumption in Doering's (and Dewar's) analysis is that substituents at positions 2 and 5 will exert *no* effect on the stability (and thus rate) of the concerted (pericyclic) transition state. Indeed, these positions are referred to as nodal carbons. However, the most recent ab initio[39] and valence-bond treatments[40] predict a sizable lowering of activation energy from conjugating substituents at positions 2 and 5. In contrast to the assumptions by Doering, these calculations do not locate diradical intermediates on the energy surface. It was concluded that the reactions are concerted.

Thus, theoretical support is available for either the biradicaloid intermediate or a concerted pericyclic transition state. The present study offers no direct experimental support for diradical intermediates. We have adopted a position that, in the absence of manifestations of the diradical,[41] we will analyze our results within the framework of a concerted reaction. Although this may not be entirely satisfactory, the absence of compelling experimental evidence for diradical intermediates and the current state of diametrically opposed theoretical predictions regarding substituent effects on pericyclic reactions persuades us to adopt this more conservative approach. Efforts are under way, however, to probe the question of possible diradical intermediates in related rearrangements of bismethylene cycloalkanes.

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(44) White, W. N.; Wolfarth, E. F. *J. Org. Chem.* **1970**, *35*, 2196.
(45) Coats, R. M.; Rogers, B. D.; Hobbs, S. J.; Peck, D. R.; Curran, D. P. *J. Am. Chem. Soc.* **1987**, *109*, 1160.
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Conclusion

The present study has quantified the phenyl substituent effect on the chair and boat transition states of the Cope rearrangement. The enthalpy of activation of both reactions is lowered by a similar amount. The results are consistent with secondary orbital interactions playing a minor role in the origin of the chair–boat energy difference of the Cope rearrangement. In addition, the results are not consistent with the conclusions of Dewar that the chair and boat transition states proceed by different mechanisms. A proposal is made to account for the anomalous entropy of activation of the Cope rearrangement in terms of phenyl substituents influencing on the degree of "looseness" of the Cope transition state. Finally, a simple force field analysis is found to adequately model the chair–boat energy differences.

Experimental Section

General Procedure. Reactions were conducted in oven-dried (160 °C) or flame-dried glassware under a positive nitrogen atmosphere unless otherwise stated. Transfer of anhydrous solvents or mixtures was accomplished with oven-dried syringes or cannula. Solvents and reagents were distilled before use: methanol from potassium hydroxide; acetonitrile, dichloromethane, and dimethylformamide from calcium hydride; ether, tetrahydrofuran, and toluene from sodium benzophenone ketyl. Thin layer chromatography (TLC) was performed on plates of silica precoated with 0.25-mm Kieselgel 60 F_{254} (Merck). Flash columns were packed with 230–400-mesh silica gel (Merck). Chromatotron chromatography was carried out on plates coated with 4-mm Kieselgel 60 F_{254} (Merck). Melting points were obtained on a Thomas-Hoover apparatus in open capillary tubes and are uncorrected.

Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker WM-250 (250 MHz) or General Electric GN-500 (500 MHz). The chemical shifts are reported on the δ scale (ppm) downfield from tetramethylsiloxane. Coupling constants (J) are reported in hertz (Hz). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; m, multiplet; br, broad; dd, doublet of doublets; dt, doublet of triplets; etc. Carbon nuclear magnetic resonance spectra (^{13}C NMR) were obtained at 125.8 MHz on a General Electric GN-500 instrument and are reported (ppm) relative to the center line of a triplet at 77.7 ppm for deuteriochloroform.

Infrared (IR) spectra were measurd with a Nicolet 5DXB FTIR spectrophotometer. Low-resolution mass spectral data were acquired on a Finnigan Model 4000 GC/MS/DS and are reported as mass/charge (CI, isobutane) or mass/charge (EI, 70 eV) and percent relative abundance. High-resolution mass spectra (EI, 22 eV) were obtained on a VG-7070e high-resolution mass spectrometer.

Capillary GC analyses were performed on a Hewlett-Packard Model 5790A gas chromatograph connected to a 3390A recorder–integrator. A methyl silicone support capillary column (length 25 m, i.d. 0.20 mm) was used with helium carrier gas and a flame ionization detector (FID). Preparative vapor-phase chromatography (VPC) was performed on a Varian Aerograph Model 920 equipped with a thermal conductivity detector and Soltec chart recorder. Samples were collected at −78 °C utilizing U-shaped Pyrex collecting tubes in a dry ice/acetone bath. The collection tubes were maintained air and water free by nitrogen backflow using a small septa and needle apparatus. Standard Pyrex columns (3 ft × $^3/_8$ in. i.d.) packed with 10% Supelco SP-2100 on 80/100 Suppelcoport were used with helium as carrier gas.

1-Tetralone 2,4,6-Triisopropylsulfonylhydrazone (2). A solution of 2,4,6-triisopropylsulfonylhydrazine[21] (2.30 g, 7.65 mmol) and distilled 1-tetralone (1.10 g, 7.52 mmol) in CH_3CN (15 mL) was treated with concentrated HCl (1 mL) and then the resultant mixture stirred at room temperature for 22 h. Vacuum filtration gave a white amorphous powder which was rinsed with pentane and dried in vacuo over P_2O_5. After drying, 1.72 g of hydrazone **2** was obtained (4.04 mmol, 54% yield, mp 162–165 °C, lit.[21] mp 176–178 °C). ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.93 (dd, 1 H, J = 1.2 Hz, 7.7 Hz, aromatic), 7.81 (s (br), 1 H, aromatic), 7.12 (m, 5 H, aromatic), 4.33 (quintet, 2 H, J = 6.7 Hz, ArCH(CH$_3$)$_2$), 2.89 (m, 1 H, ArCH(CH$_3$)$_2$), 2.72 (t (br), 2 H, Ar(C=NR)CH_2), 2.47 (t, 2 H, J = 6.5 Hz, ArCH_2CH$_2$), 1.91 (quintet (br), 2 H, ArCH$_2$CH_2), 1.31 (d, 12 H, J = 6.8 Hz, ArCH(CH_3)$_2$), 1.24 (d, 6 H, J = 6.9 Hz, ArCH(CH_3)$_2$). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 154.0, 152.0, 151.4, 140.2, 132.4, 130.0, 129.0, 126.9, 125.8, 124.5, 34.8, 30.7, 30.0, 25.9, 25.5, 24.2, 22.1. IR (KBr) 3240, 2957, 2929, 2869, 1459, 1391, 1334, 1315, 1168, 1154, 1091, 1037, 1012, 765, 718, 666 cm^{-1}.

3,4-Dihydro-1-naphthalenecarboxaldehyde (3). A mixture of trisylhydrazone **2** (1.55 g, 3.63 mmol) and a 10% TMEDA solution in hexane (15.6 mL) was cooled to −50 °C, and n-BuLi (8.50 mL of a 0.98 M hexane solution, 8.35 mmol) was added dropwise. The dark orange reaction mixture stirred at −50 °C for 45 min, and the bath was removed and replaced by an ice-water bath. After the mixture was stirred for 1 h at 0 °C, DMF (0.56 mL, 530 mg, 7.26 mmol) was syringed in and stirring continued for an additional 1 h. The reaction mixture was poured into saturated NH_4Cl (50 mL), and Et_2O (50 mL) was added. The layers were separated, and the aqueous layer was reextracted with Et_2O (100 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The residual yellow oil was purified via column chromatography (petroleum ether/Et_2O, 6:1), giving 374 mg of aldehyde **3** (2.36 mmol, 65% yield). ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.57 (s, 1 H, aldehyde), 8.10 (m, 1 H, aromatic), 7.11 (m, 3 H, aromatic), 6.91 (t, 1 H, J = 4.8 Hz, vinyl), 2.71 (t, 2 H, J = 7.8 Hz, ArCH_2CH$_2$), 2.45 (m, 2 H, ArCH$_2$CH_2). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 193.2, 153.6, 138.6, 136.3, 129.9, 128.8, 127.2, 126.4, 27.6, 24.9. IR (neat) 2943, 2887, 2836, 2722, 1691, 1489, 1453, 1437, 1232, 1135, 1070, 835, 788, 765, 736, 705, 693 cm^{-1}.

1-Ethoxy-3,4-dihydronaphthalene (4). A solution containing distilled 1-tetralone (18.20 mL, 137 mmol), absolute ethanol (20 mL), distilled triethyl orthoformate (27.20 mL, 164 mmol), and three drops of concentrated H_2SO_4 was refluxed for 30 min and then stirred for 2 days at room temperature. Sodium ethoxide was added, and ethanol was removed in vacuo. Subsequent vacuum distillation provided 18.76 g (78%) of a clear liquid (bp 101 °C/2 mm). ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.55 (m, 1 H, aromatic), 7.15 (m, 3 H, aromatic), 4.95 (t, 1 H, J = 4.7 Hz, vinyl), 3.86 (q, 2 H, J = 7.0 Hz, OCH_2CH$_3$), 2.73 (t, 2 H, J = 7.8 Hz, ArCH_2), 2.33 (m, 2 H, C=CHCH_2), 1.39 (t, 3 H, J = 7.0 Hz, OCH$_2$CH_3). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 152.5, 137.6, 132.7, 127.6, 126.8, 122.2, 96.3, 63.1, 29.0, 22.6, 15.3. IR (neat) 3068, 3024, 2978, 2933, 2886, 2833, 1718, 1685, 1639, 1489, 1455, 1371, 1342, 1286, 1251, 1190, 1144, 1116, 1100, 1062, 768, 740 cm^{-1}.

1-(Hydroxymethyl)-3,4-dihydronaphthalene (5). To a toluene solution (180 mL) containing aldehyde **3** (4.85 g, 30.7 mmol) at 0 °C was added via syringe DIBAH (30.7 mL of a 1.8 M toluene solution, 46.0 mmol). The reaction stirred at 0 °C for 1 h and then was diluted with Et_2O (50 mL) followed by addition of NaF (5.2 g). The reaction was stirred for 10 min and the mixture then poured into H_2O (100 mL). The aqueous layer was separated, and additional H_2O (100 mL) and NaF (4 g) were added. This procedure was repeated three times until most of the aluminum salts were removed. The ether layer was dried ($MgSO_4$) and filtered and the solvent removed in vacuo. The residual yellow oil was purified via column chromatography (petroleum ether/Et_2O, 3:2), giving 3.66 g of allylic alcohol **5** (22.9 mmol, 75% yield). ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.28 (m, 1 H, aromatic), 7.15 (m, 3 H, aromatic), 6.06 (t, 1 H, J = 4.5 Hz, vinyl), 4.45 (s (br), 2 H, CH_2OH), 2.74 (t, 2 H, J = 8.1 Hz, ArCH_2CH$_2$), 2.28 (m, 2 H, ArCH$_2$CH_2). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 137.0, 136.5, 133.7, 128.3, 127.6, 127.4, 127.1, 123.3, 64.3, 28.5, 23.5. IR (neat) 3333 (OH), 3059, 3030, 2953, 2882, 2831, 1490, 1450, 1438, 1427, 1239, 1133, 1079, 1007, 822, 792, 768, 757, 737 cm^{-1}.

(±)-(*R*,*R*)-2-[2-(1-Methylene-1,2,3,4-tetrahydronaphthalenyl)]-1-tetralone (6). A 10-mL capacity, sealable glass tube was charged with 1.65 g (10.3 mmol) of **5**, 3.38 g (19.4 mmol) of **4**, 0.042 g (0.33 mmol) of oxalic acid dihydrate, and 0.0085 g (0.77 mmol) of hydroquinone. The tube was freeze–thaw–degassed (3×), sealed under vacuum, and heated for 14 h at 100 °C in an oil bath. The tube was cooled, broken open, and immediately columned on silica with ether/hexanes (1:10) as eluent and N_2 as the pressurizing gas to yield 2.09 g (70%) of a white solid (mp 107–108 °C). ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.04 (dd, 1 H, J = 1.0 Hz, 7.7 Hz, aromatic), 7.62 (m, 1 H, aromatic), 7.45 (m, 1 H, aromatic), 7.20 (m, 5 H, aromatic), 5.56 (s, 1 H, vinyl), 4.93 (d, 1 H, J = 1.3 Hz, vinyl), 3.43 (m, 1 H, (C=O)CH), 2.90 (m, 5 H), 2.22 (m, 1 H), 2.00 (m, 2 H), 1.68 (m, 1 H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 199.5, 145.5, 143.9, 137.4, 135.7, 133.4, 133.1, 128.9, 127.8, 126.8, 126.4, 125.1, 108.4, 50.5, 38.9, 28.8, 28.7, 25.1, 24.3. IR (KBr) 2397, 1683, 1621, 1598, 1485, 1454, 1321, 1296, 1280, 1219, 923, 902, 774, 747, 734 cm^{-1}. Mass spectrum (CI, isobutane, relative percent) m/z 289 (MH$^+$, 100), 146 (16), 117 (1). High-resolution mass spectrum calcd for $C_{21}H_{20}$O: 288.1514. Found: 288.1504. A single crystal suitable for X-ray crystallography was obtained from dilute ether solutions which were allowed to stand at −20 °C for about 30 days.

An isomerized product was occasionally observed during column chromatography of **6** in which the exocyclic methylene moved into the ring. When nitrogen was used for pressurizing the column, this isomerized product was minimized (mp 97–98 °C). ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.07 (dd, 1 H, J = 1.2 Hz, 7.8 Hz, aromatic), 7.46 (dt, 1 H, J = 1.4 Hz, 7.4 Hz, aromatic), 7.20 (m, 6 H, aromatic), 3.85 (dd, 1 H, J = 4.8 Hz, 13 Hz, (C=O)CH) 3.10 (m, 2 H), 2.64 (m, 1 H), 2.20 (m, 4 H), 2.07 (s, 3 H, CH_3). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 198.6, 144.5, 137.4, 136.7, 135.0, 133.9, 133.4, 129.3, 128.5, 127.9, 127.4, 127.2, 126.8, 126.7, 123.7, 53.2, 30.1, 29.3, 29.0, 26.5, 15.1. IR (KBr) 3059, 2931, 2885, 2828, 1676, 1599, 1485, 1451, 1348, 1307, 1220, 1151, 1004,

931, 892, 766, 741 cm^{-1}. Mass spectrum (EI, 70 eV, relative percent) m/z 288 (M$^+$, 16), 155 (8), 146 (100), 128 (19), 115 (18), 90 (17). High-resolution mass spectrum calcd for $C_{21}H_{20}O$: 288.1514. Found: 288.1509.

(±)-(*R*,*S*)-2-[2-(1-Methylene-1,2,3,4-tetrahydronaphthalenyl)]-1-tetralone (7). To a solution of anhydrous MeOH (15 mL) containing **6** (275 mg, 0.955 mmol) was added K_2CO_3 (200 mg, 1.45 mmol), followed by heating under reflux for 50 min. The mixture was poured into saturated brine, and Et_2O (50 mL) was added. The layers were separated, and the aqueous layer was reextracted with Et_2O (50 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The residual yellow oil was purified by chromatotron (hexane/Et_2O, 40:1). Separation was complete, giving 159 mg of a white solid **7** and 106 mg of **6** (60:40). ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.04 (m), 8.04 (m, 1 H, aromatic), 7.50 (m, 2 H, aromatic), 7.20 (m, 5 H, aromatic), 5.48 (d, 1 H, J = 0.7 Hz, vinyl), 5.05 (s, 1 H, vinyl), 3.15 (m, 3 H), 2.80 (m, 2 H), 2.62 (m, 1 H), 2.04 (m, 4 H, $ArCH_2CH_2$). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 200.4, 145.5, 143.7, 136.7, 134.2, 133.2, 132.5, 129.1, 128.8, 127.9, 127.4, 126.5, 126.0, 125.3, 110.6, 45.8, 39.6, 26.3, 26.1, 25.8, 25.4. IR (KBr) 2925, 2857, 1673, 1632, 1598, 1484, 1453, 1438, 1292, 1195, 1012, 891, 798, 777, 744, 736 cm^{-1}. Mass spectrum (CI, isobutane, relative percent) m/z 289 (MH$^+$, 22), 146 (100), 128 (5), 115 (5). High-resolution mass spectrum calcd for $C_{21}H_{20}O$: 288.1514. Found: 288.1502.

(*d*,*l*)-Bis-2,2′-(1-methylene-1,2,3,4-tetrahydronaphthalene (8). To a stirred suspension of zinc powder (0.410 g, 6.25 mmol) in THF (7 mL) was added distilled diiodomethane (0.279 mL, 3.46 mmol) at room temperature. After 30 min, the mixture was cooled to 0 °C and a solution of $TiCl_4$ in dichloromethane (1 M, 0.694 mmol) was added dropwise. The solution was warmed to room temperature and stirred for 30 min. A solution of **6** (0.200 g, 0.694 mmol) in THF (1.5 mL) was then added dropwise. After the mixture was stirred for 30 min, ether (10 mL) was added and the mixture was extracted with saturated $NaHCO_3$ (20 mL). The aqueous layer was extracted with ether (2 × 20 mL), and the combined organics were dried ($MgSO_4$), filtered, and evaporated. The crude oil was columned on silica with hexanes as eluent to yield 0.094 g (47%) of a white solid. All manipulations of this material had to be conducted at or below 0 °C to prevent the Cope rearrangement which occurs slowly at room temperature. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (dd, 2 H, J = 1.4 Hz, 7.6 Hz, aromatic), 7.14 (m, 4 H, aromatic), 7.03 (dd, 2 H, J = 0.8 Hz, 7.0 Hz, aromatic), 5.40 (d, 2 H, J = 1.3 Hz, vinyl), 4.58 (d, 2 H, J = 1.2 Hz, vinyl), 2.74 (m, 2 H, allylic), 2.55 (m, 4 H, $ArCH_2$), 1.81 (m, 4 H, $ArCH_2CH_2$). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 145.9, 135.1, 129.1, 127.6, 126.3, 125.6, 125.1, 110.1, 40.9, 25.8, 25.0.

***meso*-Bis-2,2′-(1-methylene-1,2,3,4-tetrahydronaphthalene) (9).** To a stirred suspension of zinc powder (0.414 g, 6.34 mmol) in THF (7 mL) was added distilled diiodomethane (0.283 mL, 3.51 mmol) at room temperature. After 30 min, the mixture was cooled (0 °C) and a solution of $TiCl_4$ in dichloromethane (1 M, 0.704 mmol) was added dropwise. This was warmed to room temperature and stirred for 30 min. A solution of **7** (0.203 g, 0.704 mmol) in THF (1.5 mL) was then added dropwise. After an additional 30 min, ether (10 mL) was added and the mixture was extracted with saturated $NaHCO_3$ (20 mL). The aqueous layer was extracted with ether (2 × 20 mL), and the combined organics were dried ($MgSO_4$), filtered, and evaporated. The crude product was columned on silica with hexanes as eluent to yield 0.145 g (72%) of a white solid (mp 163–168 °C dec). This product was subsequently sublimed under high vacuum (100 °C) to give 0.119 g of pure **9**. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.57 (dd, 2 H, J = 1.6 Hz, 7.4 Hz, aromatic), 7.15 (m, 6 H, aromatic), 5.43 (d, 2 H, J = 1.3 Hz, vinyl), 5.02 (d, 2 H, J = 1.2 Hz, vinyl), 3.08 (m, 2 H, benzylic), 2.76 (m, 2 H, benzylic), 2.57 (s, 2 H, $H_2C{=}CCH$), 2.00 (m, 2 H, $ArCH_2CH_2$), 1.81 (m, 2 H, $ArCH_2CH_2$). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 147.2, 137.1, 135.3, 129.7, 128.4, 126.6, 126.1, 110.8, 40.5, 26.4, 25.5. IR (KBr) 3070, 2923, 2856, 1631, 1481, 1449, 1431, 1125, 1092, 941, 891, 867, 801, 771, 733 cm^{-1}. Mass spectrum (EI, 70 eV, relative percent) m/z 286 (M$^+$, 9), 156 (8), 142 (100), 128 (63), 115 (24), 58 (15). High-resolution mass spectrum calcd for $C_{22}H_{22}$: 286.1722. Found: 286.1721.

2-(2-Propenyl)-1-tetralone (10). Into a 10-mL capacity, sealable glass tube were added oxalic acid dihydrate (50 mg, 0.397 mmol), hydroquinone (10 mg, 0.091 mmol), distilled allyl alcohol (1.0 mL, 14.7 mmol), and **4** (3.84 g, 22.1 mmol). The tube was freeze–thaw–degassed (3×), sealed under vacuum, and placed in an oil bath for 15 h at 120 °C. The crude mixture was columned on silica with ether/hexanes (1:10) as eluent to provide 2.72 g (99%) of **10** as a clear oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.03 (dd, 1 H, J = 0.99 Hz, 7.9 Hz, aromatic), 7.45 (dt, 1 H, J = 1.4 Hz, 7.6 Hz, aromatic), 7.23 (m, 2 H, aromatic), 5.82 (m, 1 H, vinyl), 5.09 (m, 2 H, vinyl), 2.97 (m, 2 H, $ArCH_2$), 2.75 (m, 1 H), 2.52 (m, 1 H), 2.23 (m, 2 H), 1.85 (m, 1 H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 200.0, 144.7, 136.8, 133.8, 133.1, 129.3, 128.1, 127.2, 117.4, 47.8, 24.7, 29.2, 28.6. IR (neat) 3074, 2931, 2863, 1685, 1601, 1455, 1434, 1299, 1281, 1221, 1156, 912, 745 cm^{-1}. Mass spectrum (CI, isobutane, relative percent) m/z 187 (MH$^+$, 100), 145 (1), 118 (1). High-resolution mass spectrum calcd for $C_{13}H_{14}O$: 186.1045. Found: 186.1052.

1-Methylene-2-[3-(1-propenyl)]-1,2,3,4-tetrahydronaphthalene (11). To a stirring suspension of zinc powder (6.30 g, 96.3 mmol) in THF (107 mL) was added distilled diiodomethane (4.30 mL, 53.5 mmol) at room temperature. After 30 min, the mixture was cooled to 0 °C and a solution of $TiCl_4$ in dichloromethane (1 M, 10.7 mmol) was added dropwise. The solution was warmed to room temperature and stirred for 30 min. A solution of **10** (2.00 g, 10.7 mmol) in THF (22 mL) was then added dropwise. After the mixture was stirred for 30 min, ether (50 mL) was added and the mixture was extracted with saturated $NaHCO_3$ (100 mL). The aqueous layer was extracted with ether (2 × 100 mL), and the combined organics were dried ($MgSO_4$), filtered, and evaporated. The crude oil was columned on silica with hexanes to yield 1.29 g (65%) of a clear oil. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.58 (m, 1 H, aromatic), 7.10 (m, 3 H, aromatic), 5.82 (m, 1 H, vinyl), 5.45 (s, 1 H, vinyl), 5.00 (m, 3 H, vinyl), 2.80 (m, 2 H), 2.56 (m, 1 H), 2.25 (m, 2 H), 1.98 (m, 1 H), 1.77 (m, 1 H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 147.2, 137.4, 136.6, 134.9, 129.2, 127.7, 126.2, 125.2, 116.2, 108.4, 41.1, 37.4, 27.8, 26.9. IR (neat) 3073, 2926, 2860, 1640, 1627, 1485, 1454, 1433, 995, 911, 887, 774, 734 cm^{-1}. Mass spectrum (CI, isobutane, relative percent) m/z 185 (MH$^+$, 100), 141 (13), 131 (2), 117 (3). High-resolution mass spectrum calcd for $C_{14}H_{16}$: 184.1252. Found: 184.1239.

1-[4-(1-Butenyl)]-3,4-dihydronaphthalene (12). Compound **11** (70 mg, 0.38 mmol) was placed in a Carius tube, and toluene (40 mL) was added. The contents of the Carius tube were degassed on a high-vacuum line (four freeze–thaw cycles) and heated (210 °C, 3 h). Contents of the Carius tube were concentrated and purified by preparative VPC (120 °C, 10% SP-2100 on 80/100 Suppelcoport). ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.18 (m, 4 H, aromatic), 5.87 (m, 2 H, vinyl), 5.01 (m, 2 H, vinyl), 2.73 (t, J = 8.0 Hz, 2 H, $ArCH_2$), 2.28 (m, 4 H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 138.8, 137.0, 136.1, 135.1, 127.8, 126.8, 126.5, 125.3, 122.8, 114.8, 32.9, 32.3, 28.7, 23.3. IR (neat) 3064, 3029, 2932, 2885, 2832, 1640, 1488, 1450, 911, 763 cm^{-1}. Mass spectrum (CI, isobutane, relative percent) m/z 185 (MH$^+$, 100), 185 (100), 171 (5), 157 (4). High-resolution mass spectrum calcd for $C_{14}H_{16}$: 184.1252. Found: 184.1241.

1,2-Bis[1-(3,4-Dihydronaphthalenyl)]ethane (13). ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.18 (m, 8 H, aromatic), 5.87 (t, 2 H, J = 4.5 Hz, vinyl), 2.74 (t, 4 H, J = 8.0 Hz, $ArCH_2CH_2$), 2.66 (s, 4 H, ethane bridge), 2.25 (m, 4 H, $ArCH_2CH_2$). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 137.0, 136.6, 135.2, 127.8, 126.8, 125.6, 125.3, 122.3, 32.1, 28.7, 23.4. IR (KBr) 2924, 2852, 1459, 1449, 1425, 1262, 1157, 1096, 1068, 1018, 821, 792, 776, 740 cm^{-1}. Mass spectrum (EI, 70 eV, relative percent) m/z 286 (M$^+$, 36), 258 (5), 156 (12), 142 (100), 128 (69), 115 (21), 91 (7). High-resolution mass spectrum calcd for $C_{22}H_{22}$: 286.1722. Found: 286.1706.

2,2′-Bis(methyl-3,4-dihydronaphthalene) (14). Initial kinetic studies on compound **9** produced compound **14**, an isomerized product, in high yield. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.20 (m, 8 H, aromatic), 2.85 (m, 4 H, $ArCH_2CH_2$), 2.35 (m, 4 H, $ArCH_2CH_2$), 1.97 (m, 6 H, CH_3). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 137.7, 136.5, 135.6, 127.1, 126.4, 126.2, 123.2, 28.7, 27.9, 15.5. IR (KBr) 3056, 3019, 2896, 1696, 1653, 1617, 1465, 1374, 1243, 1218, 1203, 833, 800 cm^{-1}. Mass spectrum (EI, 70 eV, relative percent) m/z 286 (M$^+$, 100), 271 (21), 165 (11), 155 (25), 143 (71), 129 (74), 115 (43), 91 (31). High-resolution mass spectrum calcd for $C_{22}H_{22}$: 286.1722. Found: 286.1711.

Kinetic Studies of 1-Methylene-2-[3-(1-propenyl)]-1,2,3,4-tetrahydronaphthalene (11). Compound **11** (11.2 mg, 0.061 mmol, purified by preparative VPC) and dodecane (6 μL) were added to a 10-mL volumetric flask, and the mixture was diluted with benzene. All samples for kinetic analysis were prepared by placing 100 μL of this stock solution into a small thermolysis ampule. Ampules were degassed (three freeze–thaw cycles) and sealed under vacuum.

Thermolysis ampules were constructed of 3 in. × $^3/_8$ in. i.d.) Pyrex tubing. Ampules were washed with acetone (2×) and distilled water (2×) and soaked in 10% NH_4OH solution. Following a thorough rinse with distilled water, tubes were dried (24 h, 145 °C) and stored in a desiccator until use. Measurements of the rate of Cope rearrangement of compound **11** were carried out using a refluxing solvent bath as a heat source. The data are obtained from eight samplings at four different temperatures. The temperatures were calibrated with IUPAC standardized thermometers with readings to 0.1 °C. The rates determined at each temperature are given below.

solvent bath	temp (°C)	rate (s^{-1})
p-xylenes	138.2 ± 0.2	0.000 025 2
n-nonane	150.4 ± 0.2	0.000 061 4
tert-butylbenzene	168.8 ± 0.2	0.000 237
o-dichlorobenzene	179.6 ± 0.2	0.000 512

A plot of $1/T$ vs $-\ln k$ is linear, and the derived activation energy parameters are given in Table I.

Solvent Effects on the Rate of Cope Rearrangement of 1-Methylene-2-[3-(1-propenyl)]-1,2,3,4-tetrahydronaphthalane (11). Compound **11** (ca. 11 mg) was placed in a vial and diluted to 5 mL with dry nanograde hexanes. This solution was divided into four portions and each portion concentrated in a small thermolysis ampule. Each concentrated sample was diluted with 100 μL of a different solvent (octane, benzene, *o*-dichlorobenzene, or THF) along with 3 μL of dodecane as internal reference. From these solutions, two samples were prepared for each of the four solvents. Samples were thermolyzed simultaneously at 150.4 ± 0.2 °C in refluxing *n*-nonane. Calculated three-point rate constants are summarized below.

reaction solvent	rate (s^{-1})
octane	5.23×10^{-5}
THF	5.79×10^{-5}
benzene	7.15×10^{-5}
o-dichlorobenzene	8.99×10^{-5}

Kinetic Studies of *d,l*-Bis-2,2′-(1-methylene-1,2,3,4-tetrahydronaphthalene) (8). Compound **8** (93.7 mg, 0.327 mmol) was dissolved in distilled benzene-d_6 (32.7 mL). Portions of this solution (0.6 mL) were placed in thermolysis ampules (2 in. × $^1/_2$ in i.d.) and degassed (three freeze–thaw cycles) on a high-vacuum line. All tubes were sealed using a gas torch and exposed to the indicated temperatures in a thermally controlled water bath for the designated times. Care was taken to maintain samples at 0 °C before and after exposure to thermal conditions. All thermal reactions were quenched by subjecting the ampules to a −78 °C bath. Immediately before analysis by ^{1}H NMR, ampules were warmed to 0 °C and the contents transferred to an NMR tube. NMR tubes were maintained at 0 °C until they were placed in the NMR probe. All kinetic runs were analyzed by taking the ratio of the starting material (**8**) vinyl protons to the vinyl protons of the product (**13**). The data obtained from these studies are given below.

temp (°C)	rate (s^{-1})
40.3	0.000 0854
50.0	0.000 239
60.0	0.000 856
70.0	0.001 80

A plot of $-\ln k$ vs $1/T$ shows a well-behaved first-order reaction.

Kinetic Studies of *meso*-Bis-2,2′-(1-Methylene-1,2,3,4-tetrahydronaphthalene) (9). Initial attempts to survey the Cope rearrangement of **9** to diene **13** resulted in near-quantitative yield of the isomerized product **14**. Many different tube conditioning techniques and thermal conditions were tried. It was found that small amounts of Proton Sponge in the thermolysis ampule with compound **9** completely suppressed isomerization to product **14**. Thus, the use of Proton Sponge in the thermolysis mixture allowed the Cope rearrangement to proceed without interference from competing isomerizations.

Thermolysis ampules (3 in. × $^3/_8$ in. i.d.) were prepared by washing with a concentrated KWIP soap solution (2×), flushing with excess distilled water (continuous flush 10 min), and drying in a vacuum oven (185 °C, 24 h). No metal syringes or spatulas were used. Thermolysis ampules were slowly cooled in a vacuum oven and stored in a desiccator until use (within 1 day).

Sublimed **9** (ca. 0.2–0.4 mg) was placed in an ampule via a glass pipet. Similarly, Proton Sponge (ca. 0.1–0.2 mg) was placed in the ampule, and the contents were degassed (under vacuum at room temperature). Ampules were sealed and submitted to the thermal conditions in a salt bath consisting of 40% $NaNO_2$, 7% $NaNO_3$, and 53% KNO_3 and heated by 2 Vicor heaters controlled to ±0.2 °C by a thermal gauge. All thermal reactions were quenched by quickly placing the tube in a water bath (room temperature). The ampules were broken open, and benzene (150 μL) was added. Analysis of this solution by capillary GC (200 °C) gave well-behaved first-order rate data. The data obtained from these kinetic studies are shown below.

temp (°C)	rate (s^{-1})
239.8	0.000 206
254.6	0.000 556
260.9	0.000 985
269.9	0.001 90
283.0	0.003 40

The activation energies for the isomerization of the three substrates are summarized in Table I.

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