

While detailed configuration interaction calculations are complex, the qualitative consequences of configuration interaction and the import of state-correlation diagrams are quite uncomplicated and accessible.

In some circumstances the dichotomy between orbital symmetry allowed and disallowed reactions may be more profitably replaced by a dichotomy based on how state-conservation may be achieved. Thus the rearrangements leading to dihydroindene treated above,  $7 \rightarrow 8 \rightarrow 10 \rightarrow 11$ , might be described as a sequence of three state-conservative isomerizations,  $[\pi 2_s + \sigma 2_s + \pi 2_s]$  (OS),  $[\pi 2_s + \sigma 2_s]$  (CI), and  $[\pi 2_s + \pi 2_s + \sigma 2_s]$  (OS), giving in each case the stereochemistry of utilization of the two-electron components and a label (OS or CI) for the way in which state conservation may be realized. Tables giving orbital symmetry allowed and disallowed reaction types might be usefully relabeled "state-conservative through OS" and "state-conservative through CI." Compounds having no low-energy OS-dominated state-conservative path, but having electronic structural features appropriate for a low activation energy conversion (describable through effective configuration interaction), might be expected to show the CI-dominated reaction path.

The recognition of delocalization accompanying progress along a reaction coordinate as a great facilitator of effective configuration interaction and thus

a patron of state-conservative CI dominant processes may also provide an understanding of how calculations based on thermochemical data and radical models may be so successful in predicting activation energies<sup>28</sup> even for hydrocarbon rearrangements that seem to be entirely nonradical. Parallels between estimated radical stabilization and bond delocalization capacities for various substituents would not be surprising.

Better calculations of reacting systems including configuration interaction, and a wider appreciation of its energy-influencing and "orbital-symmetry inverting" manifestation, may contribute to a new stage of work on cycloadditions, one in which the concepts of orbital symmetry conservation and energetic concertedness are separate and independent. Experiments testing for the energetic concertedness of reactions and for the characteristics of short-lived singlet intermediates, suggested by this new conceptual framework, may well prove rewarding.

*We gratefully acknowledge financial support for our studies on cycloaddition chemistry contributed by the National Science Foundation, and by The Cities Service Oil Co., The Du Pont Co., and Hoffmann-LaRoche Inc.*

(28) S. W. Benson, "Thermochemical Kinetics," John Wiley, New York, N. Y., 1968; S. W. Benson and H. E. O'Neal, "Kinetic Data on Gas Phase Unimolecular Reactions," NSRDS-NBS 21, U.S. Government Printing Office, Washington, 1970.

## Orbital-Symmetry-Forbidden Reactions

JEROME A. BERSON

*Department of Chemistry, Yale University, New Haven, Connecticut 06520*

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The organic chemist, for all his modern sophistication, remains fundamentally a maker of compounds. Heritage, training, and experience teach him that syntheses of complex molecules are laborious and require construction of most of the bonds one at a time. This accounts, as much as any other factor, for his abiding fascination with concerted reactions, in which two or more bonds are made or broken simultaneously.

The traditional criteria of concert follow directly from the idea that bonding of the reactive sites is maintained throughout. Thus, the recovery of part of the cost of bond breaking by bond making should depress the activation energy below that expected for a rate-determining complete rupture of any of the relevant bonds of the reactant. Since the reactive sites must

remain in close proximity to preserve bonding, concerted reactions would tend to be stereospecific. Moreover, the same proximity requirement often would result in a low Arrhenius preexponential term or low entropy of activation because of the conversion of internal rotational to vibrational degrees of freedom in the transition state.

Not many thermal reactions clearly satisfy both the kinetic and the stereochemical criteria of concert. In the bimolecular group, perhaps the best known example is the Diels-Alder reaction,<sup>1</sup> while the unimolecular cases include the cyclobutene  $\rightarrow$  butadiene electrocyclic reaction,<sup>2</sup> the Claisen and Cope rearrangements,<sup>3</sup> and the retroene reaction that converts *cis*-2-methyl-1-vinylcyclopropane to *cis*-1,4-hexadiene.<sup>4</sup>

(1) A. Wassermann, "Diels-Alder Reactions," Elsevier, New York, N. Y., 1965.

(2) (a) E. Vogel, *Justus Liebig's Ann. Chem.*, **615**, 14 (1958); (b) R. Criegee and K. Noll, *ibid.*, **627**, 1 (1959); R. Criegee, D. Seebach, R. E. Winter, B. Boretzen, and H.-A. Brune, *Chem. Ber.*, **98**, 2339 (1965), and references cited therein.

(3) S. J. Rhoads in "Molecular Rearrangements," Part 1, P. de Mayo, Ed., Interscience, New York, N. Y., 1963, Chapter 11; (b) W. von E. Doering, V. G. Toscano, and G. H. Beasley, *Tetrahedron*, **7**, 25299 (1971).

*Jerome A. Berson took his undergraduate degree from the College of the City of New York, and his Ph.D. from Columbia University. He has taught chemistry since 1950, first at the University of Southern California, then at the University of Wisconsin, and now at Yale University, where he is professor of chemistry and (until 12:01 a.m., July 1, 1974) chairman of the department. His present research is directed toward an understanding of the mechanisms of molecular rearrangements, thermal processes, and the properties of diradicals and other reactive intermediates.*

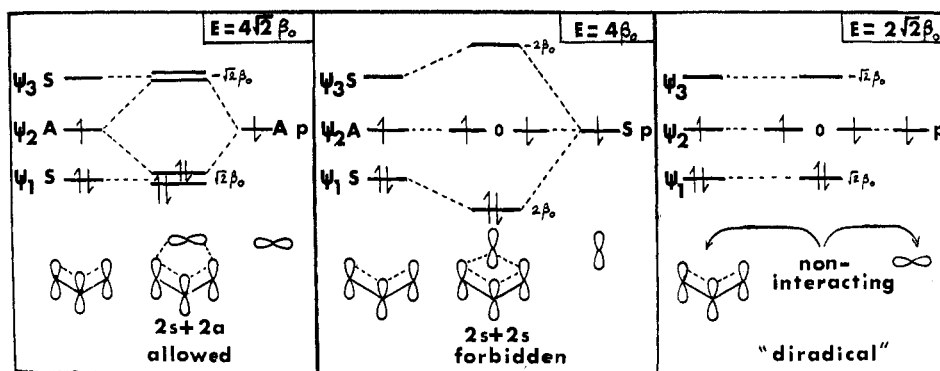


Figure 1. Schematic diagram of orbital energies and topologies of three different suprafacial 1,3-sigmatropic rearrangement transition states derived by interaction of an allyl unit with a carbon p orbital.

Until recently, the search for concerted reactions was empirical, guided by intuition rather than theory. The application of experimental criteria, especially the energetic one, was frequently controversial, largely because of uncertainty about the behavior to be expected of nonconcerted processes.

It is therefore easy to understand the excitement caused by the advent of the orbital symmetry rules of Woodward and Hoffmann, which at one stroke dispelled a whole area of confusion. These exceptionally fruitful ideas have been summarized as "orbital symmetry is conserved in concerted reactions",<sup>5a</sup> a statement that implies the exclusionary form, "a reaction in which orbital symmetry is not conserved cannot be concerted." This dictum has guided all recent effort in the field. It is now a simple matter to determine whether concert in a process under consideration is "allowed" or "forbidden." Violations ("There are none!"<sup>5b</sup>) are permitted only under extreme thermodynamic driving force (as when a highly strained reactant lacks an allowed pathway) or under "demonic intervention."<sup>5b</sup>

And yet, one doubts. Is admission to the elect company of concerted reactions really so restricted? Are the forbidden processes forever banished with the cold finality of dogma? The following exploration of these questions consists of two parts. The first contains some simple theoretical considerations, new but not really heretical exegeses of the canon, that show the permissibility of forbidden concerted reactions. The second describes some relevant experiments.

**The Electronic Basis for the Order of Preference Allowed > Forbidden > Diradical in 1,3-Sigmatropic and Other Transition States. The Role of Subjacent Orbitals.**<sup>6,7</sup> Transition states with orbital topologies corresponding to allowed processes are electronically

favored. The reasons for this can be expressed by a number of formalisms, among which may be listed those relying upon the phase properties of the highest occupied<sup>9</sup> or frontier<sup>10</sup> molecular orbitals, the symmetry designations of the reactant and product occupied orbitals and states,<sup>11</sup> the symmetries of vibrational modes of reactant and transition state,<sup>12</sup> and the aromaticity of the transition state.<sup>13-15</sup>

However, many reactions occur in which extrasymmetric factors (steric repulsions, poor orbital overlap, etc.) preclude the allowed process. What is the proper description of these reactions?

A forbidden concerted reaction may be defined as one in which bonding between the reacting sites is maintained throughout, but the orbital topology does not conform to the Woodward-Hoffmann rules. The term "forbidden" implies that such a reaction would have a transition state with net antibonding character. Previous discussion<sup>5b</sup> explicitly postulates that in such cases the system would shun the forbidden concerted pathway and proceed by a nonconcerted mechanism involving discrete diradical (or zwitterionic) intermediates. This is equivalent to a proposal that orbital phase considerations predict the order of preference of transition states to be allowed > diradical > forbidden.

Two corollaries of this position are that, in order to avoid generating forbidden character, the orbitals at the reactive sites in the diradical would overlap as little as possible, and consequently, that reactions occurring by other than allowed pathways would tend to occur stereorandomly. The following discussion reaches different conclusions.

Figure 1 shows the essentials of the argument applied

(8) For reasons different than those given here, concert in some symmetry-forbidden processes has been invoked by W. Schmidt, *Tetrahedron Lett.*, 581 (1972), and by N. D. Epiotis, *J. Amer. Chem. Soc.*, **94**, 1924 (1972).

(9) R. B. Woodward and R. Hoffmann, *ibid.*, **87**, 395 (1965); R. Hoffmann and R. B. Woodward, *Accounts Chem. Res.*, **1**, 17 (1968).

(10) K. Fukui, *ibid.*, **4**, 57 (1971).

(11) H. C. Longuet-Higgins and E. W. Abrahamson, *J. Amer. Chem. Soc.*, **87**, 2045 (1965).

(12) L. Salem, *Chem. Phys. Lett.*, **3**, 99 (1969).

(13) (a) H. E. Zimmerman, *J. Amer. Chem. Soc.*, **88**, 1563, 1566 (1966); (b) *Accounts Chem. Res.*, **4**, 272 (1971).

(14) M. J. S. Dewar, *Tetrahedron Suppl.*, **8**, 75 (1966); *Angew. Chem., Int. Ed. Engl.*, **10**, 761 (1971).

(15) The classification of thermally allowed reactions as those involving an odd number of suprafacial reaction elements<sup>5</sup> is a useful mnemonic for recognizing aromatic transition states.

(4) W. R. Roth and J. König, *Justus Liebigs Ann. Chem.*, **688**, 28 (1965).

(5) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970: (a) p 1. (b) p 173.

(6) We were pleased to learn through personal communication that Professor Lionel Salem also had been working on the problem of forbidden concerted reactions and independently had reached theoretical conclusions similar to our own. The form of the argument presented here is one developed collaboratively.<sup>7</sup>

(7) J. A. Berson and L. Salem, *J. Amer. Chem. Soc.*, **94**, 8917 (1972).

to the case of thermal suprafacial 1,3-sigmatropic rearrangement of carbon. There are two idealized transition-state geometries for concerted processes, one in which the migrating carbon retains configuration (a forbidden  $2_s + 2_s$  reaction), another in which inversion occurs (an allowed  $2_s + 2_a$  reaction). The energy level scheme is derived by permitting interaction between the allyl and p orbitals in the two topological combinations corresponding to the transition-state geometries. We consider first, for didactic purposes, the case in which the energies themselves are derived from simple Hückel calculation on the assumption of equal nearest-neighbor interactions (all nonzero off-diagonal matrix elements =  $\beta_0$ ).

A hypothetical "diradical" rearrangement would have a transition-state electronic energy approximating that of the noninteracting allyl and p orbitals. It is clear from Figure 1 that the transition state for the allowed reaction is stabilized relative to the "diradical" case largely because of the lowering of an antisymmetric and nonbonding level, the highest occupied molecular orbital (HOMO) of the allyl unit, to a strongly bonding level.

However, Figure 1 also shows that there can be appreciable stabilization of the forbidden transition state. This results not from an effect on the HOMO but instead from the interaction of the carbon p orbital with a *subadjacent*, bonding allyl orbital. Two of the four electrons involved thus can be accommodated in a more stable orbital than is the case in the separated fragments. The energies of the electrons in the allyl HOMO ( $\psi_2$ ) and the original p orbital are hardly affected. The allyl  $\psi_2$  orbital does not mix with the p orbital, and although  $\psi_1$  and  $\psi_3$  both mix with p, the interactions approximately cancel each other. Similar conclusions emerge from a corresponding treatment of reactions in which the migrating group retains configuration and rearranges either by an allowed antarafacial or a forbidden suprafacial one.<sup>16</sup>

In most geometries corresponding to the forbidden transition state of Figure 1, there is substantial overlap between the migrating p orbital and the orbital on the center carbon of the allyl system. This further depresses the energy of the subadjacent level (to  $2.56\beta_0$  if the interaction is assumed equal to the nearest-neighbor interactions) and reinforces the effect.

Subadjacent orbital control of the transition-state geometry normally would not be expected to become important until steric factors became unfavorable to the operation of Woodward-Hoffmann control. However, it must be kept in mind that, even in the most favorable cases known, the allowed suprafacial-inversion 1,3-sigmatropic transition state is only slightly preferred experimentally, the geometric distortions needed to achieve it being very severe.<sup>17</sup> Conse-

quently, it should not be difficult to present steric or other extrasymmetric obstacles to its achievement and thereby bring the forbidden concerted reaction to the fore. In such circumstances, the assumptions of equal interaction terms used to derive the orbital energies in Figure 1 become quite unsatisfactory, but calculations based on perturbation theory provide a more realistic comparison of the two types of stabilization. Applied to a model reaction, the 1,3-sigmatropic rearrangement of methylenecyclobutane, the calculations give stabilization energies of 2.9–5.8 kcal/mole for the allowed reaction and 1.6–3.2 kcal/mole for the forbidden. The calculations are too crude to permit a prediction on the stereochemistry of the rearrangement but clearly suggest that the allowed and forbidden pathways are closely balanced in energy.<sup>18</sup>

The major conclusion from Figure 1 is that the same basic argument used to demonstrate that the allowed concerted topology is best necessarily implies that the forbidden concerted one, not the diradical, is second best. In any real case, of course, other electronic factors<sup>19</sup> or steric effects may reverse this, but there is a general underlying bias toward the order of preference allowed > forbidden > diradical. To the extent that the subjacent orbital factor controls the reaction under study, concerted and hence stereospecific behavior is to be expected, even when the system is forced to adopt the forbidden topology. This is in effect a return to the organic chemist's intuitive pre-1965 assumption that there usually is energetic benefit in maximizing orbital overlap between the reactive sites.

**Sigmatropic Rearrangements with Forbidden Stereochemistry. The Magnitude of the Energy Benefit in the Allowed Process.** As the preceding discussion implies, some of the fruitful systems to examine for experimental verification of forbidden concerted processes should be those in which extrasymmetric factors have at least partially counterbalanced the normal preference for the allowed process. Unfortunately, this approach necessarily sacrifices some or all of the kinetic driving force, one of the experimental criteria of concert. However, it is likely that, pending the availability of much more reliable estimates of heats of formation of diradicals, decisions on concert often will have to be made on other than energetic grounds.

The allowed suprafacial 1,3 pathway requires inversion of configuration of the migrating group by bonding of the *back lobe* of the migrating carbon to the terminus of migration. This somersaulting action

(c) 22nd National Organic Chemistry Symposium, Ann Arbor, Mich., June 13–17, 1971, Abstracts, p 28; (d) G. L. Nelson, Ph.D. Dissertation, University of Wisconsin, 1969.

(18) The stabilization energy calculated for the allowed reaction is based upon a geometry in which the allyl residue is twisted to improve overlap with the migrating orbital. If the loss of allylic resonance thus incurred were taken into account, the allowed process would become even less favorable.

(19) For example, since the conclusions are based upon one-electron considerations, it is not inconceivable that the important two-electron energies characteristic of open shells<sup>20</sup> could reverse, in certain cases, the ordering of the nonconcerted and forbidden transition-state energies.

(20) L. Salem and C. Rowland, *Angew. Chem., Int. Ed. Engl.*, **11**, 92 (1972).

(16) Very similar arguments apply to electrocyclic reactions. For example, the transition state for the cyclobutadienoid forbidden reaction (disrotatory opening of cyclobutene) also has a stabilized subadjacent level, the behavior of which may be seen in ref 13.

(17) (a) J. A. Berson and G. L. Nelson, *J. Amer. Chem. Soc.*, **89**, 5303 (1967); (b) J. A. Berson, *Accounts Chem. Res.*, **1**, 152 (1968);

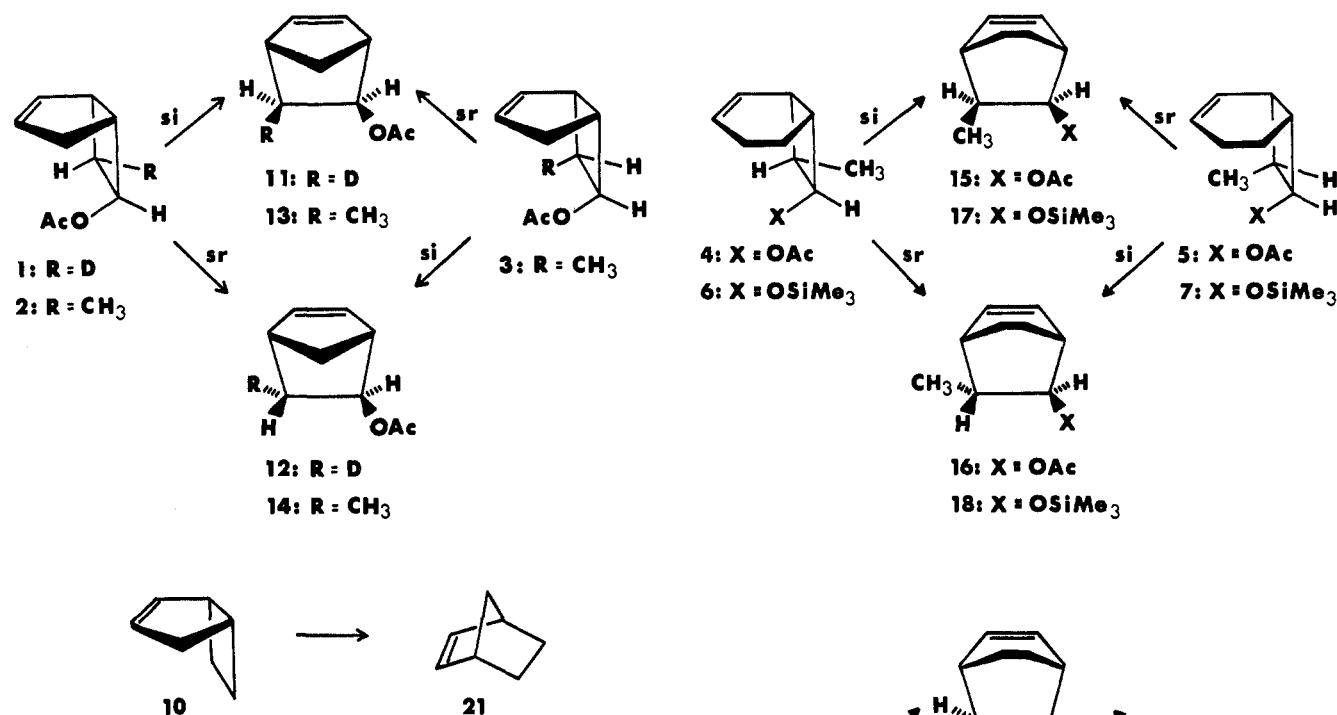


Figure 2.

Table I

Reactant	$E_a^a$ (log $A$ ) <sup>b</sup>	Rate ratio, <sup>c</sup> allowed (si)/ forbidden (sr)	Ref
Bicycloheptenes			
1	46.8 (13.7)	19	17, 21
2	47.1 (14.2)	10	17, 22
3		0.14	22
10	48.6 (14.8) <sup>e</sup>	?	24a
Bicyclooctenes			
4		2.2	23
5		0.08	23
6	46.7 (13.2)	2.4	23
7		0.065	23
8	37.3 (11.9)	>250	23
9		<i>d</i>	23

<sup>a</sup> Arrhenius activation energy in kilocalories/mole for 1,3-sigmatropic rearrangement. <sup>b</sup> Logarithm of preexponential term (in seconds). <sup>c</sup> Ratio of rates of formation of products by *si* and *sr* reactions, obtained by kinetic analysis and/or by extrapolation of product ratio to zero time. <sup>d</sup> The ratio could not be measured because **9** suffers side reactions. <sup>e</sup> Values for total disappearance of starting material.

produces the allowed transition-state topology, but the overlap is necessarily weak. Some feeling for the magnitude of the preference for the allowed process is provided by the following results.

Figures 2 and 3 show two series of thermal rearrangements, bicyclo[3.2.0]- to bicyclo[2.2.1]heptenes, and bicyclo[4.2.0]- to bicyclo[2.2.2]octenes. All of these reactions now have been investigated. The stereochemical results of the pyrolysis experiments are given in Table I,<sup>21-24</sup> which also lists the available Arrhenius

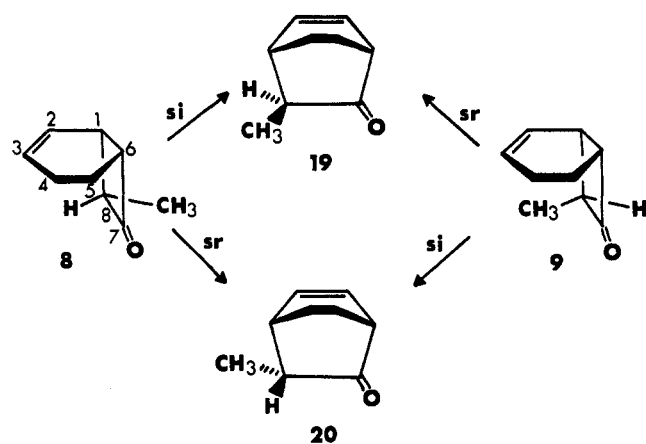
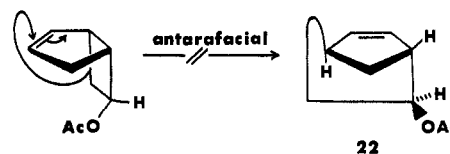


Figure 3.

parameters. In both of these series, the structure of the reactant ensures suprafacial rearrangement, since an antarafacial reaction would produce a highly strained trans-bridged product (e.g., **22**).



In the case of compound **1**, the observed 19-fold preference for inversion over retention would correspond (at 300°, the pyrolysis temperature) to only 3.4 kcal/mole of free energy benefit for the allowed pathway over the forbidden one (or 2.5 kcal/mole over a hypothetical diradical pathway giving equal amounts of inversion and retention product). Those who have tried to estimate activation energies for thermal homolytic reactions from bond energy tables will recognize that differences this small usually are within the error limits of the estimates. It is not surprising,

(24) (a) A. T. Cocks and H. M. Frey, *J. Chem. Soc. A*, 2564 (1971). (b) In this connection, Cocks and Frey<sup>24a</sup> report the  $E_a$  and log  $A$  terms for **10**, which are those expected for a diradical process. The absence of a stereochemical label in their experiment precludes the application of the more sensitive criterion of concert.

(21) (a) J. A. Berson and G. L. Nelson, *J. Amer. Chem. Soc.*, **89**, 5503 (1967); (b) J. A. Berson, *Accounts Chem. Res.*, **1**, 152 (1968).

(22) J. A. Berson and G. L. Nelson, *J. Amer. Chem. Soc.*, **92**, 1096 (1970).

(23) R. W. Holder, unpublished work; R. W. Holder, Ph.D. Dissertation, Yale University, 1972.

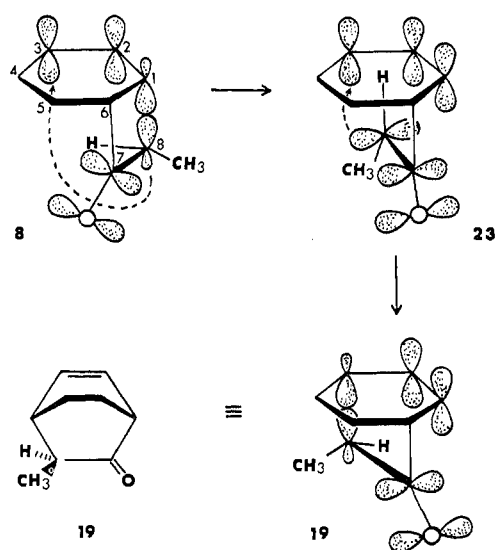


Figure 4.

therefore, to observe that the experimental activation energies for the rearrangements of **1** and **2** (Table I) are only slightly (and perhaps not significantly) below the estimated<sup>21b</sup> value for the hypothetical diradical reaction (48–51 kcal/mole). These rearrangements show no strong evidence of kinetic driving force despite the obvious control of the reaction stereochemistry by orbital symmetry forces.<sup>24b</sup>

When the substituent on the migrating carbon is deuterium (**1**) or exo methyl (**2**, **4**, **6**, **8**), the allowed inversion reaction is the predominant pathway in these rearrangements. However, there are some striking variations in the stereospecificity. The most remarkable of these is the rearrangement of the ketone **8** to give exclusively *exo*-3-methylbicyclo[2.2.2]oct-5-en-2-one (**19**), the unstable epimer of the **19**–**20** pair. This reaction is much more stereospecific than any of the other predominantly allowed rearrangements of Table I. Accompanying the increased stereospecificity is a 10<sup>6</sup>-fold increase in rate as compared to those of model systems, *e.g.*, **4** or **6**, which lack the carbonyl group. The rate enhancement is caused largely by a decrease of about 9 kcal/mole in  $E_a$ , which in turn seems to result from cooperative action between the somersaulting motion favored by orbital symmetry and the stabilization of the transition state by conjugation involving the carbonyl group. The carbonyl  $\pi$  orbital is virtually orthogonal to the breaking C<sub>1</sub>–C<sub>8</sub>  $\sigma$  bond of **8** in the ground state (Figure 4), but as reaction proceeds the allowed rotation about the C<sub>7</sub>–C<sub>8</sub> bond brings these orbitals into good alignment in the transition state (**23**). Continuation of the rotation gives the product of rearrangement with inversion (**19**).

To interpret some of the other variations in stereospecificity shown in Table I, it first will be necessary to discuss 1,3 rearrangements in which the normal inversion is prevented by the deliberate construction of a steric blockade.

**The Sense of Rotation in the Suprafacial-Inversion Rearrangement.** The orbital symmetry rules not only require overall inversion of configuration of the mi-

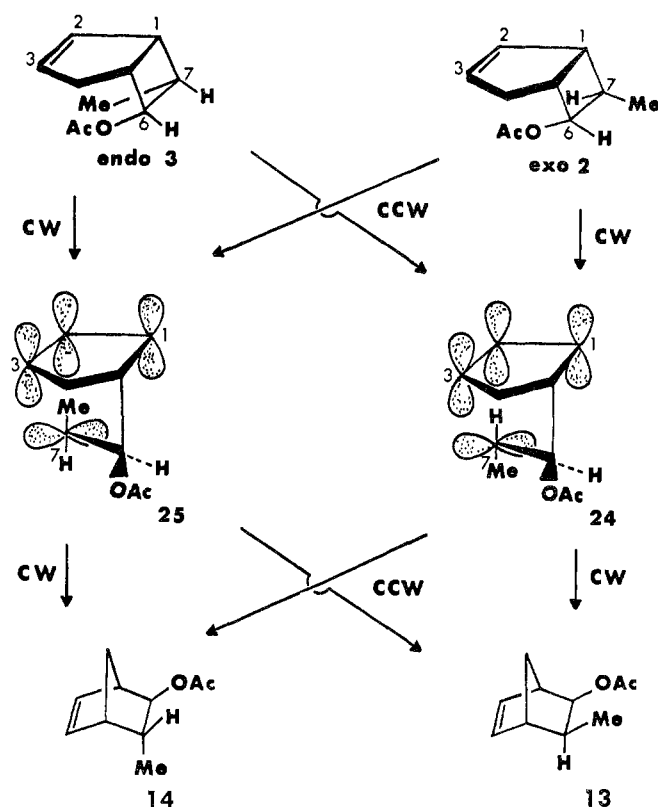


Figure 5.

grating group in the allowed suprafacial 1,3-sigmatropic rearrangement but also imply, for the systems under study here, that the inversion should occur by rotation *in a specific sense* about the bond joining the migrating carbon to the molecular framework. In the conventional drawings used in this discussion, the required rotational sense is clockwise (CW), because in that process overlap between the back lobe of the migrating carbon and the appropriate lobe of the migration terminus grows most rapidly.

Although the clockwise (CW) and counterclockwise (CCW) rotations give the same product from a particular reactant, there is an experimental method for distinguishing the two paths. This is based on the rationale shown in Figure 5. An endo substituent on the migrating carbon of the reactant will be forced into the face of the allylic framework in the transition state (or intermediate) for CW inversion, whereas in the CCW inversion it is the exo substituent that turns inside. Thus, because of the severe steric repulsions generated, the rate of rearrangement with inversion in the CW mode from endo methyl reactant (**3**) should be substantially less than that from exo methyl reactant (**2**), whereas inversion by the CCW path should lead to  $k_{inv}(endo) > k_{inv}(exo)$ . The results of this test<sup>22</sup> show that  $k_{inv}(exo)$  is at least 54 times  $k_{inv}(endo)$ . An endo substituent thus sterically blocks the inversion mechanism, as is predicted by the orbital symmetry requirement for CW rotation.

**Mechanism of the Rearrangement with Retention.** In the endo-substituted cases of Table I for which information is available (compounds **3**, **5**, and **7**), rearrangement occurs with predominant retention of

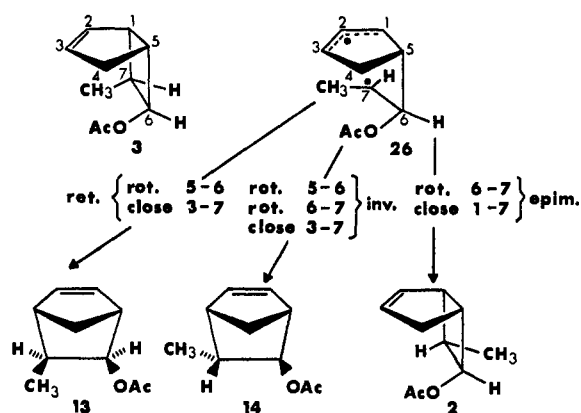


Figure 6.

configuration. Conforming to the prevailing reluctance to invoke forbidden concerted reactions, we first interpreted this behavior in the case of **3** as a manifestation of a diradical process.<sup>22</sup> Some support for this interpretation was provided by the observed epimerization of **3** to **2**.<sup>22</sup> Similar epimerizations occur in the pyrolyses of **4**, **5**, **6**, and **7**.<sup>23</sup>

Superficially, at least, epimerization might be a reasonable alternative fate for the hypothetical diradical, e.g., **26**, Figure 6. However, more detailed examination of the idea reveals some awkward aspects. For example, the total rate of rearrangement of *endo*-methylbicyclo[3.2.0]heptene (**3**) to **13** and **14** is only about 1.5 times that of its epimerization to **2**.<sup>22</sup> The *endo*-methylbicyclo[4.2.0] compound **7** rearranges about four times as rapidly as it epimerizes, but the *exo* methyl isomer **6** actually epimerizes faster than it rearranges. The epimerization products are highly strained cyclobutanes, whereas the rearrangement products are much less strained cyclohexanes. If a common diradical is the intermediate in both processes, the experimental observations suggest the somewhat surprising conclusion that, despite the unfavorable strain-energy difference, the rate of ring closure of the diradical to epimerization product competes with and sometimes exceeds that to rearrangement product. Thus, although the epimerization may involve a diradical, it is not clear that the same species is an intermediate in the rearrangement.

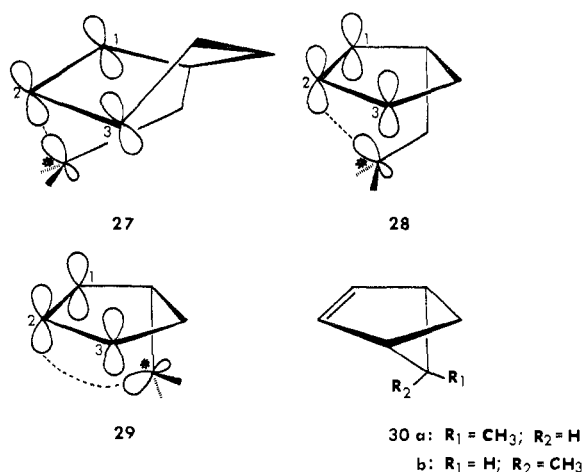
More generally, by the application of ordinary experimental criteria, it is difficult to distinguish the alleged diradical retention mechanism from the presumably concerted inversion mechanism. For example, the rate of rearrangement with inversion ( $k_{inv}$ ) from *exo* methyl compound **2** is seven times as great as the rate of rearrangement with retention ( $k_{ret}$ ) from *endo* methyl compound **3**. This is in the right direction for concert in **2** and not in **3**, but the factor is not impressive. The magnitudes of the stereospecificities, factors of 10 favoring the allowed inversion from **2** and **7** favoring the forbidden retention from **3**, again provide little support for a sharp discontinuity in mechanism. In the comparisons of the bicyclo[4.2.0] series (Table I), the preferences for retention in the *endo* methyl compounds, **5** and **7** (factors of 12.5 and 15, respectively), are actually greater than the preferences for

inversion in the *exo* methyl counterparts, **4** and **6** (2.2 and 2.4, respectively). Moreover, the absolute rate,  $k_{ret}$ , from **7** is also greater than  $k_{inv}$  from **6**, the ratio being about 4.6 at 300°. With these data in mind, it is instructive to ask whether a chemist who had never heard of orbital symmetry rules would be able to tell which preference, inversion or retention, denoted a concerted reaction.

It is conceivable that, by a judicious assignment of properties to the hypothetical species on the reaction pathway, a concordant diradical mechanism could be constructed to account for the rearrangements that proceed with retention. The mere fact that the ascription of such properties is *ad hoc*, of course, does not necessarily damage the diradical explanation, since it can be argued that the experimental results are acting as a guide to an understanding of diradicals. However, the working hypothesis that both the allowed inversion and the forbidden retention reactions are concerted requires no additional assumptions and, at least for the present, offers substantial pragmatic advantages in the interpretation of these and other puzzling observations.

As Table I shows, the *exo* methyl compounds, **2**, **4**, and **6**, all give predominant inversion of configuration, but the stereospecificity is lower in the bicyclo[4.2.0]octene cases, **4** and **6** (inversion:retention ratios = 2.2 and 2.4), than in the bicyclo[3.2.0]heptene case, **2** (inversion:retention ratio = 10). In the *endo* methyl cases, **3**, **5**, and **7**, where retention predominates, the stereospecificity in the bicyclo[4.2.0]octenes, **5** and **7** (retention:inversion ratios = 12.5 and 15), now is greater than in the bicyclo[3.2.0]heptene, **3** (ratio = 7). These variations may be included under one phenomenological description if we recognize that in both *exo* and *endo* methyl series expansion of the ring containing the allylic framework from five to six membered favors the retention pathway relative to the inversion. We persist in a so far unsuccessful attempt to explain this in terms of a diradical mechanism for both the inversion and retention pathways. A competition between concerted inversion and diradical retention reactions could conceivably account for the observed trends, for example, if it is assumed that product strain effects retard the retention reaction more than the inversion. There is no obvious independent basis for such an assumption. However, the hypothesis of competing concerted reactions offers the following natural interpretation of the data.

The previous discussion emphasized the strong subadjacent orbital stabilizing effect of interaction between the front lobe of the migrating carbon and the suprafacial lobe of  $C_2$  of the allylic framework. This stabilization favors the forbidden concerted suprafacial-retention pathway and should be very sensitive to geometric factors. An inspection of molecular models clearly shows that the greater flexibility introduced by the extra methylene group of the bicyclo[4.2.0]octene substrates makes possible a conformation and a suprafacial-retention transition state **27** derived from it



in which overlap of the relevant orbital lobes at  $C_2$  and the migrating carbon ( $C^*$ ) is more favorable than in the corresponding transition state **28** from the rigid bicyclo[3.2.0]heptenes.

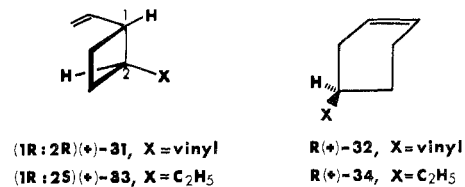
As a corollary, we may infer that geometric factors which decrease this overlap should further retard the rearrangement with retention. An appropriate test case would be the bicyclo[2.1.1]hexene system **30**, where the overlap in the retention transition state (**29**) is much worse even than in the bicyclo[3.2.0]heptenes. It is gratifying to find experimental confirmation already available in the work of Roth and Friedrich,<sup>25</sup> who report an inversion:retention ratio of 197 for the exo methyl isomer, **30a**, and a retention:inversion ratio of 0.45 for the endo compound, **30b**. Both results are in agreement with the predicted sharp decline in the retention component (bicyclo[4.2.0]octene > bicyclo[3.2.0]heptene  $\gg$  bicyclo[2.1.1]hexene).

By the same argument, the forbidden suprafacial-retention reaction might be expected to become more important in systems where the allylic framework is set free to adopt an optimum conformation. The following experiments support this.

**Allowed vs. Forbidden Pathways in Systems with a Free Migrating Group and a Free Allylic Framework.** So far, we have been concerned with rearrangements that were necessarily suprafacial (*s*). To explore the possibility of an antarafacial (*a*) migration, we now free the allylic framework of geometric constraints. If the migrating group also is free to move with retention (*r*) or inversion (*i*) of configuration, products of two allowed (*si* and *ar*) and two forbidden (*sr* and *ai*) reactions are conceivable.

Our first analysis<sup>26</sup> of the free framework-free migrating group type is a limited one, since the substrate, *trans*-1,2-divinylcyclobutane (**31**), has no stereochemical labels on its double bonds and therefore cannot answer the suprafacial *vs.* antarafacial question. The inversion *vs.* retention problem, however, can be solved by the use of optically active **31**.<sup>27</sup> The absolute

configuration and maximum rotation of **31** are established by correlation with  $\alpha$ -pinene and those of the 1,3-rearrangement product, 4-vinylcyclohexene (**32**),



by correlation with 3-methylcyclohexanone. The signs of rotation correspond to the absolute configurations shown.

Pyrolysis of (1*R*,2*R*)-(+)-*trans*-1,2-divinylcyclobutane at 146.5° gives (*R*)-(+)-4-vinylcyclohexene. After correction for partial racemization of the starting material, the sign and magnitude of rotation of **32** show that the rearrangement of the portion of **31** that has not undergone prior racemization gives 54% (*R*)-(+)-**32** and 46% (*S*)-(–)-**32**, the products respectively of rearrangement with inversion and retention of configuration.

At first glance, the observed stereochemistry might be interpreted as the result of the superposition of a small inversion component, contributed by a last faint residuum of orbital symmetry control, upon a largely stereorandom, chirality-destroying process passing through planar or rapidly rotating diradical intermediates. The expected strong allylic stabilization at each end of the breaking  $C_1$ - $C_2$  bond of **31** could provide some not wholly unreasonable basis for a proposal that the diradical transition-state energy now might be lower than that of any concerted process. However, this picture loses some of its appeal when a saturated group, ethyl, is substituted for one of the vinyls of **31**. Pyrolysis of optically active 2-ethyl-1-vinylcyclobutane (**33**) gives 4-ethylcyclohexene (**34**), with virtually the same stereospecificity (59% inversion, 41% retention) as does the divinyl compound **31**.<sup>29</sup>

A clearer insight into the actual processes in the divinyl case is provided by a study of the *trans*-1,2-dipropenylcyclobutanes.<sup>30</sup> Here the attachment of a stereochemical label to the allylic receptor framework permits the suprafacial *vs.* antarafacial analysis. This in turn provides a means of detecting internal rotations analogous to those which could have been responsible for the extensive racemization observed in the divinyl case.

The experimental design is outlined in Figure 7. The allowed and forbidden 1,3-sigmatropic rearrangements of a *trans*-2-substituted 1-*trans*-propenylcyclobutane (*e.g.*, **TTT**, Figure 7) would give, respectively, a *trans* and a *cis* 3,4-disubstituted cyclohexene. Thus, an

studied previously with optically active **31**,<sup>28</sup> but since the enantiomeric configurations and purities of **31** and **32** were unknown, the observed<sup>28</sup> optical activity of **32** permitted no conclusions on the sense or magnitude of the stereospecificity.

(25) W. R. Roth and A. Friedrich, *Tetrahedron Lett.*, 2607 (1969). Cf. also S. Masamune, N. Nakatsuka, R. Vukov, and E. N. Cain, *J. Amer. Chem. Soc.*, **91**, 4322 (1969).

(26) J. A. Berson and P. B. Dervan, *ibid.*, in press.

(27) The stereochemistry of the **31**  $\rightarrow$  **32** rearrangement has been

(28) G. S. Hammond and C. D. DeBoer, *J. Amer. Chem. Soc.*, **86**, 899 (1964).

(29) L. M. Jordan, Ph.D. Dissertation, Yale University, 1972.

(30) J. A. Berson and P. B. Dervan, *J. Amer. Chem. Soc.*, submitted for publication.

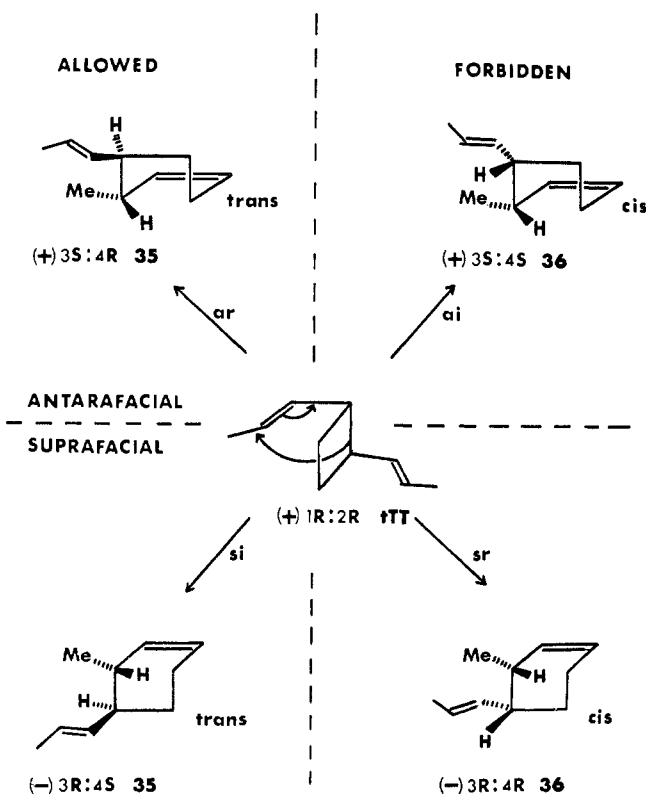
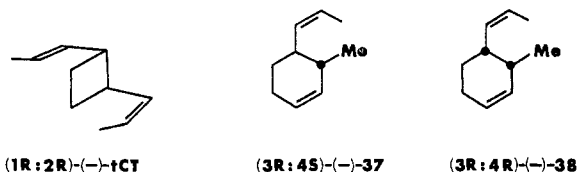


Figure 7.

evaluation of the relative importance of the two processes would be available merely from a determination of the *trans/cis* product ratio.<sup>31</sup> However, a more complete dissection into the contributions of the four conceivable pathways requires the use of optically active reactants.

The allowed pathways, *ar* and *si*, lead from one enantiomer of *trans*-1,2-*trans,trans*-dipropenylcyclobutane (**tTT**) to optical antipodes of *trans*-3-methyl-4-*trans*-propenylcyclohexene (**35**), whereas the forbidden ones, *ai* and *sr*, lead to antipodes of the *cis* compound (**36**, Figure 7). Thus, the relative rates of each of the four processes can be evaluated from the product composition combined with the relationships of the observed rotations, absolute configurations, and maximum rotations of **tTT**, **35**, and **36**. This information is provided by synthesis of optically active **tTT**, **35**, and **36** from appropriate precursors of known configuration and maximum rotation.

The pyrolysis of (1*R*,2*R*)-(+)-**tTT** at 146.5° gives the *trans* and *cis* rearrangement products (3*R*,4*S*)-(–)-**35** and (3*R*,4*R*)-(–)-**36** with survival of 80.9 and 96.1%, respectively, of the maximum optical purity. More-



(31) Experiments with racemic substrates leading to the two-path dissection of the rearrangement of 2-substituted 1-alkenylcyclopropanes have been reported by (a) P. Mazzochi and H. J. Tamburini, *J. Amer. Chem. Soc.*, **92**, 7220 (1970), and by (b) W. R. Roth, work cited in ref 31a.

**Table II**  
Analysis of Pathways in 1,3-Sigmatropic Rearrangements of *trans*-1,2-Dipropenylcyclobutanes

Reactant	Rel rate of product formation			
	Allowed		Forbidden	
	<i>si</i>	<i>ar</i>	<i>sr</i>	<i>ai</i>
<b>tTT</b>	50.8	5.4	43.0	0.8
<b>tCT</b>	49.5	2.7	47.8	0.0

over, the pyrolysis of (1*R*,2*R*)-(–)-*trans*-1,2-*cis,trans*-dipropenylcyclobutane (**tCT**) to *trans*- and *cis*-3-methyl-4-*cis*-propenylcyclohexene (**37** and **38**, products of migration across the *trans*-propenyl framework) reveals similarly high stereospecificity. The assignments of relative rates to the four pathways in each case are summarized in Table II.

The picture of these rearrangements that emerges from this study is quite different from the superficial implications of the divinylcyclobutane (**31**) results. Table II shows that the gross inversion:retention ratios from **tTT** and **tCT**, (*si* + *ai*)/(*sr* + *ar*), are 51.6:48.4 and 49.5:50.5, which again might suggest near-randomization of stereochemistry by way of an intermediate diradical with a planar carbon skeleton or its mechanistic equivalent, a diradical in which internal rotations are fast relative to ring closure. However, this interpretation would require that a substantial portion of the product be formed by antarafacial participation of the allylic framework. As Table II shows, there is only a small amount of *ar* or *ai* component in each case. In fact, only 12% of the **tTT** and 5.5% of the **tCT** 1,3 rearrangements can pass through a planar intermediate or its equivalent. The near-balance in the inversion:retention ratio thus is due to the near-equivalence in rate of two highly stereospecific reactions, *si* and *sr*, and not to the occurrence of a stereorandom intermediate. It seems likely that the same balancing is at work in the case of divinylcyclobutane (**31**).

In one interpretation of the present results (Figure 8), **tTT** gives a diradical intermediate (**39**). All four pathways from **39** require bond rotation about C<sub>4</sub>–C<sub>5</sub> to permit juncture of the migrating carbon (C<sub>3</sub>) to the terminus (C<sub>8</sub>). Pathway *sr* (not shown), a shearing motion of the two allylic units past each other, requires no additional rotations. Pathways *si* and *ar* each require one (or an odd number) of additional rotations, *si* about C<sub>3</sub>–C<sub>4</sub> and *ar* about C<sub>5</sub>–C<sub>6</sub>. Pathway *ai* (not shown) requires an odd number of additional rotations about each of C<sub>3</sub>–C<sub>4</sub> and C<sub>5</sub>–C<sub>6</sub>.

If the C<sub>3</sub>–C<sub>4</sub> and C<sub>5</sub>–C<sub>6</sub> rotational barriers were identical and the ring-closure rates to products **35** and **36** were not very different, the relative rates through each of the pathways would be controlled largely by probability and would rank *sr* > *si* = *ar* > *ai*. The experimental order (Table II) is *si* > *sr* >> *ar* > *ai* from both **tTT** and **tCT**. It seems unlikely that product stabilities make any significant contribution to this ordering, and in two cases, *si* >> *ar* and *sr* >> *ai*, this factor is ruled out rigorously because the pairs of products are enantiomeric.

Since the magnitudes of rotational barriers in di-



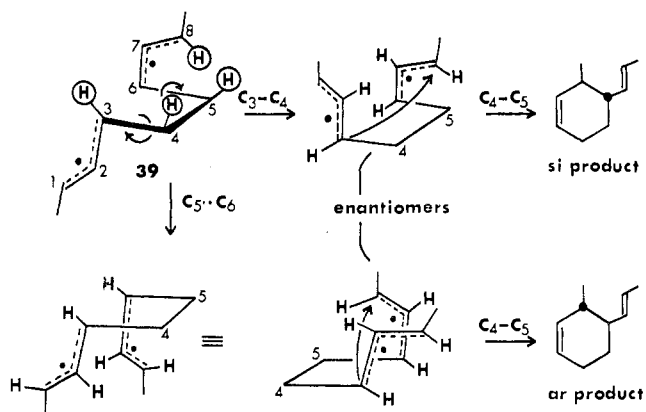


Figure 8.

radicals are imperfectly known, it is conceivable that, perhaps because of differences in steric interactions between the circled hydrogens (Figure 8), the rotational rate ratios  $(C_3-C_4)/(C_5-C_6)$  could be as large as the values (9.4 from **tTT** and 18.4 from **tCT**) needed to fit the observed *si/ar* ratios. On the other hand, the diradical mechanism offers no obvious explanation for the observations that in the suprafacial mode inversion is preferred over retention, but the reverse is true in the antarafacial mode.

For the present, a simpler and hence preferable interpretation would describe the major reactions *si* and *sr* as concerted processes, *si* allowed,<sup>5</sup> and hence slightly preferred over *sr*, which is forbidden.<sup>7</sup> Both antarafacial reactions are slow because of the difficulty of migration through the  $\pi$  nodal plane, but *ar* (allowed) is faster than *ai* (forbidden).

These results confirm and extend the trends in stereospecificity shown by the previous members of the series of sigmatropic rearrangements. The forbidden *sr* rearrangement competes even more favorably with the allowed *si* reaction in the dipropenylcyclobutane cases (**tTT** and **tCT**), where the allylic framework is not bound in a ring, than it does in the *exo*-methylbicyclo[4.2.0]octene cases (**4** and **6**).

The *sr/si* (forbidden/allowed) ratio is less than unity in all the cases where there is no "inside" substituent to block the somersault required for the allowed *si* reaction, but the increase in relative importance of the *sr* reaction can be clearly seen in the ratios *sr/si* 0.005 (**30a**) < 0.053 (**1**) < 0.1 (**2**) < 0.42 (**6**)  $\sim$  0.46 (**4**) < 0.85 (**tTT**)  $\sim$  0.97 (**tCT**) observed in passing from bicyclo[2.1.1] to bicyclo[3.2.0] to bicyclo[4.2.0] to monocyclic substrates.

In the blocked series, the trend continues, with

*sr/si* ratios 0.45 (**30b**) < 7 (**3**) < 12 (**5**)  $\sim$  15 (**7**). Again, *sr* becomes relatively more important as the conformational restrictions are eased. The data are consistent with the hypothesis that allylic  $C_2$ -migrating carbon overlap is important in stabilizing a subjacent orbital of the *sr* transition state. This is just the behavior expected of two competing concerted reactions.

**Conclusion.** The rapidly increasing number of cases of 1,3-sigmatropic rearrangements occurring with stereochemistry forbidden by orbital symmetry exposes a theoretical vacuum. What is the mechanism of such "forbidden" processes? At present, two approaches seem to be taking form.

The first and less completely developed of these identifies such rearrangements as diradical reactions passing through intermediates which display stereochemical properties that cannot yet be specified in advance. Because of their so far ill-defined nature, the diradicals can be used to fit, *a posteriori*, virtually any observation. For the same reason, however, they have obvious shortcomings as predictive or correlative constructs.

The second recognizes the possibility that some forbidden sigmatropic reactions may nevertheless be concerted. A simple theoretical argument supporting this view emphasizes the role of subjacent orbitals. The stereochemical properties of these forbidden reactions are readily predicted. So far, the experimental results are in good agreement with the predictions.

Of course, the available tests still lack extent and variety. Although the subjacent orbital effect favoring forbidden reactions is surely present, one might question whether it is large enough to be the decisive cause of the results described here. Conceivably, what our data may signify is how diradicals behave, and a practical unifying theory of diradicals, or, alternatively, some completely new concept, may yet emerge. Until then, the formulation of further tests of the hypothesis of forbidden concerted reactions should provide fruitful tasks for investigators of reaction mechanisms.

*My coworkers, P. B. Dervan, R. W. Holder, L. M. Jordan, and G. L. Nelson, contributed all of the experimental results and many of the concepts in this paper. I am pleased to record my thanks to them and to Professor Lionel Salem for many stimulating collaborative encounters. Financial support from the National Science Foundation, the National Institute of General Medical Sciences, the Petroleum Research Fund, administered by the American Chemical Society, and the Hoffmann-La Roche Fund is gratefully acknowledged.*