JOURNAL

OF THE AMERICAN CHEMICAL SOCIETY

VOLUME 109, NUMBER 20 SEPTEMBER 30, 1987

Mechanism of the Cope Rearrangement

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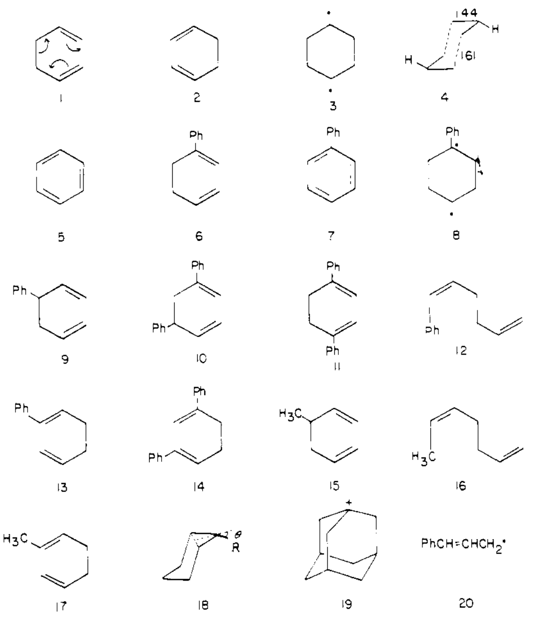
Abstract: AM1 calculations for the Cope rearrangements of 1,5-hexadiene (**1**) and its 2-phenyl (**6**), 3-phenyl (**9**), 3-methyl (**15**), 2,4-diphenyl (**10**), and 2,5-diphenyl (**11**) derivatives, via chair transition states, support the Doering biradicaloid mechanism previously predicted by MINDO/3. The relative rates for **1**, **6**, **9**, and **15** are reproduced closely, the calculated heats of activation being uniformly too large by 3.35 kcal/mol. Larger deviations for **10** and **11** can be attributed to solvent effects and experimental error. The degenerate rearrangements of **1**, **6**, and **11** were predicted to involve 1,5-cyclohexylene biradicaloids as marginally stable intermediates, the lengths of the C_1C_6 and C_3C_4 bonds being 1.60–1.65 Å. The other rearrangements were predicted to be concerted but not synchronous. Calculations for **1** and **6** with the C_1C_6 and C_3C_4 bond lengths set equal to 2.06 Å, as expected for a synchronous transition state, predicted retardation by phenyl as predicted by PMO theory. Deuterium kinetic isotope effects calculated for **1**, **6**, and **11** agreed with Gajewski's measurements, within the limits of error of the calculations and experiments.

Cope represented[2] the rearrangement[3] now named after him in terms of what would now be called a concerted pericyclic mechanism, using[2] the current curved-arrow symbolism (**1** → **2**) to represent the concerted cyclic migration of bonds around a six-membered ring. Following the MO description of the Diels–Alder reaction which Evans and Warhust[4] had given some years earlier, this mechanism for the Cope rearrangement can be interpreted in terms of a structure for the transition state (TS) where each of the six carbon atoms uses three AOs to form σ bonds to its neighbors, the fourth AO contributing to a set of delocalized cyclic six-center MOs; see Figure 1. Such a TS is isoconjugate with benzene and hence aromatic,[4] accounting for the ease of the reaction. The geometry of the TS is moreover ideal for the necessary σ-type overlap of the AOs of the terminal atoms in each allyl moiety, unlike the situation in the Diels–Alder reaction where there is a bad mismatch between the terminal 2p AOs in the olefin and diene. Combined with the discussion by Woodward and Hoffmann,[5] these arguments seemed to leave no doubt concerning the mechanism of the reaction. The only remaining ambiguity,[6] i.e., a choice between possible chair (Figure 1a) and boat (Figure 1b) conformations for the TS, was settled in favor of the former by an ingenious experimental study by Doering and Roth.[6]

This representation was challenged in 1971 by Doering et al.,[7] who pointed out that the observed activation energy for the rearrangement of 1,5-hexadiene (**1**) itself was consistent with a mechanism where the new CC bond is formed before the old one begins to break, the symmetrical intermediate (SI) being the 1,4-cyclohexylene biradical (**3**) rather than an aromatic nonclassical species. While this suggestion was largely ignored at the time, strong support for it was provided some years later by theoretical and experimental work by our group.

Chart I



MINDO/3 calculations[8] for the chair rearrangement of **1** led to a reaction profile of the type indicated in Figure 2b. The SI corresponded to a shallow (2 kcal/mol) minimum on the potential

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[1] On leave from Lanzhou University, Lanzhou, the People's Republic of China.

(2) Cope, A. C.; Hardy, E. M. *J. Am. Chem. Soc.* **1940**, *62*, 441.

(3) Frey, H. M.; Walsh, R. *Chem. Rev.* **1969**, *69*, 103.

(4) Evans, M. G.; Warhurst, E. *Trans. Faraday Soc.* **1938**, *34*, 614.

(5) Woodward, R. B. Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.

(6) Doering, W. v. E.; Roth, W. R. *Tetrahedron* **1962**, *18*, 67.

(7) Doering, W. v. E.; Toscano, V. G.; Beasley, G. H. *Tetrahedron* **1971**, *27*, 299.

(8) Dewer, M. J. S.; Ford, G. P.; McKee, M. L.; Rzepa, H. S.; Wade, L. E., Jr. *J. Am. Chem. Soc.* **1977**, *99*, 5069.

(9) Hoffmann, R.; Inamura, A.; Mehre, W. J. *J. Am. Chem. Soc.* **1968**, *90*, 1499.

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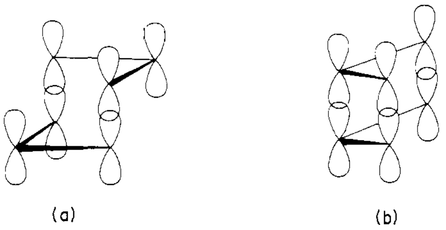

Figure 1. Orbital interactions in aromatic TSs for Cope rearrangements of 1,5-hexadiene (**1**): (a) chair; (b) boat.

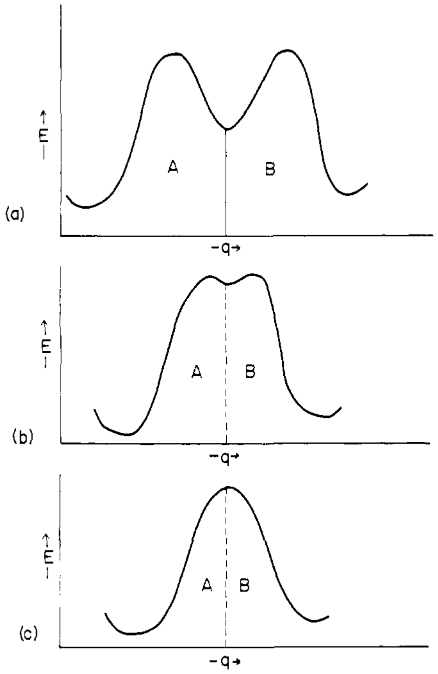

Figure 2. Transition (a → b → c) from a two-step reaction to one that is concerted but not synchronous, i.e., of two-stage type.

energy (PE) surface. Both the enthalpy of activation ($\Delta H^{\ddagger}$) and the entropy of activation ($\Delta S^{\ddagger}$) agreed well with experiment. The reaction profile calculated for the boat rearrangement was similar to that for the chair and the difference in free energy of activation between the chair and boat rearrangements agreed well with experiment. While MINDO/3 predicted similar values for $\Delta S^{\ddagger}$ for both processes, the experimental value reported for the boat rearrangement was much less negative than that for the chair. However, it seemed likely that this discrepancy was due to experimental error, given that the kinetic measurements for the boat rearrangement were stated to be much less accurate than those for the chair and given that the values of $\Delta S^{\ddagger}$ would be expected to be similar if both reactions have similar mechanisms.

While the agreement between the calculated and observed activation parameters supports the validity of the calculations, the SIs could well be transition states (TS) rather than stable intermediates, the depths (2 kcal/mol) of the calculated potential wells being less than the known limits of error in MINDO/3.

The structures calculated for the SIs seemed to provide strong support for the Doering mechanism, being consistent with their representation[7] as biradical-like species (**3**). Thus the lengths (1.61 Å) of the C_1C_6 and C_3C_4 bonds in the chair SI (**4**) were little greater than that of a saturated CC σ bond while the other CC bonds were only a little shorter (1.44 Å) than a $C(sp^2)$–$C(sp^2)$ σ bond. In an analogous aromatic species of the type implied in Figure 1, C_1C_6 and C_3C_4 would be expected to be much longer and the lengths of the remaining CC bonds similar to those in benzene (1.40 Å).

The chair SI cannot, however, be a true biradical. If it was, the corresponding MINDO/3 energy would have been far too positive. It must be a "nonclassical" closed shell species, derived from 3 by a through-bond[9] interaction between the radical centers, i.e., a *biradicaloid*. This interpretation also accounts for the lengthening of the C_1C_6 and C_3C_4 bonds and shortening of the others and also for the surprising fact that C_2 and C_5 were found to be pyramidal, as indicated in **4**. Pyramidalization of these atoms increases[10] the through-bond coupling between the radical centers.

A similar structure was found for the boat intermediate,[8] the relevant CC bond lengths being 1.63 and 1.44 Å.

Further support for this interpretation was provided by experimental studies[11] of the rearrangements of phenyl derivatives of **1**.

Consider the union[12] of two alternant hydrocarbons (AH: RH and SH) to form a single larger AH, R–S. According to PMO theory,[12] the change in π energy, i.e., the energy of union, is always the same, being given by 0.5β where β is the resonance energy of the bond linking them in RS. This prediction is supported by experiment. Thus thermochemical data[13] indicate that the heat of reaction of the following process is essentially zero (0.8 ± 0.8 kcal/mol)

$$\text{Ph-H} + \text{PhCH=CH}_2 \rightarrow \text{Ph—Ph} + \text{CH}_2\text{=CH}_2 \qquad (1)$$

Similar PMO arguments indicate that the energy of union of *any* pair of even alternant conjugated systems, i.e., the corresponding change in delocalization (resonance) energy, should also be given by 0.5β, β again being the resonance energy of the linking bond. If the TS for the rearrangement of **1** is indeed an analogue of benzene (**5**), the same should then be true for union of it with other even conjugated systems. The difference in delocalization (resonance) energy between the TS from **1** and the TS from **6** should then be equal to 0.5β where β is the resonance integral of the Ph–C_2 bond. Since C_2 remains unsaturated throughout the reaction, β should also remain unchanged. The delocalization energy of the TS from **6** should therefore be the same as that in **6** where phenyl is also attached to an even AH, i.e., ethylene. The phenyl substituent in **6** should not then affect the rate of rearrangement. Experiment[11] indicated, however, that **6** rearranges 69 times faster than **1**, showing that the TS is not a simple analogue of **7**. Such an acceleration would, on the other hand, be expected if the TS is **3**, or a biradicaloid derived from **3**, because the corresponding species (**8**) derived from **7** is a benzyl radical.

The same argument was used in a recent study[14] of the Diels–Alder reaction where there is a similar choice between aromatic and biradicaloid mechanisms. Here the PMO prediction was confirmed by calculations that indicated that introduction of even alternant substituents (CN) would lead to no increase in rate if the reaction took place via an aromatic benzene-like TS.

The 3-phenyl derivative (**9**) of **1** also rearranged faster[11] than **1** itself, though the ratio of rates was less (17:1). This result again indicates that the intermediate cannot be a simple biradical where phenyl would still be attached to a saturated carbon atom. The through-bond interaction between the radical centers weakens the C_1C_6 and C_3C_4 bonds, changing the geometries and hybridization of the corresponding carbon atoms toward planarity and sp^2. This change strengthens the CC bond linking the phenyl substituent in the analogous species derived from **9**.

These results could alternatively be attributed to variations in the structure of the TS, the TSs from **1** and **9** being aromatic while that from **6** is displaced toward **3** by the 2-phenyl substituent. While the observed[11] rates of rearrangement of **6**, **9**, and the 2,4- (**10**) and 2,5- (**11**) diphenyl derivatives of **1** seemed to suggest[11] that the effects of substituents are additive, Gajewski and his collaborators[15] have concluded from studies of secondary deuterium kinetic isotope effects (SDKIE) in the rearrangements of a number of derivatives of **1** that the corresponding TSs vary in structure with the substituents.

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(10) Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 669.

(11) Dewar, M. J. S.; Wade, L. E., Jr. *J. Am. Chem. Soc.* **1977**, *99*, 4417.

(12) See: Dewar, M. J. S. *The Molecular Orbital Theory of Organic Chemistry*; McGraw-Hill: New York, 1969; Section 6.7.

(13) Cox, J. D.; Pilcher, G. *Thermochemistry of Organic and Organometallic Compounds*; Academic: London, 1970.

(14) Dewar, M. J. S.; Olivella, S.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1986**, *108*, 5771.

(15) Gajewski, J. J.; Conrad, N. D. *J. Am. Chem. Soc.* **1978**, *100*, 6268; **1979**, *101*, 6693.

There are several questions to be answered concerning the Cope rearrangement. Is it concerted? If it is concerted, is it also synchronous? Is it a typical pericyclic reaction, involving a benzene-like aromatic TS, or does it take place by the Doering mechanism, via a biradical-like species as the TS or as a stable intermediate? Or is it perhaps a chameleon-like reaction whose mechanism changes with changes in the structure of the diene?

The evidence presented above suggests that the reaction is not synchronous, the new CC bond having been almost completely formed in the TS while the one that breaks during the reaction is still almost intact. However, even if this is true, it would not in itself imply that the reaction is not concerted. While the bond forming (A) and bond breaking (B) processes may indeed take place in two distinct steps, as indicated in Figure 2a, it is equally possible for the steps to overlap, leading to a progressive coalescence, as indicated by a → b → c in Figure 2. The final result is a two-stage reaction (Figure 2c), i.e., one which is concerted but not synchronous, the changes in bonding involved in A taking place mainly in the first half of the reaction and those involved in B taking place mainly in the second. As noted above, MINDO/3 predicted the Cope rearrangement of **1** to be marginally of two-step type, the intermediate corresponding to a minimum on the PE surface too shallow for this prediction to be reliable. The SI could correspond to the TS.

In the case of the Cope rearrangement, the distinction between the various possible mechanisms would be of practical importance only if the reaction involved a stable intermediate lying in a deep potential well, which is almost certainly not the case. Otherwise the choice between them has no bearing on practical applications of the reaction, e.g., in synthesis. Equally, if the reaction is not synchronous, the distinction between a concerted mechanism (cf. Figure 2c) and a two-stage one involving a marginally stable intermediate (cf. Figure 2b) is of little or no theoretical interest. Therefore the only significant question is that concerning the synchronicity of the reaction. This distinction *is* important in connection with the general theory of pericyclic reactions because of the commonly held belief that "allowed" pericyclic reactions are necessarily synchronous unless special factors oppose synchronicity. Here the only factor militating against synchronicity is a recently formulated[16] rule that multibond reactions tend not to be synchronous. Demonstration that the Cope rearrangement is nonsynchronous would provide striking support for the new rule.

The conclusion,[8] that the Cope rearrangement is not synchronous, has recently been challenged by Osamura et al.[17] on the basis of MCSCF calculations for the rearrangements of **1**, using the STO-3G and 3-21G basis sets. The calculations were carried out both with two-configuration (TCSCF) wave functions and with multiconfiguration (MCSCF) ones involving configurations derived from the three highest occupied and three lowest unoccupied MOs. The latter choice rested on the intuition that these are the MOs primarily involved in the bonds that migrate during the reaction; cf. **1** → **2**. The results from both TCSCF calculations and the STO-3G MCSCF calculation agreed with MINDO/3 in predicting a two-step mechanism with a biradical-like species as a stable intermediate. Lack of computer facilities prevented the authors from carrying out the MCSCF 3-21G calculation. Instead, it was simulated by a CI procedure with results that refuted the Doering mechanism, the SI being predicted to have a structure corresponding to a normal aromatic TS.

While "state-of-the-art" ab initio procedures are undoubtedly superior to ours, the procedure used by Osamura et al. certainly does not fall in this category. Their work is also open to criticism, quite apart from doubts concerning the validity of the unnecessary[18] simulation, because no attempt was made to optimize geometries at the correlated level or to characterize stationary points. A further problem, inherent in the MCSCF method, is the dependence of the results on the choice of configurations, which is made on a purely subjective basis. The choice adopted by Osamura et al. might indeed be expected[20] to favor an aromatic TS.

Table I. Heats of Formation (ΔH_f) for 1,5-Hexadienes and Their Cope Products

	ΔH_f (kcal/mol)			ΔH_f (kcal/mol)	
compd	calcd	exptl[a]	compd	calcd	exptl[a]
1	18.6	20.2	**11**	72.6	67.4
6	45.6	43.7	**15**	14.2	12.5
9	48.8	45.9	**13**	42.5	43.0
10	75.5	69.6	**17**	8.7	12.6

[a] See ref 18.

A high-level ab initio calculation for the Cope rearrangement of **1**, if properly carried out, would clearly be of interest. Indeed, we are currently trying to do this. However, even if we are successful, and even if the results could be trusted, conclusions drawn from them would not necessarily apply to other Cope rearrangements because the simplest example of any reaction is often untypical.[22] Unambiguous conclusions cannot in any case be drawn from calculations by any current procedure because the errors in energies given by even the best of them are too large. A better approach[14] is to calculate a number of examples of the reaction for which activation parameters are available, e.g., **6**, **9**, **10**, and **11**. Even if the errors in the calculated activation parameters for the individual reactions are too large for definite conclusions to be drawn from them, the relative values for a number of related reactions are likely to be reproduced, at least qualitatively. Comparison of the predicted pattern of rates with experiment should then provide a more reliable test of the predicted mechanism than any calculation for a single case.

The conventional ab initio SCF approach gives satisfactory results for reactions only if a large basis set is used and if adequate allowance is made for electron correlation.[23] While calculations of this kind are marginally feasible for **1**, using current supercomputers, the cost in the case of its phenyl derivatives would be prohibitive. Equally, our earlier semiempirical procedures (MINDO/3 and MNDO) are open to criticism in connections such as this in view of indications[14] (cf. ref 24) that they tend to favor unsymmetrical TSs in cycloadditions. If so, similar problems might arise in other pericyclic reactions. This deficiency[25] has, however, been corrected in the new AM1[26] procedure. We have accordingly used it to study the Cope rearrangements of **1** and its derivatives, following the lines indicated above.

Theoretical Procedure

The calculations were carried out with the standard AM1[26] procedure, as implemented in the AMPAC program.[27] Transition

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(16) Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 209.

(17) Osamura, Y.; Kato, S.; Morokuma, K.; Feller, D.; Davidson, E. R.; Borden, W. T. *J. Am. Chem. Soc.* **1984**, *106*, 3362.

(18) A precisely analogous MCSCF calculation has been carried out by Bernardi et al.[19] for a somewhat more complex system (ethylene + butadiene Diels–Alder reaction), with full geometry optimization and with a larger basis set (4-31G).

(19) Bernardi, F.; Bottoni, A.; Robb, M. A.; Field, M. J.; Hillier, I. H.; Guest, M. F. *J. Chem. Soc., Chem. Commun.* **1985**, 1051.

(20) The CASSCF (Complete Active Space SCF) MCSCF procedure used by Osamura et al. included configurations derived from the three highest occupied and three lowest unoccupied MOs, these being assumed to contain the three pairs of electrons directly involved in the migrating bonds. An MCSCF treatment based on these configurations is expected to overemphasize the correlation energy of the six electrons in question. As Dewar and McKee[21a] have shown, aromaticity is largely due to an increase in correlation energy of the π electrons in appropriate cyclic conjugated molecules. An overestimation of the correlation energy of the six delocalized electrons in a Cope TS is therefore likely to lead to an overestimation of the stability of an aromatic structure for the TS in comparison with other alternatives.

(21) (a) Dewar, M. J. S.; McKee, M. L. *Pure Appl. Chem.* **1980**, *52*, 1431. (b) Haddon, R. C.; Raghavachari, K. *J. Am. Chem. Soc.* **1985**, *107*, 289.

(22) Thus ethyl chloride is the *only* alkyl chloride with a β hydrogen that does not give an olefin with alcoholic potash while methylamine is the *only* primary aliphatic amine that does not form an alcohol with nitrous acid.

(23) See e.g.: Breulet, J.; Schaefer, H. F., III *J. Am. Chem. Soc.* **1984**, *106*, 1221.

(24) Caramella, P.; Houk, K. N.; Domelsmith, L. N. *J. Am. Chem. Soc.* **1977**, *99*, 4514.

(25) Contrary to earlier suggestions,[24] the fault was found[22] to lie in the known tendency of MINDO/3 and MNDO to overestimate interatomic repulsions at distances >1.5 times the covalent bond distance.

(26) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

Table II. Transition States (TS) and Intermediates (SI) for Cope Rearrangements

reactant	ΔH_f[a]	$\delta\Delta H$[b]	$\Delta H^{\ddagger}$ calcd	$\Delta H^{\ddagger}$ obsd	θ, deg
1, chair TS	55.6	22.2	37.1[c]	33.3[d,e]	14.4
1, boat TS	66.4	23.9	47.8[d,c]	44.7[d,e]	17.6
6, TS	78.6	18.5	32.9	29.3[c,f]	11.1
6, SI	78.2	18.1			11.0
9, cis TS	87.7	21.4	38.9	35.3[c,f]	15.8
9, trans TS	83.9	19.1	35.1	31.6[c,f]	13.0
10, TS	107.0	12.8	31.5	24.7[c,f]	11.1
11, TS	101.6	7.7	29.0	21.1[c,f]	18.8
11, SI	100.3	14.7			10.3
15, cis TS	52.2	21.6	38.0	34.6[c,g]	15.1
15, trans TS	50.3	20.4	36.1	33.1[c,g]	13.7

[a] Heat of formation calculated for the TS or stable intermediate, in kcal/mol. [b] Difference in energy between this RHF and HE–CI values of DHf. [c] Reference 11. [d] Reference 7. [e] Reference 36. [f] Estimated from reported kinetic data; see text. [g] Frey, H. M.; Sally, R. V. *Trans. Faraday Soc.* **1968**, *64*, 1858.

Table III. Entropies of Activation for Rearrangement of 1,5-Hexadiene

reaction	entropy of activation (cal/deg) calcd	entropy of activation (cal/deg) obsd
chair Cope	−15.6	−13.0 ± 1.0
boat Cope	−11.0	−3.0 ± 3.6

states were located by the reaction coordinate method[28] or by a new procedure[29] recently developed here, refined by minimizing the norm of the gradient,[30] and characterized by calculating force constants.[30] All geometries were found by minimizing the energy without making any assumptions. Options for these procedures are included in AMPAC. Calculations for potentially biradical-like species were carried out with the "half-electron" approximation with 3 × 3 CI (AM1-HE-CI),[31] this having proved superior to the corresponding UHF treatment (UAM1).

Results and Discussion

Calculations were carried out for **1** and for its chair and boat Cope rearrangements; for **6** and **11** and their chair rearrangements; for **9** and its chair rearrangements to *cis*- (**12**) or *trans*- (**13**) 1-phenyl-1,5-hexadiene; for **10** and its chair rearrangement to *trans*-2,6-diphenyl-1,5-hexadiene (**14**); and for 3-methyl-1,5-hexadiene (**15**) and its chair rearrangements to *cis*- (**16**) or *trans*- (**17**) 2,6-heptadiene. The calculations were carried out with the standard (RHF) version of AM1 as indicated in the previous section.

Table I shows the heats of formation calculated for **1** and its derivatives and for the products of their Cope rearrangements. While thermochemical data seem to be available[13] only for **1**, reasonable estimates of the heats of formation of the other compounds can be derived from that of **1** by assuming group additivity.[32] The corresponding values are listed, together with the experimental value for **1**, in Table I. The agreement with our calculations is within the normal limits of error for AM1. The calculated geometries are not reported because they showed no unexpected features.

The chair Cope rearrangement of **1** was predicted to be concerted, in formal agreement with the earlier MINDO/3[8] calculations. The corresponding depression in the potential surface was, however, even more marginal (0.1 kcal/mol). Similar small minima were also found for **6** (0.4 kcal/mol) and **11** (1.3 kcal/mol). All are too small to have any definite significance. The heats of formation calculated for the TSs, and for the symmetrical intermediates from **6** and **11**, are shown in Table II and their geometries in Figure 3. As in the earlier MINDO/3 study[8] of **1**, C_2 and C_5 were predicted in all cases to be pyramidal. The angle (θ; see **18**) through which the attached atom or group is tilted out of planarity with the adjacent carbon atoms is indicated in Table II. The other reactions studied, i.e., the rearrangements of **9**, **10**, and **15**, were predicted to be concerted. The chair rearrangements of **9**, **10**, and **15** can take place in two distinct ways, leading to products in which the terminal phenyl or methyl group occupies a cis or trans orientation. Calculations were carried out for both alternatives for **9** and **15**. The geometries and heats of formation, calculated for the corresponding TSs are shown in Table II and Figure 3.

Table II compares the corresponding heats of activation ($\Delta H^{\ddagger}$) with experiment. Most reports of experimental studies have listed Arrhenius activation energies (EA) rather than heats of activation. Values for the latter were calculated from the relation

$$\Delta H^{\ddagger} = \mathrm{EA} - RT \tag{2}$$

where T is the middle of the temperature range used in the kinetic measurements.

Table III shows entropies of activation calculated for the boat and chair rearrangements of **1**. These are discussed in a later section of this paper.

A remarkable feature of the SIs derived from **1**, **6**, and **11** is the shortness of the C_1C_6 and C_3C_4 bonds. In agreement with the earlier MINDO/3[8] calculations for **1**, these are little longer than the C–C bonds in paraffins. CC bonds that are forming or breaking during a reaction usually have lengths greater than 2 Å in the corresponding TSs and this has been true for all the pericyclic reactions that have been studied theoretically and predicted to be synchronous.[33] The lengths predicted in the present case are therefore definitely inconsistent with a synchronous mechanism for the Cope rearrangement. Their shortness would, however, be expected on the basis of the Doering mechanism where the symmetrical intermediate is a perturbed 1,4-cyclohexylene biradical (cf. **3**). The fact that they are longer than normal CC σ bonds can be attributed to sigmaconjugative/hyperconjugative[19] interactions between the radical centers. Indeed, their lengths are the same as those (1.44, 1.62 Å) found[34] recently for CC bonds analogously oriented with respect to the trivalent carbon atom in 1-adamantyl cation (**19**). Since sigmaconjugative/hyperconjugative[35] interactions are stronger for carbocations than for analogous radicals, it is not surprising that the single cationic center in **19** has the same effect as the synergism of two radical centers in **1**. Note also that the C_1C_6 and C_3C_4 bonds in the TS from **6** are predicted (Figure 3) to be a little shorter than those in the TS from **1** while those in the symmetrical intermediate from **11** are shorter again. These differences are again consistent with the formulation of these species as biradicaloids derived from **3** because phenyl substituents at C_2 or C_5 should stabilize the radical centers in **3** and consequently reduce the through-bond interaction between them. Similar comments apply to the pyramidal geometries predicted for C_2 and C_5 in the TSs. Sigmaconjugation is possible only if the relevant AOs are of hybrid type.[35] Experimental evidence for pyramidalization of these atoms in the SI has been presented recently by Doering and Troise.[36]

The identification of the SIs as biradicaloids does, however, raise a problem. RHF procedures give energies for biradicals that

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(27) Available from the Quantum Chemistry Program Exchange (QCPE), Program No. 506.

(28) Dewar, M. J. S.; Kirschner, S. *J. Am. Chem. Soc.* **1971**, *93*, 4290.

(29) Dewar, M. J. S.; Healy, E. F.; Stewart, J. J. P. *J. Chem. Soc., Faraday Trans. 2* **1984**, *80*, 227.

(30) McIver, J. W.; Komornicki, A. *J. Am. Chem. Soc.* **1972**, *94*, 2625.

(31) See: Dewar, M. J. S.; Merz, K. M., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 5146.

(32) The heats of formation were estimated, using data from ref 13, assuming the heat of reaction for each of the following processes to be zero:

$\mathbf{1} + PhC(CH_3){=}CH_2 \rightarrow \mathbf{6} + CH_3CH{=}CH_2$

$\mathbf{1} + 2PhC(CH_3){=}CH_2 \rightarrow \mathbf{10} + 2CH_3CH{=}CH_2$

$\mathbf{1} + RCH(CH_3)_2 \rightarrow (\mathbf{9}\text{ or }\mathbf{15}) + C_3H_{10}\ (R = Ph\text{ or }CH_3)$

$\mathbf{1} + PhC(CH_3){=}CH_2 + RCH(CH_3)_2 \rightarrow \mathbf{11} + CH_3CH{=}CH_2 + C_3H_{10}$

$\mathbf{1} + RCH{=}CH_2 \rightarrow (\mathbf{13}\text{ or }\mathbf{17}) + C_3H_8$

(33) The lengths of CC bonds that are forming or breaking during reactions are usually in the range 1.9–2.2 Å. See, e.g., ref 20, 21, and 26. Many other examples could be cited.

(34) Laube, T. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 349.

(35) Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 669.

(36) Doering, W. v. E.; Troise, C. A. *J. Am. Chem. Soc.* **1985**, *107*, 5739.

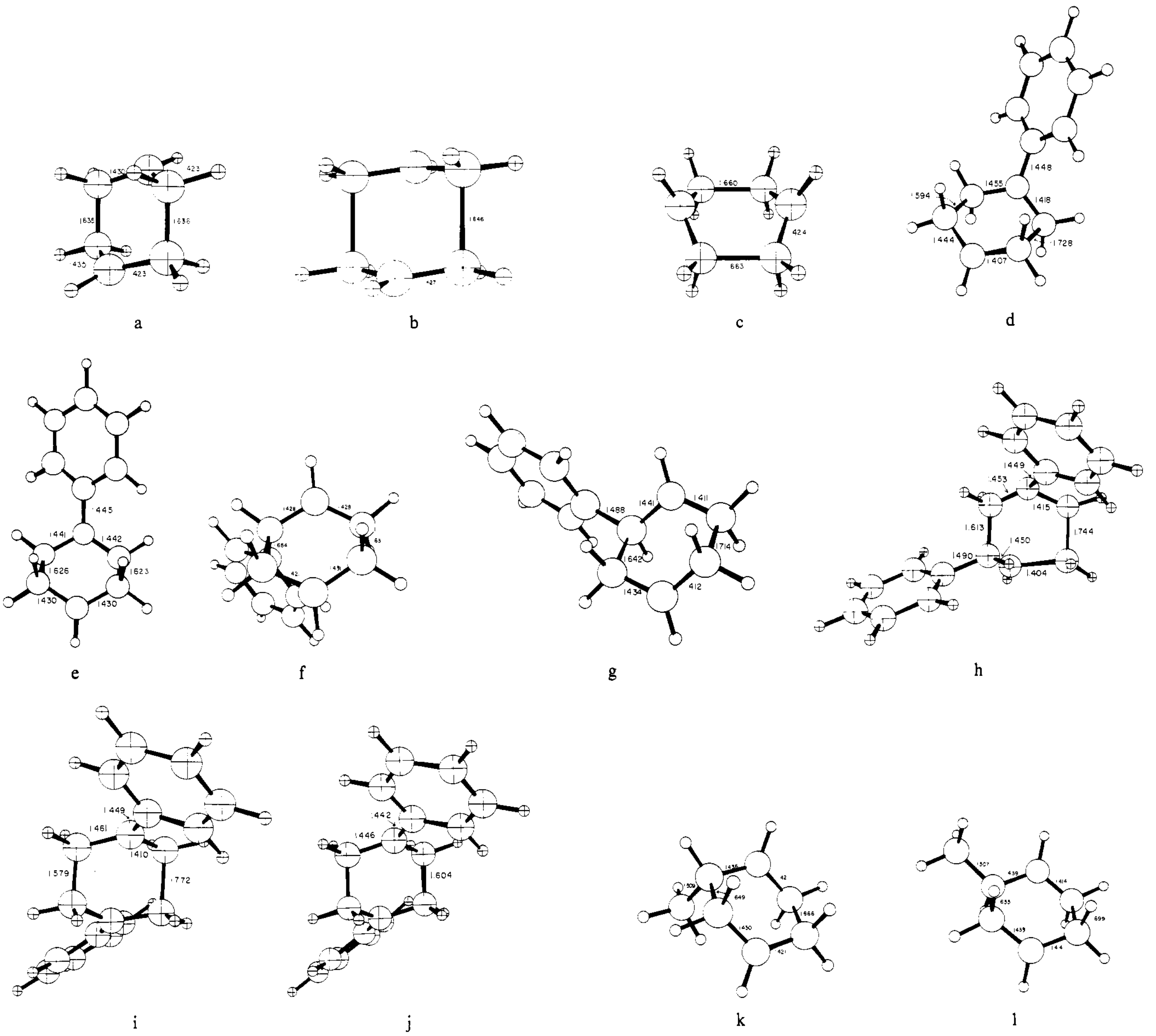

Figure 3. Ortep plots and bond lengths (Å) for (a) chair TS from **1**, (b) chair SI from **1**, (c) boat TS from **1**, (d) TS from **6**, (e) SI from **6**, (f) TS (cis) from **9**, (g) TS (trans) from **9**, (h) TS from **10** (i) TS from **11**, (j) SI from **11**, (k) TS (cis) from **15**, and (l) TS (trans) from **15**.

are much too positive, the errors in the case of MINDO/3, MNDO, and AM1 being commonly 40–60 kcal/mol. Analogous open-shell treatments have to be used in such cases. Similar but smaller errors might be expected in the case of biradical-like species. Since the TSs in Cope rearrangements seemed to be of this type, our use of an RHF procedure (AM1) to study them clearly needs justification.

In our procedures, inclusion of CI has very little effect on the energies of normal closed shell molecules whereas the decrease ($\delta\Delta H$) is large for biradicals. The values for species of intermediate type, i.e., biradicaloids, are, as would be expected, intermediate. The value of $\delta\Delta H$ should thus serve as an indication of the "biradical character" of a biradicaloid. There is, however, a further problem. The HE–CI energies for genuine biradicals are systematically too negative by ca. 20 kcal/mol, due to overestimation of the correlation energy.[14] The energy calculated for a biradical should therefore be corrected by adding 20 kcal/mol. The corresponding correction for a biradicaloid remains uncertain because of a lack of experimental data. Studies of a number of reactions involving biradical-like intermediates have, however, suggested that the correction in fact remains relatively constant, the best estimate of the heat of formation of a molecule usually being given by the more negative of two calculated values, one the RHF value and the other the HE–CI one plus 20 kcal/mol.

We therefore carried out single-point calculations for the various TSs and for the symmetrical intermediate from **11**, using AM1–HE–CI. Table II shows in each case the corresponding decrease ($\delta\Delta H$) in energy, relative to the (RHF) AM1 values. These clearly fall in the awkward range, being ca. 20 kcal/mol. Since the RHF version of AM1 predicted shallow minima for two of the symmetrical intermediates, i.e., those from **6** and **10**, it seems likely on balance that the same may be true for all of them. However, even if this is the case, the effect on the activation barrier is likely to be small, leading at most to a systematic decrease of a few kcal/mol. The subsequent discussion of the rates of the reactions is therefore based on the RHF potential surfaces.

One point of interest in Table II is the fact that the CI correction *decreases* along the series **1** < **6** < **11**, apparently implying a corresponding progressive decrease in biradical character. This would be contrary not only to chemical intuition but also to the corresponding changes in the CC bond lengths, which, as noted above, indicate biradical character to *increase* along this series. The reason for this can be seen immediately by considering why RHF methods give energies for biradicals that are too positive. The repulsion between the two unpaired electrons in a biradical segregates them between the two "singly occupied" orbitals, ϕ_1 and ϕ_2, the coulombic repulsion between them being correspondingly small. An RHF wave function for the biradical assigns

Table IV. Formal Charges Calculated for Transition States and Intermediates

species	C1	C2	C3	C4	C5	C6	Ha	Hb	R1	R2
1	−0.226	−0.156	−0.131	−0.131	−0.156	−0.226	+0.120	+0.120		
TS (**1**, chair)	−0.123	−0.241	−0.122	−0.122	−0.242	−0.123	+0.120	+0.120		
TS (**1**, boat)	−0.126	−0.234	−0.126	−0.126	−0.234	−0.126	+0.118	+0.118		
6	−0.208	−0.070	−0.118	−0.132	−0.157	−0.224		+0.116	−0.012	
TS (**6**)	−0.116	−0.160	−0.109	−0.127	−0.215	−0.139		+0.121	−0.024	
int. (**6**)	−0.110	−0.163	−0.109	−0.128	−0.217	−0.130		+0.122	−0.024	
9	−0.216	−0.153	−0.039	−0.127	−0.158	−0.224	+0.121	+0.119	−0.051	
TS (**9**, trans)	−0.132	−0.226	−0.036	−0.118	−0.245	−0.125	+0.127	+0.120	−0.046	
TS (**9**, cis)	−0.121	−0.227	−0.033	−0.120	−0.238	−0.123	+0.120	+0.122	−0.040	
10	−0.206	−0.071	−0.115	−0.040	−0.151	−0.216		+0.119	−0.012	−0.052
TS (**10**)	−0.115	−0.163	−0.105	−0.040	−0.203	−0.145		+0.128	−0.023	−0.045
11	−0.206	−0.072	−0.120	−0.120	−0.070	−0.208			−0.016	−0.016
TS (**11**)	−0.129	−0.136	−0.115	−0.115	−0.136	−0.129			−0.018	−0.018
int. (**11**)	−0.118	−0.139	−0.115	−0.115	−0.139	−0.118			−0.017	−0.016
15	−0.223	−0.153	−0.078	−0.129	−0.156	−0.226	+0.119	+0.119	+0.019	
TS (**15**, trans)	−0.128	−0.234	−0.071	−0.120	−0.243	−0.125	+0.121	+0.120	+0.024	
TS (**15**, cis)	−0.122	−0.239	−0.067	−0.122	−0.238	−0.124	+0.119	+0.120	+0.027	

[a] Linked to C_2. [b] Linked to C_5.

them, however, to a common MO ($\phi_1 + \phi_2$) a description that gives equal weights to configurations where the electrons occupy different orbitals (ϕ_1 and ϕ_2) and where they occupy the same orbital. The corresponding energy is therefore too positive, by an amount δE, given by

$$\delta E = 0.25(J_{11} + J_{22}) \qquad (3)$$

where J_{11} is the coulombic repulsion between a pair of electrons in ϕ_1 and J_{22} that between a pair of electrons in ϕ_2. In the case of a simple biradical, such as **3**, ϕ_1 and ϕ_2 are AOs and the J integrals are correspondingly large. In the corresponding species from **6** or **11** (cf. **8**), one or both of the orbitals is an MO for which the J integral is much smaller. The error in the RHF energy is therefore correspondingly less.

Figure 4 shows a plot of the heats of activation (Table II) for the chair rearrangements of **1** and its derivatives against the corresponding experimental values, together with a line of unit slope, drawn through the first six points, i.e., omitting those for the diphenyl derivatives, **11** and **12**. With these exceptions, the points all lie within 0.45 kcal/mol of the line and the standard deviation is 0.29 kcal/mol. The line corresponds to a systematic error of +3.35 kcal/mol in the calculated values. To our knowledge, no previous theoretical study of a system of this degree of complexity has ever provided such good results. Indeed, the systematic error of 3.35 kcal/mol could be due simply to our use of the RHF AM1 procedure for species that clearly have significant biradical character. As noted above, the corrections to the HE–CI values for species of this kind are still uncertain.

Even if the uncorrected values were taken for **11** and **12**, the agreement would normally be regarded as satisfactory. However, there are in fact good reasons for regarding the published experimental values with suspicion. The activation parameters for **11** were derived from just two measurements at two temperatures while the Arrhenius plot for **12** showed marked curvature. The measurements for both compounds were moreover carried out in solution (*o*-dichlorobenzene) whereas the others, except that for **6**, referred to the gas phase. The Arrhenius preexponential factors (A) for all the latter reactions were almost identical ($\log A = 10.7 \pm 0.1$). The A factors for **10** and **11** were, on the other hand, less than this by one and two orders of magnitude, respectively. Furthermore, the rates of rearrangement of **9** differed in the gas phase and in *o*-dichlorobenzene, the rate in solution being much greater and the activation parameters smaller, the activation energy being less by 3.4 kcal/mol, and the A factor being less an order of magnitude. It does therefore seem as if some of the reactions in solution took place by an alternative route, with a lower activation energy and a smaller A factor. This suggestion is supported by the fact that if the activation parameters for **12** are estimated from the rates at the two highest temperatures, the corresponding A factor is normal ($\log A = 10.84$) and the corresponding point in Figure 4, indicated by a cross, lies close to the line.

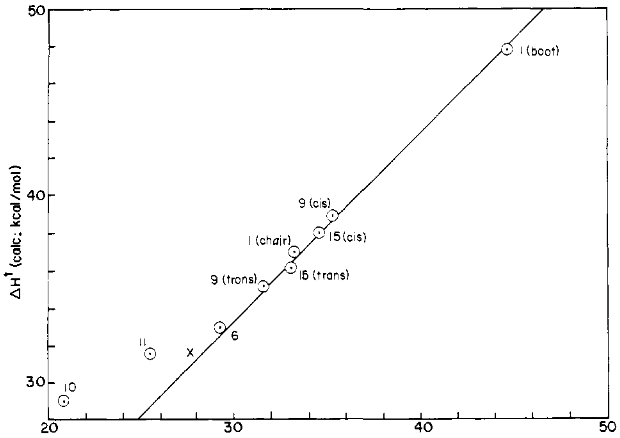

Figure 4. Plot of calculated vs. experimental heats of activation ($\Delta H^{\ddagger}$) for Cope rearrangements of **1** and its derivatives.

These discrepancies might be attributed to solvation. *o*-Dichlorobenzene does indeed strongly accelerate other analogous reactions, e.g., the Diels–Alder reaction between isoprene and maleic anhydride.[37] Here, however, solvation seems unlikely to be responsible because effects of this kind depend on electrostatic interactions between the reacting system and the solvent and here both the reactants and the TSs should be almost nonpolar. Indeed, the calculated formal charges (Table IV) imply that the TSs are *less* polar than the reactants. There is moreover no distinction in this respect between **6**, where normal results were obtained in *o*-dichlorobenzene solution, and **9**, where the results in solution differed significantly from those in the gas phase. The results for **10** furthermore suggest that the discrepancies relate to measurements at lower temperatures.

It seems more likely that the discrepancies were due to catalysis by some adventitious impurity, the catalyzed reactions having lower activation energies and A factors. A reasonable candidate would be a two-step radical chain reaction involving an allyl radical as chain carrier, e.g.

$$\underset{\mathbf{19}}{(\mathrm{PhCHCHCH_2})^{\bullet}} + \mathbf{9} \rightarrow$$

$$\mathrm{PhCH{=}CHCH_2CH_2{}^{\bullet}CHCH_2CHPhCH{=}CH_2} \rightarrow \mathbf{9} + \mathbf{19} \qquad (4)$$

For this to be possible, neither step must be too endothermic. Since the overall reaction is thermoneutral, the heat of reaction of each step must then be small. Since addition of an alkyl radical to an olefin is intrinsically exothermic by ca. 20 kcal/mol, this condition will be met only if the resonance energy of the corresponding allyl radical is of comparable magnitude. Since the resonance energy

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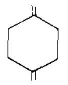
(37) Dewar, M. J. S.; Pyron, R. S. *J. Am. Chem. Soc.* **1970**, *92*, 3098.

Table V. Comparison of Biradicaloid SIs with Synchronous TSs for Cope Rearrangements of **1** and **6**

	biradicaloid SI				synchronous TS[a]			
	bond lengths (Å)				bond lengths (Å)			
compd	16	12	56	angle θ (deg)	16	12	56	angle θ (deg)
1	1.646	1.427	1.427	14.4	(2.062)	1.391	1.391	11.1
6	1.623	1.442	1.430	11.1	(2.062)	1.401	1.389	8.3

[a] Assuming the lengths of the C_1C_6 and C_3C_4 bonds to be 2.06 Å; see text.

Chart II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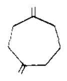
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of cinnamyl radical **20** is much greater than that of the radicals (allyl or 2-phenylallyl) that would be involved as intermediates in the other reactions, this mechanism would explain why problems arose only with the 3-phenyl derivatives (**9** and **10**) of **1**. The alternative mechanism clearly cannot involve fission into allyl radicals and recombination because the Arrhenius *A* factor for such a process would be very large.

In the case of the Diels–Alder reaction, we were able to carry out separate calculations both for the synchronous (aromatic) mechanism and for the biradicaloid one, because AM1, being an RHF procedure, favored the former sufficiently to make it the preferred outcome. Comparison of the AM1 rates with those calculated with AM1–HE–CI led to an unambiguous distinction between the two mechanisms. Here the results of a synchronous reaction cannot be predicted because even AM1 leads to the biradicaloid mechanism.

The fact that RHF AM1 calculations predict a biradicaloid mechanism is in itself highly significant. Any RHF procedure is inherently biassed against biradical-like species, tending to favor any available closed shell alternative. Here such an alternative is available in the form of the synchronous mechanism where the TS would have a normal closed shell aromatic structure. The prediction, that the Cope rearrangement involves biradicaloid intermediates, is therefore very strong, and it is of course further strengthened by the truly remarkable agreement between the AM1 results and experiment. Nevertheless it would clearly be of interest to have some indication of what the results would be if the reaction were synchronous. It occurred to us that this might be achieved by repeating the calculations with the lengths of the relevant bonds in the TS set equal to the values expected for an aromatic TS. We therefore repeated the calculations for **1** and **6**, assuming the TSs to be symmetrical and setting the lengths of the C_1C_6 and C_3C_4 bonds equal to 2.06 Å but optimizing all other geometrical parameters. Table V shows the results. While the energy of the TS for **1** increased by 7.8 kcal/mol, that for **6** increased by 12.6 kcal/mol. The corresponding "activation energies" for **1** and **6** are then almost identical, being 44.9 and 45.3 kcal/mol, respectively. Thus when the reactions are constrained to take place via "aromatic" TSs, a 2-phenyl substituent leaves the activation energy for **1** unchanged. This result supports the conclusion reached above, that such a substituent would have no effect on the rate if the reaction were synchronous.

It seems in any case clear that no calculation for **1** alone could in itself provide an unambiguous distinction between the two alternative mechanisms for **1** because the difference in activation energy between them is likely to be less than the possible error in *any* available procedure.[38] To be of real significance, any future study of the Cope rearrangement must not only be carried out with an adequate procedure but must also, like ours, be based on calculations for a number of examples for which experimental activation parameters are available.

Entropies of Activation

Entropies of activation serve as a qualitative indication of the relative tightness of binding of the reactants and TS in a unimolecular reaction. Comparison with values calculated theoretically can also serve as a quantitative check on calculated possible mechanisms. One of the advantages of our procedures is the relative ease with which molecular entropies, and hence entropies of activation, can be calculated. The results are moreover much more accurate in chemical terms than corresponding enthalpies, the errors being usually less than 1 eu for molecules without internal rotation and less than 3 eu if there are no unusually low torsional barriers.[39] We accordingly calculated entropies of activation for the chair and boat rearrangements of **1**, the results being compared with experiment[40] in Table III.

The agreement for the chair rearrangement is clearly very good, particularly since the entropy calculated for **1** is expected to be too large by 2–3 eu in view of the possibility of internal rotation. In the case of the boat rearrangement, however, there is a large discrepancy. According to AM1, the entropies of activation for both reactions are similar. Indeed, even the small difference can reasonably be attributed to the fact that the chair SI is predicted to be a marginally stable intermediate whereas the boat SI is the TS. The reported experimental value for the boat rearrangement is, however, less negative by more than 10 eu. It is extremely difficult to see how such a difference could exist if both reactions take place by similar mechanisms, as has been generally assumed and as calculations have indicated. Further studies of boat Cope rearrangements are in progress. Meanwhile the close agreement between the (corrected) calculated and observed values of ΔH^{*} for the boat rearrangement of **1** must be regarded as fortuitous.

Kinetic Isotope Effects

As noted earlier, Gajewski et al.[15] have reported studies of SDKIEs for the Cope rearrangements of various derivatives of **1** which they have taken as evidence for a concerted mechanism in which the structure of the TS changes extensively with the nature of the substituents, ranging from species corresponding to a weakly coupled pair of allyl radicals at one extreme to a diradical-like species, analogous to **3**, at the other. Their arguments rest on the assumption that the value of a SDKIE is directly related to changes in the strengths of the bonds formed by the adjacent carbon atom. This assumption, while intuitively reasonable, is, however, suspect. CH(D) SDKIEs depend on the frequencies of molecular vibrations involving motion of the relevant atoms of hydrogen or deuterium. These in turn depend on the relevant stretching and bending CH(D) force constants and hence on the hybridization of the carbon AOs used to form the CH(D) bonds. Computational evidence indicates that formation of a very weak bond in a TS can lead to an almost complete change in geometry of carbon from planar to tetrahedral[41] and that this can in turn lead to a correspondingly large SDKIE.[42] Thus while absence of a SDKIE, or a very small SDKIE, can be taken as evidence that the adjacent atom has undergone little or no change in bonding, a large SDKIE does not necessarily imply a large change in bonding. If a relatively large SDKIE arises from formation of a weak bond, small changes in the strength of the latter, too small to be of any real chemical significance, may lead

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[38] For example, the error in the activation energy calculated[23] for a much simpler reaction, namely electrocyclic ring opening in cyclobutene, using a full double-ζ-plus-polarization basis set and full singles-plus-doubles CI (CISD), was 9.8 kcal/mol.

[39] Dewar, M. J. S.; Ford, G. P. *J. Am. Chem. Soc.* **1977**, *99*, 7822.

[40] Goldstein, M. J.; Benzon, M. S. *J. Am. Chem. Soc.* **1972**, *94*, 7147.

[41] Dewar, M. J. S.; Olivella, S. *J. Am. Chem. Soc.* **1978**, *100*, 5290.

[42] Canadell, E.; Poblet, J. M.; Olivella, S. *J. Phys. Chem. Soc.* **1983**, *87*, 424.