Alternative Transition States in the Cope Rearrangements of Hexa-1,5-diene

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AM1 calculations show that the boat and chair Cope rearrangements of hexa-1,5-diene can each proceed by two different paths, one involving an aromatic and the other a biradical-like transition state, distinguishable by their entropies of activation.

The Cope rearrangement of hexa-1,5-diene (**1**) derivatives was long regarded as a classic example of an 'allowed' pericyclic reaction,[1] taking place *via* an aromatic[2] transition state (TS) (**2**) isoconjugate with benzene and with a chair geometry.[3] This view was challenged some years ago by Doering *et al.*,[4] who suggested that the reaction might be nonsynchronous, the TS being a biradical-like species derived from the 1,4-cyclohexylene biradical (**3**) by a through-bond interaction between the radical centres, *i.e.* a biradicaloid.

The two mechanisms should correspond to transition states with different geometries, the lengths of the forming/breaking CC bonds, C(1)–C(6) and C(3)–C(4), differing significantly, and substituents at C-2 or C-5 should also exert different effects. On the basis of these criteria, Doering's mechanism was supported strongly by experimental studies[5] and theoretical (MINDO/3)[6] calculations[7] in these laboratories, and we have recently further confirmed this mechanism by a detailed theoretical investigation[8] of the chair Cope rearrangements of the hexadiene (**1**) and five of its derivatives, using AM1.[10] In particular, the calculations predicted the lengths of C(1)–C(6) and C(3)–C(4) to be 1.61—1.65 Å, corresponding to long single bonds, whereas analogy suggests that in the aromatic TS they would be >2 Å.

While this evidence for the biradical mechanisms seems very strong, two pieces of evidence to the contrary remained. Osamura *et al.*[10] have reported an *ab initio* calculation for the chair Cope rearrangement of (**1**) which apparently predicted the TS to be 'aromatic', the lengths of C(1)–C(6) and C(3)–C(4) being 2.06 Å. This work was admittedly marred by lack of proper geometry optimization and failure to carry out the MCSCF calculation properly. Furthermore, no effective attempt was made to locate an alternative biradicaloid TS.

The second problem was more serious. If the chair and boat Cope rearrangements have similar mechanisms, as has been generally assumed and as both MINDO/3[7] and AM1[8] predict, their entropies of activation should be similar. Both calculations[7,8] indeed predicted this to be the case. Yet the reported experimental values differ by 10 cal K^{-1} mol^{-1}; see Table 1. While the possible experimental error for the boat value was rather large, comparable entropies of activation have recently been reported[11] for Cope rearrangements of cyclic derivatives [(**4**) and (**5**)] of (**1**) where geometric constraints enforce rearrangement by the boat mechanism.

In the case of the Diels-Alder reaction, where there is a similar choice between aromatic and biradicaloid transition states, a detailed investigation[12] suggested not only that such reactions normally take place by the biradicaloid mechanism but also that the two mechanisms represent discrete alternatives, not ends of a graded series of 'merging' mechanisms. It seemed possible that the same situation might hold in the case of the Cope rearrangement, the aromatic and biradicaloid mechanisms corresponding to distinct transition states with

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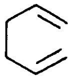
Table 1. Activation parameters and transition state geometries for Cope rearrangements of hexa-1,5-diene (**1**).

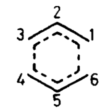
	$\Delta H^{\ddagger b}$		$\Delta S^{\ddagger c}$		Bond lengths (Å)	
Reaction[a]	Calc.	Obs.	Calc.	Obs.	C(1)–C(2)	C(3)–C(4)
Chair (birad)	37.1	33.3[d,e]	−15.6	−13.1 ± 1.0[d,e]	1.656	1.427
(aro)	43.6		−8.1		1.992	1.394
Boat (birad)	47.8	44.7[e]	−11.0	−3.0 ± 3.6[e]	1.661	1.424
(aro)	50.5		−6.3		1.983	1.394

[a] Cope rearrangements of (**1**) *via* aromatic (aro) or biradicaloid (birad) transition state. [b] Enthalpy of activation (kcal mol^{-1}; cal = 4.184 J). [c] Entropy of activation (cal mol^{-1} K^{-1}). [d] Ref. 5. [e] Ref. 15.

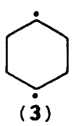
Table 2. Calculated secondary deuterium isotope effects at 250 °C.

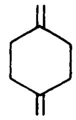
	k_D/k_H		k_H/k_D	
Reaction	birad	aro	birad	aro
Chair	1.135	1.131	1.001	1.028
Boat	1.126	1.126	1.030	1.030

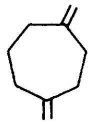

(**1**)



(**2**)


(**3**)


(**4**)


(**5**)

different geometries and entropies. The greater lengths of C(1)–C(6) and C(3)–C(4) in the aromatic TS should make it more flexible than the corresponding biradicaloid and hence increase its entropy. The difference in entropy of activation between the chair and boat rearrangements could then be understood if they take place by different mechanisms, the chair being biradicaloid and the boat aromatic. The *ab initio* results would also be accommodated since no effective attempt was made to find an alternative TS.

Our previous AM1 calculations[8] for the chair and boat rearrangements of (**1**) were carried out using the length of the forming CC bond as a reaction co-ordinate,[13] and therefore tended to lead to biradicaloid transition states. We have now found a second 'aromatic' TS in each of these reactions. All four transition states had C_{2v} symmetry and all were characterized as saddle points on the potential surface by calculating force constants.[14] The lengths of the CC bonds and the calculated and observed activation parameters are listed in Table 1. The calculated bond lengths follow the pattern just predicted C(1)–C(6) and C(3)–C(4) being much longer in the aromatic transition states.

The entropies of activation calculated for the aromatic rearrangements are, as expected, less negative than those for the biradicaloid ones. The value (-6.3 cal K^{-1} mol^{-1}) calculated for the aromatic boat rearrangement agrees with experiment (3.0 ± 3.6 cal K^{-1} mol^{-1}) to within the limits of experimental error and even better with the seemingly more accurate value (-6.9 Å; 1.8 cal K^{-1} mol^{-1}) reported[11] for (**5**). The value for (**4**) was less negative (-3.7 Å; 3.2 cal K^{-1} mol^{-1}), as would be expected in view of its greater rigidity. Our results thus support our suggestion that the difference in entropy of activation between the boat and chair rearrangement reflects a difference in mechanism, and our calculated activation parameters are also consistent with it. Thus while the calculated free energies of activation for the biradicaloid and aromatic boat rearrangements are almost identical (53.6 *vs.* 53.8 kcal mol^{-1}) at the temperature (523 K) used in the experimental study,[15] the free energy of the chair biradicaloid TS is lower than that for the aromatic TS by 2.6 kcal mol^{-1}.

The preference for the aromatic mechanism in the case of the boat rearrangement can be attributed to the eclipsing interactions across the C(1)–C(6) and C(4)–C(5) bonds. Since these bonds are much shorter in the biradicaloid than in the aromatic TS, the interactions should selectively destabilize the biradicaloid boat TS.

The conclusion, that the Cope rearrangement of (**1**) can take place by two distinct paths involving mechanisms that are basically different and yet involve transition states with such similar structures, is very surprising. To our knowledge, no situation of this kind has been previously encountered in the case of any other reaction. Our work suggests that the same will prove true for other pericyclic processes, *e.g.* the Diels-Alder reaction,[11] where there is a similar choice between aromatic and biradicaloid mechanisms. It seems likely that these also take place by one or other of two distinct alternative reaction paths with distinct and different transition states rather than by a graded series of intermediate mechanisms *via* transition states with variable structures, as Gajewski[16] has suggested in the case of the Cope rearrangement.

In view of the implications of this work, further experimental confirmation would clearly be of value. According to current ideas, secondary deuterium kinetic isotope effects can serve as a criterion of bonding at the carbon atom adjacent to H(D). If so, the k_H/k_D rate ratios for deuterio derivatives of (**1**) should differ significantly for the aromatic and biradicaloid mechanisms. Moreover, our calculated k_H/k_D values for the chair Cope rearrangements of several deuteriated hexa-1,5-dienes agreed well with experiment.[8] We therefore carried out similar calculations for the aromatic boat and chair rearrangements of (**1**). As Table 2 shows, the results were almost identical with those found earlier[8] for the corresponding biradicaloid rearrangements, implying that the difference in bonding between the two types of TS leads to no change in the related kinetic isotope effects. It therefore seems unlikely that measurements of this kind would lead to a distinction between the aromatic and biradicaloid Cope mechanisms and our results also throw further doubt[8] on the use of kinetic isotope effects in general as a quantitative criterion of bonding.

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