Theoretical perspectives on the Cope rearrangement in bullvalene systems

Pebam Munindro Singh & R H Duncan Lyngdoh*
Department of Chemistry, North-Eastern Hill University, Shillong 793 022, India.
Received 23 May 2003; accepted (revised) 16 January 2004

Using the semi-empirical AM1 SCF-MO method, transition states have been located for Cope rearrangements in various bullvalene systems, including degenerate unsubstituted and difluoro substituted cases as well as non-degenerate monofluoro substituted cases. Transition states have been located for non-degenerate cases using the routine SADDLE keyword of the MOPAC package. By assuming transition state symmetry about the reaction coordinate for degenerate cases, computational time is substantially saved with no loss of essential accuracy. All these transition states incorporate a boat-shaped cyclic six-membered moiety. Activation energy barriers range between 24.0 and 32.5 kcal/mol, rather high compared with experimental values reported, and thus systematically corrected. The non-degenerate cases have transition states whose positions along the reaction coordinate (as gauged by appropriate geometry markers) agree well with their slightly “late” character predicted from reaction endothermicity by the Hammond postulate. The effects of fluorine substitution on activation energy and transition state geometry as predicted by these calculations accord well with chemical intuition based on the inductive effect. The application of a systematic correction to the activation barriers leads to more reasonable values. For the non-degenerate monofluoro substituted cases, these corrected activation barriers are used to construct an energy profile diagram to represent all the interconversions, which lead us to infer a minimal energy requirement of 19.22 kcal/mol for complete scrambling of the carbons during Cope rearrangement of these systems.

IPC: Int.Cl. 7 C 07 C 13/23

The Cope rearrangement\(^1\), long considered as a typical pericyclic reaction, is believed to be a one-step concerted process occurring via a cyclic transition state and abiding by the conservation of orbital symmetry\(^3\). The thermal prerequisite and stereochemistry of this [3,3] sigmatropic rearrangement have been satisfactorily explained by frontier orbital analysis and the correlation diagram method\(^4\). This theoretical study examines the Cope rearrangement in some bullvalene systems, including degenerate cases with reactant and product identical.

Cope rearrangements in 1,5-hexadienes are [3,3] sigmatropic carbon-carbon bond migrations over a diene framework, subjected to intense experimental study\(^6\). Originally described as a “no mechanism” reaction\(^\text{15}\), the Cope rearrangement was then labeled as a pericyclic concerted reaction via a cyclic aromatic transition state. Later semi-empirical theoretical work raised the possibility of it being an asynchronous process involving biradicaloid intermediates\(^16\). More recently, accurate theoretical calculations\(^17\) indicate a concerted process as a more correct description. Probably the actual situation depends upon the particular system involved, including substituent and conformational effects, as well as the theoretical method used.

The degenerate Cope rearrangement is a special case where the reactant and product are identical, e.g. for unsubstituted or symmetrically substituted acyclic 1,5-hexadiene systems, besides complex systems like semibullvalene and bullvalene involving valence tautomerism. Bullvalene, first synthesised by Schroeder\(^18\), involves a Cope rearrangement (Figure 1) attracting much attention due to the phenomenon of complete scrambling of its 10 carbon atoms by multiple Cope rearrangements\(^\text{19}\) which distribute the position of the cyclopropane ring among all the carbons. At room temperature four \(^{13}\)C NMR signals are obtained as expected, but at about 100\(^\circ\)C they coalesce into only one signal\(^20\), signifying indistinguishability of all 10 carbons when the rapid rate of interconversion between the 1093 different tautomers becomes comparable to the NMR time scale. The molecule adopts a “fluxional” structure,

Figure 1 — Degenerate Cope rearrangement of bullvalene showing the reactant, transition state and product.
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A C

A

B

C

D

Figure 2 – Positional isomers of monofluorobullvalene showing the possible one-step interconversion. Cross mark shows that there is no direct conversion between the isomers.

Figure 3 – Degenerate Cope rearrangement of difluorosubstituted bullvalene showing the Reactant, transition state and product.

Six unique inter-conversons may be envisioned, viz., A→B, A→C, A→D, B→C, B→D and C→D. Of these, only the A→D, C→B and C→A cases can proceed via single Cope rearrangements (Figure 2), the others occurring only through multiple Cope rearrangements. The net result is that, at a particular temperature like the unsubstituted case, all four isomers should inter-convert at a rate comparable with the NMR time scale so that complete scrambling of all the carbons occurs. Thus, no spectroscopic differentiation between the four isomers is evident, a single $^{13}C$, $^1H$ or $^{19}F$ peak being observed.

Our study of degenerate Cope rearrangements includes difluoro substituted bullvalenes, which exist as twelve positional isomers (six corresponding to three antipodal pairs) having 27 unique isomerisation processes. We choose only cases where disubstitution occurs such that the rearrangement can proceed in degenerate fashion. This leaves only five difluoro substituted bullvalenes which undergo degenerate Cope rearrangements, labeled as E, F, G, H and I in Figure 3, which also portrays the transition state and product for each case.

We seek to compare Cope rearrangement feasibility for these different bullvalene systems...
through study of the reaction pathways and transition states, laying focus on transition state stability and geometry. The transition state geometries for the non-degenerate cases (involving monosubstituted fluorobulvalenes) are also gauged to see if they are “early”, “midway” or “late” along the reaction coordinate. This is related to the endothermicity or exothermicity of the net reaction in each case as per the Hammond postulate. Finally, we attempt to correct the AM1 values for the activation energies, and use these corrected values to plot an energy level profile diagram for cases of multiple Cope rearrangements in monofluorosubstituted bulvalenes.

**Theoretical methodology**

Both the AM1 and PM3 semi-empirical SCF-MO methods of the MOPAC 6.0 package were used initially to calculate energy-minimised geometries and wave-functions for the reactants, products and transition states in the unsubstituted bulvalene case. Since the PM3 heats of formation for all species were found invariably higher than the AM1 values, we opted for the AM1 method to carry out all further calculations. All equilibrium geometries were optimised by the Davidson-Fletcher-Powell algorithm. We used the PRECISE keyword of the MOPAC package to sharply reduce the threshold for gradient norm during energy minimisation, resulting in improved accuracy and reproducibility.

**Location of transition states**

Different methods were applied to locate transition states for degenerate and non-degenerate cases. Non-degenerate cases were located by using the standard SADDLE keyword of the MOPAC package, which interpolates between reactant and product geometries through a reverse search strategy, resulting in the transition state. Degenerate cases were treated in two ways as described below.

We firstly assumed symmetry about the reaction coordinate for the transition state in any degenerate Cope rearrangement. We had earlier applied this concept of symmetry to rapidly locate transition states in some degenerate cases of the 1,5-sigmatropic hydrogen shift in 1,3-pentadienes. Following this concept, a putative transition state with symmetry different from reactant or product may be located by adopting a trial geometry of the appropriate symmetry, which is then simply energy-minimised subject to this symmetry constraint. This procedure results in a transition state if the starting point for optimisation occurs close enough to the transition state itself, or if that is the only possible option on the energy hypersurface. For transition states having the same symmetry as the reactant, we ensured that the starting geometry for energy-minimisation was closer to the transition state than the reactant. This was performed by simply adopting the energy-minimised transition state for the unsubstituted bulvalene case as a basis to build up starting geometries for the degenerate substituted cases. The advantage of this symmetry constraint method lies in substantial reduction of computational effort expended in evaluating integrals, gradients and second derivatives.

The other method to locate transition states for degenerate cases was to simply apply the SADDLE keyword described earlier. This procedure was computationally more rigorous than the symmetry-constrained search described above, but is more general in its application, besides being less ambiguous.

Whatever be the method for locating transition states, confirmation of a given stationary point as a transition state was performed by applying the FORCE keyword, which set up and diagonalised the Hessian (second derivative) matrix. The emergence of only one negative eigenvalue confirmed the given structure as a transition state.

**Results and Discussion**

We present our results for both degenerate and non-degenerate cases of Cope rearrangements in bulvalene systems as given below.

**Degenerate Cope rearrangement in unsubstituted bulvalene**

Table I presents AM1 and PM3 values of the heats of formation $\Delta H_f$ (R) and some geometrical parameters for unsubstituted bulvalene, the PM3 energy being higher than the AM1 value by 1.44 kcal/mol. Only four different carbon-carbon bond types exist in bulvalene, represented as $a$, $b$, $c$ and $d$ (Figure 4a). All other bonds are equivalent to one of these due to the $C_2$ symmetry of bulvalene. To these four C-C bonds, we note a fifth carbon-carbon distance $e$ (Figure 4a) which forms a new type $a$ C-C bond after the rearrangement (Figure 1). We also note the distance $f$ between the two vertices, besides the angles $\theta_1$ and $\theta_2$ of Figure 4a which interchange during the rearrangement.

The AM1 values for lengths of bond types $a$, $b$, $c$ and $d$ are respectively 1.5185, 1.4598, 1.3386 and
Table I — AM1 and PM3 heats of formation and geometrical parameters of unsubstituted bullvalene* (reactant) along with results of higher level theory and experiment#

<table>
<thead>
<tr>
<th>Method</th>
<th>$\Delta H_f$</th>
<th>$a$</th>
<th>$b$</th>
<th>$c$</th>
<th>$d$</th>
<th>$e$</th>
<th>$f$</th>
<th>$\theta_1$</th>
<th>$\theta_2$</th>
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<tr>
<td>AM1</td>
<td>75.40</td>
<td>1.5185</td>
<td>1.4598</td>
<td>1.3386</td>
<td>1.4953</td>
<td>2.4580</td>
<td>3.0340</td>
<td>60.00</td>
<td>122.04</td>
</tr>
<tr>
<td>PM3</td>
<td>76.84</td>
<td>1.5160</td>
<td>1.4685</td>
<td>1.3354</td>
<td>1.4976</td>
<td>2.4630</td>
<td>3.0330</td>
<td>60.00</td>
<td>122.22</td>
</tr>
<tr>
<td>HF/6-31+G**</td>
<td>-</td>
<td>1.5178</td>
<td>1.5192</td>
<td>1.3255</td>
<td>1.4831</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HF/6-311++G*</td>
<td>-</td>
<td>1.5366</td>
<td>1.5244</td>
<td>1.3369</td>
<td>1.4845</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MP2/6-31+G**</td>
<td>-</td>
<td>1.5326</td>
<td>1.5102</td>
<td>1.3529</td>
<td>1.4677</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>X-ray diff.</td>
<td>-</td>
<td>1.5352</td>
<td>1.5157</td>
<td>1.3450</td>
<td>1.4727</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Neutron diff.</td>
<td>-</td>
<td>1.5330</td>
<td>1.5160</td>
<td>1.3420</td>
<td>1.4730</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Heats of formation in kcal/mol; bond lengths in angstrom; angles in degrees

#For theoretical results, see ref 24; for experimental values, see ref 52.

Table II — AM1 and PM3 data* for degenerate Cope rearrangement in unsubstituted bullvalene and geometrical parameters for the transition state

<table>
<thead>
<tr>
<th>Method</th>
<th>$\Delta H_f$</th>
<th>$v_1$</th>
<th>$E_a$</th>
<th>$g$</th>
<th>$h$</th>
<th>$l$</th>
<th>$f$</th>
<th>$\theta$</th>
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<tr>
<td>AM1(Sad)</td>
<td>104.46</td>
<td>-0.2260</td>
<td>29.06</td>
<td>2.1908</td>
<td>1.3800</td>
<td>1.4882</td>
<td>2.9900</td>
<td>94.76</td>
</tr>
<tr>
<td>AM1(Sym)</td>
<td>104.45</td>
<td>-0.2218</td>
<td>29.05</td>
<td>2.1906</td>
<td>1.3804</td>
<td>1.4875</td>
<td>2.9900</td>
<td>94.75</td>
</tr>
<tr>
<td>PM3(Sad)</td>
<td>108.08</td>
<td>-1.1431</td>
<td>31.24</td>
<td>2.1027</td>
<td>1.3823</td>
<td>1.4899</td>
<td>2.9930</td>
<td>89.76</td>
</tr>
<tr>
<td>PM3(Sym)</td>
<td>108.08</td>
<td>-1.1132</td>
<td>31.24</td>
<td>2.1025</td>
<td>1.3820</td>
<td>1.4899</td>
<td>2.9920</td>
<td>89.76</td>
</tr>
</tbody>
</table>

*Heats of formation and activation energy in kcal/mol; Hessian eigenvalue in $10^5$ dyne/cm; bond lengths in angstrom; angle in degrees

Figure 4 — Geometry markers for (a) reactant, (b) transition state and (c) carbon numbering.

1.4953 Å (PM3 values respectively 1.5160, 1.4685, 1.3354 and 1.4976 Å). These values are compared in Table I with those obtained from higher level theoretical calculations and with the results of experiment using X-ray and neutron diffraction methods, with which there is substantial qualitative agreement. A normal C-C single bond is indicated for bond type $a$ within the cyclopropane moiety, despite the strain effect, and a usual C=C double bond for bond type $c$, relatively strain-free. Lengths for the single-bond types $b$ and $d$ are shorter than the single bond type $a$ since the termini of bond types $b$ and $d$ are connected to doubly-bonded $sp^2$ carbons. The carbon-carbon distance $e$ (AM1 value 2.4580 Å) indicates absence of covalent bonding, while the distance $f$ between the vertices has an AM1 value of 3.0340 Å. The cyclopropane angle $\theta_1$ is necessarily exactly 60° by symmetry, while the angle $\theta_2$ to which it converts after the rearrangement has an AM1 value of 122.04°.

Table II gives AM1 and PM3 values for the heat of formation $\Delta H_f$ of the transition state, the activation energy $E_a$ and the single negative Hessian eigenvalue $v_1$, where the SADDLE and symmetry-constrained methods are labeled “Sad” and “Sym” respectively (as for all tables in this paper). These two methods both yield practically the same values for heat of formation, activation energy and single negative eigenvalue (for both AM1 and PM3 hamiltonians). The symmetry-constrained approach is much less compute-intensive than the SADDLE strategy, using less than 10% of the computational time, clearly pointing to the effectiveness of the symmetry-constrained method. The values for the activation energy (29.05 kcal/mol for AM1 and 31.24 kcal/mol for PM3) may be compared with the experimental value of 12.8 kcal/mol, which indicates that the semi-empirical AM1 and PM3 hamiltonians yield values appreciably larger in comparison. A systematic error of about 15-16 kcal/mol had been suggested by Dewar et al. in calculating AM1 activation barriers for these kinds of tricyclic systems. Since absolute values are not what
are sought here, but rather trends among a series, this semi-empirical methodology may yet yield meaningful results.

Table II further presents some PM3 and AM1 determinants of transition state geometry (Figure 4b) in the degenerate Cope rearrangement of unsubstituted bullvalene, where both the SADDLE and the symmetry-constrained approaches converge to the same results. The transition state symmetry ($C_{2v}$) differs from that of the reactant ($C_{3}$), but the labelling system of Figure 4b also applies to more general cases (see later). Important characteristics of transition state geometry are the bond lengths and bond angles involved in the opening of the cyclopropane ring and shift of the π-electron system during the reaction. Apart from one ethylenic double bond and the C-C single bonds not directly involved in the rearrangement, there remain three types of carbon-carbon bonds in the transition state, represented by the bond types g, h and i (Figure 4b). The bond type g in the transition state (equivalent to $g'$ opposite) corresponds to the bond type a in the reactant (Figure 4a), while the bond type h here corresponds to the bond type b in the reactant. Due to symmetry, the bond h here is equivalent to the adjacent bond $h'$ (Figure 4b) which corresponds to the bond type c in the reactant (Figure 4a). The bond type i in the transition state corresponds to the bond type d in the reactant. The distance f between the vertices is again taken note of. The angles $\theta$ and $\theta'$ noted here in the transition state are the same on both sides (Figure 4b) for degenerate cases, corresponding to the angles $\theta_1$ and $\theta_2$ of the reactant (Figure 4a). We quote values of geometry markers or heats of formation here as derived from the symmetry-constrained methodology rather than from the standard SADDLE keyword whenever differences arise (all very small in any case).

The AM1 value of 2.1906 Å (PM3 value 2.1025 Å) for the bond length g in the transition state is much larger than the AM1 value of 1.5185 Å (PM3 value 1.5160 Å) for this bond (type a) in the cyclopropane ring of the reactant, indicating cleavage of this bond during the reaction. The AM1 bond length value for the bond types h and $h'$ is 1.3804 Å (PM3 value 1.3820 Å), intermediate between the single bond length for bond type b (AM1 value 1.4598 Å) and the double bond length for bond type c (AM1 value 1.3386 Å), indicating that single-double bond interconversion occurs symmetrically here in the transition state. The bond length i (AM1 value 1.4875 Å; PM3 value 1.4899 Å) in the transition state differs little from that of the corresponding bond d in the reactant (AM1 value 1.4953 Å). This is also noted for the distance f between the two vertices, having an AM1 value of 2.9900 Å (PM3 value 2.9920 Å).

The bond angles angles $\theta$ and $\theta'$ on both sides of the transition state have an AM1 value of 94.76° (PM3 value 89.76°). The increase from the $\theta_1$ value of 60° in the reactant is due to lengthening of the cyclopropane C-C bond a of the reactant as it cleaves during the reaction. The decrease from the AM1 $\theta_2$ value of 122.04° in the reactant is due to shortening of the non-bonded carbon-carbon distance e in the reactant as a new bond forms.

We see that the bullvalene Cope rearrangement centers around a non-planar cyclic six-membered ring moiety which is boat-shaped, the two allylic moieties connected by two bonds of the bond type g which undergo breaking and forming (of the bond types a and e in the reactant). It also resembles an open book of $C_{2v}$ symmetry with a dihedral angle of about 130.21° between the two halves. It thus differs from the chair-shaped or skew-shaped transition states reported for the Cope rearrangement in acyclic 1,5-hexadiene systems, which can incorporate a boat-shaped species as well. The conformational flexibility of the 1,5-hexadiene system allows for a variety of shapes for the transition state, each depending upon the conformer chosen for reactant and product. The bullvalene system is conformationally less flexible, with only this boat-shaped transition state envisioned so far for the Cope rearrangement here.

Non-degenerate Cope rearrangements in monosubstituted fluorobullvalenes

From the six inter-conversions among the four monosubstituted fluorobullvalene isomers (Figure 2), only the A--D, the C--B and the C--A cases proceed through single Cope rearrangements (Figure 2). The first two of these involve symmetrical transition states ($C_{1}$ symmetry) which are calculated by both SADDLE and symmetry-constrained strategies. The other three inter-conversions A--B, B--D and C--D occur only through multiple Cope rearrangements (see later).

Table III gives the AM1 values for the heats of formation $\Delta H_{f}(R)$ along with the symmetry point group of the four positional isomers A, B, C and D (Figure 2). For the purpose of this paper, bracketed point groups in the tables, e.g. [$C_{2v}$], indicate arrival at
the most stable one being that for the C→A conversion, and the least stable being that for the A→D conversion, reflecting on the differing effects of position of the fluorine substituent in the transition state.

Calculated AM1 values for the activation energy $E_a$ range from 23.99 to 31.20 kcal/mol, comparable to the AM1 value for the unsubstituted case (29.05 kcal/mol), but certainly on the large side when compared with experimental expectation. The forward and reverse reaction feasibilities as given by the activation barriers $E_a(F)$ and $E_a(R)$ predict that the C↔A inter-conversion would be kinetically most facile, and the A↔D one least facile, regardless of reaction direction. Note that the order of absolute magnitude for the negative Hessian eigenvalues runs parallel to that for the activation energies, which we have noted in our other theoretical work.$^{56}$

The positive values of reaction enthalpy $\Delta H_r$ predict endothermicity for the three conversions A→D, C→B and C→A ($\Delta H_r = 1.64, 0.73$ and $4.32$ kcal/mol respectively). This endothermicity depends, of course, on the direction taken for the reaction, where our choice is as above. The reaction enthalpies give the ordering for degree of endothermicity as: C→A > A→D > C→B. Since the reaction enthalpies for these reactions are small compared with the activation energies, the Hammond postulate predict the transition states to be quite different from either reactant or product, but located approximately midway along the reaction pathway and yet a little closer to the product, viz. having some small degree of “late” character. We confirm these inferences by examining aspects of transition state geometry relating to bond breaking and making, besides angle inter-conversions occurring during the reaction, which we define by referring to the general case of transition state geometry given in Figure 4b. These aspects include lengths of the bonds $g$ and $g'$, lengths of the bonds $h$ and $h'$, as well as the values of the angles $\theta$ and $\phi$.

<table>
<thead>
<tr>
<th>Isomers</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Delta H_r$</td>
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<td>29.98</td>
<td>29.25</td>
<td>35.21</td>
</tr>
<tr>
<td>Point group</td>
<td>$C_1$</td>
<td>$C_1$</td>
<td>$C_1$</td>
<td>$C_1$</td>
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<tr>
<td>$\Delta H_f$</td>
<td>4.32</td>
<td>0.73</td>
<td>0.00</td>
<td>5.96</td>
</tr>
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</table>

*Enthalpies in kcal/mol

Table IV — AM1 data* on heats of formation of four positional isomers for monosubstituted fluorobullvalene

<table>
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<tr>
<th>Reaction</th>
<th>$\Delta H_r$ (TS)</th>
<th>$\Delta H_r$</th>
<th>$E_a(F)$</th>
<th>$E_a(R)$</th>
<th>$\nu$</th>
<th>Pt Gp(TS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A→D(Sad)</td>
<td>64.77</td>
<td>1.64</td>
<td>31.20</td>
<td>29.56</td>
<td>-0.2656</td>
<td>[C,]</td>
</tr>
<tr>
<td>A→D(Sym)</td>
<td>64.77</td>
<td>-</td>
<td>31.20</td>
<td>29.56</td>
<td>-0.2651</td>
<td>$C_1$</td>
</tr>
<tr>
<td>C→B(Sad)</td>
<td>58.43</td>
<td>0.73</td>
<td>29.18</td>
<td>28.45</td>
<td>-0.1955</td>
<td>[C,]</td>
</tr>
<tr>
<td>C→B(Sym)</td>
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<td>-</td>
<td>29.18</td>
<td>28.45</td>
<td>-0.1939</td>
<td>[C,]</td>
</tr>
<tr>
<td>C→A(Sad)</td>
<td>57.56</td>
<td>4.32</td>
<td>28.31</td>
<td>23.99</td>
<td>-0.0880</td>
<td>$C_1$</td>
</tr>
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</table>

*Heat of formation and activation energies in kcal/mol; $\nu$ in $10^3$ dynes/cm
\( \theta' \), as given for the general case of Figure 4b. Each of these pairs of geometry markers has exactly equal values for the "midway" transition state in the degenerate Cope rearrangement for unsubstituted bullvalene. They are not equal for non-degenerate cases, though, and the ratios \( g/g', h/h' \) and \( \theta/\theta' \) may give some idea of the position of the transition state along the reaction pathway. Late transition states are expected to have values of \( g/g' \) and \( \theta/\theta' \) larger than unity and values of \( h/h' \) smaller than unity, and conversely for early transition states. For the \( C\rightarrow A \) case, due to the transition state asymmetry, two sets of \( h \) and \( h' \) bonds exist with two values for the \( h/h' \) ratio.

Table V gives AM1 values of these geometry markers along with the \( g/g', h/h' \) and \( \theta/\theta' \) ratios for the three processes. The values of these ratios all closely approach unity, indicating the approximately "midway" character of all these transition states. The precise values of the \( g/g' \) and \( h/h' \) ratios indicate that these transition states all possess some degree of "late" character. The values of the \( g/g' \) ratio for the processes \( A\rightarrow D, C\rightarrow B \) and \( C\rightarrow A \) (1.00320, 1.00502 and 1.00270 respectively) are all slightly larger than unity and indicate that the transition states are "late" to a small extent. The \( h/h' \) ratios are all slightly smaller than unity, being 0.99877, 0.99812 and 0.98029 (0.99573) for the processes \( A\rightarrow D, C\rightarrow B \) and \( C\rightarrow A \) respectively. Likewise inferring the slightly "late" character of all these transition states. This inference, however, is not drawn uniformly from the values of the \( \theta/\theta' \) ratio, which are larger than unity for the processes \( C\rightarrow B \) and \( C\rightarrow A \) as expected, but smaller than unity for \( A\rightarrow D \). Apparently, the bond length ratios are more effective in corroborating the Hammond postulate since the bonds involved are directly present in the rearranging cyclic moiety of the transition states, while the angles \( \theta \) and \( \theta' \) are not.

In most aspects, transition state geometries for these 3 non-degenerate Cope rearrangements closely resemble that for the degenerate unsubstituted case, invoking the same boat-shaped type of moiety at the center. This may be seen by comparing the values of the \( g \), \( g' \), \( h \), \( h' \), \( \theta \) and \( \theta' \) geometry markers for these non-degenerate transition states with the corresponding values of the \( g \), \( h \) and \( \theta \) markers for the unsubstituted case (Table II).

The effect of fluorine substitution upon transition state stability and activation energy \( E_a \) depends upon the site of substitution in the transition state, and may be gauged by comparison with the unsubstituted case having an \( E_a \) value of 29.05 kcal/mol. Figure 4c presents a numbering system for identifying substitution sites in the transition state, given as \( C^1, C^2, C^3 \) and \( C^4 \). Substitution at the \( C^1 \) position is on a double bond not involved in the rearranging moiety of the transition state, and has only a slight destabilising effect. Fluorine substitution at the \( C^2 \) position (the \( A\rightarrow D \) case) increases \( E_a \) to 31.20 kcal/mol (Table IV). This may be explained by invoking the \(-1\) effect of the fluorine at a cyclopropane ring which has been predicted to have a destabilising effect on the ring55 owing to a increased 2s character in the orbitals present in the carbon atom as it bonds. Fluorine substitution at the \( C^3 \) position (the \( C\rightarrow A \) case) lowers \( E_a \) to 28.31 kcal/mol. This destabilising effect is due to the lone-pairs on fluorine being in conjugation with the cyclopropane ring bond being formed thereby assisting its formation during the pericyclic process.

\( \text{Degenerate Cope rearrangements in difluorosubstituted bullvalenes} \)

Table VI presents AM1 values for \( \Delta H_0(R) \) and \( \Delta H_0(TS) \), the heat of formation of the reactants and transition states, \( E_a \), the activation energy, along with the Hessian negative eigenvalue and computational

<table>
<thead>
<tr>
<th>Reaction</th>
<th>( g )</th>
<th>( g' )</th>
<th>( h )</th>
<th>( h' )</th>
<th>( \theta )</th>
<th>( \theta' )</th>
<th>( g/g' )</th>
<th>( h/h' )</th>
<th>( \theta/\theta' )</th>
</tr>
</thead>
<tbody>
<tr>
<td>A\rightarrow D (sad)</td>
<td>2.1950</td>
<td>2.1870</td>
<td>1.3784</td>
<td>1.3807</td>
<td>93.62</td>
<td>94.57</td>
<td>1.00366</td>
<td>0.99870</td>
<td>0.98995</td>
</tr>
<tr>
<td>A\rightarrow B (sym)</td>
<td>2.1940</td>
<td>2.1870</td>
<td>1.3785</td>
<td>1.3802</td>
<td>93.62</td>
<td>94.59</td>
<td>1.00320</td>
<td>0.99877</td>
<td>0.98975</td>
</tr>
<tr>
<td>C\rightarrow B (sad)</td>
<td>2.2030</td>
<td>2.1920</td>
<td>1.3788</td>
<td>1.3815</td>
<td>95.47</td>
<td>95.07</td>
<td>1.00502</td>
<td>0.99804</td>
<td>1.00421</td>
</tr>
<tr>
<td>C\rightarrow B (sym)</td>
<td>2.2030</td>
<td>2.1920</td>
<td>1.3788</td>
<td>1.3815</td>
<td>95.46</td>
<td>95.08</td>
<td>1.00502</td>
<td>0.99812</td>
<td>1.00400</td>
</tr>
<tr>
<td>C\rightarrow A (sad)</td>
<td>2.2260</td>
<td>2.2200</td>
<td>1.3724</td>
<td>1.4000</td>
<td>96.76</td>
<td>95.90</td>
<td>1.00270</td>
<td>0.98029</td>
<td>1.00918</td>
</tr>
<tr>
<td>A\rightarrow D (sym)</td>
<td>2.1940</td>
<td>2.1870</td>
<td>1.3768</td>
<td>1.3827</td>
<td>93.62</td>
<td>94.57</td>
<td>1.00366</td>
<td>0.99870</td>
<td>0.98995</td>
</tr>
</tbody>
</table>
time $T$ for the 5 degenerate Cope rearrangements involving the five difluoro substituted bullvalenes $E$, $F$, $G$, $H$ and $I$ portrayed in Figure 3, listing also the symmetry point groups for the reactants and transition states. Heats of formation for the reactants range between -14.99 and -6.10 kcal/mole, giving the stability order $G > F > I > H > E$ for the 5 isomers. The Cope rearrangements involving the systems $E$, $F$ and $G$ have transition states with $C_{2v}$ symmetry, so we used the symmetry-constrained method to locate them besides the routine SADDLE keyword. Transition states for the $H$ and $I$ cases have $C_1$ and $C_2$ symmetry respectively, and may also be calculated using the symmetry-constrained method.

Both SADDLE and symmetry-constrained methods lead to essentially the same results regarding geometry and energy of the transition states of $C_{2v}$ symmetry (for systems $E$, $F$ and $G$), demonstrating immense reduction of computational time when the latter method is employed. The transition states have heats of formation $\Delta H_f(\text{TS})$ ranging from 10.85 to 25.63 kcal/mole, giving the stability order $I > H > F > G > E$. The calculated AMI values for the activation energies range from 23.09 to 32.54 kcal/mol, yielding the order of magnitude $G > E > F > H > I$, implying the reverse order for kinetic facility of the reaction. Here again, the AMI values for the activation enthalpies are appreciably larger than what would be expected from experiment or higher level theoretical calculations.

Table VII presents geometrical parameters pertaining to the transition states for degenerate Cope rearrangements in these 5 difluoro substituted bullvalenes. These geometry markers correspond directly to those of the general case portrayed in Figure 4b, the characteristic geometry changes being represented by the bond types $g$ and $h$ along with the bond angle $\theta$. The values of these markers indicate that the transition states for these 5 degenerate Cope rearrangements again closely resemble that of the unsubstituted bullvalene case (Table II), giving the same boat shape. It may be noted that for the $H$ and $I$ cases, the lowering of symmetry in the transition states calls for two sets of $h$ values, where the first referring to the $h$ bond towards the viewer (Figure 3) and the second referring to that directly behind it.

The chief difference between these degenerate reactions and the unsubstituted case is the symmetrical difluoro substitution. The effect of fluorine substitution upon transition state geometry is gauged from the lengths of the bonds directly attached to a fluorine atom. Fluorine substitution at either terminus of an $h$ type bond has the effect of

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**Table VI** — AM1 data* on reactants and transition states for degenerate Cope rearrangements involving difluoro substituted bullvalene systems

<table>
<thead>
<tr>
<th>Reaction</th>
<th>$\Delta H_f(R)$</th>
<th>$\Delta H_f(TS)$</th>
<th>$E_a$</th>
<th>$\nu_1$</th>
<th>$T$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E \rightarrow E$ (Sad)</td>
<td>[C1]</td>
<td>[C2v]</td>
<td>-6.10</td>
<td>25.63</td>
<td>31.73</td>
</tr>
<tr>
<td>$E \rightarrow E$ (Sym)</td>
<td>[C1]</td>
<td>C2v</td>
<td>-</td>
<td>25.63</td>
<td>31.73</td>
</tr>
<tr>
<td>$F \rightarrow F$ (Sad)</td>
<td>[C1]</td>
<td>[C2v]</td>
<td>-14.25</td>
<td>14.25</td>
<td>28.50</td>
</tr>
<tr>
<td>$F \rightarrow F$ (Sym)</td>
<td>[C1]</td>
<td>C2v</td>
<td>-</td>
<td>14.25</td>
<td>28.50</td>
</tr>
<tr>
<td>$G \rightarrow G$ (Sad)</td>
<td>[C1]</td>
<td>[C2v]</td>
<td>-14.99</td>
<td>17.55</td>
<td>32.54</td>
</tr>
<tr>
<td>$G \rightarrow G$ (Sym)</td>
<td>[C1]</td>
<td>C2v</td>
<td>-</td>
<td>17.55</td>
<td>32.54</td>
</tr>
<tr>
<td>$H \rightarrow H$ (Sad)</td>
<td>C1</td>
<td>[C1]</td>
<td>-11.88</td>
<td>11.31</td>
<td>23.19</td>
</tr>
<tr>
<td>$I \rightarrow I$ (Sad)</td>
<td>C1</td>
<td>[C1]</td>
<td>-12.24</td>
<td>10.85</td>
<td>23.09</td>
</tr>
</tbody>
</table>

*Enthalpies in kcal/mol; $\nu$, in $10^4$ dynes/cm; $T$ in seconds

**Table VII** — AM1 data* on geometrical parameters for transition states of degenerate Cope rearrangements involving difluoro substituted bullvalene systems

<table>
<thead>
<tr>
<th>Reaction</th>
<th>$g$</th>
<th>$h$</th>
<th>$i$</th>
<th>$\theta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E \rightarrow E$ (Sad)</td>
<td>2.1900</td>
<td>1.3782</td>
<td>1.5044</td>
<td>93.42</td>
</tr>
<tr>
<td>$E \rightarrow E$ (Sym)</td>
<td>2.1900</td>
<td>1.3783</td>
<td>1.5043</td>
<td>93.43</td>
</tr>
<tr>
<td>$F \rightarrow F$ (Sad)</td>
<td>2.2050</td>
<td>1.3798</td>
<td>1.4853</td>
<td>95.77</td>
</tr>
<tr>
<td>$F \rightarrow F$ (Sym)</td>
<td>2.2040</td>
<td>1.3797</td>
<td>1.4853</td>
<td>95.79</td>
</tr>
<tr>
<td>$G \rightarrow G$ (Sad)</td>
<td>2.1880</td>
<td>1.3951</td>
<td>1.4854</td>
<td>94.76</td>
</tr>
<tr>
<td>$G \rightarrow G$ (Sym)</td>
<td>2.1880</td>
<td>1.3951</td>
<td>1.4853</td>
<td>94.76</td>
</tr>
<tr>
<td>$H \rightarrow H$ (Sad)</td>
<td>2.2463</td>
<td>1.3927</td>
<td>1.5070</td>
<td>97.67</td>
</tr>
<tr>
<td>$I \rightarrow I$ (Sad)</td>
<td>2.2580</td>
<td>1.3940</td>
<td>1.5052</td>
<td>96.96</td>
</tr>
</tbody>
</table>

*Bond lengths in angstrom and angles in degrees
lengthening it. The fluorine-bonded \( h \) type bonds in the \( \text{G} \rightarrow \text{G}, \text{H} \rightarrow \text{H} \) and \( \text{I} \rightarrow \text{I} \) cases show this increase, with lengths from 1.3927 to 1.3951 Å. Other \( h \) type bonds are shorter, ranging between 1.3731 and 1.3797 Å. The \( \rightarrow \text{I} \) effect of fluorine diminishes the \( h \) bond electron density, reducing its partial double bond character further. A similar bond lengthening effect occurs for the \( i \) type bonds, which are fluorine substituted in the \( \text{E} \rightarrow \text{E} \) case, as well as on one side each for the \( \text{H} \rightarrow \text{H} \) and \( \text{I} \rightarrow \text{I} \) cases.

The effect of fluorine substitution upon the activation energy \( E_a \) is again site-dependent, reproducing the trends shown for the monosubstituted cases. Difluoro substitution at the two \( \text{C}^2 \) sites (the \( \text{E} \rightarrow \text{E} \) case) increases the \( E_a \) value as compared with the unsubstiuted case, as occurs for the \( \text{C}^2 \)-monosubstituted case dealt with earlier, and may be explained by a similar rationale. Disubstitution at the two \( \text{C}^3 \) sites (the \( \text{H} \rightarrow \text{H} \) and \( \text{I} \rightarrow \text{I} \) cases) has the effect of lowering activation energy, as occurs for the \( \text{C}^3 \)-monosubstituted case dealt with earlier, and may be similarly rationalised. Disubstitution at the two \( \text{C}^4 \) positions (the \( \text{G} \rightarrow \text{G} \) case) has a destabilising effect not dealt within the monosubstituted cases. It may be explained by the electron-releasing effect of the fluorine atoms (through their lone pairs) which should have a destabilising effect as concluded by Hoffmann \( et \ al.^{27} \) in their work on similar systems.

Corrected values of activation barriers

We now attempted prediction of realistic activation energy values for all these Cope rearrangement reactions on the basis of the systematic error of 15-16 kcal/mol suggested by Dewar \( et \ al.^{40} \) for this type of system. Fixing this error at the value of 16.3 kcal/mol proposed by them for bullvalene, Table VIII presents our AM1 values of activation enthalpy \( E_a \) along with the corrected values for all the 9 systems treated here. The corrected values (6.79 kcal/mol to 16.24 kcal/mol), are probably more in line with observed ranges of values as obtained for these kinds of systems, but require experimental verification. Relative kinetic facility for the Cope rearrangement in the various systems studied then assumes the following order: \( \text{I} \rightarrow \text{I} > \text{H} \rightarrow \text{H} > \text{C} \rightarrow \text{A} > \text{F} \rightarrow \text{F} > \text{unsubstituted case} > \text{C} \rightarrow \text{B} > \text{A} \rightarrow \text{D} > \text{E} \rightarrow \text{E} > \text{G} \rightarrow \text{G} \).

Multiple Cope rearrangements in monofluorobullevalenes

The corrected values of \( E_a \) are used to plot an energy profile diagram (Figure 5) depicting the enthalpy changes accompanying the multiple Cope rearrangements in monofluorobullevalenes.

<table>
<thead>
<tr>
<th>System</th>
<th>unsubtd</th>
<th>( \text{A} \rightarrow \text{D} )</th>
<th>( \text{C} \rightarrow \text{B} )</th>
<th>( \text{C} \rightarrow \text{A} )</th>
<th>( \text{E} \rightarrow \text{E} )</th>
<th>( \text{F} \rightarrow \text{F} )</th>
<th>( \text{G} \rightarrow \text{G} )</th>
<th>( \text{H} \rightarrow \text{H} )</th>
<th>( \text{I} \rightarrow \text{I} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( E_a ) (AM1)</td>
<td>29.05</td>
<td>31.20</td>
<td>29.18</td>
<td>28.31</td>
<td>31.73</td>
<td>28.50</td>
<td>32.34</td>
<td>23.19</td>
<td>23.09</td>
</tr>
<tr>
<td>( E_a ) (corrected)</td>
<td>12.75</td>
<td>14.90</td>
<td>12.88</td>
<td>12.01</td>
<td>15.43</td>
<td>12.20</td>
<td>16.24</td>
<td>6.89</td>
<td>6.79</td>
</tr>
</tbody>
</table>

*All enthalpies in kcal/mol

Figure 5 — Reaction profile of multiple Cope rearrangement of monofluorobullevalene systems.
rearrangements for the multi-step inter-conversions among monofluorosubstituted bullvalenes, which include the $A \leftrightarrow B$, $B \leftrightarrow D$ and $C \leftrightarrow D$ conversions, along with the three unique transition states TS1, TS2 and TS3. We plot Figure 5 taking the starting point corresponding to the lowest energy isomer C as zero. This diagram portrays energetically all the possible processes (conversions) occurring in the Cope rearrangement reaction involving monosubstituted fluorobullvalenes. In order to ensure complete scrambling of all the carbons among these monofluoro bullvalenes, the energy requirement would be the enthalpy difference between the lowest energy isomer C and the highest energy transition state TS3. From this diagram, it emerges that a minimum energy requirement of 19.22 kcal/mol would be required to be supplied in order for complete scrambling of carbon atoms to occur among these four monofluoro substituted bullvalenes.

**Conclusions**

These semi-empirical AM1 calculations predict that a pericyclic one-step reaction is possible and feasible for all these cases of bullvalene Cope rearrangements, each involving a boat-shaped six-membered cyclic rearranging moiety within the transition state. While transition states for the degenerate cases (unsubstituted and symmetrically difluoro substituted) are exactly midway along the reaction coordinate, those for the non-degenerate monofluorosubstituted cases are slightly “late” in character, which observation is supported by their geometries in accordance with the Hammond postulate. The use of symmetry constraints to locate transition states for the degenerate cases is found to be highly effective in reducing computational cost. The effects of fluorine substitution on activation energies and on transition state geometries as predicted here are rationalised qualitatively by appealing to the inductive effect. A systematic correction is applied to the activation energy barriers, yielding an energy profile diagram for all the six inter-conversions among the monofluorosubstituted bullvalenes which predicts a minimum enthalpy requirement of 19.22 kcal/mol for the complete scrambling of carbon atoms in these systems.

**References**

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