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Sequential Transition States and the Valley–Ridge Inflection Point in the Formation of a Semibullvalene

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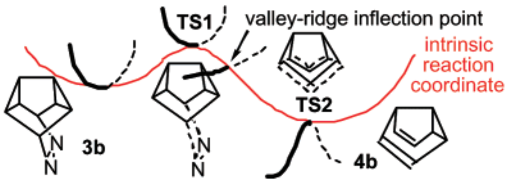
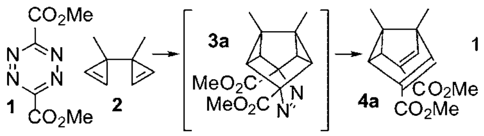
ABSTRACT

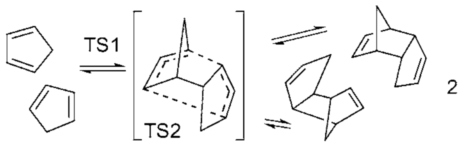


Two sequential transition states are calculated at the B3LYP/6-31G(d,p) level for the deazetization of 3b. The intrinsic reaction coordinate for loss of nitrogen passes through a transition state and then a valley–ridge inflection point and ultimately leads to the transition state for the Cope rearrangement of semibullvalene 4b. The energetic and geometrical consequences are discussed.

Sauer recently published an elegant one-pot synthesis of the semibullvalene **4a** from the tetrazine **1** and the bis-cyclopropene **2** as shown in eq 1.[1] We were intrigued by the lengthy cascade of pericyclic reactions suggested for the mechanism. In particular, concerted loss of nitrogen from the proposed intermediate (**3a**) might well lead not to an intermediate, but if the symmetry of the system were preserved, might instead lead to the transition state for the degenerate Cope rearrangement of **4a**.



It is a common but overly simplistic assumption that one transition state connects one reactant (or intermediate) to one product (or intermediate). While this is often the case, there has recently been increasing interest in reactions in which the intrinsic reaction coordinate (IRC)[2] from one transition state connects not to an intermediate or to the product but to a second transition state.[3−7] Carpenter has reported several beautiful examples of such reactions.[4] We are aware of only two recent examples of organic reactions which could be classified as one chemical transition state leading to another.[5] Caramella et al. have calculated that the transition state for the Diels−Alder dimerization of cyclopentadiene is followed by the transition state for the Cope rearrangement as shown in eq 2.[5b] A similar situation is calculated for the dimerization of acrolein.[5a]



It has long been argued on theoretical grounds that there must be exactly two valleys leading downhill from a transition state.[6] However, following the IRC down one or both valleys may lead not to a minimum energy structure but to another transition state. Somewhere between them the

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[1] Sauer, J.; Bäuerlein, P.; Ebenbeck, W.; Schuster, J.; Sellner, I.; Sichert, H.; Stimmelmayr, H. *Eur. J. Org. Chem.* **2002**, 791−801.

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valley opens into a ridge at the valley−ridge inflection point (VRI).[3e,7] This is a bifurcation on the reaction path; it is downhill from the first transition state to two different products. The reaction dynamics thus control the product distribution.[3,4] These features are illustrated in Figure 1.

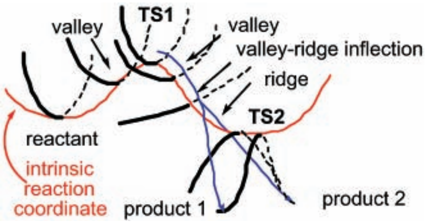
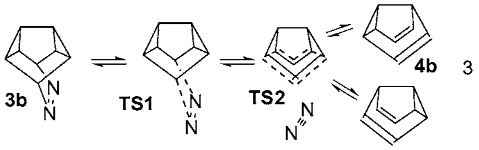


Figure 1. Generalized potential energy surface showing two valleys descending from a transition state (**TS1**), leading to a minimum (reactant) and a second transition state (**TS2**). The valley−ridge inflection point along the intrinsic reaction coordinate (red) and the steepest descents (blue) are indicated.

Beyond product studies, there are not clear-cut experimental techniques for studying such potential energy surfaces (PES). However, computational methods are of sufficient reliability to offer useful insights on appropriate model systems. The conversion of **3b** to **4b** (eq 3) was therefore chosen for study. It retains the essential features of the experimental system, including the ring strain and preorganization of the semibullvalene system.[8]



The PES for the formation of **4b** from **3b** was calculated at the B3LYP/6-31G(d,p) level[9] using Gaussian 98.[10] This method has been shown to give reliable geometries and energies for transition structures of related pericyclic reactions,[11] including the Diels−Alder cycloaddition[12] and the Cope rearrangement.[8b,13] The transition structures and minima were characterized by frequency calculations and had one or zero imaginary frequencies, respectively. The relative energies are summarized in Table 1; all energies discussed in the text include unscaled zero-point vibrational energy corrections. As anticipated, two transition structures were located (**TS1** and **TS2**) corresponding to loss of N_2 and the Cope rearrangement, respectively.

Table 1. B3LYP/6-31G(d,p) relative energies (RE), zero-point vibrational energies (ZPE), relative energies with ZPE correction (kcal/mol), and low or imaginary frequencies (cm^{-1})

	relative energy	zero-point energy	RE with ZPE	low frequency
3b	0	92.8	0	357.7
TS1	16.1	89.9	13.2	481.5i
VRI	12.7	88.8	8.7	31.8i
TS2	−24.4	83.3	−30.4	227.0i
4b	−30	84.8	−34.5	304.9

The IRC was followed in both directions from **TS1**; it indeed connects with **3b** and **TS2**. The frequencies were manually examined at a number of structures along the IRC to ensure that those considered corresponded to the two reaction coordinates; the VRI was located as that point where

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the vibration corresponding to the Cope rearrangement was closest to zero. Specifically, at a C1−N bond distance of 2.113 Å, this frequency was 32.4 cm^{-1}, and at 2.114 Å it was 31.8i cm^{-1}. From the calculated frequencies along the IRC, a portion of the PES was generated, as shown in Figure 2. This clearly shows the change in curvature of the orthogonal reaction coordinate, i.e., the Cope rearrangement, at the valley−ridge inflection point (**VRI**). Optimized geometries of all stationary points and the **VRI** are shown in Figure 3.

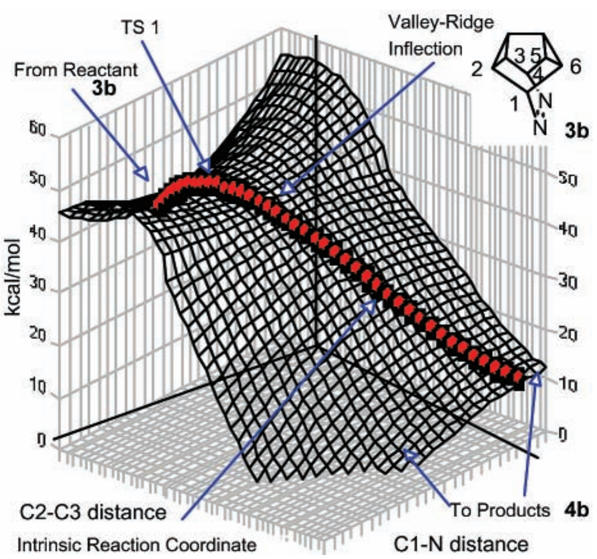

Figure 2. Potential energy surface for the deazetization of **4b** at the B3LYP/6-31G(d,p) level. Reaction coordinates are the C1−N and the C2−C3 bond distances. The IRC (in red) was calculated using the algorithm in Gaussian 98. The black surface was extrapolated from frequencies calculated at several points along the IRC.

The valley−ridge inflection point is *not* the inflection point along the IRC. This second derivative is negative at **TS1**, by definition; it also happens to be negative at **VRI**. (It is the second derivative corresponding to the Cope rearrangement that is zero at the **VRI**.) Along the IRC, the second derivative corresponding to loss of N_2 eventually changes to positive. We did not explore this area in great, detail but this inflection occurs between the C1−N distances of 2.281 Å (54.0i cm^{-1}) and 2.302 Å (107.9 cm^{-1}). This emphasizes the need to carefully examine the vibrational frequencies in the search for a VRI.

All of the structures along the intrinsic reaction coordinate, up to **TS2**, maintain C_{2v} symmetry. The reaction coordinates for the loss of N_2 and the Cope rearrangement are orthogonal in that the least motion pathways involve atomic motions of different symmetries. This may contribute to the existence of two sequential transition states. Although deazetizations of dialkyldiazo compounds can be stepwise,[4b,14] the cleavage of the C1−N and C4−N bonds is calculated to be synchronous. This is reasonable; in this case, the cyclopropane rings would be expected to participate in the deazetization and enable the reaction to be synchronous.[15] The C1−N and C4−N bonds are relatively long in **3b** (1.517 Å) as expected due to the ring strain of the system. They lengthen smoothly along the IRC, 1.969 Å in **TS1** and 2.114 Å in **VRI**. These bonds are relatively short (<2 Å) in **TS1** as expected for an exothermic reaction (30.4 or 34.5 kcal/mol to **TS2** or **4b**). The C2−C3 (C5−C6) bonds lengthen gradually from 1.509 Å in **3b** to 1.621 Å in **TS1**, 1.688 Å in **VRI**, and then more (2.103 Å) in **TS2**. Similarly, the C1−C2 and symmetry-related bonds shorten from 1.531 Å in **3b** to 1.458 Å in **TS1**, 1.432 Å in **VRI**, and 1.391 Å in **TS2**, as expected for the increasing double-bond character. Both these changes are consistent with the participation of the cyclopropane bonds even in the early stages of the deazetization. In the product (**4b**), the symmetry is of course broken; the nonbonded C2−C3 distance is 2.363 Å, while the remaining cyclopropane bond (C5−C6) is 1.611 Å. This latter distance is quite long for a carbon−carbon bond but consistent with long bonds found in other semibullvalenes.[8]

What are the consequences of this potential energy surface? In terms of dynamics, **TS1** is rate determining as the nitrogen starts to leave. Immediately past this structure, nonsymmetrical distortions still raise the energy of the

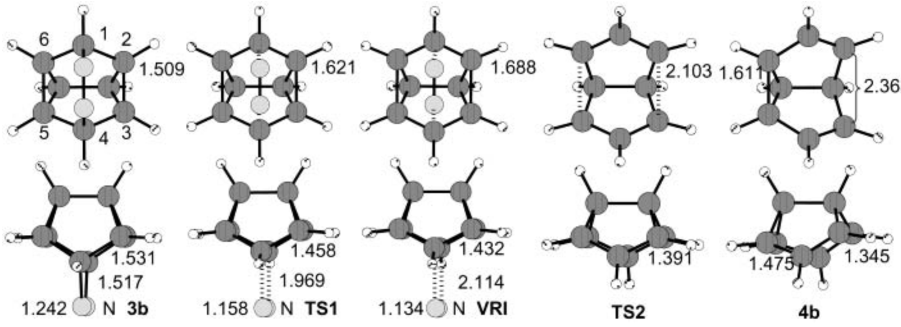

Figure 3. Side and bottom views of the B3LYP/6-31G(d,p)-optimized geometries for structures along the intrinsic reaction coordinate for the deazetization of **3b**. Selected distances are in Ångstroms. Full geometries are in Supporting Information. Carbons are dark, nitrogens are light, hydrogens are small, and partial bonds are dashed.

system, so that the lowest energy pathway would be along the IRC until the **VRI**. This point is quite close to **TS1**, only 0.145 Å longer and 4.5 kcal/mol lower in energy. By definition, past the **VRI**, the steepest descent is off of the ridge, breaking symmetry and distorting toward one of the degenerate products **4b**. In chemical terms, this means that shortly past **TS1** the molecule can be stabilized by breaking symmetry and forming the cyclopropane C−C bond and the new π-bonds. In this particular example, there is no chemical consequence of the VRI, because the two products are identical; in general, this is not required.

However, we note that **TS1** maintains the symmetry of both the reactant **3b** and the following transition state **TS2**. There is no necessity for this; one could imagine two transition states for loss of N_2 leading to **4b** with participation of only one of the cyclopropyl rings.[4a] The Hammond Postulate[16] suggests that the transition state should show some distortion toward the products. It appears that the geometry of **TS1** reflects the geometry of **TS2** and not that of the final product. If this is a general phenomenon, then it suggests an additional, novel consequence of sequential transition states, specifically that the transition state can be stabilized by the following one, more so than by the final products.[11b,15,17] Although a correlation has been observed in other cases between the barrier height and the product stability,[15,17] the similarity in energy of **TS2** and **4b** makes it impossible to say which one influences the energy of **TS1**.

Finally, it is appropriate to put this system into context with prior organic reactions that have been suggested to have sequential transition states (See eq 2 and Supporting Information, Scheme S1). The conceptually simplest systems are those in which a conformational transition state leads to a second transition state. An elegant example of this is cyclooctatetraene, in which the transition state for tub−tub interconversion connects to the D_{6h} transition state for double-bond switching,[3e] studied by photodetachment spectroscopy by Wenthold et al.[18] A similar situation is found in the rearrangements of bicyclo[*n*.1.0]polyenes.[4d] The second transition state could result from destabilization of an intermediate, as originally proposed for the cyclopropane-1,3-diyl.[4a] The ring opening of cyclopropylidene to allene studied by Ruedenberg[7b,c] as well as an electrocyclization studied in this laboratory[3a] and the proton shift in the enol of acetone[19] can all be viewed as having separated a pericyclic reaction into the constituent pseudopericyclic bond forming and rotational steps. And last, the Diels−Alder/Cope sequences studied by Caramella[5] and the deazetization/Cope sequence studied here are examples where the two transition states are both bond-forming/breaking reactions. These might each be described as the “synthesis of a transition state”.

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Supporting Information Available: Cartesian coordinates and absolute energies of all stationary points and the VRI and a Scheme showing additional reactions with VRIs. This material is available free of charge via the Internet at http://pubs.acs.org.

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