

# Trajectories through an Intermediate at a Fourfold Branch Point. Implications for the Stereochemistry of Biradical Reactions

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**Abstract:** Trajectory calculations across a fourfold symmetric potential energy surface with a central depression (corresponding to two reactants and two products linked by a common intermediate) show that the product distribution need not always be that predicted by transition-state theory. In particular conservation of momentum tends to take trajectories from a reactant, through the intermediate, and on to the product that is closest to the straight-line path. The implications of this phenomenon are discussed in general and for the special case of stereochemistry in reactions that could be classified as formal [1,1]-sigmatropic shifts.

Many reactions in organic chemistry can be described in principle by the mechanism summarized in (a) of Scheme I. A and A' are reactants, B and B' are products, and I is a steady-state intermediate whose existence might be inferred but is frequently not directly detected. For example, virtually all sigmatropic reactions and intramolecular cycloadditions can be written in terms of a biradical (or radical pair) mechanism that will conform to the scheme if the reactants and products are chiral or if they contain stereochemical markers at the sites of bond formation and cleavage.

When the relationship between A and A' and between B and B' is enantiomeric, a normal kinetic analysis requires that equal amounts of B and B' be formed at all times, regardless of the initial proportions of A and A'. A similar conclusion can be derived if A and A' (and B and B') are related as epimers at an isotopically labeled center, provided that both differential kinetic and equilibrium isotope effects can be considered negligible (which is frequently the case). Failure to observe equal amounts of B and B' under these circumstances is sometimes interpreted in terms of competitive pathways that convert a single isomer of the reactant to a single isomer of the product as in (b) of Scheme I. Alternatively, as shown in (c), one might hypothesize the existence of two subspecies of I that can interconvert but do not reach equilibrium under the reaction conditions (rotamers of a biradical, for example).

The purpose of this article is to point out that the original premise (that (a) in Scheme I would require formation of equal amounts of B and B') is not correct under all circumstances and that formation of unequal amounts of B and B' is therefore insufficient evidence to invoke the more complex mechanisms (b) or (c).

I have approached the problem by calculating trajectories across an idealized surface that is supposed to represent the situation summarized in (a) of Scheme I. In order to reduce the computation time I have chosen a function that describes a surface with fourfold symmetry; i.e., the potential energy wells are identical for A, A', B, and B'. It seems reasonable to believe that the qualitative conclusions derived from this surface would apply to the more general twofold symmetric surface in which the potential energy wells are deeper for B and B' than for A and A'. The form of the function is summarized in eq 1 and shown pictorially in Figure 1.

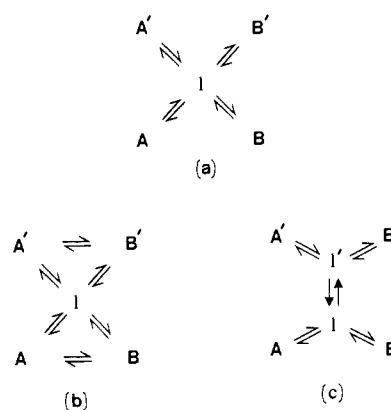
$$Z = D(e^{2a(r-0.5)} - 2e^{a(r-0.5)}) + E(e^{br} - 1) \cos^2(\theta + \pi/4) \sin^2(\theta + \pi/4) + F(e^{-2cr} - 2e^{-cr}) \quad (1)$$

$$r^2 = x^2 + y^2$$

$$\theta = \tan^{-1}(y/x)$$

The first of the three major terms in eq 1 describes a simple Morse potential with a minimum at  $r = 0.5$ , corresponding to the reactants and products. The third term is a Morse potential for

Scheme I



the intermediate with a minimum at  $r = 0$ . Together these two terms would describe a surface with cylindrical symmetry and with no saddle points. The fourfold symmetry and the saddle points are provided by the second term.

The values of the constants  $a$ ,  $b$ ,  $c$ ,  $D$ ,  $E$ , and  $F$  can be chosen such that the changes in  $Z$  (potential energy) in the range  $0 \leq r \leq 0.5$  approximate the expected changes in potential energy (measured in kcal/mol) for a typical thermal reaction. Thus with the constants specified in Figure 1, the four equivalent saddle points representing the transition states occur at 31.02 units above the reactants/products and 1.42 units above the intermediate.<sup>1</sup>

Trajectories were started at one of the four equivalent minima<sup>2</sup> and angles for the initial direction explored in  $2^\circ$  increments. Initial kinetic energies between 31.12 and 34.02 kcal/mol were evaluated in 0.1 kcal/mol increments. The equations of motion were evaluated numerically, and the validity of the trajectory was verified at each step by confirmation of total energy conservation (within 0.1% over the entire path). The proportions of the various

(1) The function with  $F = 0$  would have fourfold symmetry but would lack a local minimum at  $r = 0$ . Such a function is not a realistic model for a potential energy surface: (a) McIver, J. W.; Komornicki, A. *J. Am. Chem. Soc.* **1972**, *94*, 2625-2633. (b) McIver, J. W.; Stanton, R. E. *J. Am. Chem. Soc.* **1972**, *94*, 8618-8620. (c) McIver, J. W.; Stanton, R. E. *J. Am. Chem. Soc.* **1975**, *97*, 3632-3646. (d) Ceulemans, A.; Beyens, D.; Vanquickenborne, L. G. *J. Am. Chem. Soc.* **1984**, *106*, 5824-5837.

(2) A truly complete evaluation of trajectories across the surface would include starting points other than at the potential energy minimum, corresponding to all possible combinations of kinetic and potential energy for the starting state. (I thank Professor John Wiesenfeld for emphasizing this point.) Since this was not done, the calculated stereoselectivities will not be quantitatively correct. The qualitative conclusions should be valid, however, because trajectories starting far from the minimum have, for a given total energy, high potential energy and therefore low kinetic energy. As a consequence, most simply return to the minimum in the time span allotted for reaction. This qualitative expectation was verified by calculation of a representative set of such trajectories.

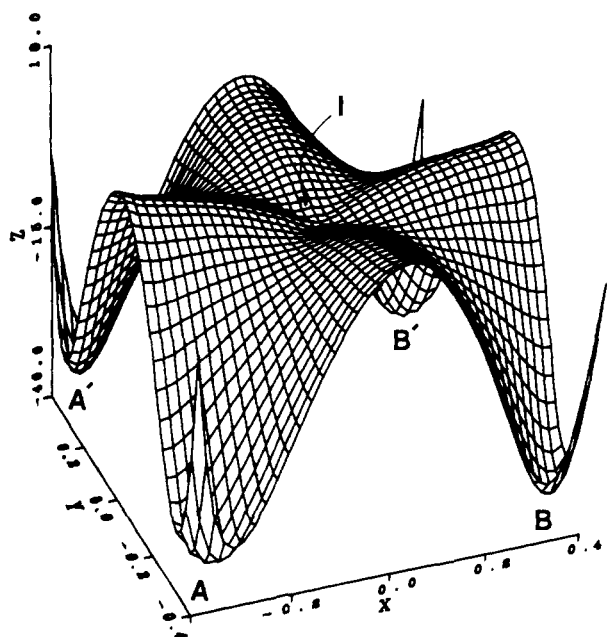


Figure 1. Graphical representation of the surface described by eq 1 with  $a = 10$ ,  $b = 8$ ,  $c = 10$ ,  $D = 35$ ,  $E = 4$ , and  $F = 5$ .

products were determined for each energy and then the overall product distribution was determined by using Boltzmann weighting at a selected temperature.<sup>3</sup>

The outcome was *very* different from the predictions of transition-state theory. Starting with A the products were 89% B' and 11% B at 353 K.<sup>2</sup> This product ratio was effectively temperature independent over a typical experimentally accessible range (353–438 K).

The reason for the preferred formation of B' became apparent when the trajectories were inspected graphically. For those molecules with a total energy only slightly above the threshold, initial trajectories that deviated much from the straight line connecting reactant to intermediate were ineffective because the potential energy rose too steeply. Thus reacting molecules necessarily approached the intermediate on paths close to the diagonal. Once at the intermediate *conservation of momentum* carried them through and on to the diagonally related product B'. Trajectories of molecules with higher total energy could approach the intermediate from other directions and give other products, but the Boltzmann factor ensured that these trajectories were given relatively low weighting. Large contribution from these higher energy trajectories would require temperatures not accessible in a normal thermal experiment.

Increasing the depth of the central depression, corresponding to the intermediate, had very interesting consequences: two effects were observed. First, increasing the well depth increased the number of trajectories that got "lost" in the center, as one might have anticipated. Second, increasing the well depth *decreased* the number of trajectories that made it from A to B (or to A') with a single pass through the region of the intermediate (more exactly described as the circle through the four saddle points projected onto the  $xy$  plane). This latter effect could be traced to a phenomenon in which the lower potential energy of the intermediate caused trajectories that might otherwise have strayed far from the straight diagonal (A through I to B') to be drawn

(3) Trajectories that returned more than five times to the reactant were discounted as being unreactive on the grounds that the time for reaction would then be comparable to the mean time between collisions for a solution-phase reaction and that, on the average, a collision would tend to deactivate the molecule to a point below the threshold energy. Trajectories suffering more than five reflections within the intermediate potential well were considered to give each possible product with equal probability on the grounds that here a collision would, on the average, tend to activate the molecule but would do so by imparting a random trajectory. Trajectories leading to the isomeric reactant A' were noted and then the fate of this material determined by symmetry at the end of the calculation.

back nearer to it. The two effects opposed each other in their influence on the overall product distribution. Interestingly, for well depths less than about 10 kcal/mol the second was more important and the selectivity for formation of B' from A actually *increased*. For intermediates in a well more than 10 kcal/mol deep the first effect began to take over and selectivity again decreased. Clearly, the particular value of the well depth at which one effect or the other dominates must be very dependent on the nature of the surface and is thus not of special significance. The qualitative point, that dynamic phenomena can still play an important role even for reactions involving an intermediate in a substantial potential energy well, is significant, I think.

So how, then, does the traditional kinetic analysis of the situation ever work? Why does one, for example, ever see racemization by passage through an intermediate whose equilibrium geometry is achiral? The answer, presumably, is that in most reactions of complex molecules the intermediate has many more degrees of freedom than are represented by the two geometrical coordinates of the present model surface. The exit channels to products will be found with lower probability in an intermediate with more degrees of freedom, and so the tendency will be to spend more time near the intermediate potential minimum and, thereby, to lose the directional information in the trajectory. But this will not *always* be true. For certain types of reactions of even quite complex molecules the number of effective degrees of freedom of an intermediate can be quite restricted.

Cases in point are the formal  $[1,n]$ -sigmatropic shifts in bicyclic molecules. These transformations can be approximated by changes in three independent coordinates: the first,  $R$ , measures the distance of the migrating carbon from the migration origin; the second,  $\xi$ , measures the pyramidal configuration at the migrating carbon; the third,  $\phi$ , measures the dihedral angle around the bond to the migrating carbon (see Figure 2). Other bond distances and angles do change of course, but they can be considered to be of secondary importance because they are restricted to a relatively narrow range of values at all times during the reaction. Of the three principal coordinates,  $\phi$  deserves special attention. If the reaction in fact involved a biradical intermediate, one could expect that changes in  $\phi$  for the intermediate would be accompanied by little if any change in energy. This expectation is based on the experimental observation of very low barriers to rotation about bonds connecting  $sp^2$  to  $sp^3$  carbon,<sup>4</sup> including the ethyl radical.<sup>5</sup> Thus the hypothetical biradical in the sigmatropic shift could presumably begin a descent to products with a wide range of values of  $\phi$ ; the angle could be adjusted to that appropriate for the product without any significant energy penalty. If this is really true, the problem reduces to one with two principal geometrical coordinates,  $R$  and  $\xi$ , and the model described above begins to become germane.

The progress from reactant to intermediate is likely to involve changes in both  $R$  and  $\xi$ . The C–C bond obviously has to lengthen and the arrangement of ligands around the migrating carbon is likely to move from tetrahedral toward trigonal planar.<sup>6</sup> One now only has to replace the  $x$  and  $y$  coordinates of Figure 1 by the  $R$  and  $\xi$  coordinates of this example to foresee the outcome. Conservation of momentum requires that for most molecules the passage through the intermediate will occur by continuous increase in  $R$  and *continuous change in*  $\xi$  such that the product is formed with *inversion of configuration* at the migrating carbon. Furthermore, and most important for experimental verification of the model, the ratio of products formed with inversion to those formed with retention should be effectively *temperature independent*. This predicted temperature independence serves to differentiate the

(4) Benson, S. W. "Thermochemical Kinetics", 2nd ed.; Wiley-Interscience: New York, 1976; p 306.

(5) Pacansky, J.; Coufal, H. *J. Chem. Phys.* **1980**, *72*, 5285–5286.

(6) Even if the biradical did not have a planar equilibrium geometry at the migrating carbon it would almost certainly be less pyramidal than that in the reactant. The *tert*-butyl radical, for example, apparently differs from planarity by only 11.5° in its equilibrium geometry (Griller, D.; Ingold, K. U.; Krusic, P. J.; Fischer, H. *J. Am. Chem. Soc.* **1978**, *100*, 6750–6752) while the ethyl radical is fully planar (ref 3).

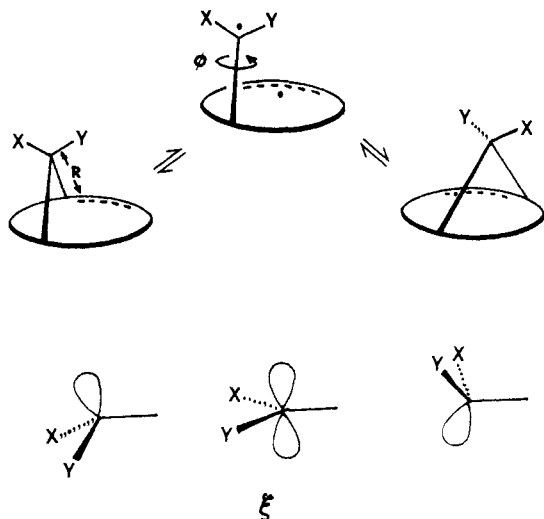


Figure 2. Principal coordinates for describing a formal  $[1,n]$ -sigmatropic shift in a bicyclic molecule.

present proposal from those in (b) and (c) of Scheme I where, barring an unlikely coincidence of barrier heights, temperature dependence of the product ratio would be expected.

Work carried out in this laboratory has recently shown that 1-phenyl- and 2-phenylbicyclo[2.1.1]hexenes do rearrange with a strong preference for inversion and that the product ratio is, within experimental error, temperature independent.<sup>7</sup> The parent compound showed temperature-dependent stereoselectivity and is, therefore, a candidate for one of the more traditional mechanisms ((b) or (c) in Scheme I).

Looking further afield, one can hypothesize that the phenomenon proposed here could explain the observed preference for inversion in the formal  $[1,5]$ -sigmatropic shifts of 7,7-dimethylbicyclo[4.1.1]octadiene<sup>8</sup> and norcaradiene derivatives.<sup>9</sup> It might also have a role in the mysterious inversion observed in pyrazoline deazetizations.<sup>10</sup>

(7) Newman-Evans, R. H.; Carpenter, B. K. *J. Am. Chem. Soc.* **1984**, *106*, 7994-7995.

(8) Borden, W. Y.; Lee, J. G.; Young, S. D. *J. Am. Chem. Soc.* **1980**, *102*, 4841-4843.

(9) (a) Klärner, F.-G.; Yaslak, S.; Wette, M. *Chem. Ber.* **1979**, *112*, 1168-1188. (b) Klärner, F.-G.; Brassel, B. *J. Am. Chem. Soc.* **1980**, *102*, 2469-2470.

What is still unclear is how much the phenomenon would be attenuated for intermediates with larger numbers of degrees of freedom. If it persists in cyclopropane,<sup>11</sup> cyclobutane,<sup>12</sup> and cyclopentane<sup>13</sup> stereomutations or in reactions such as the vinyl-cyclopropane<sup>14</sup> rearrangement, then a considerable amount of reinterpretation of reaction stereochemistry will be necessary. Experiments are under way in this laboratory to probe these questions.

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## Synthetic and Structural Studies in the [4.4.4.5]Fenestrane Series

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**Abstract:** Photolysis of dienone **16** furnishes **20**, which by way of diazoketone **22c** is cyclized through carbene insertion to **24**. Reductive removal of the carbonyl group of **24** followed by deketalization gives **30**, and photochemical Wolff rearrangement of the derived  $\alpha$ -diazoketone **31b** in methanol gives **32** and **33**. X-ray crystallographic analysis of the related *p*-bromoanilide **37** confirmed these assignments and provided structural information. The two angles that reflect flattening at the central quaternary carbon atom are 128° and 129°. These are the first examples of [4.4.4.5]fenestrans (tetracyclo[4.3.1.0<sup>3,9</sup>.0<sup>8,10</sup>]decanes) to be prepared.

Synthetic efforts in recent years have resulted in preparation of several ring systems related to the unknown hydrocarbon

tetracyclo[3.3.1.0<sup>3,9</sup>.0<sup>7,9</sup>]nonane ([4.4.4.4]fenestrane, windowpane), of which the most frequently discussed<sup>2-5</sup> isomer is **1**. There are