

Nonexponential decay of reactive intermediates: new challenges for spectroscopic observation, kinetic modeling and mechanistic interpretation

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epoc ABSTRACT: A thermally generated reactive intermediate is generally presumed to consist of a population with a distribution of lifetimes characterized by a single, well-defined parameter, τ . The decay of an instantaneously generated population, whose conversion to products occurred by parallel unimolecular steps, would be expected to be defined by a simple, single-exponential expression: $A(t) = A_0 \exp(-t/\tau)$, where $A(t)$ is the population at time t , and A_0 is the population at $t=0$. In this model, the lifetime is also related to the first-order rate constants, k_i , for the unimolecular product-forming steps; specifically $\tau = (\sum_i k_i)^{-1}$. The ratio of the products is equal to the ratio of the rate constants for their formation. Given an accurate potential energy surface (PES) for the reaction, one would expect to be able to compute the values of the k_i under the specified reaction conditions, and hence both the lifetime of the intermediate and the ratio of products. This simple picture, which has formed the basis for most mechanistic investigation of reactive intermediates, and most kinetic modeling of reactions in which they are involved, has been challenged in recent years by molecular dynamics (MD) simulations, which have predicted that a variety of thermally generated intermediates should exhibit bimodal or even multimodal lifetime distributions. In several cases the shortest lifetime populations have been found to lead to products in a ratio quite different from that for the longer-lived populations, and also quite unlike that expected from RRKM or transition state theory calculations based on the same PES used for the MD simulations. This commentary reviews the origins of this behavior and discusses the challenges of designing experiments to test the predictions. Copyright © 2003 John Wiley & Sons, Ltd.

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KEYWORDS: reactive intermediates; dynamics, IVR; lifetime; mechanism; RRKM

INTRODUCTION

Between the late 1920s and early 1950s two opposing models of unimolecular chemical reaction kinetics were being developed. One was due to Rice and Ramsperger,¹ and to Kassel,² and was later extended by Marcus³—the RRKM model.^{4–7} The other was due to Slater.⁸ At heart, the principal point of disagreement between the models had to do with the rate of intramolecular vibrational energy redistribution (IVR). On one hand, the RRKM model explicitly invoked the *statistical approximation*, treating excess vibrational energy in a microcanonical (i.e. identical total energy) ensemble of molecules as being always statistically distributed among the available modes. This approximation is equivalent to assuming that IVR is always much faster than any conceivable reaction.

The Slater model, on the other hand, treated molecules as if they were a collection of harmonic oscillators. Since harmonic oscillators are unable to exchange kinetic energy, the Slater model effectively implied that the IVR rate was zero. Both models had a sufficiently large number of adjustable parameters that they could be made to fit experimental kinetic data equally well, and so both remained in play for several years.

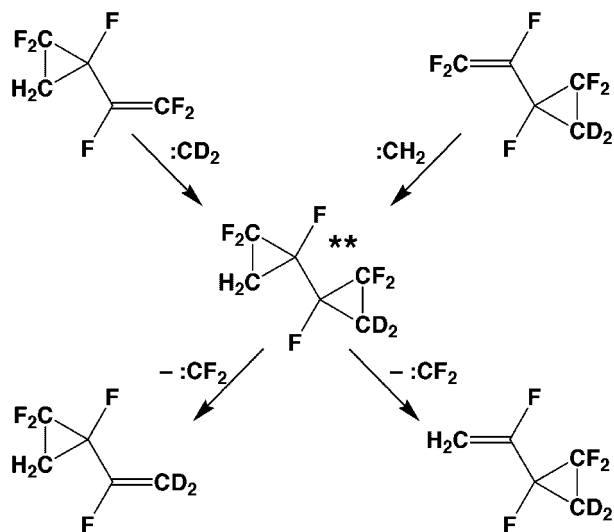
That situation changed in 1960 when Butler and Kistiakowsky reported the results of a clever test to distinguish between the RRKM and Slater models.⁹ They prepared chemically activated methylcyclopropane from singlet methylene by two different routes: cycloaddition to propene and C—H insertion into cyclopropane. The vibrationally hot methylcyclopropane underwent isomerization to a number of products whose ratios could be determined. Butler and Kistiakowsky argued that, if the Slater model were correct, the vibrational modes excited by the two methods of preparation of the methylcyclopropane ought to be quite different, and therefore the product ratios should also be different. However, if IVR were as fast as the RRKM model posited, the means of preparation of the methylcyclopropane ought not to

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Scheme 1. The reaction designed by Rynbrandt and Rabinovitch to look for incomplete IVR prior to reaction

matter, and so the same product ratio should be observed from both reactions.

Most books on unimolecular reaction rate theory cite this experiment as playing a pivotal role in acceptance of the RRKM model and rejection of the Slater model⁴⁻⁷ since, it is frequently claimed, the result was that the two reactions gave identical product ratios. A reexamination of the original paper might lead the reader to a less dogmatic conclusion, since the experimental uncertainty in the product ratios was quite large. The original authors were more cautious in their interpretation than many of the subsequent reporters of their work. Nevertheless, it is fair to say that the results looked more like those expected for fast IVR than for slow or nonexistent IVR, and to that extent the RRKM model was favored.

In 1970, Rynbrandt and Rabinovitch reported the results of an experiment that was similar in spirit to that of Butler and Kistiakowsky, but designed to afford a more sensitive measure of the extent of IVR.^{10,11} They also relied on the generation of a chemically activated cyclopropane from singlet methylene, but they selected a system that created an effective symmetry element in the vibrationally hot intermediate, so that the product ratio would be 1:1 (except for a possible secondary isotope effect, whose magnitude could be determined) in the case of complete IVR. The reaction is shown in Scheme 1. The question that these researchers asked was whether one would see preferential extrusion of CF_2 from the newly formed cyclopropane ring, or whether it would occur with equal probability (after isotope correction) from either ring. The former result would indicate incomplete IVR prior to product formation, whereas the latter would support the complete IVR expected from the RRKM model. The result turned out to be dependent on the pressure of the bath gas used in the reaction. At 1 torr, there was a preferential loss of CF_2 from the nascent

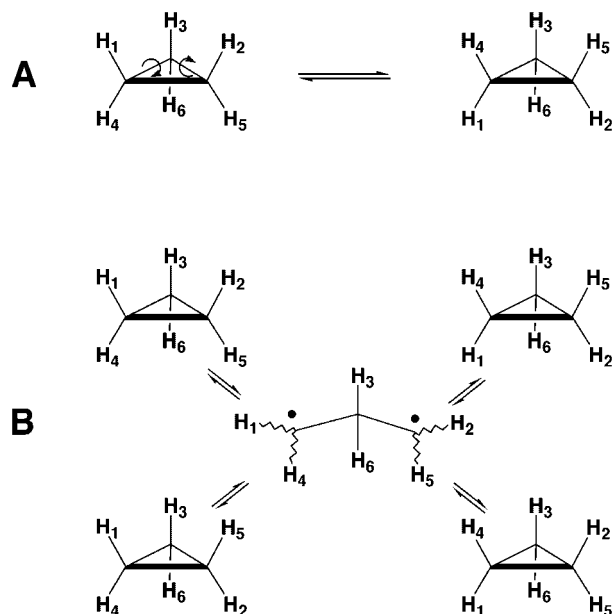
cyclopropane ring, but only to the extent of 3.5%. However at 3300 torr, the asymmetry was substantial: 27% excess fragmentation of the newly formed ring. The authors explained the pressure dependence by relating the lifetime of the chemically activated intermediate to its branching ratio. They argued that there should be a distribution of lifetimes for the chemically activated bicyclic propyl, and that those molecules with the shortest lifetimes ought to be the ones that would show the greatest asymmetry in branching ratio, since they would be the most likely to have reacted before IVR was complete. The high pressure of bath gas collisionally deactivated all but the fastest-reacting component of the distribution, and hence revealed the intrinsically asymmetric fragmentation of the noninterceptible intermediates. From their data the authors could estimate a magnitude for the IVR 'rate constant,' which they put at about 10^{12} s^{-1} .

Several secondary sources cite this experimental result as an anomaly in the generally uniform adherence of reactions to RRKM-like behavior, although none describes what feature of this particular reaction explains its claimed pathology.⁴⁻⁶ I will take an alternative view. Given the results of recent computational and experimental studies, I will argue that phenomena like that observed by Rynbrandt and Rabinovitch may be quite common, and that the RRKM extreme of complete IVR prior to reaction is not necessarily the norm for reactive intermediates.

PLATEAUS ON THE POTENTIAL ENERGY SURFACE

While a principal claim of this article will be that the behavior of reactive intermediates cannot generally be determined *only* by inspection of the PES in their vicinity, it is nevertheless certain that the shape of the PES is one important controlling factor. In recent years, as *ab initio* electronic-structure calculations have become more feasible and more reliable, there has been increasing recognition that certain classes of reaction involve 'intermediates' that sit on energetic plateaus on the PES. The implication is that these species can undergo fairly large changes in geometry, at least in certain coordinates, without significant change in potential energy. Among the classes of intermediates that seem routinely to exhibit this property are singlet biradicals¹²⁻¹⁵ and hydrocarbon radical cations.¹⁶

If the plateau region had several truly barrierless exits leading to stable molecules (reactants and products), one would be in a situation where kinetic models such as RRKM or transition state theory (TST) had nothing to say about what the product ratio should be. It's not that these models would make incorrect predictions—they simply could not be applied. In reality one often finds that *ab initio* electronic-structure calculations predict very small



Scheme 2. Competing mechanism for the stereomutation of cyclopropane. **A:** concerted conrotation; **B:** formation of a trimethylene biradical minimum with loss of stereochemical information

barriers, $\sim k_B T$, for entrance to and exit from the plateau. These barriers do formally allow TST or RRKM calculations to be carried out, but their validity remains open to question. Greater insight has come from applying quasiclassical trajectory simulation methods.

I will summarize here the results from trajectory simulations of two reactions for which the best *ab initio* theory does indicate the involvement of biradical plateaus: cyclopropane stereomutation and the vinylcyclopropane rearrangement.

For cyclopropane stereomutation, the key question has been whether the scission and reformation of a carbon-carbon bond occurs preferentially with correlated double rotation of the terminal methylenes, as originally proposed by Hoffmann,¹⁷ or in a stereorandom fashion, as implied by thermochemical calculations of Benson¹⁸ (see Scheme 2). The stereochemistry and thermochemistry are related because one can reformulate the question to ask whether the ‘trimethylene’ biradical, formed by C—C scission, has a barrier to reclosure that is larger than the barrier to internal rotation of its terminal methylenes. If it does, as suggested by Benson, then one might expect (at least from traditional kinetic analysis) stereorandom reclosure. If it does not, the situation is potentially complicated. Already in 1970, Hoffmann’s extended Hückel calculations had suggested that singlet biradicals might sit on PES plateaus, giving them properties somewhere between those expected for an intermediate and a transition state (hence his proposed name of ‘twixtyl’ for such entities).¹⁹ His prediction of correlated double rotation for trimethylene came from a symmetry analysis of the interaction between the $2p$ -like orbitals of the

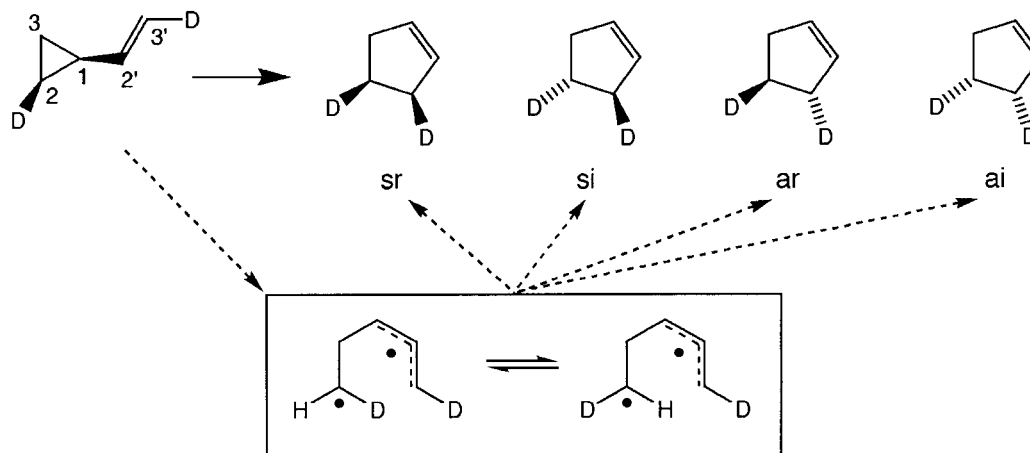
terminal methylenes and the C—H σ and σ^* orbitals of the central methylene.

The experimental test of these predictions proved to be very difficult and controversial. At one extreme there seemed to be evidence for as much as a 50:1 preference for correlated double rotation,^{20,21} while at the other there was apparent experimental support for essentially stereorandom behavior.²²

The highest levels of electronic-structure calculation^{23,24} did give credence to Hoffmann’s ‘twixtyl’ suggestion, and they did also show that the lowest energy pathway for breaking a C—C bond should be by correlated conrotation, as he had predicted. However, the transition states for C—C scission accompanied by disrotation or monorotation were found to be much closer in energy to that for conrotation than Hoffmann’s calculations had suggested.¹⁷ They were close enough that it was not at all certain that the overall stereochemical situation could be reliably deduced from a TST analysis. For that reason, two different sets of collaborative research groups undertook quasiclassical trajectory simulations of the reaction, using somewhat different technical approaches. Despite the different details, the two simulations gave gratifyingly similar results. They showed that there should indeed be a preference for correlated double rotation, by about 2.9–3.5:1 according to one simulation²⁵ and 4.7:1 according to the other.²⁶ However, this preference had a strong component of nonstatistical dynamics, meaning phenomena that could not be captured by models such as RRKM or TST, which use the fast-IVR approximation. Specifically, both studies found that the behavior of a particular trimethylene was dependent on the mode of its formation. If it had been formed from a conrotation TS, it selected the exits to reclosure of the ring with different probabilities than if it had been formed from a disrotation or monorotation TS. There was a notable tendency for the internal rotational motions initiated by the bond cleavage to persist in the biradical long enough to play an important role in determining which TS to reclosure was encountered first. This kind of stereochemical memory is clearly at odds with the ‘amnesia’ that should have resulted if IVR had been complete before product formation occurred. Of particular relevance to this article is the fact that one of the groups examined the decay of the trimethylene biradical in their simulation and found that it was nonexponential.

About 3/4 of the trajectories took the first exit to product that they encountered, and spent an average of about 130 fs on the biradical plateau. The remaining 1/4 spent over 400 fs there and executed multiple internal rotations of the terminal methylenes before finally closing the ring.²⁷ Prediction of a bimodal, or in some cases multimodal, lifetime distribution will be a recurring theme in this article, as will the linkage between lifetime and stereoselectivity.

Let us now turn to the vinylcyclopropane rearrangement,²⁸ depicted (somewhat unrealistically, as described



Scheme 3. A schematic representation of the stereochemical pathways for the vinylcyclopropane rearrangement

below) in Scheme 3. The overall transformation is clear: one must break the bond between C1 and C2 of the reactant, and then reconnect C2 to C3'. However, controversy resides in the details of the stereochemistry and timing of these two events.^{29–40} First the stereochemistry: the bond formation at C2 can occur with retention or inversion of its original configuration. In addition, the bond formation at C3' can occur to the same face—suprafacial—of the allylic unit (C1—C2'—C3') to which C2 was originally attached, or to the opposite face—antarafacial. These two stereochemical variables combine to create four possible stereoisomeric products, for which the two-letter designations shown in Scheme 3 indicate suprafacial (s) or antarafacial (a), and retention (r) or inversion (i). Experimental study of the stereochemistry would appear to allow one to differentiate between two extremes of the timing question. If the breaking of the C1—C2 bond and the formation of the C2—C3' bond occurred concertedly, the reaction would be pericyclic—a [1,3] sigmatropic rearrangement—and hence subject to the Woodward–Hoffmann rules of orbital symmetry conservation.⁴¹ These rules indicate that, for a thermal reaction, the products designated si and ar would be ‘allowed’ whereas the other pair, sr and ai, would be ‘forbidden.’ The alternative, stepwise mechanism would presumably involve the singlet-state biradical depicted in Scheme 3. If able to explore all of its energetically accessible conformations, this biradical would be expected to be achiral. In addition, it might be expected to undergo facile internal rotations about the remaining C—C bond to C2. Since the intermediate is achiral, and since achiral intermediates are supposed to give only achiral or racemic products, this mechanism would seem to predict that the product isomers related to each other as enantiomers should be formed in equal amounts, namely $[sr] = [ai]$ and $[si] = [ar]$.

Of course, the reaction could not really be persuaded to go exactly as shown in Scheme 3, because the C1—C3 bond would certainly break at very nearly the same rate as C1—C2. In the experiments actually conducted by

Baldwin and coworkers,³¹ this problem was resolved by deuterium labeling *both* C2 and C3, creating diastereomerically pure but achiral molecules. Even then, there remained a large number of technical difficulties which, in the end, the researchers were able to overcome. Their results indicated that the four stereochemical courses for the reaction run at 300 °C were: sr 23%, si 40%, ar 13% and ai 24%. These numbers do not fit the expectations from either mechanism. Clearly the Woodward–Hoffmann ‘forbidden’ and ‘allowed’ products are formed in nearly equal amounts ($[sr] + [ai] = 47%$; $[si] + [ar] = 53%$)—hardly what one would expect for a pericyclic reaction. In contrast, the stereochemical paths do not show the pairwise equalities expected from the stepwise mechanism.

The current explanation of these results comes from a combination of high-level *ab initio* electronic-structure calculations and molecular-dynamics simulations.^{42–46} The picture that emerges from the electronic-structure calculations is that breaking the C1—C2 bond of the reactant creates a biradical that, once again, sits on a plateau on the PES. There are exits to all four possible products from the plateau region, with little or no barrier to the formation of any of them.

Doubleday, Hase and coworkers have carried out extensive quasiclassical trajectory studies on this reaction.⁴² Their simulations matched the experimental outcome very well: the computed product ratios were 42:30:10:18 (si:sr:ar:ai) whereas the experimental ratios³¹ were 40:23:13:24. It was clear that the simulations again revealed that the reaction was dominated by non-statistical dynamics. Just as seen in cyclopropane stereomutation, the decay of the biradical was nonexponential, and the stereoselectivity highly correlated with the amount of time spent on the plateau. Thus, trajectories that completed the passage to products in <200 fs gave a ratio of 53:43:0:4 whereas those taking >600 fs gave 20:22:30:28. Clearly, the reaction becomes more stereorandom the longer the trajectories last. This is just the picture one would expect if IVR were occurring

on a timescale comparable to that for product formation. The simulations also revealed that the product ratio could be strongly influenced by the distribution of kinetic energy among the vibrational modes of the TS from which the trajectories were initiated. This too is unambiguous nonstatistical behavior.

There is every reason to believe that the results found for the vinylcyclopropane rearrangement are typical of those to be expected for reactions involving biradicals (and presumably other reactive intermediates) on energetic plateaus. Other examples for which there is experimental and/or computational support for this picture include the rearrangements of bicyclo[2.1.1]hexene derivatives,⁴⁷ bicyclo[3.1.0]hex-2-ene,⁴⁸ bicyclo[3.2.0]hept-2-ene¹² and 9,9-dicyanobicyclo[6.1.0]nona-2,4,6-triene.⁴⁹ These reactions cannot be completely understood within the context of any statistical kinetic model.

GENERATION OF CHEMICALLY ACTIVATED INTERMEDIATES

In the preceding examples, the best evidence suggests that the biradicals involved sit on energetic plateaus. Neither the conversions of the biradicals to products nor their return to the reactants apparently face any significant barrier. The behavior of the biradicals seems to be dictated by a potentially complex interaction between the dynamics of entry to the plateau region, which dictates the initial direction of motion, and the influence of small (often ≤ 1 kcal mol⁻¹) conformational barriers on the plateau itself. However, when the return of an intermediate to the reactant constitutes a reaction for which there is a substantial barrier, the dominant contributor to its dynamics (in the forward direction) may be the kinetic energy acquired in the descent to the intermediate from the preceding transition state. This is very similar to the scenario investigated by Butler and Kistiakowsky⁹ in 1960 and by Rynbrandt and Rabinovitch^{10,11} in 1970. However, I will be concerned in this commentary with situations in which the chemically activated species is an unisolable reactive intermediate rather than a stable molecule, as it was in these earlier experiments. That difference has one important practical consequence. In the Rynbrandt and Rabinovitch experiment, increased collisional interception of the chemically activated intermediate caused all but the fastest reacting molecules to be trapped permanently in the bicyclic well. At high pressures there was little of the final products formed, but what there was showed substantial asymmetry in the CF₂ extrusion, indicative of incomplete IVR. When the chemically activated intermediate is not stable, collisional interception can only temporarily trap species in the intermediate well; eventually the progress on to the final products will occur, presumably with a ratio that could be deduced from

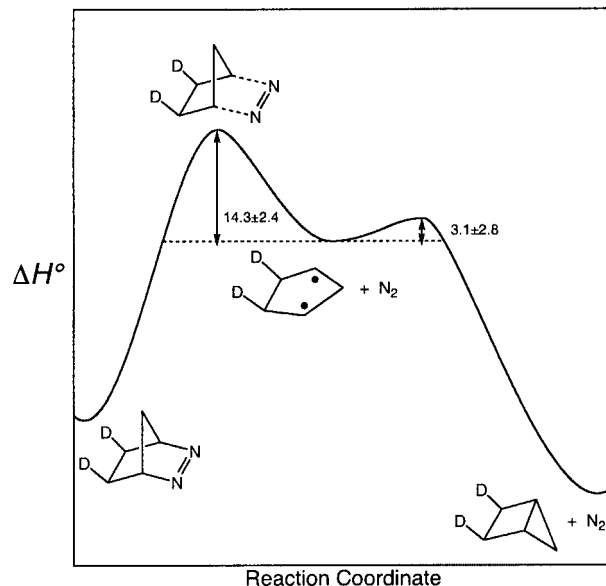


Figure 1. Experimental enthalpy profile, and experimentally preferred stereochemistry for the deazetization of DBH

statistical rate theory. Hence, in this case, collisional interception should have no effect on the total yield of final products but should change their ratio in a way that now *reduces* the dynamical asymmetry.

Again I have chosen two examples to discuss in some detail: nitrogen extrusion from 2,3-diazabicyclo[2.2.1]hept-2-ene (DBH) and methyl radical loss from the acetone radical cation.

The principal mechanistic issue in the thermal nitrogen loss from DBH is the reason for the preferred inversion of configuration, revealed by deuterium labeling of the reactant (Fig. 1).^{50–56} Several mechanisms have been advanced to explain this result, but those ascribing a key role to a diazenyl biradical (generated by homolyzing just one C—N bond of DBH) were called into question when it was discovered that CASPT2//CASSCF(6,6)/6–31G(d) calculations showed the preferred mechanism to involve synchronous C—N scission.⁵⁷ The diazenyl biradical was found to be 7 kcal mol⁻¹ higher in enthalpy than the synchronous transition state. A plausible mechanism was revealed when a single CASSCF direct-dynamics trajectory was run forward from this transition state. Even without any ZPE in the real-frequency normal modes, this trajectory picked up enough kinetic energy (the experimental value^{58–62} is 14.3 ± 2.4 kcal mol⁻¹) in its descent to cyclopentane-1,3-diyl + N₂ to surmount the small barrier to ring closure of the biradical (experimentally 3.1 ± 2.8 kcal mol⁻¹) on the first attempt. It is significant that this event occurred with the inversion of configuration observed experimentally. The conformational change can be traced to simple Newtonian conservation of momentum: as the N₂ departs in one direction, the carbons to which it was attached move in the opposite direction and thereby induce the flap inversion in the five-membered ring.⁵¹ This is equivalent to

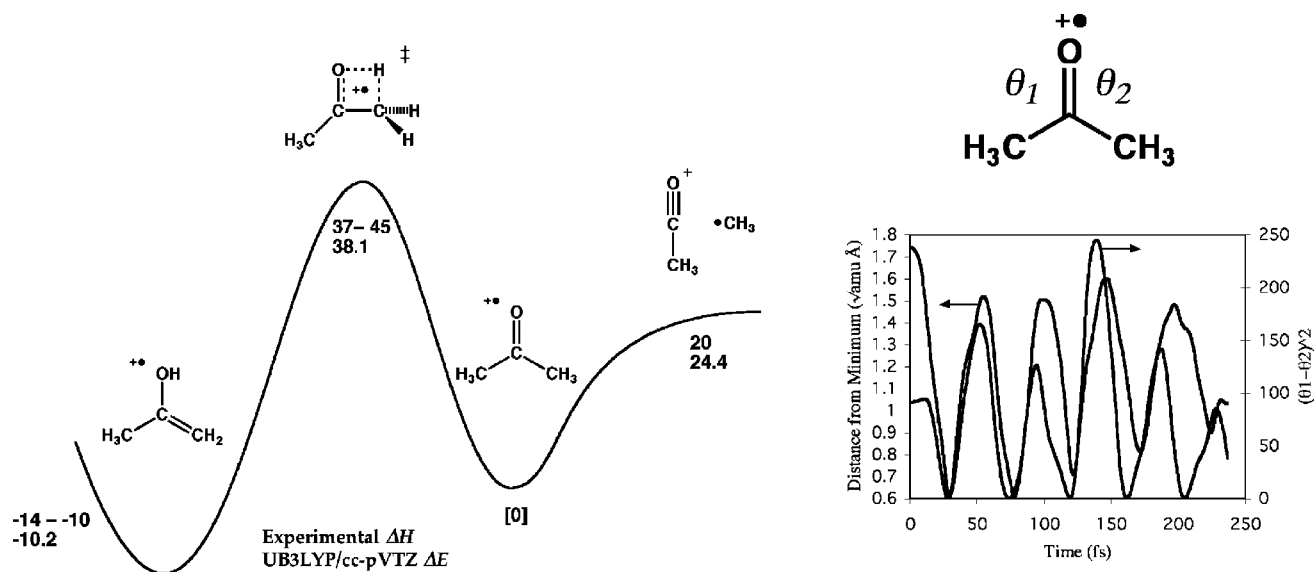


Figure 2. Left-hand panel: experimental enthalpy and calculated potential energy profile for the formation and dissociation of the acetone radical cation. Right-hand panel: observation and identification of periodic motion about the PE minimum due to kinetic energy picked up during formation of the acetone radical cation

saying that the vibrational kinetic energy acquired by the descent from the TS is deposited selectively into a few vibrational modes, and *does not* completely redistribute itself to the other modes before reaction of the intermediate occurs. Instead, this vibrational excitation plays a key role in determining which exit channel is encountered first.

Experimental support for this mechanism could be found when the reaction was studied in supercritical fluids. In supercritical propane, the ratio of rate constants for formation of the inversion and retention products dropped from near 5 at the lowest pressure to about 2 at the highest (where the fluid had a density of roughly 1/3 that for liquid propane). The functional dependence of the ratio on pressure could be fitted to a model in which there was a bimodal distribution of lifetimes for the cyclopentane-1,3-diyl. The shorter-lifetime (nonstatistical) population was assumed to give only the inversion product, whereas the longer-lifetime (statistical) population was assumed to give the two products in a 1:1 ratio. An analytical mathematical model that leads to such a picture is described below. From the fit to the data, a lifetime for the nonstatistical population of 100–130 fs could be deduced.⁵⁷ This is very much in line with what MD simulation suggests.

Interest in the acetone radical cation dissociation has almost as long a history as the DBH controversy. In 1970 McLafferty and coworkers⁶³ reported that enol radical cations generated in a mass spectrometer would undergo unimolecular rearrangement to the keto tautomer, followed by alkyl radical loss. Shortly thereafter,⁶⁴ they reported the results of isotopic labeling studies indicating that when the enol radical cation of acetone rearranged to its keto form, the newly formed methyl was lost more readily than the existing one, despite the fact that the

intermediate from which the dissociation occurred should have C_{2v} symmetry. They postulated that this phenomenon was a sign of incomplete IVR prior to reaction.⁶⁴ Subsequent studies^{65–68} showed unambiguously that the asymmetry in methyl dissociation was indeed the result of some sort of nonstatistical dynamical phenomenon. In particular, Brauman and coworkers deduced an important role for the in-plane bending vibration of the carbonyl group.⁶⁸

The experimental enthalpy profile^{69,70} for the formation and dissociation of the acetone radical cation could be quite well reproduced by calculations at the UB3LYP/cc-pVTZ level (Fig. 2). When a single direct-dynamics trajectory run at this level of theory was launched from the H-migration TS, without ZPE, it accessed the deep minimum for the acetone radical cation, but did not proceed on to the products as had been observed with DBH. Nevertheless, the trajectory was informative. If behavior implied by use of the statistical approximation were observed, the trajectory should have moved chaotically around the minimum on the PES. However, it exhibited quite periodic behavior for several hundred femtoseconds. Specifically, when the distance of the radical cation from the C_{2v} minimum-energy geometry (computed as the RMS difference in mass-weighted distance-matrix elements) was plotted as a function of time, it revealed a more-or-less sinusoidal form that coincided in frequency and phase with an in-plane bending motion of the carbonyl group (Fig. 2). That such a motion should receive a disproportionate share of the released kinetic energy is certainly reasonable, given the geometry difference between the TS and the acetone radical cation minimum, but it is also of significance for the subsequent dissociation. The reason is that loss of a methyl radical generates the acylium ion, for which the

CCO angle has an optimum value of 180° . The methyl dissociation therefore tends to occur from a geometry with one large and one small CCO angle. Consequently, the excited in-plane bend of the carbonyl brings the trajectory close to one and then the other exit channel to dissociation. This oscillatory behavior has real consequences for the chemistry, as revealed when a full-scale simulation was undertaken.⁷¹ 1800 trajectories were run from the vicinity of the H-migration TS, using the AM1-SRP direct-dynamics method,⁷² parameterized to fit the UB3LYP/cc-pVTZ results. When the loss of each methyl was analyzed as a function of time, three important results were found. First, the methyl loss showed a periodicity with a frequency matching that of the in-plane carbonyl bending motion. Second, the overall rate of loss of methyl groups was significantly higher than observed when trajectories corresponding to the same total energy were initiated in the region of the acetone radical cation minimum. Third, when the cumulative branching ratio was calculated, it was found that more newly formed than pre-existing methyls had been lost, as observed experimentally. All of these observations point to the failure of the statistical approximation, *despite the fact that the acetone radical cation sits in a PE minimum some 20 kcal mol^{-1} deep.*

A PLACE FOR FEMTOSECOND SPECTROSCOPY?

Increasing evidence suggests that the bimodal or multimodal lifetime distributions predicted for the intermediates in the DBH and acetone radical cation dissociations are examples of a more general phenomenon that was first brought to the community's attention in the Rynbrandt and Rabinovitch experiment.^{10,11} It now appears that an IVR rate of roughly 10^{12} s^{-1} is simply not sufficient for the statistical approximation to be universally valid. There is also no experimental evidence that IVR gets much faster than this as the vibrational state density increases, and, in fact, there are theoretical reasons to think that it may not.⁷³

A direct experimental test of this claimed failure of the statistical approximation would obviously be desirable. In particular, one may wonder whether the relatively recent advances in femtosecond spectroscopy⁷⁴ could be brought to bear on the problem. Could one, for example, directly detect the periodic alternation in methyl-group loss predicted for the acetone radical cation dissociation? The answer, I fear, is 'no,' or at best 'not easily.' The problem is that the reactions of interest are necessarily thermal; the acquisition of kinetic energy in specific vibrational modes as an intermediate is formed from its preceding transition state is a key component of the problem. Generating the intermediate in some other way will not lead to the same behavior. Of course, the direct detection of a reactive intermediate in a thermal

reaction is extremely challenging because its instantaneous concentration is so low and the background signal due to structurally similar reactants and products is so high. In a simulation one can synchronize the timing clocks for each reacting molecule so that the inherent periodicity comes out when one 'signal averages'—i.e. looks at the collective behavior of a large set of trajectories. However, in a thermal reaction, reactive intermediates will be formed in an incoherent fashion as molecules pass over the preceding transition state at infrequent and random times. Signal averaging under these circumstances would wash out any intrinsic periodicity because of the random offset in time of birth of the intermediate. Unless some clever chemical physicist can either devise a way to cause a 'pulse' of molecules to pass coherently over the same transition state on the way to forming a reactive intermediate, or can do single-molecule femtosecond spectroscopy, there is no obvious way in which direct spectroscopic detection of the claimed nonstatistical behavior can be accomplished.

A SIMPLE ANALYTICAL MODEL

If there is no obvious way to detect the nonstatistical dynamics of thermally generated reactive intermediates by direct spectroscopy, one might ask whether any indirect test can be devised. One possibility is revealed by constructing a simple analytical model for the behavior suggested by the simulation experiments. Suppose a 'pulse' of molecules *could* be caused to pass coherently over a transition state on the way to an intermediate, and suppose that the kinetic energy picked up in the descent from the transition state were localized in a single vibrational mode, of frequency ω , driving trajectories first to one exit channel (A) and then another (B), as was the case for both the DBH and acetone radical cation reactions. Let the probability of taking an exit to products be p on each encounter, meaning that, if nothing else occurred, the mole fraction of product formed in channel A would be p on the first cycle, $p(1-p)^2$ on the second, $p(1-p)^4$ on the third, and so on. While the first encounter with the B channel would generate a mole fraction of $p(1-p)$ product, the second $p(1-p)^3$, etc. Now suppose that, in competition with this oscillatory behavior, there is a simple first-order relaxation of the localized kinetic energy into an equilibrium, statistical, distribution among the available vibration modes. Let us assign a rate constant k_{IVR} to that process. Finally, let us assume that the statistical population selects the A or B channel with equal probability, and decays with an exponential distribution of lifetimes, having an exponent k_{RRKM} . This description implies that the ensemble of reactive intermediates is microcanonical, which is probably reasonable, even for a thermal reaction, provided that the kinetic energy acquired in the formation of the intermediate is $\gg k_{\text{B}}T$. The mathematical development of this model

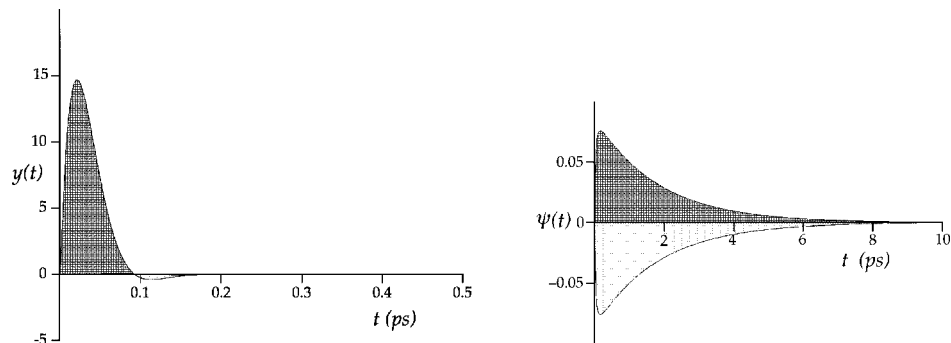


Figure 3. Lifetime distributions from the analytical model, using parameter values to simulate the DBH reaction. The left-hand panel depicts the nonstatistical component and the right-hand panel the statistical component. Positive values of $y(t)$ and $\psi(t)$ indicate formation of the *exo*-labeled product, whereas negative values indicate formation of the *endo*-labeled product

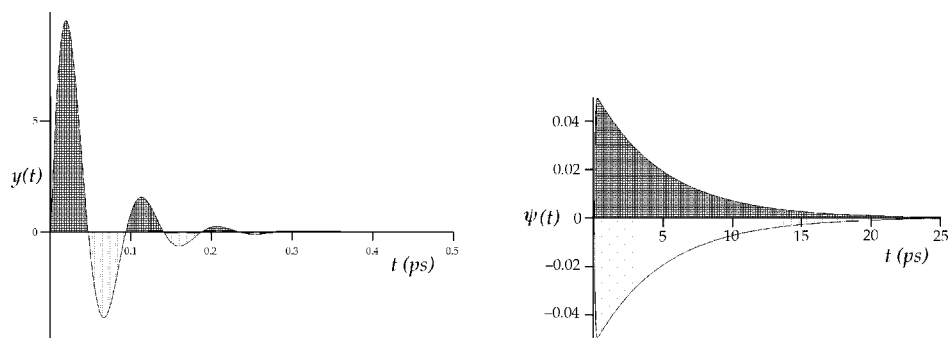


Figure 4. Lifetime distributions from the analytical model, using parameter values to simulate the acetone radical cation reaction with a final product ratio of 1.5. Positive values of $y(t)$ and $\psi(t)$ indicate dissociation of the newly formed methyl group, whereas negative values indicate loss of the existing methyl group

is given in the supporting information. Two functions, $y(t)$ and $\psi(t)$, define respectively relative yields of product per unit time derived from the nonstatistical and statistical populations of the intermediate. When these functions have positive values, product is being formed predominantly in the A channel, and when they have negative values, product is being formed mostly in the B channel. Graphical depictions of $y(t)$ and $\psi(t)$ with various values of ω , k_{IVR} , k_{RRKM} , and p are interesting. For the DBH reaction, the key vibrational mode of the cyclopentane-1,3-diyl intermediate is the out-of-plane flapping of carbon 2. From GVB/6-31G(d) calculations on the intermediate, this motion has a harmonic frequency of 180 cm^{-1} . Using that value, and with $k_{\text{IVR}} = 10^{12}\text{ s}^{-1}$, one finds that the observed gas-phase ratio of products (4.7 : 1) can be fitted if $p = 0.93$. (The product ratio is not influenced by the value of k_{RRKM} .) This very high probability of taking an exit to products on first encounter is consistent with the result of the *ab initio* direct-dynamics trajectory calculation described above. The functional form of $y(t)$ with these values for the parameters is shown in the left-hand panel of Fig. 3. The right-hand panel of Fig. 3 shows the time-dependent yield for the product derived from the statistical pool. It is based on an RRKM calculation, which gave $k_{\text{RRKM}} = 5.53 \times 10^{11}\text{ s}^{-1}$. Together, these components define a more-or-less bimodal distribution of lifetimes for product

formation, as had been posited in the analysis of the experimental data from the supercritical fluid studies.

For the acetone radical cation, the key mode driving trajectories between the methyl-dissociation exit channels is the in-plane carbonyl bend, for which the simulation suggested a frequency of 362 cm^{-1} . Keeping the IVR rate constant fixed at 10^{12} s^{-1} , one finds that the experimental branching ratio of 1.1–1.7 can be fitted if $p = 0.15\text{--}0.40$. With these values of the parameters, $y(t)$ takes on the early time oscillatory behavior observed in the MD simulation (Fig. 4, left-hand panel).

The potential value of this exercise is revealed when one starts to enquire about the effect of changing k_{IVR} on the overall branching ratios (Fig. 5). For the DBH reaction, the model predicts the intuitively reasonable result that the product ratio should asymptotically approach 1 as k_{IVR} increases. However, for the acetone radical cation dissociation, the model predicts an initial *increase* in the branching ratio, followed by the asymptotic approach to 1. This is a potentially interesting outcome, although obviously only if it is not due to some artifact of an overly simplistic model.

That there could be real physical significance to the prediction becomes apparent when one investigates its origin. The key observation is that, when there is oscillatory behavior in the early stages of product formation, measurement of the total yields in the A and B channels

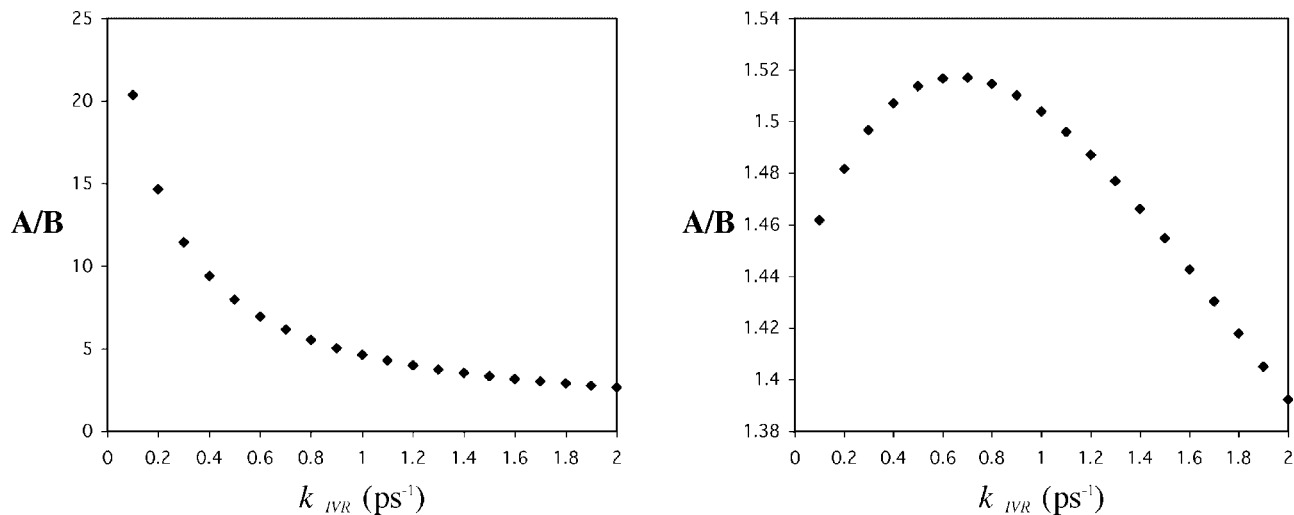


Figure 5. Dependence of total product ratios on k_{IVR} from the analytical model. The left-hand panel uses parameter values to simulate the DBH reaction. The right-hand panel uses parameter values to simulate the acetone radical cation dissociation with a branching ratio of 1.5 at $k_{IVR} = 10^{12} \text{ s}^{-1}$.

will afford an underestimate of the extent of nonstatistical behavior, because the product formed in the B channel at short time reduces the overall A/B ratio. For example, with parameters that lead to a product ratio of 1.50 for the representation of the acetone radical cation dissociation, the model suggests that the branching ratio would have been 2.25 if all of the nonstatistical population had dissociated in the A channel. Consequently, suppression of the oscillations leading to early product formation in the B channel can increase the product ratio. This is what happens when the IVR rate constant has the right value. If the first spike of oscillation in the A direction can still occur, but the return to the B channel is significantly diminished by population loss due to IVR, then the result can be an increase in the total product ratio.

The question, of course, is whether this prediction can be turned into a real experimental test. How does one go about changing k_{IVR} for a molecule? In a very rough way, this is what the supercritical fluid experiments described earlier were designed to do. The collision frequency of a reactive intermediate with the surrounding molecules can be about 10^{13} s^{-1} in a high-pressure supercritical fluid. Under such circumstances, collisions can be occurring on timescales similar to those for IVR and for reaction. It is likely that collisions promote IVR, and to that extent, change of collision frequency provides some control on the IVR rate. Where this approach obviously deviates from the assumptions of the analytical model is that collisions will also promote *intermolecular* energy exchange, implying that the intermediates will settle into a more-or-less thermal distribution of energies, rather than being isoenergetic as assumed in the model. Nevertheless, the qualitative effect of increasing the collision frequency ought to be similar to the effect of increasing k_{IVR} . In particular, for reactions that have the kind of intrinsic oscillatory behavior predicted for the acetone radical cation dissociation, one would expect to see an

initial increase and then a decrease in branching ratio as the pressure of supercritical fluid is raised. Observation of such a phenomenon would provide indirect evidence for the existence of the nonstatistical oscillations, since there is no obvious alternative mechanism that would lead to such a result. The acetone radical cation dissociation itself clearly would not be a very promising candidate for trying this experiment, but there are other reactions, including the formation and subsequent Wolff rearrangement of singlet diformylcarbene, for which similar behavior is predicted.

CONSEQUENCES OF THE PREDICTED BEHAVIOR

The claimed failure of the statistical approximation, if true, has consequences that are disturbing to mechanistic chemists and kinetic modelers alike. For mechanistic chemists it would mean that examining the structure of the equilibrium geometry of an intermediate may not be sufficient to predict how it will react. For example, an achiral intermediate might give optically active products (provided it was formed from a chiral, nonracemic reactant, of course). If the behavior of an intermediate is strongly influenced by the kinetic energy acquired during its formation, then the chemistry that it exhibits may depend on how it is made, whereas many of us have thought and taught that the opposite is true. For the kinetic modeler, the problem is no less severe. In complex schemes, such as those describing hydrocarbon combustion, the involvement of chemically activated species is generally handled by a master-equation approach.⁷⁵ Solution of master equations can be a daunting task,⁷⁶ even if one assumes the validity of an RRKM-like model, but the problem would become a good deal more complex if the chemically activated intermediates were

susceptible to the kinds of phenomena described in this article. For a kinetic scheme in which several intermediates are linked sequentially, and where some or all of them may branch to several products, an error in prediction of the branching ratio at even one place can have an effect that becomes amplified as it spreads through the scheme. It would thus seem prudent to examine in detail some of the key exothermic reactions in combustion chemistry (and probably atmospheric chemistry as well) to find out whether they really are adequately described by standard, statistical kinetic models.

Since the ramification of a widespread failure of the statistical approximation for reactive intermediates could be substantial, it would be desirable to conduct the most direct experimental tests of its validity that can be devised. For the reasons described in this commentary, that looks like a difficult task, but perhaps the reader might rise to the challenge.

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