

THE REVIEW OF PHYSICAL CHEMISTRY OF JAPAN, VOL. 50, 1980

THE VOLUME PROFILE OF CHEMICAL REACTIONS

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The volume profile of a chemical reaction has the same significance to the high pressure investigator that the energy profile has for the kineticist. In some ways, it conveys more information. This paper discusses its general features and how it is determined, considers the simplest cases of concerted reactions, analyzes the meaning of "early" and "late" transition states, and weighs the possibility of pressure mediated changes in mechanism.

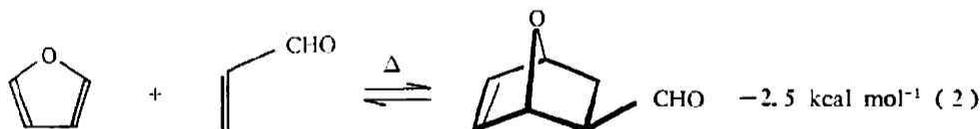
1. Introduction

One of the clearest indications of progress in a branch of science can be found in its jargon. Once general agreement is reached concerning some phenomenon, a name is chosen for it, a symbol assigned to it, and an equation is written for it. After that, it is no longer necessary in the next stage to engage in long, preliminary descriptions: the equation is written, and zork! everyone in the audience knows the starting point.

Chemists wishing to discuss a chemical reaction have two such devices of indicating their experience. One of these is the stoichiometric equation, which tells one at a glance which molecules are being converted into which, and how many of each. For example:



Various elaborations and extensions are possible, as in:



It is clear that the layman would have to be given some years of instruction to appreciate fully the centuries of experience that have culminated in this shorthand, or the extent of the corollaries implied in it; but to chemists discussing research, it provides a common level below which there is no disagreement.

A second means of such communication, interestingly enough, is not an equation but a drawing; that of the energy profile of the reaction. Thus, for the Diels-Alder reaction written above, one might draw Fig. 1. It tells us at a glance that there is a transient intermediate I

(Received August 28, 1980)

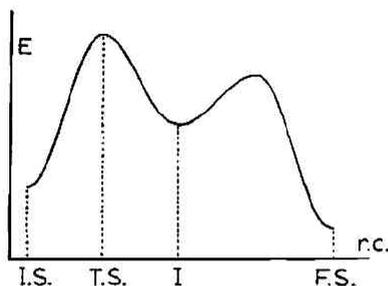


Fig. 1. Energy profile for reaction (2).

(which happens to be the *endo*-stereoisomer) the formation of which is rate controlling and the concentration of which is low, and that the reaction is exothermic and reversible. Some of the most important principles of chemistry, such as that of Evans and Polanyi, the Hammond postulate, the overall thermodynamics, certain selection rules, and so on, can all be indicated in the fleeting instant required to draw the curve. An algebraic equation representing concerted reactions was recently proposed¹¹; although it is of course completely empirical, all of these important principles can be derived from it.

2. The Volume Profile

It is a sign of the growing maturity of high pressure chemistry that the volume profile can now be considered as our means of instant communication. Figure 2 represents one of the simplest volume profiles imaginable: that of a homolytically breaking bond in the reaction

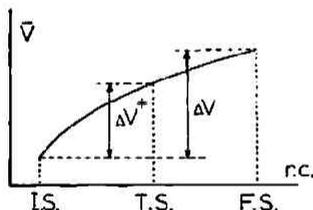


Fig. 2 Volume profile for a homolytically breaking bond.

The following points can be raised in a comparison with the energy profile. First of all, reactions in which the net overall energy change is positive are usually not observable unless they are entropy-driven; however, both positive or negative reaction volumes are frequently encountered. This is so because the work term $p\Delta V$ at atmospheric pressure is generally four or five orders of magnitude smaller than the energy and entropy, and its contribution to the free energy change—and therefore, to the equilibrium position—is negligible. It is perhaps interesting to reflect that reactions which are uphill so far as the volume is concerned will not be observable if the pressure is high enough. Thus, chemistry at the surface of the planet Jupiter, say, must be quite different from what we used to here on earth, even after the low

temperatures prevailing there have been taken into account. Homolytically breaking bonds are not likely to be known in Jovian laboratories.

A second and related point is that the activation energy, for all practical purposes, is always positive, but the activation volume may have either sign.²⁾ When the sign is plus and expansion is indicated in the transition state, the reaction is retarded by pressure.

Thirdly, we note that the transition state is defined by the maximum in the energy profile; however, volume profiles need not—and frequently do not—exhibit an extremum. Thus, if we look back at our homolytic bond cleavage in Fig. 2, the expansion may amount to 10 ml/mol in the transition state, and to 20 in the final state. In those cases in which an extremum does occur—as in the case, for instance, of displacement reactions—, it is not necessary that the energy maximum and the volume extremum coincide along the reaction coordinate, but it is impossible to explore this question experimentally.

Next, a very important distinction between the two profiles is the fact that for the energy diagram, only differences can be determined, whereas for the volume analog, absolute values can be assigned to both initial and final states, and since the difference ΔV^\ddagger can also be measured, an absolute value can be assigned to V^\ddagger . The importance of this fact lies in the opportunity open to high pressure chemists, to make a definite identification of the species responsible when unusual activation characteristics are encountered. This advantage has already served well in several instances, as in the interpretation of the Winstein-Fainberg diagram,³⁾ and in the assignment of mechanism to the cycloaddition of tropone to cyclopentadiene⁴⁾; it is in fact so unique that high pressure chemists should stress it more and measure and report \bar{V}^\ddagger on a routine basis.

3. Determination of the Profile

We now turn to the kinds of measurement necessary to fix the profile (Fig. 3).

The initial and final state volumes are obtained from density measurements as a function of concentration. From each datum, an apparent molal volume can be calculated and extrapolation to infinite dilution is then carried out.⁵⁾ The availability of commercial tuning fork densimeters has greatly improved the accuracy to which these terms can be asayed.⁶⁾

The reaction volume ΔV provides an important cross check on the measurements because it can be determined in at least two, and sometimes three completely independent ways. One of these, is simply calculating $\Sigma \bar{V}_p - \Sigma \bar{V}_r$; it is unavailable only if anyone species on either side

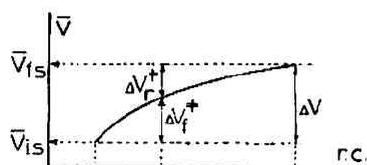


Fig. 3. The measurable components of the volume profile.

cannot be obtained in pure form (in case of a rapidly established equilibrium, for example). A second way is the dilatometric one: the volume change during the reaction is measured directly, and with good temperature control this can be done with good precision even at low concentration. The third way consists of measuring the pressure dependence of the equilibrium constant and the use of the well-known equation

$$\Delta V = \frac{\partial \Delta G}{\partial P} = -RT \frac{\partial \ln K}{\partial P}.$$

It will of course not routinely be possible in all instances to measure ΔV by all three routes; however, the circumstances limiting the use of each are too obvious to elaborate further here.

The activation volume requires knowledge of the rate constant over a range of pressures, so that one can apply

$$\Delta V^{\ddagger} = \frac{\partial \Delta G^{\ddagger}}{\partial P} = -RT \frac{\partial \ln k}{\partial P}.$$

This simple concept was first devised by van't Hoff,⁷⁾ first understood in modern terminology by Eyring⁸⁾ and fleshed out in the last two decades with measurements for hundreds if not thousands of reactions in several dozens of laboratories around the world.⁹⁾ It goes without saying that a folklore has correspondingly developed about what kind of equipment to use, how analytical procedures can be adapted to high pressure, how best to extract the information desired from the data obtained, and how all the information gained can be incorporated in modern mechanistic chemistry; however, these features have been reviewed and need not be discussed here.

4. Characteristics of Common Profiles

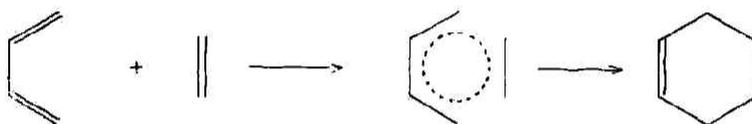
In simple, one-step, concerted reactions, the most common volume profiles are those without an extremum. Simple bond cleavages (whether single or multiple) that produce no additional electrical charges, usually lead to continuously rising profiles, while cleavages that do produce additional charges give rise to continuously declining profiles. Extrema are of course the rule in stepwise reactions, but some concerted reactions have them as well. Sigmatropic shifts such as the Claisen rearrangement¹⁰⁾ show minima because of the newly forming bond; a maximum was observed in the degenerate Wagner-Meerwein shift shown on p.211 because of charge delocalization.¹¹⁾ This reaction is of interest in that the solvated molecule essentially goes through a breathing motion, with exhalation inhibited by the pressure.





5. Diels-Alder Reactions

A particularly interesting profile is exhibited by certain cycloaddition reactions. When such reactions are concerted as appears to be the case in the large majority of Diels-Alder reactions symbolized by



the activation volume is large and negative, comparable to the reaction volume.¹²⁾ This similarity in volume of the transition state and product would suggest that the former is "late": *i. e.*, that in the transition state the nuclei are already near their final positions. This is in very sharp contrast indeed to the commonly held belief¹³⁾ that Diels-Alder reactions have "early" transition states: organic chemists have interpreted the small activation energies and large overall enthalpy changes in this way. Which point of view is right?

In the author's opinion, the two positions are not necessarily at variance, and that a transition state can be both "early" in energy terms, and "late" in terms of nuclear positions.

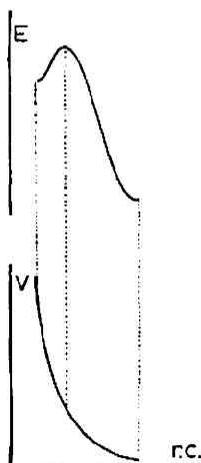


Fig. 4. The energy and volume profiles of Diels-Alder reactions: the transition state is early, but the nuclei are near their final positions.

This would be so if the bonding does not progress monotonically as the nuclei progress to their final positions (see Fig. 4). It is noteworthy that the entropies of activation in Diels-Alder reactions are also very large and negative. What all this seems to say is that in the Diels-Alder reaction, the nuclei must be near their final positions before the electrons begin to flow.

Even more amazing is the finding by Eckert,¹⁴⁾ since confirmed by others,¹⁵⁾ that the activation volume is sometimes even more negative than the reaction volume! In these instances, the volume profile is a minimum. In the maelstrom of success surrounding the newly enunciated principle of conservation of molecular orbital symmetry, these workers were quick to interpret their observations as an indication of the so-called secondary orbital interactions, a notion advanced by Woodward and Hoffman¹⁶⁾ to explain the long-standing puzzle of *endo*-stereochemistry. In confirmation, Eckert also found that in closely similar reactions in which geometric constraints inhibit such interactions, the minimum is not observed.¹⁷⁾ In retrospect, however, some caution must be sounded.

First of all, while the reasons for this need not concern us here, very large pressure effects on k are notoriously difficult to measure. Secondly, even if all claims made to date are true, some nagging questions remain. Thus, in some instances, the Diels-Alder reaction produces both *endo*- and *exo*- products, and both with virtually identical activation volumes.¹⁸⁾ Since the effect of pressure on product distribution can be measured with much greater accuracy, one has to become suspicious. Likewise, when there is a minimum in the volume profile, the reaction rate must be enhanced by pressure in *both* directions. In the retro Diels-Alder reaction, this would be exceedingly interesting since it would be a rare case of a molecule breaking up and shrinking at the same time. Retro Diels-Alder reactions are common; however, to date no case of pressure enhancement has come to light. Should such hoped-for developments occur, that would still not guarantee that the then-proven minimum in the volume profile is indeed due to secondary orbital interactions: a slight increase in polarity at the transition state in the rather non-polar solvents generally used in Diels-Alder reactions could also be responsible, and one should have to rule this out by studying solvent effects on the rate. Before this reservation is dismissed as overly conservative, it should be recalled that the [2+2] cycloreversion of certain cyclobutanes is *strongly* enhanced by pressure;¹⁹⁾ in these instances, the breaking bonds lead to a product quite akin to a simple zwitterion.²⁰⁾

6. Transition State Location

One of the more fruitful applications of the volume profile has been the verification of the Hammond postulate—the principle that is generally understood to convey the idea that among a group of similar reactions, the less exothermic ones have the later transition states (see Fig. 5).²¹⁾ It had long been known that the pressure-enhanced Menschutkin reactions show

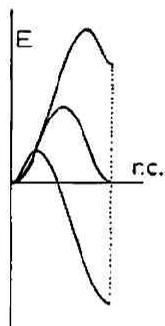


Fig. 5. The Hammond postulate illustrated: as the activation energy is lowered, the transition state becomes more product-like.

the greatest acceleration in the most hindered cases.²³⁾ A complete set of measurements of both JV^* ,²³⁾ and \bar{V} of both reactants and products⁵⁾ showed that JV^*/JV increases from rather low values indicative of early transition states to values close to unity when the reaction is made subject to very large hindrance.²⁴⁾ Clearly, the transition state is "later" in those cases. Independent confirmation was obtained from measurements of k^{35}/k^{37} in the methylation of pyridine and 2,6-lutidine with methyl chloride; the latter had the larger isotope effect, and the difference is roughly in agreement with that predicted on the basis of the activation volumes.²⁵⁾

7. Transition State Progression

The volume profile has also played a role in the question whether there can be transition state progression, not now among a series of reactions as a function of substituents, but in a single reaction as a function of pressure. The basic thought is that if $|JV^*|$ is reasonably large and very high pressures are used, the work term pJV may cause measurable shifts in the transition state location, as shown in Fig. 6. The corresponding shift in transition state location was first mentioned by Walling,²⁶⁾ who claimed that it might be playing a role in his results concerning the Diels-Alder reaction. This idea was attacked by Benson and Berson,²⁷⁾ who estimated that the effect was negligibly small. The lively polemic which ensued was

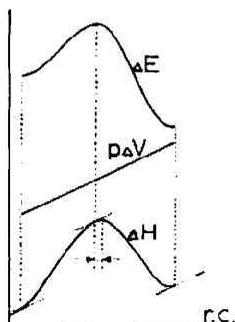


Fig. 6. The volume profile is assumed to be linear for the sake of clarity. The slope is obviously different from zero for JH at the three locations where E has extremum.

hard to follow at first because the phenomenon was then described as the "compressibility" of the transition state, which it obviously is not. In later years one further claim has been made,²⁸⁾ and this one also drew a negative comment¹⁾; however, the principle is sound, and estimate is in order of what it will take to demonstrate.

Since $|JV^\ddagger|$ must always decrease as the pressure is raised, the work term $|pJV^\ddagger|$ cannot be made indefinitely large by increasing the pressure without limit, and in fact, with $1 \text{ cm}^3 \times 1 \text{ bar}$ equalling about 0.025 cal, it seems that a work term much larger than 10 kcal/mole is hard to imagine in any reaction at any pressure. While such an amount is of enormous interest in the case of competing reactions of synthetic importance, its superposition on the normal energy profile with a ΔE^\ddagger of 25 kcal/mole or more is likely to cause only minimal shifts not easily detected. In those instances where this shift appears to play a role, confirmation by means of accurate measurements of isotope effects appears mandatory.

The detection of the impact of the work term appears to be far more promising in reactions with small energetic barriers, of 5-10 kcal/mole, say. These reactions will obviously be extremely fast, and since kinetic studies at very low temperature and very high pressures do not seem practical as yet, the choices will have to be made from among degenerate equilibrations. In such reactions, $A \rightleftharpoons A$ with at least some of the nuclei exchanging positions, it is obvious that the transition state is located halfway and symmetrically between the initial and final states in both the energy and volume profiles, and hence that no shifts will occur; however, the intriguing possibility exists that the addition of a large work term will stabilize the transition state so as to leave it a "stable" molecule. The creation of the bridged bishomobenzene from semifullvalene has been mentioned as an example.^{1,29)} Obviously only spectral techniques will permit the laboratory appraisal of this speculation.

Another area of interest, in this connection, is photochemistry. The product controlling steps here are often those involving high energy intermediates, ready to race downhill in sometimes competing ways, and impeded by very little need for further activation.

This effect of pressure on the mechanism of reactions, which we have referred to as transition state progression or retrogression, should not be confused with another and much more common effect, that of pressure on the relative importance of competing pathways to a common product. The effect of pressure in such instances then appears as in Fig. 7; they result simply from a minor contribution becoming the major one because of a more negative or less positive activation volume.^{30,31)}

One other pressure effect on mechanism may be mentioned here, namely that on those reactions in which tunnelling makes a significant contribution. Isaacs has described several

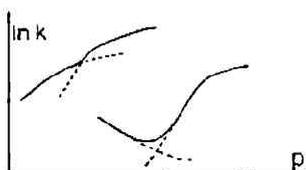


Fig. 7. The cases of competing mechanisms, and the resulting rate vs. pressure plots.

such reactions³²¹; in each case, the tunnelling contribution is reduced by the application of pressure. Interestingly, the transition states in these reactions appear to be the only known cases in which isotopic substitution results in a substantially different volume; *i. e.*, $V_D^\ddagger \neq V_H^\ddagger$, for example.

In considering pressure effects on very fast reactions, it should be remembered that the transition state formalism begins to lose its validity as the barrier becomes vanishingly low and the concept of equilibrium between the initial and transition states becomes untenable. While one may still observe pressure effects and may in fact still be able to express the effect in terms of an "activation volume", the intuition connected with this concept must at some point break down.³³¹

It is at present not clear how rapid rates would have to be to force consideration of this breakdown; however, the late Professor Jost had obtained one of the promising results in this connection.³⁴¹ Activation volumes of reactions whose rates are closet to diffusion controlled, and which have to be determined from pressure effects in reactions approachable only by means of T-jump techniques, are entirely similar in direction and magnitude to those determined for vastly slower reactions by means of conventional techniques. There is therefore little reason to fear, for now, that high pressure in ultrafast reactions won't play the same vital role that it has come to play in the traditional slow chemistry.

Acknowledgements.

The author is indebted to the National Science Foundation for supporting his investigations in this area. He thanks Professor J. Osugi for inviting him to contribute to this issue commemorating the 50th volume of *The Review of Physical Chemistry of Japan*, one of his many brain children.

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