Reply to “Comment on Phantom Activation Volumes”

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In the preceding article,[1] le Noble and Asano (L&A) criticize our paper on phantom activation volumes (PAV)[2] on the grounds that our thesis leads to the conclusion that all kinetic equations of the Arrhenius−Eyring type would have to be revised or even abandoned. Since these equations have “served. . . mechanistic chemists very well” and have “been a useful gauge in the elucidation of reaction mechanisms”, they “state categorically” that the conjecture of PAV “is fundamentally false if the transition state theory (TST) is valid”.

Our position is that the TST is certainly valid but that calculations of volume of activation (V_a) contain inaccuracies, usually small but sometimes large, arising from the failure of eq 4[1] to take into account ancillary nonvolume-related events that occur over the span of pressure that gives rise to variations in reaction rate. If these ancillary events affect the rate, then a portion of the apparent V_a will have arisen from them and ipso facto be a phantom V_a. The fact that eq 4 furnishes a quantity which is *labeled* a volume does not prove that this quantity has no other component.

What pressure-induced events other than volume could affect reaction rates? We proposed viscosity, on the grounds that it is pressure-sensitive, and the rates of some reactions are viscosity-sensitive. From the response of rates to viscosity,[3−5] the effects of pressure on viscosity,[6] and the effect of pressure on rates,[7] we calculated, in an approximate way, what percentage of the apparent V_a’s of Diels−Alder and 1,3-dipolar cycloadditions and of Claisen rearrangements arises from changes in viscosity rather than volume.[2] These are in effect corrections to eq 4 and range from very small up to 61%.

We hold that PAV is a valid concept *and* so is the TST, if imprecise.

It seems paradoxical that L&A oppose the concept of PAV when they provide important examples of it themselves. We cited one example out of many by Asano and co-workers in which an isomerization is slowed by raising the pressure, even though the volume of the transition state (TS) differs little from that of the reactants.[8] Asano attributed the depression in rate not to volume but, rather, to the increase in viscosity created by the pressure. Clearly, in this case, eq 4 provides an apparent V_a which is, for the most part, not a true volume at all. The fact that they understand how all this comes about does not change the fact that it is partially a phantom, not a physically accurate V_a.

They cite another excellent case of PAV. Radical−radical combination exhibits negative V_a’s since it is a bond-making reaction. Yet the termination of free-radical polymerization, like other diffusion-limited reactions, is pressure-retarded, giving rise to a *positive* apparent V_a.[9] Once again, the obvious explanation is that rising pressure induces rising viscosity. Clearly, the apparent V_a must have a phantom component during termination.[10]

We also discussed[2,3,11] Diels−Alder (DA) reactions in which the apparent V_a was more negative than the volume of reaction V_r. It is obviously physically impossible for the TS of a nonpolar cycloaddition to be smaller than the cycloadduct. Therefore, the TST-derived V_a cannot be the true one. This difficulty has elicited several explanations in the past. One is that “One may picture the DA reaction as one in which it is necessary for the nuclei to approach their final places closely before the electrons will flow to theirs”.[7] This conflicts with not only the TST but also the Born−Oppenheimer approximation, the bedrock of chemistry, so it is not convincing. Another is secondary orbital interactions (SOI),[7] in which atoms not bound to each other in either the reactants or products approach closer than their van der Waals distances in the TS. This can be disregarded for two reasons: (1) SOI is conceivable only for the endo, not the exo TS so that the V_a for endo should be significantly more negative than for exo. However, in many cases that are candidates for SOI, it is not.[12] (2) SOI do not exist. Since 1962, it has been known that methyl, which cannot participate in SOI, is more endo-seeking than carbomethoxy,[13] COOH,[14] Ac,[14,15] CHO,[14,15] CN,[14−16] etc., all of which can. Clearly, steric and not electronic effects govern here.

Non-PAV explanations are conceivable. (3) Polar substituents in a DA might be positioned to give the TS an exceptionally high dipole moment, evoking enhanced solvent electrostriction, and this would give rise to a more negative V_a.[17] This would be a true, not a phantom, volume effect. However, the TS would have to be more polar than the cycloadduct, an unlikely circumstance. Furthermore, among DA’s in general,[7] there is no correlation between apparent V_a and either (a) structural features that might affect the TS’s dipole moment or (b) solvent polarity, which affects electrostriction strongly.[18] (4) The dominant influence on apparent V_a in DA reactions is the increase in packing fraction at the TS *v-a-v* the reactants.[11] This too is a true volume effect. One might then propose that the packing fraction of the TS exceeds that of the cycloadduct also, but the physical basis is not apparent.

Extreme cases exist where the TST-derived V_a is so distant from any physical possibility that the PAV dominates it altogether. In the DA between isoprene and maleic anhydride in CO_2, as the critical point is crossed while raising the pressure, the TST-derived V_a becomes more negative than -500 cm^3/mol![19] This is $>3\times$ the total volume of the reactants. Under normal circumstances in dichloromethane, it is -39.9 cm^3/mol.[20] Similarly, a V_a of -750 cm^3/mol at the critical point was reported for isoprene + methyl acrylate.[21] Although this paper was criticized for sampling errors in product composition,[22] it is not clear that the rate constants also were in question. An enormous negative apparent V_a was reported near the critical temperature in the neat dimerization of chlorotrifluoroethylene.[23] Finally, in a Z/E-type isomerization of dimethylindigo, a TST-derived V_a of about 100 cm^3/mol was obtained by Asano’s group[24] at a pressure just above the point where a sudden downturn in rate is observed. The true V_a for the reaction is only ca. a few cubic centimeters per mole, so the bulk of the apparent V_a has to be a PAV, whatever its origin. They suggested

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that the TST was invalid (cf. first paragraph) in this region, with which we heartily agree.

All the above extreme examples except Asano's are predicted by the fact, first reported by us,[3] that the reactions in question are accelerated by rising viscosity. Nonpolar reactions typically proceed significantly slower in the gas than the liquid phase, a phenomenon we have interpreted on the basis of viscosity,[3,4] since crossing from even the most mobile liquid into the gas phase entails a sudden fall in viscosity of about 10-fold. Even a small change in rate over a very small range of pressure will produce an unrealistically large apparent V_a. Does this make the TST invalid? Not in general, but certainly when crossing discontinuous states, just as L&A say.

They cast doubt on our assertion that viscosity is the relevant solvent property that gives rise to our rate effects: "The correlation between reaction rate constants and [solvent] molecular weights, *if true*. . ."[1] (Italics are ours). The correlation between rates and viscosity—not molecular weights, as we showed in 1981[3]—is an experimental *fact*, not a conjecture.[4] A more proper question is whether viscosity is the *effective* parameter. We believe it is. Furthermore, there is literature that supports this viscosity-rate link. We cited[3,4] a number of papers by others in which rates rise with viscosity. Of particular interest is a study of the same reaction we did, cyclopentadiene dimerization, but in a large varied group of common, mobile, polar and nonpolar solvents.[25] At that time, they did not have viscosity in mind, but they did try to find a correlation between rate and just about every other solvent property: boiling point, MVE, surface tension, dielectric constant, Hildebrand's solubility parameter δ, E_T, Kosower's Z, and μ. None of them correlates. This rules out L&A's suggestions of "dielectric constant, surface tension. . . and so on". These rates were plotted[26] against the cohesive energy density (CED), δ^2_s, affording a "rough correlation" with a very low slope, after omission of the point with the largest deviation. However, the correlation is very rough, with tremendous scatter. It is even worse with the missing point restored, and then the slope falls to zero. This means that rate is independent of CED in this system,[27] ruling out their unsupported suggestion of internal pressure, "which is closely approximated by the CED".[1] In contrast, our plot[4] of these rates[25] versus solvent viscosity is incomparably more coherent than any of the others.

Finally, L&A suggest that if viscosity is indeed responsible, ". . . there is apparently a diffusion process which is facilitated by reduced volume, difficult though that may be to imagine". It is indeed difficult to imagine that diffusion is faster when there is less mobility and less available empty space. In any case, this argument cannot be applied to our experiments, which were done at constant pressure.

They then point out that if viscosity were someday found to affect an equilibrium constant, then eq 3[1] would also need revision, a circumstance unacceptable to them.

This is correct but so what? First, the situation is purely hypothetical and may never arise. Second, if it did, there is nothing intrinsically unbelievable about a viscosity-sensitive K_{eq}, since K_{eq} is the quotient of the forward and reverse reaction rates. There is no law stating that both rates must respond identically to viscosity or any other solvent property and no law stating that reactants' and products' relative thermodynamic stabilities are invariant with all solvent properties.[30]

Finally, L&A say that our thesis inexorably leads further to phantom activation energies (PAE), since solvent viscosities fall with rising temperature. Thus, the Arrhenius equation would also need revision. This is also correct. We pointed out in our first paper of the series in 1973 that for those reactions that are viscosity-accelerated, PAE's should be negative.[31] They are usually very small because viscosity changes over small ΔT's are not large enough to affect the rate significantly. However, just as PAV's can be most unambiguously identified when they dwarf true V_a's, PAE's can be made visible in the same way. In this instance, we cannot greatly enlarge PAE's, but there are many reactions in which the true E_a is so small that the PAE emerges from the shadow. In bimolecular cases where the true $E_a \cong 0$, often—perhaps always—the apparent E_a is negative; i.e., raising the temperature lowers the rate. The following are a few of the many examples: recombination of two Me•'s,[32] two Cl•'s,[33] two allyl•'s,[34] OH• + many olefins,[35] *t*-Bu• + HBr,[36] Me_2Cl^+ + Ph-Me,[37] and atom recombination in general, with discussion.[38] These E_a's run from −1 to −2 kcal/mol, and while the magnitude is of course a soft number, the sign cannot be mistaken. The PAE can also be positive, e.g., in the isomerization of azo compounds and benzylideneaniline, which is pressure-retarded owing to a viscosity effect.[8] This leads to a positive PAV (vide supra) but also to a positive PAE because the fall in viscosity over ΔT_P means less pressure retardation and, thus, a steeper rise of k with T.

In summary, we agree with L&A that the concept of PAV and PAE conflict with the TST and Arrhenius equations but not that the conflict is irremediable. These equations have indeed served chemists very well and, with revision, will continue to do so. However, the V_a's and E_a's from them have been taken by chemists to have physical reality—that's how they serve as a "gauge in the elucidation of reaction mechanisms"—and yet misrepresent that reality, sometimes in a small way, occasionally in a significant way. The solution is to recognize arcane quantities such as V_a and E_a, not merely by the names they have been given but, rather, by considering the actual processes by which they are determined. In this way, we will be able to approach physical reality more closely than we do now.[39]

References and Notes

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(27) This is not surprising because CED, a weak effect in any case (ref 18, p 132), is the square of Hildebrand's δ (vide supra), which is connected to the energy required to form a cavity (to make room for a molecule) in the solvent from no cavity.[28] This is clearly much more demanding than merely rearranging the shape of an existing cavity, as in the Claisen rearrangement or intramolecular DA,[3−5] or merging two existing cavities, as in the intermolecular DA.[4] Furthermore, in the series *n*-butane to dodecane, δ is almost constant, changing smoothly in tiny, diminishing increments.[29] In the heart of our series, octane-dodecane, $(\delta_{C(n+1)} - \delta_{Cn})/\delta_{C(n+1)}$ is less than 1%, and even for CED, it is less than 2%! The series δ_o, δ_d, δ_p, and δ_h are even more compressed. These data show that CED, internal pressure, and δ have no connection with our viscosity-rate results.

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(39) L&A properly present scientific arguments to counter our position but also engage in one-upmanship by citing, but refusing to cite properly, two of our papers,[3,11] thus giving the false impression that we do not have priority in two important areas. Our 1989 paper,[11] the first to report accurate molecular and void volumes in cycloadditions, precedes their ref 15 (1998), and our 1981 paper,[3] the first to report a noncage viscosity-rate link for any reaction, precedes all of their ref 17 (1991−2000).