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COMMENTS

Comment on "Phantom Activation Volumes"

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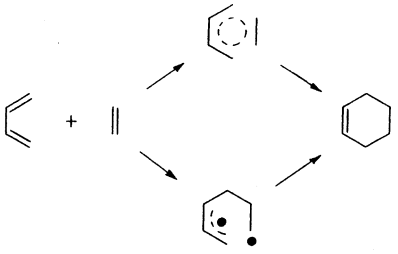
Introduction

Few ideas in physical organic chemistry have proved to be more fruitful than that of molecular orbital symmetry control of the stereochemistry of pericyclic reactions.[1] A simple count of electrons suffices to divide such reactions into "allowed" and "forbidden" ones and then to predict their configurational outcomes. Despite its usefulness, only two generally applicable approaches have been designed to serve as experimental support for the concerted nature of allowed reactions: stereochemistry and piezochemistry. The Diels−Alder reaction may serve to illustrate the point.



If the reaction is concerted, with a single transition state, the dienophile centers *must* maintain the same configuration throughout the process, including the product stage; if it is stepwise, the open-chain diradical intermediate *need* not. Bartlett has on that basis provided beautiful examples of some Diels−Alder reactions that fit the concerted mold, and others that do not.[2] To make the distinction, it is necessary to assume that the diradical intermediate is sufficiently long-lived to undergo one or more single-bond rotations. The iconoclast may of course maintain that retention of configuration only proves that the intermediate was too short-lived to permit such rotations, and not that it did not occur at all.[3]

The high-pressure approach makes use of the fact that bond formation is characterized by volume shrinkage. Because the activation volume of Diels−Alder reactions thought to be concerted is generally close in magnitude to the overall reaction volume, the argument is that both bonds must have made significant progress toward formation when the transition state is reached.[5] In this field, Stewart has provided[6] striking examples of Diels−Alder reactions in which some of the molecules do, and others do not, follow the concerted pathway. In recent times, Klärner has refined[7] the argument by accounting in detail for other volume elements affecting the reaction profile, and ruling them out as invalidating the approach.

However, in the past few years, the high-pressure argument has been revisited by Swiss and Firestone (S&F), who were led to do so by the well-known fact[8] that the viscosity of liquids tends to rise when the pressure is raised. Presenting data[9] apparently showing that the rates of some Diels−Alder reactions are higher in more viscous media, they argued[10] that the activation volume needs to be corrected because it is partly of a phantom nature, and that when this is done, the remaining and presumably real part is insufficient to support the claim of concertedness. S&F further used their data to support the concept of "vibrational activation", in which the cycloaddition process requires "reactants, one of which is vibrationally excited." These ideas were subsequently questioned[11] and defended[12] on theoretical grounds.

The two cycloaddition reactions studied by S&F[9] were the dimerization of cyclopentadiene and the dipolar addition of diphenyldiazomethane (DPDM) and ethyl phenylpropiolate (EPP). The first of these two reactions, the rates of which were measured in a series of *n*-alkanes ranging from octane to heptadecane, showed a pronounced maximum in *n*-dodecane, followed by a decline in the higher MW solvents. S&F used the rising part of the curve to support their notion of phantom activation volumes, but offered only unsubstantiated suggestions[13] to explain the return to more nearly normal values in the most viscous solutions. When new data are used to propose the negation of a substantial body of literature and its replacement by a radical new idea, one criterion on which its possible acceptance must rest is laboratory information of unquestionably superior quality. Van Eldik therefore tried to extend the available rate data for the first reaction by measuring the monomer concentration over a wider range of conversion but came to the conclusion[14] that there simply was no viscosity dependence of the sort that S&F had claimed, and which they subsequently defended.[15] We have now carefully scrutinized S&F's data for the second reaction,[9] the details of which have hitherto appeared only in their unpublished Supporting Information, and report our analysis here.

One reason for our interest was the fact that S&F treated the data as a pseudo-first-order process,[16] the initial concentration of the EPP having been about 10 times higher than that of the DPDM. We therefore recalculated the second-order rate constants more rigorously on the basis of the exact expression (1):

$$k_2 = \frac{1}{t(a-b)} \ln \frac{b(a-x)}{a(b-x)} \qquad (1)$$

where *a* and *b* represent the initial concentrations of EPP and DPDM and *x* is the concentration of the product formed in a time *t*. The results are recorded in Table 1; the values of k_2 are those arrived at by means of a linear least-squares fitting procedure, which assumes no error in *t* and which allows a nonzero intercept. An example of our calculations may be seen in our Supporting Information. Table 1 reveals several features worth noting.

One of these is the precision of the measurements: this is uniformly good, with an average deviation of the individual

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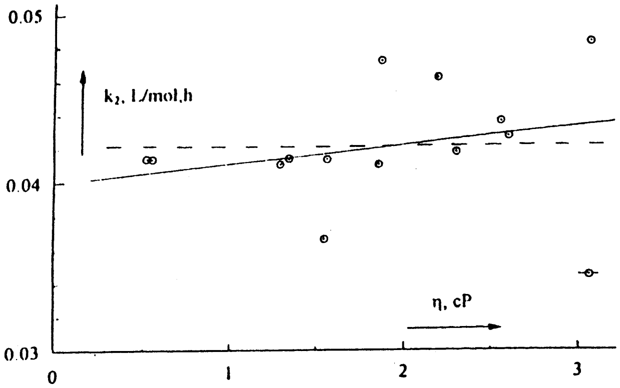

Figure 1. Plot of the rate constants of the reaction of DPDM and EPP in various *n*-alkane solvents vs solution viscosity. In one of the two "3 cP experiments", the viscosity was not measured and was assumed (by us) to be the same as in the other.

TABLE 1: Summary of S&F's Rate Data for the Reaction of DPDM with EPP in Various *n*-Alkanes at 30 °C

n-alkane	exp no.	% reacn	no. of data	k_2, L/(mol h)	% error	η, cP
C_8H_{18}	1	42	8	0.0415	2.6	0.54
	2	40	7	0.0415	0.5	0.56
$C_{12}H_{26}$	1	60	7	0.0415	0.2	1.35
	2	42	11	0.0410	1.7	1.30
$C_{13}H_{28}$	1	34	10	0.0368	1.7	1.55
	2	73	9	0.0415	1.2	1.57
$C_{14}H_{30}$	1	50	10	0.0474	0.4	1.88
	2	53	7	0.0411	1.3	1.87
$C_{15}H_{32}$	1	41	9	0.0464	1.2	2.21
	2	38	7	0.0420	0.3	2.31
$C_{16}H_{34}$	1	51	9	0.0429	0.4	2.62
	2	68	11	0.0438	0.5	2.58
$C_{17}H_{36}$	1	35	6	0.0346	0.3	
	2	57	8	0.0486	1.6	3.08

points from the least squares lines of only 1%. The accuracy is much less impressive, however; in only three of the seven solvents do the duplicate values agree to within the precision limits, whereas in the four others differences between duplicate runs occur which amount to 10−35%. It seems certain that some uncontrolled or poorly controlled experimental variable suffuses S&F's study.

A second point becomes more obvious when the rate constants are plotted against viscosity, as shown in Figure 1: the sort of dependence discerned by S&F[9] is just not there. There is no peak. Though fitting a least-squares straight line through these points (as S&F did for an intramolecular Diels−Alder reaction in a series of glymes) does produce a slightly rising dependency (solid line in Figure 1; $k_2 = 0.00117\eta + 0.0400$), the average deviation of the rate constants from this line amounts to 5.7%, and when the possibility of no viscosity dependence at all is tested in the same way (dashed line; $k_2 = 0.0422$), the average deviation is only barely larger, at 6.0%. It is obvious that no reliable nonzero relation between k_2 and η has been demonstrated.

These results left us wondering how S&F, using the same data, arrived at their conclusions; the errors introduced by their assumption of a pseudo-first-order process should not have exceeded a few percent. Figure 4 in S&F's paper[9] is a graph of "relative rate constants" vs the solution viscosity; these constants, shown without units, are portrayed as being in the range 1747−2216. The value in *n*-octane appears at about 1890. The same numbers are given in their Supporting Information, there called "Relative Second-Order Slopes" (RSOS). By trial and error, we established that the numerical values of the RSOS conform to the following relationship:

$$\mathrm{RSOS} = 10^6 \frac{b}{ta} \ln \frac{b}{b-x} \qquad (2)$$

To give one example, the first run in *n*-octane is reported as having a slope, $-[\ln\{b/(b-x)\}]/t$, equal to -0.01692 [h^{-1}], and indeed, if this value and the initial concentration values, $a = 0.423$ and $b = 0.0479$ mol L^{-1}, are substituted into eq 2, RSOS is found to be 1916 h^{-1}, which is the value reported (though without the units). All RSOS given in S&F's Supporting Information agree closely with the values calculated on the basis of eq 2, except for the second run in *n*-heptadecane where it is reported as 1770, whereas eq 2 yields a value of 2165 h^{-1}. Equation 2 is obviously wrong as a means of calculating second-order rate constants, whether relative or absolute. That can be seen simply from the fact that the concentration units in eq 2 cancel and that the values of RSOS therefore have the units of "time^{-1}" only, instead of "time^{-1} × concentration^{-1}". The correct relation for the pseudo-first-order approximation in a bimolecular reaction is

$$k_{2(\mathrm{approximately})} = \frac{1}{ta} \ln \frac{b}{b\text{-}x} \qquad (3)$$

which has the right units. Comparing this with eq 2, we see that, in addition to the factor 10^6, S&F have mistakenly multiplied (3) by the initial concentration b, which, in their experiments, varied arbitrarily by up to 23% for various reaction runs. That was the main cause of their errors. However, there is another aspect of the results that astonishes us. The RSOS duplicate results, as reported by S&F on the basis of an incorrect relationship equivalent to eq 2, agree much more closely with each other than do the corresponding duplicate values of k_2, which we have calculated from the same experimental data using the exact correct rate eq 1 and the approximation (3). This may be seen in Table 2.

TABLE 2: RSOS- and k_2 Ratios in Duplicate Runs

n-alkane	RSOS (2)/RSOS(1)[a]	$k_2(2)/k_2(1)$[b]	$k_{2\mathrm{app}}(2)/k_{2\mathrm{app}}(1)$[c]
C_8H_{18}	0.97	1.00	1.02
$C_{12}H_{26}$	0.98	0.99	1.00
$C_{13}H_{28}$	1.02	1.13	1.11
$C_{14}H_{30}$	1.02	0.87	0.86
$C_{15}H_{32}$	1.03	0.91	0.90
$C_{16}H_{34}$	1.00	1.02	1.01
$C_{17}H_{36}$	1.01	1.40	1.38

[a] Reported by S&F.[9] [b] Calculated by the present authors on the basis of eq 1. [c] Calculated by the present authors on the basis of the approximate eq 3.

Finally, if one assumes that the viscosity effect is real, it is of interest to recalculate the phantom activation volumes based on the correct values of k_2. Firestone[10] has recommended the use of an expression containing the slope $\delta \ln k_2/\delta \ln \eta$, which he gave the value of 0.277. The actual magnitude of this term, if it is real at all, would be 0.0346, 8 times smaller than claimed. The plot from which we calculate this value and which is similar in appearance to Figure 1, is shown in our Supporting Information. The phantom activation volumes for all of the 11 1,3-dipolar cycloadditions quoted by Firestone[10] should be reduced accordingly, to the range −0.50 to −0.71 cm^3/mol, which is generally less than the uncertainty in the activation volumes themselves.

Conclusion

We have shown that serious errors were made by S&F in their computations of the effect of solution viscosity on the rate constant of the cycloaddition of DPDM to EPP. *When the calculations are done correctly, no effect is discernible.* This removes the reaction as one supporting the novel notion of "phantom activation volumes", which, to borrow a phrase,[17] "are not useful as criteria of the Diels–Alder mechanism".

Acknowledgment. We appreciate the very thorough perusal of our Comment by the Referees.

Supporting Information Available: The S&F rate data in their first run in *n*-octane, the linear least squares calculation of the rate constant, and a plot of ln k_2 vs ln η. This material is available free of charge via the Internet at http://pubs.acs.org.

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