Criteria for the cation radical *vs.* electrophilic mechanistic distinction: the aminium salt-catalysed Diels–Alder reaction

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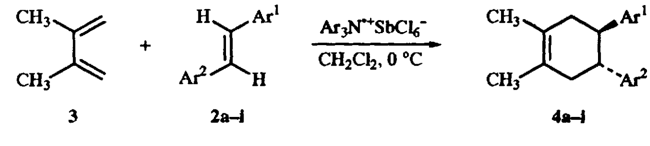
The tris(4-bromophenyl)aminium salt-catalysed Diels–Alder additions of stilbenes to 2,3-dimethylbuta-1,3-diene are shown to proceed *via* ionization of the stilbenes to the corresponding cation radicals by demonstrating that the reactions involve the generation of a unit positive charge in an essentially symmetrical distribution on the stilbene substrates; a hypothetical electrophilic mechanism is unequivocally ruled out by the present results.

The discovery of the triarylaminium salt-catalysed Diels–Alder reaction has stimulated interest in cation radical chemistry and facilitated the development of a wide range of cation radical pericyclic chemistry.[1] The ability to generate cation radicals of a variety of substrates using catalytic quantities of the commercially available and shelf-stable cation radical salt tris-(4-bromophenyl)aminium hexachloroantimonate $(\mathbf{1}^{\bullet+})$[2] is an especially attractive feature of the method. The reactions are often stereospecific and surprizingly selective, as well as extraordinarily fast and efficient. The scope and limitations of aminium salt catalysed pericyclic chemistry have already been discussed.[2,3] In a few interesting cases, $\mathbf{1}^{\bullet+}$ has been found to induce Brønsted acid-catalysed, carbocation-mediated chemistry, rather than the expected cation radical chemistry.[4] Fortunately, a simple diagnostic test for distinguishing these two mechanistic types has been developed.[5,6] Specifically, inclusion of a hindered base such as 2,6-di(*tert*-butyl)pyridine in the reaction medium completely suppresses Brønsted acid catalysed processes but allows most cation radical processes to proceed. Recently, the possibility that $\mathbf{1}^{\bullet+}$ could act as an electrophile *via* one of its electron deficient aryl positions has been suggested as an alternative mechanism for generating carbocations, which would not necessarily be suppressed by hindered bases. Such an electrophile-catalysed, carbocation mediated mechanism was, in fact, proposed for the Diels–Alder cyclodimerization of cyclohexa-1,3-diene, which is widely considered to be a prototypical cation radical reaction.[7] While it is important to realize that the assignment of a cation radical mechanism for this and other aminium salt-catalysed Diels–Alder reactions rests upon a far broader base than the hindered base criterion,[3,8] it nevertheless appeared important to develop definitive mechanistic criteria which would decisively rule out (or rule in) the hypothetical electrophilic mechanism. Beyond this, the ultimate goal of this research was to develop a strong criterion which would point positively and uniquely to a cation radical mechanism for these reactions.

It is here proposed that for a symmetrical pi system (such as *trans*-stilbene), the development of a full unit of positive charge distributed symmetrically over the system is a unique and positive indication of cation radical formation. In contrast, electrophilic addition yielding a carbocation intermediate generates a highly unsymmetrical positive charge distribution. Symmetrical bridging by the electrophile could result in a symmetrical charge distribution, but in that case a portion of the charge would be borne by the bridging electrophile, rather than the substrate. In any case, symmetrical bridging would not appear to be a viable possibility for the triarylaminium electrophile.† The stilbene system appeared especially appropriate because the peak oxidation potentials of a very long series of symmetrically *para*-disubstituted stilbenes had been obtained and found to correlate nicely with the σ^+ parameter.[9] The $E_{1/2}$ *vs.* σ^+ equation quoted in this latter study affords a ρ value of -10.8. A subsequent study found the oxidations of the 4,4′-dimethyl- and 4,4′-dimethoxy-stilbenes to be essentially reversible.[10] The oxidation potentials found in this second study for these reversibly oxidized stilbenes are also consistent with $\rho = -10.8$. Other studies have demonstrated that ρ values for electrochemical oxidations are not very sensitive to solvent polarity.[11] The value $\rho = -10.8$ would therefore appear to be a valid indication for the generation of a full unit of positive charge (as the cation radical) in the stilbene system. This ρ value, however, is based upon a symmetrically disubstituted stilbene system wherein the σ^+ value of a single substituent is used. For example, in the case of 4,4′-dimethylstilbene, the σ^+ value of a single *para*-methyl substituent (-0.31) was used.[9] To assess the symmetry of the charge distribution, it was essential to include monosubstituted stilbenes in our experimental study. Consequently, the more general form of the Hammett–Brown equation, $\log k/k_0 = \rho\Sigma\sigma^+$, was used. In this context, 4,4′-dimethylstilbene has two *para*-methyl substituents and $\Sigma\sigma^+ = -0.62$. The effect of recasting the Hammett–Brown equation in the more general form is simply to divide the ρ value by a factor of two (*i.e.*, $\rho = -5.4$).



2a *trans*-Stilbene = SB
b 3-Methylstilbene = 3-MSB
c 3,5-Dimethylstilbene = 3,5-DMSB
d 3,3′-Dimethylstilbene = 3,3′-DMSB
e 4-Chlorostilbene = 4-CSB
f 4,4′-Dichlorostilbene = 4,4′-DCSB
g 4-Methylstilbene = 4-MSB
h 4,4′-Dimethylstilbene = 4,4′-DMSB
i 3,4′-Dimethylstilbene = 3,4′-DMSB

Scheme 1

The Diels–Alder addition of stilbene, and of a series of mono- and di-substituted stilbenes (**2**) to 2,3-dimethylbuta-1,3-diene (**3**) was selected as an appropriate reaction system (Scheme 1). The competition kinetics of the Diels–Alder reactions of a series of nine stilbenes with a five-fold excess of **3** were studied at 0 °C in dichloromethane in the presence of $\mathbf{1}^{\bullet+}$. Each relative rate constant was cross-checked by matching a specific substrate with at least two different partners.[12] The kinetic runs were always carried out to less than 10% conver-

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† Especially since the highly hindered nitrogen is non-basic and non-nucleophilic.

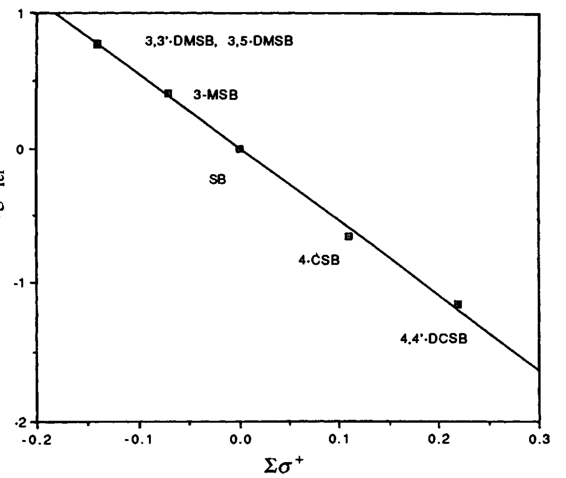

Fig. 1 Hammett–Brown plot for the aminium salt-catalysed Diels–Alder additions of substituted stilbenes to 2,3-dimethylbuta-1,3-diene

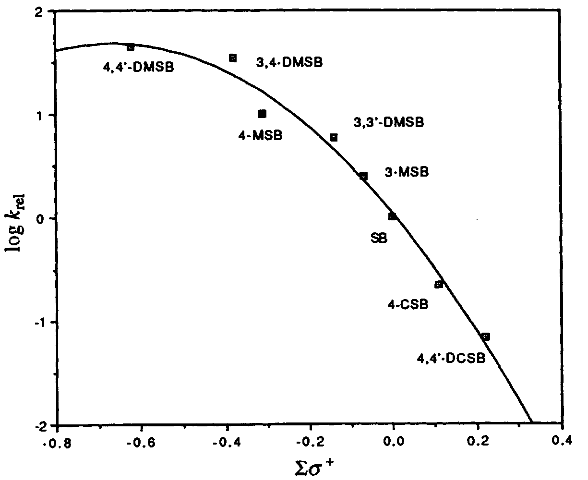

Fig. 2 Hammett–Brown plot for the aminium salt-catalysed Diels–Alder additions of substituted stilbenes to 2,3-dimethylbuta-1,3-diene

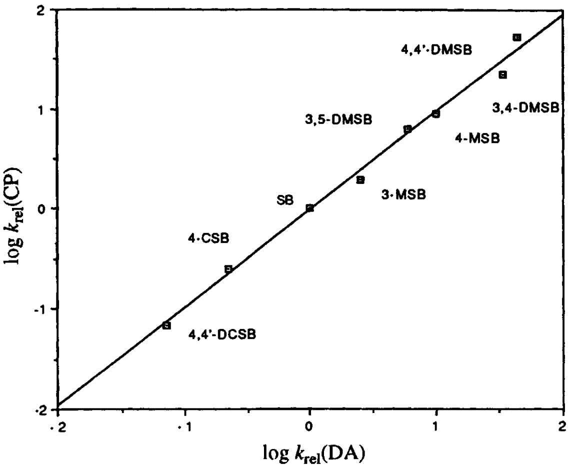

Fig. 3 Plot of log k_{rel} for aminium salt-catalysed cyclopropanation *vs.* log k_{rel} for Diels–Alder cycloaddition of substituted stilbenes to 2,3-dimethylbuta-1,3-diene

sion, and mass balances were *ca.* 98%. No products other than the Diels–Alder adducts (**4**) were detectable. The Hammett–Brown plot is very nicely linear ($r^2 = 0.998$; Fig. 1) for all but the three most easily ionizable substrates (**2g**–**i**) and has $\rho = -5.45$. The full plot (Fig. 2) shows marked curvature for the three noted substrates, suggesting a mechanistic change. The effective ρ value in this region sharply diminishes to $\rho \approx -2.7$. These observations are consistent with a mechanistic change from equilibrium controlled ionization ($\rho = -5.4$) to a kinetically controlled ionization step. According to the Marcus equation, a kinetically controlled electron transfer having no thermodynamic driving force would have a ρ value exactly one-half that for the equilibrium electron transfer.[13] A mildly endergonic ET such as that involved in the ionization of stilbene by $\mathbf{1}^{\bullet+}$ is predicted to have a slightly larger (negative) ρ value. Consistently with these interpretations, the absolute rate of reaction of 4-methylstilbene with **3** is independent of the concentration of **3**, whereas the rate of reaction of 4-chlorostilbene is approximately doubled when the concentration of **3** is doubled. The transition from an equilibrium controlled ionization with rate determining cycloaddition to rate determining ionization for the more ionizable substrates appears plausible on the basis of the less favourable (slower) back electron transfer for these substrates (Scheme 2).

$$\mathrm{SB} + \mathrm{Ar_3N^{\bullet+}} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{Ar_3N} + \mathrm{SB^{\bullet+}} \xrightarrow[\mathbf{3}]{k_2} \mathbf{4}^{\bullet+}$$

Scheme 2 Kinetic *vs.* thermodynamic control of stilbene ionization

Further strong support for the cation radical mechanism is available from a plot of log k_{rel} for these Diels–Alder reactions *vs.* the corresponding log k_{rel} values for aminium salt-catalysed cyclopropanation by ethyl diazoacetate, a reaction for which a cation radical mechanism has already been strongly supported (Fig. 3).[12] Not only are substituent effects nicely parallel, they are quantitatively virtually identical, in a statistical sense (slope = 0.98). This correlation strongly indicates that substituent effects are primarily determined in a step which does not involve the neutral components and that the two reactions have essentially identical mechanisms, including the transition from thermodynamically controlled to kinetically controlled ionization.

An analogous study was also carried out in acetonitrile solvent, and the results are very similar ($\rho = -4.7$). It therefore appears clear that the Diels–Alder reactions of those substrates on the linear part of the Hammett–Brown plot involve the generation of a full unit of positive charge. The symmetrical disposition of the charge essentially follows from the inclusion of both mono- and di-substituted stilbenes on the plot, but is better evaluated from a comparison of the rate constants themselves. For example, the first *meta*-methyl substituent accelerates the rate by a factor of 2.5 relative to stilbene, while the second *meta*-methyl substituent (3,3′-dimethylstilbene) accelerates the rate by a factor of 2.3 relative to 3-methylstilbene. Similarly, the first *para*-chloro substituent retards the rate by a factor of 0.22, while the second retards by a further 0.32. In the case of the more strongly electron donating *para*-methyl substituent, the effect of the second *para*-methyl group (4.4) is noticeably less than that of the first such substituent (10.0), but still far greater than expected for a carbocation forming process. In the rate determining protonation of *cis*-stilbenes (leading to geometric isomerization), for example, the effect of the first *para*-methyl substituent is virtually the same as found in the present work (10.5), but the second *para*-methyl accelerates the rate by only a factor of 1.4.[14] It is, of course, expected that more strongly perturbing substituents will induce asymmetry in the charge distributions of monosubstituted stilbene cation radicals, so that appreciable deviations from the ideal of multiplicative substituent effects are expected even for a cation radical forming process.

Acknowledgements

The authors thank the NSF (CHE-9123292) and the Robert A. Welch Foundation (F-149) for support of the research.

References

1 D. J. Bellville, D. D. Wirth and N. L. Bauld, *J. Am. Chem. Soc.*, 1981, **103**, 718.
2 R. I. Walter, *J. Am. Chem. Soc.*, 1955, **77**, 5999.
3 N. L. Bauld, *Tetrahedron*, 1989, **45**, 5307.
4 P. G. Gassman and D. A. Singleton, *J. Am. Chem. Soc.*, 1984, **106**, 6085.
5 P. G. Gassman and D. A. Singleton, *J. Am. Chem. Soc.*, 1984, **106**, 7993.
6 D. W. Reynolds, K. T. Lorenz, H.-S. Chiou, D. J. Bellville, R. A. Pabon and N. L. Bauld, *J. Am. Chem. Soc.*, 1987, **109**, 4960.
7 L. Eberson, B. Olofsson and J.-O. Svensson, *Acta Chem. Scand.*, 1992, **46**, 1005.
8 N. L. Bauld, *Advances in Electron Transfer Chemistry*, ed. P. S. Mariano, JAI Press, Greenwich, 1992, vol. 2, pp. 1–66.
9 T. Kubota, B. Uno, Y. Matsuhisa, H. Miyazaki and K. Kano, *Chem. Pharm. Bull.*, 1983, **31**, 373.
10 F. D. Lewis, A. M. Bedell, R. E. Dykstra, J. E. Elbert, I. R. Gould and S. Farid, *J. Am. Chem. Soc.*, 1990, **112**, 8055.
11 B. A. Sim, P. H. Milne, D. Griller and A. D. M. Wayner, *J. Am. Chem. Soc.*, 1990, **112**, 6635.
12 N. L. Bauld and W. Yueh, *J. Am. Chem. Soc.*, 1994, **116**, 8845.
13 R. A. Marcus, *Ann. Rev. Phys. Chem.*, 1964, **15**, 155.
14 D. S. Noyce, D. R. Hartter and F. B. Miles, *J. Am. Chem. Soc.*, 1968, **90**, 6333.

Paper 4/07664H
Received 15*th December* 1994
Accepted 1*st March* 1995