Mechanistic Criteria for Cation Radical Reactions: Aminium Salt-Catalyzed Cyclopropanation

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Received February 8, 1995[⊗]

Abstract: Mechanistic studies of the cyclopropanation of a series of *trans*-stilbenes by ethyl diazoacetate catalyzed by two different triarylaminium salts decisively confirm a cation radical mechanism and rule out a hypothetical electrophilic mechanism. The elucidation of key aspects of these cation radical mechanisms, including kinetic *vs* equilibrium control of ionization and chain *vs* catalytic mechanisms, has also been achieved for these systems. New mechanistic criteria for the positive identification of cation radical mechanisms are proposed.

The discovery of aminium salt-catalyzed, cation radical pericyclic reactions[1,2] has provided an important impetus for the elucidation of the fundamental chemistry of the cation radical and for the development of this chemistry into a useful repertoire of reactions of synthetic quality.[3,4] The mechanistic/theoretical aspects of this novel chemistry have not been entirely neglected, but the field could perhaps be considered to be in a relatively early developmental stage, loosely comparable to that of carbocation chemistry in the early 1950s. A number of basic issues do appear to have been satisfactorily resolved, however.[3,4] Especially important among these is the conclusion that at least many of these reactions are mechanistically pericyclic (i.e., concerted), although orbital symmetry allowedness/forbiddenness appears to play little or no part in determining reaction rates or periselectivity.[3,4] As progress in this area continues and expands, it appears increasingly important to clearly and rigorously distinguish the unique chemistry of the cation radical intermediate from that based upon other reactive intermediates, especially the carbocation. In a few interesting cases, aminium salts have been found to induce Bronsted acid-catalyzed, carbocation-mediated chemistry rather than the expected cation radical chemistry.[5] Fortunately, a simple diagnostic test for distinguishing these two mechanistic types is now available.[6,7] Specifically, inclusion of a hindered base such as 2,6-di-*tert*-butylpyridine in the reaction medium completely suppresses Bronsted acid-catalyzed processes while allowing most cation radical reactions to proceed. Recently, it has been suggested that carbocation intermediates might be generated by electrophilic addition of the aminium salt, *via* one of its electron deficient aryl ring positions, to a π bond.[8] Since carbocations, *per se*, are not necessarily trapped efficiently by the hindered base, an electrophile-catalyzed, carbocation-mediated mechanism might still formally be tenable. While it is important to realize that the assignment of cation radical mechanisms to these aminium salt-catalyzed pericyclic reactions rests upon a far broader platform of evidence than the hindered base criterion,[3,4] it nevertheless appears important to develop criteria which are capable of decisively ruling out (or ruling in) the hypothetical electrophilic mechanism. Still more challenging and desirable than simply ruling out specific contender mechanisms is the development of strong and positive mechanistic criteria which can uniquely identify cation radical mechanisms. Even within the context of cation radical mechanisms, many significant mechanistic aspects remain to be clarified. For example, is a cation radical chain mechanism or a classic catalytic mechanism operative?[2,3] Is the ionization step or the pericyclic step rate determining? And, perhaps most elusive of all, is the ionization step of the outer or inner sphere variety? The present research provides useful, and in many cases decisive, insights into all of these very basic questions.[9]

Results and Discussion

The Charge/Symmetry Criterion. For a symmetrical π electron system (as exemplified by *trans*-stilbene), the development of a full unit of positive charge distributed symmetrically over the system (e.g. equally over both phenyl rings) should represent a unique and positive criterion for 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 substantial portion of the positive charge must be borne by the bridging electrophiles rather than the substrate. Moreover, symmetrical bridging would not appear to be a plausible possibility in the case of a triarylaminium electrophile.[10] The ideal case of unit charge generation on the substrate molecule can, of course, only be achieved in an equilibrium-controlled ionization process, although highly endergonic, kinetically controlled ionization could approach this ideal. The stilbene system appeared to be especially appropriate for an experimental test of the charge/symmetry criterion because the oxidation potentials of a very long series (nitro to dimethylamino) of symmetrically *para*-disubstituted stilbenes had been measured

[⊗] Abstract published in *Advance ACS Abstracts*, May 15, 1995.

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(6) Gassman, P. G.; Singleton, D. A. *J. Am. Chem. Soc.* **1984**, *106*, 7993.

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(8) Eberson, L.; Olofsson, B.; Svensson, J.-O. *Acta Chem. Scand.* **1992**, *46*, 1005−1015.

(9) Bauld, N. L.; Yueh, W. *J. Am. Chem. Soc.* **1994**, *116*, 8845−8846.

(10) Bridging *via* nitrogen (five-membered ring) is unlikely because the highly hindered nitrogen is nonbasic and non-nucleophilic. In any case, such bridging is inherently unsymmetrical. Other formal bridging possibilities (three- or four-membered rings) are similarly unlikely.

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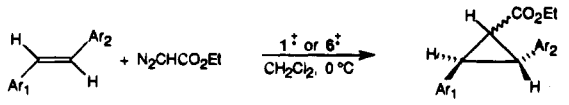
Scheme 1. Aminium Salt-Catalyzed Cyclopropanation of Stilbenes



2a-h 3 4a-h

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

$1^{\ddagger} = (4\text{-}BrC_6H_4)_3N^{\ddagger}\ SbCl_5^{\ddagger}$ $6^{\ddagger} = (2,4\text{-}Br_2C_6H_3)_3N^{\ddagger}\ SbCl_5^{\ddagger}$

and found to correlate well with the σ^+ substituent parameter.[11] The $E_{1/2}$ *vs* σ^+ equation quoted in this latter study affords a Hammett–Brown ϱ value of -10.8 for the conversion of stilbenes to the corresponding cation radicals. A subsequent study found the oxidations of 4,4′-dimethyl- and 4,4′-dimethoxystilbene to be essentially reversible.[12] The oxidation potentials found in this independent study are also consistent with the ϱ value quoted above.[13] Still other studies have found that ϱ values for electrochemical oxidations are rather insensitive to solvent polarity.[14] The value $\varrho = -10.8$ would therefore appear to be a valid index 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 series of symmetrically *di*substituted stilbenes wherein the σ^+ value of a *single* substituent is used. For example, in the case of 4,4′-dimethylstilbene, the σ^+ value for a single methyl substituent (-0.31) was used. To assess the symmetry of the charge distribution, it was essential to include monosubstituted stilbenes in the experimental study. Consequently, a more general form of the Hammett–Brown equation, $\log k/k_0 = \varrho\sum\sigma^+$, was used. In this context, 4,4′-dimethylstilbene has two *p*-methyl substituents and $\sum\sigma^+ = -0.62$. The effect of recasting the Hammett–Brown equation in the more general form is simply to divide ϱ by a factor of 2. Consequently, $\varrho = -5.4$ is now the appropriate index for cation radical formation. For a kinetically controlled ionization having no thermodynamic driving force ($\Delta G° = 0$), the Marcus equation predicts that relative free energy effects are exactly one-half those for the equilibrium, i.e., $\varrho = -2.7$.[15] The ϱ value for an endergonic ionization (positive $\Delta G°$) is predicted to be somewhat more, and that for exergonic ionization (negative $\Delta G°$) somewhat less, negative than the value -2.7.

To apply the charge-symmetry criterion, the cyclopropanations of *trans*-stilbene and a series of seven substituted *trans*-stilbenes (**2a–h**) by excess ethyl diazoacetate (**3**), catalyzed by tris(4-bromophenyl)aminium hexachloroantimonate ($\mathbf{1}^{\bullet+}$) in dichloromethane solvent at 0 °C, were studied (Scheme 1). In every case, the reactions were first carried out on a synthetic scale, and the pure cyclopropane products were isolated and characterized by ^{1}H NMR and MS. The relative rate constants for the cyclopropanation reactions of these eight substrates were thus obtained *via* competition kinetics (Table 1). Two stilbenes, each present at 0.012 M concentration, were paired in each competition experiment, which utilized a 3-fold excess (0.036 M) of ethyl diazoacetate in dichloromethane at 0 °C. Reactions were carried out to less than 10% conversion of the more reactive partner (GC analysis, corrected) and mass balances were >98%. No other volatile products were detectable. Final results are averages over three independent runs. Each relative rate constant was cross-checked by matching a specific substrate with at least two different partners. The Hammett–Brown plot (Figure 1) shows extensive curvature for the three more readily ionizable substrates (**2a–c**), indicating a possible mechanistic change for these substrates. For the remaining five substituents (**2d–h**), however, the plot is impressively linear ($r^2 = 0.999$) and, significantly, $\varrho = -5.17$, in good agreement with the value anticipated for equilibrium-controlled ionization (Figure 2). In the case of the most readily ionizable substrates, the data are too limited to define ϱ very precisely, but the effective ϱ value drops sharply from that which characterizes the linear portion

Table 1. Relative Rate Constants for the Cyclopropanation of Stilbenes by Ethyl Diazoacetate Catalyzed by Tris(4-bromophenyl)-aminium Hexachloroantimonate

stilbene	k/k_0	stilbene	k/k_0
1. 4,4′-dimethylstilbene	58.00	5. 3-methylstilbene	2.00
2. 3,4-dimethylstilbene	23.00	6. stilbene	1.00
3. 4-methylstilbene	9.20	7. 4-chorostilbene	0.25
4. 3,3′-dimethylstilbene	5.00	8. 4,4′-dichlorostilbene	0.07

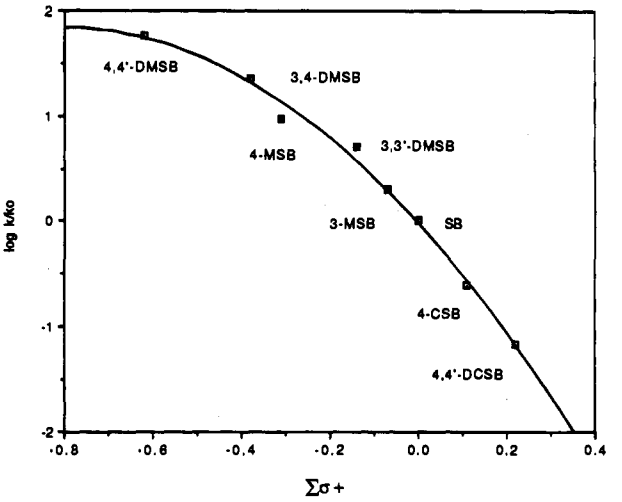


Figure 1. Hammett–Brown plot for the cyclopropanation of substituted *trans*-stilbenes (SB) by ethyl diazoacetate catalyzed by tris(4-bromophenyl)aminium hexachloroantimonate ($\mathbf{1}^{\bullet+}$); in dichloromethane at 0 °C: M = methyl, DM = dimethyl, C = chloro, and DC = dichloro.

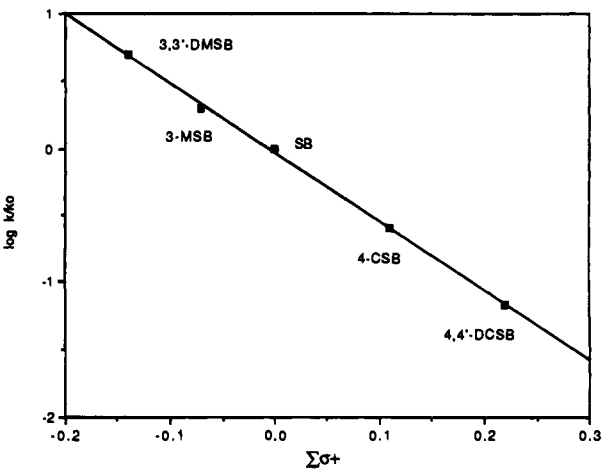
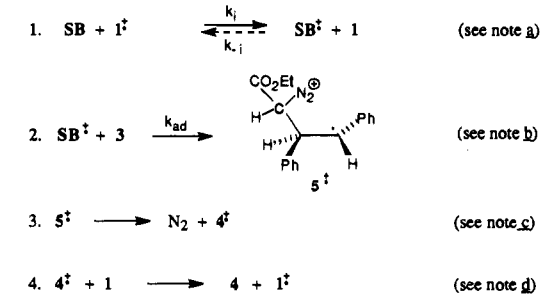


Figure 2. Linear portion of the Hammett–Brown plot of Figure 1: $\varrho = -5.17$, $r^2 = 0.999$.

(11) Kubota, T.; Uno, B.; Matsuhisa, Y.; Miyazaki, H.; Kano, K. *Chem. Pharm. Bull.* **1983**, *31*, 373–385.
(12) Lewis, F. D.; Bedell, A. M.; Dykstra, R. E.; Elbert, J. E.; Gould, I. R.; Farid, S. *J. Am. Chem. Soc.* **1990**, *112*, 8055–8064.
(13) A ϱ value of -5.3 is derived from the data in ref 12 for stilbene and the dimethyl and dimethoxy derivatives.
(14) Sim, B. A.; Milne, P. H.; Griller, D.; Wayner, A. D. M. *J. Am. Chem. Soc.* **1990**, *112*, 6635–6638.
(15) Marcus, R. A. *Ann. Rev. Phys. Chem.* **1964**, *15*, 155.

Scheme 2. Generalized Mechanism for the Cyclopropanation of Stilbenes by Ethyl Diazoacetate Catalyzed by $\mathbf{1}^{\bullet+}$



[a] For **2a**–**c**: k_{-i} [**1**]≪k_{ad} [**3**], i.e., kinetically controlled ionization. For **2d**–**h**: k_{-i} [**1**]≫k_{ad} [**3**], i.e., equilibrium-controlled ionization.[b] Nonstereospecific addition to *cis*-stilbene suggests a stepwise mechanism.[c] The structure of the product cation radical is unknown (e.g., whether it has an intact cyclopropane ring or a long bond structure).[d] Steps 1–4 constitute a classic catalytic cycle.

of the plot to a value in the range of $\varrho = -2.3$ to -2.8, consistent with kinetically controlled ionization. The assignment of the curvature in the Hammett–Brown plot to a change from equilibrium to kinetic control (see Scheme 2) is further supported by studies of the dependence of the absolute rates of cyclopropanation upon the concentration of ethyl diazoacetate (**3**). The rates of cyclopropanation of 4-methylstilbene and 4,4′-dimethylstilbene remain quite constant when the concentration of **3** is doubled, consistent with a rate-determining ionization step. In contrast, the rate of cyclopropanation of stilbene is almost exactly doubled when the EDA concentration is doubled, consistently with a rate-determining reaction of the stilbene cation radical formed in an equilibrium ionization, with **3**. The basis for the change in rate-determining step is presumably a less favorable and therefore slower rate of reversal of ionization for the more readily ionized substrates.

The inclusion of both mono- and disubstituted stilbenes on the Hammett–Brown plot implies that charge is generated on both aryl rings in an approximately symmetrical fashion. The symmetry of the charge distribution can be seen more clearly from the rate constants themselves, as opposed to log k's. The first *p*-chloro substituent, for example, retards the rate by a factor of 0.25 (Table 1). The effect of the second *p*-chloro substituent is a further retardation by a factor of 0.27. Similarly, the first and second *m*-methyl substituents accelerate the rate by factors of 2.0 and 2.5, respectively. In the case of the more strongly electron donating *p*-methyl substituent, the effect of the second methyl substituent (6.3) is somewhat less than that of the first (9.2), but still far greater than expected for a carbocation-forming process. In the rate-determining protonation of *cis*-stilbenes, for example, the effect of the first *p*-methyl substituent is nearly the same as in the present work (10.5) but the second *p*-methyl group accelerates by a factor of only 1.4.[16] It is, of course, expected that more strongly perturbing substituents will induce substantial 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 on forming process. The combination of $\varrho = -5.17$ and a relatively symmetrical charge distribution satisfies the charge/symmetry criterion and constitutes strong evidence for a cation radical mechanism, as well as specifically against an electrophilic mechanism. The correspondence of the mechanistic change suggested by the Hammett–Brown plot with the observed change in the rate law is also nicely consistent with the proposed cation radical mechanism.

(16) Noyce, D. S.; Hartter, D. R.; Miles, F. B. *J. Am. Chem. Soc.* **1968**, *90*, 6333–4637.

Rate Retardation/Selectivity Enhancement. The ionization of stilbenes by $\mathbf{1}^{\bullet+}$ produces the neutral triarylamine **1** in a hole transfer reaction which is approximately 0.53 eV (12.2 kcal/mol) endergonic.[17] The addition of **1** should therefore sharply retard the cyclopropanation rate through an exergonic reversal of the ionization step. On the other hand, hole transfer from a hypothetical benzylic carbocation intermediate to **1** is substantially endergonic and appears quite unlikely.[19] Further, in the case of a kinetically controlled ionization step, the at least partial reversal of ionization induced by added **1** might be expected to have the effect of increasing the magnitude of substituent effects *via* an increased ϱ value, which is intermediate between that for kinetically controlled and thermodynamically controlled ionization. Experimentally, the addition of 100 mol % of **1** retards the rate of cyclopropanation of stilbene by a factor of at least 100. The selectivity in the cyclopropanation of 4-methylstilbene/stilbene mixtures is enhanced from 9.2 to 20.8. In the case of the 4,4′-dimethylstilbene/4-methylstilbene pair, selectivity is enhanced from 6.3 to 9.5 by the addition of 100 mol% of **1**.

Other Criteria. In conventional electrophilic additions, *cis*-stilbene is more reactive (typically about 5 times) than *trans*-stilbene.[20] In contrast, the ionization of *cis*-stilbene (E_p^{ox} = 1.70 V) is considerably more difficult than that of *trans*-stilbene (E_p^{ox} = 1.59 V *vs* SCE). Experimentally, *trans*-stilbene is at least 100 times as reactive as *cis*-stilbene toward cyclopropanation. Further, if electrophilic addition were operative, and if the addition were to occur reversibly, *cis*-stilbene should be rapidly isomerized to *trans*-stilbene prior to cyclopropanation. Experimentally, *cis*-stilbene is not isomerized, even after several hours of exposure to the reaction conditions. Moreover, even if the hypothetical electrophilic addition step were rate determining, isomerization of *cis*-stilbene by $\mathbf{1}^{\bullet+}$ should occur in the absence of any **3**. In fact, *cis*-stilbene is stable indefinitely in the presence of $\mathbf{1}^{\bullet+}$ when **3** is absent.

Stronger Hole Catalysts. Tris(2,4-dibromophenyl)aminium hexachlorantimonate ($\mathbf{6}^{\bullet+}$) is a much more powerful catalyst [E_p^{ox}(**6**) = 1.50 V *vs* SCE] for cyclopropanation than is $\mathbf{1}^{\bullet+}$. Whereas the less reactive stilbenes require several hours to achieve even the desired 5–10% conversion to cyclopropanated products when $\mathbf{1}^{\bullet+}$ is used, the desired conversions are achieved in approximately 1–2 min or less when $\mathbf{6}^{\bullet+}$ is used. Further, the same relatively more ionizable substrates (**2a**–**c**) which engender the curved portion of the Hammett–Brown plot discussed previously fail to undergo cyclopropanation at all. Although the catalyst is consumed, these stilbene substrates are recovered rather efficiently (>95%). It appears likely that these exergonic ionizations by $\mathbf{6}^{\bullet+}$ are extremely fast and produce such a high concentration of substrate cation radicals that the catalyst is quickly consumed by cation radical/cation radical reactions such as coupling. A similar result emerges even for the mild aminium salt catalyst $\mathbf{1}^{\bullet+}$ when the cyclopropanation of 4-methoxystilbene (E_p^{ox} = 0.816 V) is attempted.

The cyclopropanations of the remaining substrates using $\mathbf{6}^{\bullet+}$ as the catalyst are efficient, however, and their competition kinetics were studied (Table 2). The Hammett–Brown plot is nicely linear ($r^2 = 0.990$), but the ϱ value (-2.31) corresponds not to a thermodynamically controlled but to a kinetically

(17) The oxidation potentials of **1**, **6**, and **2** are 1.06,[17] and 1.59[12]V *vs* SCE, respectively.

(18) Schmidt, W.; Steckhan, E. *Chem. Ber.* **1980**, *113*, 577.

(19) The oxidation potential of **1** is greater than that of the benzyl radical (0.73 V) and much greater than that of the 4-methylbenzyl radical (0.51 V *vs* SCE).[15]

(20) Bellucci, G.; Bianchini, R.; Brown, R. S.; Slevocka-Tilk, H. *J. Am. Chem. Soc.* **1991**, *113*, 8012–8016.

Table 2. Relative Rate Constants for the Cyclopropanation of Stilbenes by Ethyl Diazoacetate Catalyzed by Tris(2,4-dibromophenyl)aminium Hexachloroantimonate

stilbene	k/k_0	stilbene	k/k_0
1. 3-methylstilbene	1.62	4. 4,4'-dichlorostilbene	0.31
2. stilbene	1.00	5. 3-chorostilbene	0.15
3. 4-chlorostilbene	0.50		

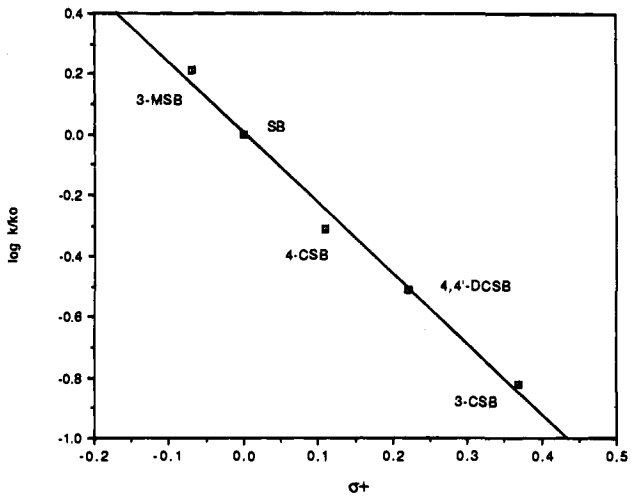


Figure 3. Hammett–Brown plot for the cyclopropanation of substituted *trans*-stilbenes by ethyl diazoacetate catalyzed by tris(2,4-dibromophenyl)aminium hexachloroantimonate ($\mathbf{6}^{\bullet+}$) in dichloromethane at 0 °C: $\varrho = -2.31$, $r^2 = 0.990$.

Scheme 3. Cation Radical Chain Mechanism for the Cyclopropanation of Stilbenes by Ethyl Diazoacetate Catalyzed by $\mathbf{6}^{\bullet+}$

1. $\mathbf{SB} + \mathbf{6}^{\ddagger} \longrightarrow \mathbf{SB}^{\ddagger} + \mathbf{6}$
2. $\mathbf{SB}^{\ddagger} + \mathbf{3} \longrightarrow \mathbf{5}^{\ddagger}$
3. $\mathbf{5}^{\ddagger} \longrightarrow N_2 + \mathbf{4}^{\ddagger}$
4. $\mathbf{4}^{\ddagger} + \mathbf{SB} \longrightarrow \mathbf{4} + \mathbf{SB}^{\ddagger}$

controlled ionization (Figure 3). This result is eminently plausible, since the reversal of ionization by neutral **6** is energetically very much less favorable than that by **1**. The ionization of stilbene by $\mathbf{6}^{\bullet+}$ is only very slightly endergonic ($\Delta G^0 = +0.09$ eV), but the observed ϱ value suggests a substantially exergonic ionization step. Consequently, a cation radical chain mechanism in which substrate ionization is effected by product cation radicals is indicated (Scheme 3). The latter hole transfer is undoubtedly exergonic and indeed is required to be for the operation of an efficient chain process.

Mechanistic Considerations. In the case of the cyclopropanations catalyzed by $\mathbf{1}^{\bullet+}$, the observation that substrate ionization is equilibrium controlled renders moot the mechanistic question of whether these substrates are ionized exclusively by $\mathbf{1}^{\bullet+}$ or product cation radicals or both. However, since the ionization by $\mathbf{1}^{\bullet+}$ controls the equilibrium supply of cation radicals, these reactions are appropriately considered to be catalytic, as opposed to chain, processes. The possibility that the equilibration of the stilbene cation radicals might occur by hole transfer between a stilbene cation radical and a neutral stilbene partner, incidentally, can be decisively dismissed by the following reasoning. The cyclopropanations catalyzed by $\mathbf{6}^{\bullet+}$ are rate controlled, i.e., they do not involve the equilibration of the cation radicals of the two competing substrates. Evidently, the rate of reaction of stilbene cation radicals with ethyl diazoacetate is much faster than hole transfer to a neutral stilbene molecule. Since the cyclopropanations involving $\mathbf{1}^{\bullet+}$ are run under identical conditions (apart from the catalyst) and since the same competing reactions are involved in this latter case (reaction with **3** *vs* hole transfer), it is evident that hole transfer equilibration cannot compete effectively with the reaction with ethyl diazoacetate.

For the substrate molecules (**2a–c**) for which kinetically controlled ionization prevails even for the cyclopropanations catalyzed by $\mathbf{1}^{\bullet+}$, the imprecision of the estimate of ϱ is too great to clearly distinguish the chain and catalytic mechanisms. However, the range of ϱ values which appear to be consistent with the data (−2.3 to −2.8) are more nearly compatible with an exergonic (chain) than a highly endergonic (catalytic) mechanism for ionization.

In the equilibrium-controlled ionizations of **2d–h** by $\mathbf{1}^{\bullet+}$, the rate-determining step of the cyclopropanation sequence must be subsequent to the ionization and presumably involves reaction with **3**. However, since the ϱ value (−5.17) rather closely approaches the estimated index for thermodynamic ionization (−5.4), there must be relatively little charge transfer to **3** in the transition state of this bimolecular reaction. The evident symmetry of the charge distribution in this transition state also suggests relatively little covalent bonding to **3**. An appropriate transition state model would therefore seem to be the ion molecule complex $\mathbf{2}^{\bullet+}/\mathbf{3}$.

Inner-Sphere *vs* Outer-Sphere Ionization. The kinetically controlled ionizations of the stilbene substrates by $\mathbf{6}^{\bullet+}$ and, for the more ionizable substrates, by $\mathbf{1}^{\bullet+}$ reveal relatively symmetrical positive charge accumulations on both aryl rings. This is nicely consistent with outer-sphere electron transfer and gives no indication of the development of covalent bonding to a specific alkene carbon of the stilbene substrate, which would seem to be implicit in the concept of inner-sphere electron transfer.

Summary. Mechanistic criteria for cation radical reactions have been developed and applied to the cyclopropanation of a series of *trans*-stilbenes (**2**) by ethyl diazoacetate (**3**) catalyzed by triarylaminium salts ($\mathbf{1}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$). For the less readily ionizable group of stilbenes, using the relatively mild catalyst tris(4-bromophenyl)aminium hexachloroantimonate ($\mathbf{1}^{\bullet+}$), the generation of substrate cation radicals in equilibrium with the reactants is decisively confirmed by demonstrating, *via* Hammett–Brown substituent effect studies, that the reactions involve the generation of a unit positive charge in an essentially symmetrical distribution over both aryl rings of the stilbene substrate. In the case of the more readily ionizable group of stilbene substrates, the ionization step reverts to kinetic control, as indicated both by the greatly diminished magnitude of ϱ and the observation that the reaction rates are independent of the concentration of **3**. The reactions of all of the stilbene substrates are subject to sharp rate retardation by adding neutral triarylamine **1**, as expected for an exergonic reversal of the highly endergonic ionization step. In the case of the more readily ionizable group of stilbenes, the conversion of a rate-controlled ionization to one which is at least partially under equilibrium control in the presence of added **1** also results in a rather dramatic enhancement of selectivity (i.e., enhanced substituent effects). When the cyclopropanations are carried out using the more potent catalyst tris(2,4-dibromophenyl)aminium hexachloroantimonate ($\mathbf{6}^{\bullet+}$), all of the reactive substrates exhibit rate-controlled ionization, and substituent effects indicate that the ionization step is exergonic, implicating a cation radical chain mechanism in which the stilbene substrate is ionized by a highly energetic product cation radical. These criteria not only rule

out the possibility of an electrophile-catalyzed, carbocation-mediated reaction mechanism, they also point specifically and directly to a cation radical mechanism. The elucidation of key aspects of the details of the cation radical mechanisms, including kinetic *vs* thermodynamic control of ionization and chain *vs* catalytic mechanisms, has also been achieved for these systems. Finally, an outer-shell electron-transfer mechanism is inferred for the kinetically controlled ionizations.

Experimental Section

Analysis. Proton magnetic resonance spectra were recorded on a General Electric QE-300 spectrometer as solutions in $CDCl_3$. Chemical shifts are reported in parts per million (ppm) downfield from the reference, tetramethylsilane (TMS). Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet. Analytic gas chromatographic (GC) analyses were performed on a Perkin-Elmer Model 8500 equipped with a flame ionization detector and a DB-1 (J & W Scientific, 30 m × 0.25 mm, 1 mm film thickness) capillary column using helium as a carrier gas. GC yields were calculated with the aid of a PE Nelson integrator, Model 1020 reporting integrator. Naphthalene was used as internal standard for all the quantitative analyses, and detector response factors were calculated for all the products. Low-resolution mass spectra (LRMS) were obtained on a Hewlett-Packard 5971A GC-MS spectrometer equipped with a DB-1 (15 m × 0.25 mm, 1 mm film thickness) capillary column.

Solvents and Reagents. Methylene chloride (CH_2Cl_2) was dried over phosphorus pentoxide (P_2O_5), dimethoxyethane and hexane were dried over CaH_2, and tetrahydrofuran (THF) was dried over Na/benzophenone. *cis*-Stilbene, ethyl diazoacetate (EDA), tris(4-bromophenyl)aminium hexachloroantimonate, and tris(*p*-bromophenyl)-amine were purchased from Aldrich Chemical Co. and used as received without further purification. *trans*-Stilbene was twice recrystallized from ethanol and dried *in vacuo* prior to use. The other stilbenes in this study were synthesized *via* a Grignard procedure (*vide infra*), except for *trans*-4,4′-dichlorostilbene, which was synthesized by a McMurry reaction. All of the stilbenes had been synthesized and characterized previously.[12,21]

Preparation of Tris(2,4-dibromophenyl)amine (6; Ar′$_3$N). A solution of 5.05 g (20.6 mmol) of triphenylamine in 20 mL of chloroform was placed in a 100 mL round-bottomed flask at room temperature. A solution of 7.0 mL (135.6 mmol) of bromine in 5 mL of chloroform was added to it slowly. The reaction mixture was stirred overnight at room temperature. Then, 30 mL of ethanol was added to the reaction mixture to give a precipitate. After evaporation of the volatile materials under reduced pressure, the title compound was recrystallized from ethanol/chloroform several times to give 13.2 g (89%, mp 226−227 °C; lit.[18] mp 216−218 °C) of Ar′$_3$N: ^{1}H NMR ($CDCl_3$) δ 7.72 (d, 3H, J = 3 Hz), 7.27 (dd, 3H, J = 3 Hz, 9 Hz), 6.73 (d, J = 9 Hz, 3H); LRMS *m/e* 724, 723, 722, 721, 720, 719 (M^+), 718, 644, 643, 642, 641, 640, 639, 638, 637, 562, 561, 560, 559, 154 (base).

Preparation of Tris(2,4-dibromophenyl)aminium Hexachloroantimonate (6$^{\bullet+}$; Ar′$_3$N$^{\bullet+}$). This compound was prepared according to the literature procedure.[18] A solution of 0.72 g (1.00 mmol) of tris-(2,4-dibromophenyl)amine in 5 mL of dry methylene chloride was placed in a 25 mL round-bottomed flask. A solution of 0.2 mL of antimony pentachloride in 2 mL of methylene chloride was added to it, and the reaction mixture was allowed to stand for 10 min. The reaction was instantaneous, and the deep green mixture which resulted was poured into 100 mL of dry hexane. The green precipitate was filtered off and washed thoroughly with dry hexane. The precipitate was dried at room temperature in vacuum overnight.

Preparation of *trans*-4,4′-Dichlorostilbene (DCSB). The title chemical was synthesized by the McMurry method.[22] A 10 g (34.5 mmol, Aldrich) sample of $TiCl_3(DME)_{1.5}$ and 10.00 g (153.0 mmol, Lancaster) of Zn−Cu couple were transferred quickly to a 250 mL round-bottomed flask containing 100 mL of dry dimethoxyethane (DME, dried over CaH_2) with nitrogen. The mixture was refluxed for 2 h to yield a black suspension. After cooling, a solution of *p*-chlorobenzaldehyde (1.93 g, 13.7 mmol) in 10 mL of DME was added slowly to the flask by a syringe. The reaction mixture was refluxed for 16 h. After being cooled to room temperature, the reaction mixture was diluted with hexane (200 mL) and filtered through a pad of Florisil. The filtrate was dried over $MgSO_4$, and the solvent was removed on a rotary evaporator to give 1.43 g (84%, mp 168−169 °C) of the title chemical: LRMS *m/e* 252, 250 (M^+), 248, 213, 212, 179, 178 (base), 177, 176, 88, 75, 74, 63, 51, 50.

General Procedure for the Grignard Method for Preparation of *trans*-Stilbenes. To a dry 250 mL round-bottomed flask equipped with a reflux condenser, stirrer, nitrogen inlet, and addition funnel were added 3.80 g (158 mmol) of dry magnesium turnings, 100 mL of dry THF, and an ice/water bath. A solution of 16.0 mL (139 mmol) of benzyl chloride in 30 mL of THF was slowly added from the addition funnel to the flask. After addition, the ice/water bath was removed, and the Grignard reagent was stirred for 1 h. Then, a solution of 75 mmol of an appropriate benzaldehyde in 10 mL of THF was added dropwise (*via* the addition funnel) to the Grignard reagent. After all of the aldehyde had been added, the reaction mixture was brought to gentle reflux for a period of 2 h and then allowed to cool to room temperature. The alkoxymagnesium bromide salt was hydrolyzed by dropwise addition of 6 M HCl until the aqueous solution was acidic to litmus paper. The layers were separated, and the aqueous layer was washed with 100 mL of diethyl ether several times. The combined ether layers were dried over anhydrous $MgSO_4$. After removal of the $MgSO_4$ and evaporation of the volatile materials under reduced pressure, the crude desired alcohol product was formed. The crude alcohol was placed in a 250 mL round-bottomed flask which was equipped with a stirrer, a nitrogen inlet, a reflux condenser, and 100 mL of pyridine. With stirring, 18 mL (193 mmol) of phosphorus oxychloride was slowly added *via* syringe through a rubber septum to the reaction mixture. After the addition was complete, the mixture was refluxed for 2 h and allowed to cool to room temperature. To this solution, 20 mL of water was slowly added, and the desired product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine solution. The ethereal solution was then dried over anhydrous $MgSO_4$. After removal of the $MgSO_4$ and evaporation of the volatile materials under reduced pressure, the product was purified by flash silica gel column chromatography with hexane/ethyl acetate (9:1 v/v) eluent and recrystallized from ethanol several times.

General Procedure for the Preparation of the Cyclopropanation Products of *trans*-Stilbenes Catalyzed by Ar$_3$N$^{\bullet+}$ (1$^{\bullet+}$). Approximately 30 mol % of tris(4-bromophenyl)aminium hexachloroantimonate was weighed into a 25 mL volumetric flask containing a magnetic stirrer. The flask was then capped with a septum, immersed in an ice/water bath, and purged with nitrogen. Methylene chloride (15 mL) was added, and the solution was stirred for 5 min. To this was then added (syringe) a solution containing 0.5 mmol of appropriate stilbenes and an excess (5-fold) of EDA in methylene chloride (10 mL). After an appropriate interval (3 h, or until the color of the aminium salts disappeared), the reaction was quenched with 3 mL of saturated methanol potassium carbonate. Wear (20 mL) and methylene chloride (10 mL) were added, and the organic layer was separated and dried ($MgSO_4$). After removal of the $MgSO_4$ and evaporation of the volatile materials under reduced pressure, the cyclopropanation products were purified by TLC (hexane/ethyl acetate, 9:1, v/v) and characterized (NMR, LRMS). In the case of stilbene and the less reactive substituted stilbenes, the reactions are relatively slow, and high conversions were not attained in the reaction times used. The faster reactions involving stilbene with *p*-methyl substituents resulted in good conversions.

Ethyl *trans*-2,3-bis(4-methylphenyl)cyclopropanecarboxylate (4a): isolated yield 78%; ^{1}H NMR ($CDCl_3$) δ 7.18 (m, 4 H), 7.03 (m, 4 H), 3.90 (q, 2 H), 3.08 (dd, 1 H), 2.79 (dd, 1 H), 2.30 (dd, 1 H), 2.28 (s, 3 H), 2.24 (s 3 H), 0.99 (t 3 H); LRMS *m/e* 294 (M^+), 265, 249, 222, 221, 220, 205, 203, 129 (base).

Ethyl *trans*-2-(3,4-dimethylphenyl)-3-phenylcyclopropanecarboxylate (4b): isolated yield 72% (two isomers, with the carboxyl group *syn* and *anti* to the phenyl substituent); ^{1}H NMR ($CDCl_3$) δ 7.25−7.06

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(m, 18 H), 3.81 (m, 2 H), 3.14 (m, 2 H), 2.75 (m, 2 H), 2.22 (m, 2 H), 2.15 (s, 3 H), 2.10 (s, 3 H), 1.11 (t, 3 H), 1.04 (t, 3 H); LRMS *m/e* 294 (M^+), 265, 249, 222, 221, 220, 205, 203, 129 (base).

Ethyl *trans*-2-(4-methylphenyl)-3-phenylcyclopropanecarboxylate (4c): isolated yield 68% (*syn* and *anti* isomers); ^{1}H NMR ($CDCl_3$) δ 7.19−7.09 (m, 18 H), 3.87 (m, 4 H), 3.01 (m, 2 H), 2.72 (m, 2 H), 2.26 (m, 2 H), 2.20 (s, 3 H), 2.15 (s, 3 H), 1.00 (t, 6 H); LRMS *m/e* 280 (M^+), 251, 235, 207 (base), 189, 129.

Ethyl *trans*-2,3-bis(3-methylphenyl)cyclopropanecarboxylate (4d): isolated yield 78%; ^{1}H NMR ($CDCl_3$) δ 7.18−7.06 (m, 8 H), 3.89 (q, 2 H), 3.11 (dd, 1 H), 2.72 (dd, 1 H), 2.29 (dd, 1 H), 2.20 (s, 3 H), 2.15 (s, 3 H), 1.04 (t, 3 H); LRMS *m/e* 294 (M^+), 265, 249, 222, 221, 220, 205, 203, 129 (base).

Ethyl *trans*-2-(3-methylphenyl)-3-phenylcyclopropanecarboxylate (4e): isolated yield 25% (*syn* and *anti* isomers); ^{1}H NMR ($CDCl_3$) δ 7.23−7.15 (m, 18 H), 3.92 (m, 4 H), 3.09 (m, 2 H), 2.70 (m, 2 H), 2.21 (m, 2 H), 2.19 (s, 3 H), 2.16 (s, 3 H), 1.04 (t, 6 H); LRMS *m/e* 280 (M^+), 251, 235, 207 (base), 189, 129.

Ethyl *trans*-2,3-diphenylcyclopropanecarboxylate (4f): isolated yield 18%; ^{1}H NMR ($CDCl_3$) δ 7.30 (s, 10 H), 3.93 (q, 2 H, J = 7.5 Hz), 3.20 (dd, 1 H), 2.86 (1 H), 2.25 (dd, 1 H), 0.99 (t, 3 H, J = 7.5 Hz); LRMS *m/e* 266 (M^+), 237, 221, 193 (base), 115, 91.

General Procedure for the Preparation of the Cyclopropanation Products of *trans*-Stilbenes Catalyzed by $Ar'_3N^{\bullet+}$ ($6^{\bullet+}$). Approximately 3−5 mol % of tris(2,4-dibromophenyl)aminium hexachloroantimonate was weighed into a 25 mL volumetric flask containing a magnetic stirrer. The flask was then capped with a septum, immersed in an ice/water bath, and purged with nitrogen. Methylene chloride (15 mL) was added, and the solution was stirred for 5 min. To this was then added (syringe) a solution containing 0.5 mmol of appropriate stilbenes and an excess (5-fold) of EDA in methylene chloride (10 mL). After an appropriate interval (30 min or until the color of the aminium salts disappeared), the reaction was quenched with 3 mL of saturated methanolic potassium carbonate. Water (20 mL) and methylene chloride (10 mL) were added, and the organic layer was separated and dried ($MgSO_4$). After removal of the $MgSO_4$ and evaporation of the volatile materials under reduced pressure, the cyclopropanation products were purified by TLC (hexane/ethyl acetate, 9:1, v/v) and characterized (NMR, LRMS).

Ethyl *trans*-2-(4-chlorophenyl)-3-phenylcyclopropanecarboxylate (4g): isolated yield 18% (*syn* and *anti* isomers); ^{1}H NMR ($CDCl_3$) δ 7.24−7.33 (m, 18 H), 3.97 (m, 4 H), 3.17 (m, 2 H), 2.89 (m, 2 H), 2.40 (m, 2 H), 1.07 (t, 3 H), 1.03 (t, 3 H); LRMS *m/e* 300 (M^+), 255, 229, 228, 227 (base), 226, 225, 193, 192, 191, 190, 189, 165, 151, 149, 116, 115, 91, 89, 77, 63, 51, 50.

Ethyl *trans*-2,3-bis(4-chlorophenyl)cyclopropanecarboxylate (4h): isolated yield 15%; ^{1}H NMR ($CDCl_3$) δ 7.43 (m, 4 H), 7.32 (m, 4 H), 4.15 (q, 2 H), 3.15 (dd, 1 H), 2.85 (dd, 1 H), 2.36 (dd, 1 H), 1.25 (t, 3 H); LRMS *m/e* 337, 335 (M^+), 300, 290, 264, 263, 262 (base), 255, 229, 228, 227, 225, 193, 192, 191, 190, 189, 165, 151, 149, 116, 115, 91, 89, 77, 63, 51, 50.

Ethyl *trans*-2-(3-chlorophenyl)-3-phenylcyclopropanecarboxylate: isolated yield 15% (*syn* and *anti* isomers); ^{1}H NMR ($CDCl_3$) δ 7.33−7.24 (m, 18 H), 3.97 (m, 4 H), 3.19 (m, 2 H), 2.85 (m, 2 H), 2.42 (m, 2 H), 1.08 (t, 3 H), 1.04 (t, 3 H); LRMS *m/e* 300 (M^+), 255, 229, 228, 227 (base), 226, 193, 192, 191, 190, 189, 165, 151, 149, 115, 91, 89, 65, 63.

General Procedure for the Competitive Cyclopropanation of Stilbenes with Ethyl Diazoacetate (EDA) Catalyzed by Aminium Salts. Approximately 2−30 mol % of tris(4-bromophenyl)aminium hexachloroantimonate or 0.4−0.5 mol % of tris(2,4-dibromophenyl)-aminium hexachloroantimonate was weighed into a 10 mL volumetric flask containing a magnetic stirrer. The flask was then capped with a septum, immersed in an ice/water bath, and purged with nitrogen. Methylene chloride (5 mL) was added, and the solution was stirred for 5 min. To this was then added (syringe) a solution containing equimolar amounts (*ca.* 0.12 mmol) of stilbenes and an excess (2−3-fold) of EDA in methylene chloride (5 mL). After an appropriate interval (timed so that the conversion was less than 10%), the reaction was quenched in a 0.5 mL aliquot of the reaction mixture with 1 mL of satured methanolic potassium carbonate. Water (5 mL) and methylene chloride (2 mL) were added, and the organic layer was separated and dried ($MgSO_4$). After removal of $MgSO_4$, the competitive ratios were determined and corrected for varying response factors. In all cases, the results of at least three runs were averaged. The resulting relative rate ratios were cross-checked by pairing each substrate with at least two other reaction partners. At the 10% conversion to product level, the mass balances were 98−99%.

Selectivity Enhancement by Added Triarylamine 1. Competition kinetic runs were carried out as described before, except for the presence of added neutral triarylamine. The runs with added triarylamine were slowed sufficiently that higher concentrations of the aminium salt catalyst were used in order to obtain measurable conversions:

compound	$[Ar_3N^{\bullet+}]$, mol %	$[Ar_3N]$, mol %	k/k_0
4-MSB/SB	3.3	0.0	9.2
4-MSB/SB	10.0	107.0	20.8
4,4′-DMSB/4-MSB	1.6	0.0	6.3
4,4′-DMSB/4-MSB	5.1	100.0	9.5

Effect of the Concentration of Ethyl Diazoacetate upon the Absolute Reaction Rates of Cyclopropanation. The conversions to cyclopropane products were measured for samples, run in parallel and for identical reaction times, which were of identical composition, except for the concentration of ethyl diazoacetate:

substrate	[**3**], M	convn (%)	time (s)
4,4′-DMSB	0.064	8.4	30
4,4′-DMSB	0.104	8.6	30
4-MSB	0.064	1.4	30
4-MSB	0.104	1.5	30
SB	0.130	8.1	600
SB	0.064	5.8	1200
SB	0.130	11.2	1200

Acknowledgment. The authors thank the NSF (CHE-9123292) for support of this research.

JA950425Z