# Is Hole Transfer Involved in Metalloporphyrin-Catalyzed Epoxidation?

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**Abstract:** The possibility of a hole-transfer mechanism for the epoxidation of alkenes catalyzed by metalloporphyrins (MP) has been investigated. In the first approach, the results of MP-catalyzed epoxidation of a series of substrates were compared to the corresponding results of epoxidation under conditions where cation radicals are demonstrably formed (using a triarylaminium salt catalyst). In sharp contrast to the MP-catalyzed epoxidations (using M = Mn), the hole-catalyzed epoxidations do not generate carbonyl compounds and alcohols as byproducts and are rigorously stereospecific. These results are of interest primarily in that they provide support for the assumption that cation radicals can be efficiently and stereospecifically epoxidized by appropriate oxygen-transfer agents. However, the differences in product composition and stereochemistry for MP- *vs* hole-catalyzed epoxidation cannot be construed mechanistically to rule out a cation radical mechanism for the former, especially because the oxygen-transfer agents are different in the two reaction systems. In a second, and more rigorous, approach, a careful search for transient cation radical intermediates in MP-catalyzed epoxidations (using M = Mn and Fe) was carried out using newly developed cation radical probe reactions. Cation radical intermediates were, in fact, not detected and, if involved, must be extremely short lived ($<2 \times 10^{-12}$ s). The results of this work, taken as a whole, are reasonably construed to suggest that, even for the relatively easily ionizable alkene functionalities present in many of the probe substrates, a hole-transfer mechanism is probably not operative in MP-catalyzed epoxidations.

The mechanism of epoxidation catalyzed by metalloporphyrins (MP) is of exceptionally broad interest but remains controversial.[1-5] Of the four basic mechanisms usually considered, only the stepwise radical addition mode (Scheme I) appears to have been rigorously excluded.[6] The mechanisms which remain viable are (1) concerted, (2) stepwise *via* a carbocation, and (3) stepwise *via* a metallaoxetane (possibly equilibrating with a carbocation). To complicate matters further, a hole-transfer (HT; also sometimes termed an electron transfer, ET) variant of each of these three mechanisms potentially exists and has received serious consideration.[2,5-9] According to this concept, an electron is transferred (ET) from the alkene substrate to the metal oxene (MPO), giving a substrate cation radical, which could then react further *via* one or more of the three basic mechanisms previously listed. An equivalent description, which is preferred here, is the transfer of a hole[10] from the oxidant to the alkene. In the case where the hole is initially on the porphyrin ligand[11] of the oxene, the HT description is more precise and still remains viable when the hole is on the metal. Our interest in this complex mechanistic issue derives generally from a continuing involvement in the catalytic chemistry of cation radicals[12,13] and, more specifically, from recent observations of authentic cation radical mediated (hole catalyzed) epoxidations.[14] These observations establish for the first time that cation radicals can be efficiently and stereospecifically epoxidized by appropriate monooxygen-transfer agents, and they invite comparison with the results of corresponding MP-catalyzed epoxidations. To search more rigorously for cation radical intermediates, several new cation radical probes, based upon rapid intramolecular hole transfer and intramolecular cyclizations, have been designed and applied to MP-catalyzed epoxidation.

## Results and Discussion

Hole-catalyzed epoxidation (Scheme II) requires a relatively ionizable (e.g., conjugated) $\pi$ substrate, but within this context it is efficient and extraordinarily site specific and regiospecific. With tris(4-bromophenyl)aminium hexachloroantimonate ($\mathbf{1}^{\bullet+}$) as the catalyst, either selenium dioxide or benzeneseleninic anhydride (BSA) as the oxidant, and dichloromethane as the solvent, epoxidation reactions are complete within 10 min (BSA) or 1 h ($SeO_2$) at 0 °C. Yields are typically in the 80% range for suitably ionizable substrates. The MP-catalyzed epoxidations were carried out using (5,10,15,20-tetraphenylporphinato)-manganese(III) chloride as the catalyst and iodosylbenzene as the oxidant in dichloromethane solution. These latter reactions were carried out to *ca.* 10% conversion. The results of corresponding MP- and hole-catalyzed epoxidations of six substrates are displayed for comparison in Table I. The salient observation is that the hole-catalyzed epoxidations are extremely clean, yielding no detectable quantities of other oxidized materials. In contrast, the MP-catalyzed epoxidations, as is well-known, all yield alcohols or carbonyl compounds or both as byproducts. Also,

(1) Groves, J. T.; Nemo, T. E. *J. Am. Chem. Soc.* **1983**, *105*, 5786–5791.
(2) Ortiz de Montellano, P. R. *Cytochrome P-450: Structure, Mechanism, and Biochemistry*; Plenum: New York, 1986.
(3) He, G.-X.; Mei, N.-Y.; Bruice, T. C. *J. Am. Chem. Soc.* **1991**, *113*, 5644–5650.
(4) Collman, J. P.; Hampton, P. D.; Brauman, J. I. *J. Am. Chem. Soc.* **1990**, *112*, 2986–2998.
(5) Traylor, T. G.; Miksztal, A. R. *J. Am. Chem. Soc.* **1989**, *111*, 7443–7448.
(6) Castellino, A. J.; Bruice, T. C. *J. Am. Chem. Soc.* **1988**, *110*, 7512–7519.
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(9) Traylor, T. G.; Xu, F. *J. Am. Chem. Soc.* **1988**, *110*, 1953–1958.
(10) Johnson, M. D.; Miller, J. R.; Green, N. D.; Closs, G. L. *J. Phys. Chem.* **1989**, *93*, 1173.
(11) Depending upon the nature of the metal, the specific porphyrin ligand, and perhaps other factors, the hole on the metalloporphyrin oxidant can reside upon the organic ligand or the metal: Groves, J. T.; Haushalter, R. C.; Nakamura, M.; Nemo, T. E.; Evans, B. J. *J. Am. Chem. Soc.* **1981**, *103*, 2884–2886.
(12) Bauld, N. L. *Advances in Electron Transfer Chemistry*; Mariano, P., Ed.; JAI Press: Greenwich, 1992; *2*, pp 1–66.
(13) Bauld, N. L. *Tetrahedron* **1989**, *45*, 5307–5363.
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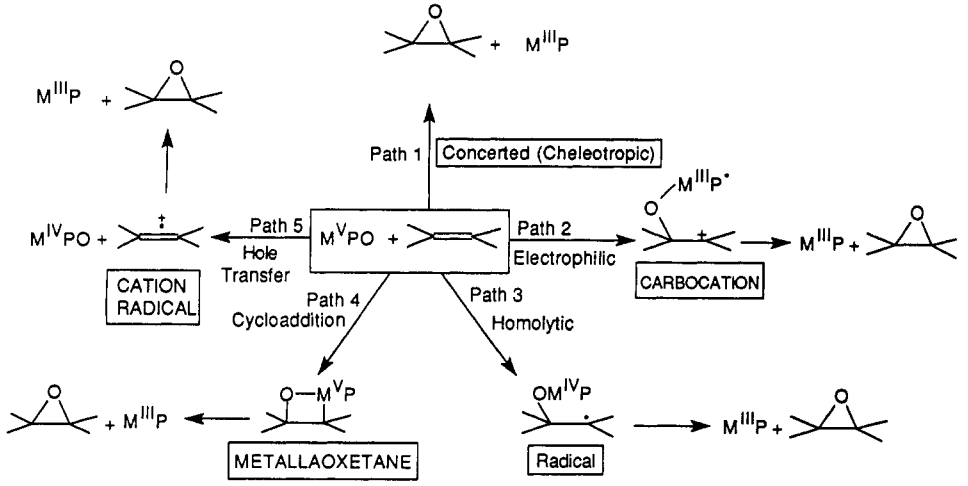
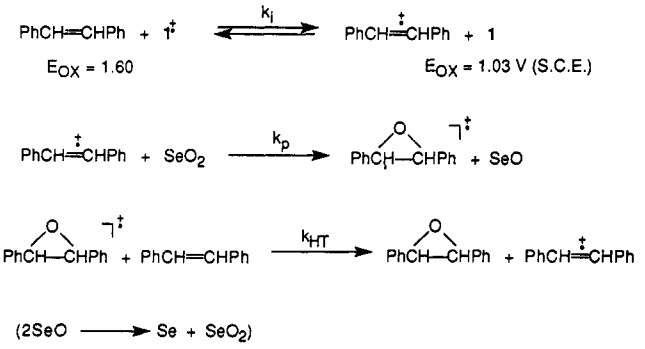
**Scheme I.** Possible Mechanisms for Metalloporphyrin-Catalyzed Epoxidation[a]




[a] $M^{III}P$ = metalloporphyrin; $M^{V}PO$ = oxidized metalloporphyrin (oxene).

**Scheme II.** Proposed Mechanism of Aminium Salt (Hole) Catalyzed Epoxidation of Stilbene by Selenium Dioxide[a]




[a] As shown, the reaction is a chain process. A plausible alternative is the classic catalytic mechanism in which the epoxide chain radical transfers its hole to the neutral form (**1**) of the hole catalyst, regenerating $\mathbf{1}^{\bullet+}$.

*cis*-stilbene is partially isomerized to the *trans* isomer, and the epoxidation is far from stereospecific. Hole-catalyzed epoxidation of the stilbenes using the more soluble oxidant (BSA) is completely stereospecific, and no *c*/*t* isomerization is observed. These latter results demonstrate that *cis*-stilbene cation radicals are configurationally quite stable, a conclusion firmly supported by spectroscopic studies.[16] This species therefore cannot be invoked to explain the geometric isomerization observed in the MP-catalyzed reaction of *cis*-stilbene. Since free radical intermediates generated by homolytic addition have already presumably been excluded,[6] a carbocation pathway appears to be the most logical path for the isomerization. Carbocation intermediates are already considered to be involved in the rearrangement pathways leading to the carbonyl-containing byproducts.[5,17] Consequently, both minor reaction channels involving the $\pi$ bond now firmly appear to involve carbocations. A third minor channel, hydroxylation, does not directly involve the double bond and is now well established as a homolytic abstraction process.[18] Unfortunately, the rather sharp differences which exist in the product distributions and stereochemistries of hole- and MP-catalyzed epoxidation cannot be rigorously construed to rule out a cation radical mechanism for the latter, especially because the oxygen-transfer agents in the two reaction systems are quite different.

**Table I.** Comparison of Products of Corresponding MP- and HT-Catalyzed Oxidations of Substrates in Dichloromethane Solutions

| substrate | method | products (rel yield,[a] %) |
|---|---|---|
| *trans*-stilbene | HTC[b] | *trans*-epoxide (100) |
| | MP[c] | *trans*-epoxide (68); 2,2-diphenylethanal (18); benzaldehyde (12); deoxybenzoin (2) |
| *cis*-stilbene | HTC | *cis*-epoxide (100) |
| | MP | *cis*-epoxide (56); *trans*-epoxide (30); 2,2-diphenylethanal (7); deoxybenzoin (2.5); *trans*-stilbene (4.5) |
| *trans*-1-propenylbenzene | HTC | epoxide (100) |
| | MP | epoxide (82); cinnamyl alcohol (8); benzaldehyde (10) |
| 1,1-diphenylethene | HTC | epoxide (100) |
| | MP | epoxide (91); 2,2-diphenylethanal (9) |
| styrene | HTC | epoxide (100) |
| | MP | epoxide (84%); phenylethanal (16) |
| indene | HTC | epoxide (100) |
| | MP | epoxide (94.5); 7-indenol (5.5) |

[a] Yield relative to total of all oxidized products; a 100% yield signifies that no other oxygenated products are detected in amounts of 1% or greater. [b] HTC = hole transfer chain (hole) catalyzed: $\mathbf{1}^{\bullet+}$, benzeneseleninic anhydride, $CH_2Cl_2$, 0 °C. [c] MP = metalloporphyrin = (5,10,15,10-tetraphenylporphinato)manganese(III) chloride.

**Regioselectivity.** The existence of a correlation between substrate ionizability and reactivity toward MP-catalyzed epoxidation is well established and is at least formally consistent with an HT mechanism.[5] However, non-HT mechanisms in which the transition state has developed some degree of HT (i.e., cation radical) character are equally compatible with the data and may actually be more consistent with the modest sensitivity of MP-catalyzed epoxidation to substrate ionizability. The hole-catalyzed epoxidation of conjugated dienes provides the first opportunity to compare site selectivity and radioselectivity in hole- and MP-catalyzed epoxidation. With 4-isopropenyl-1-vinylcyclohexene as the substrate (**2**; Scheme III), hole-catalyzed epoxidation occurs exclusively on the more ionizable, conjugated diene moiety.[14] The reaction is also 100% regiospecific for the more highly substituted, endocyclic double bond. Similar regioselections have been observed in hole-catalyzed Diels–Alder

(16) It should be noted, however, that MP-catalyzed epoxidations of the stilbenes with M = Fe tend to be more stereospecific than those which use Mn.

(17) Castellino, A. J.; Bruice, T. C. *J. Am. Chem. Soc.* **1988**, *110*, 158–162.

(18) Bowry, V. W.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1991**, *113*, 5687–5698.

(19) Garrison, J. M.; Ostovic, D.; Bruice, T. C. *J. Am. Chem. Soc.* **1989**, *111*, 4960.

(20) Jorgensen, K. A.; Schiott, B. *Chem. Rev.* **1990**, *90*, 1483–1506.

(21) This interaction could, for example, explain the greater stereospecificity of stilbene epoxidation by iron porphyrin catalysts.

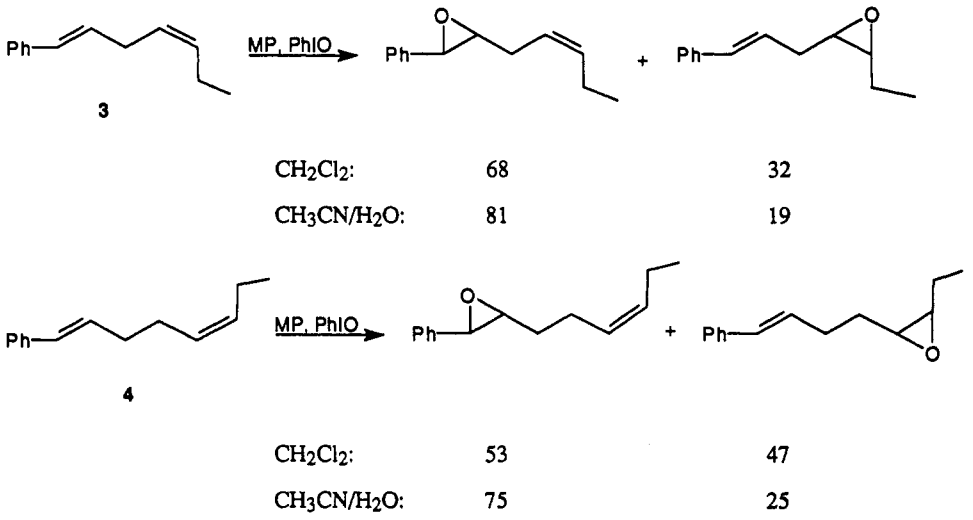
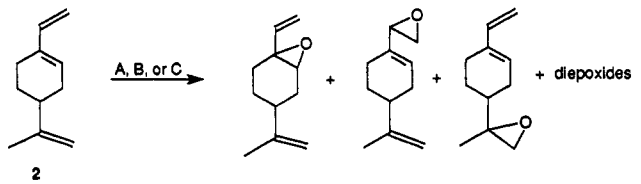



**Figure 1.** Results of metalloporphyrin-catalyzed epoxidations of the intramolecular hole transfer probe substrates.

**Scheme III.** The Regiochemistry and Site Selectivity of Aminium Salt Catalyzed and Metalloporphyrin-Catalyzed Epoxidation Contrasted to *m*-Chloroperbenzoic Acid Epoxidation




| | | | | |
|---|---|---|---|---|
| A = $Ar_3N^{\ddagger}$ | 100 | 0 | 0 | 0 |
| B = MP | 75 | 25 | 0 | 0 |
| C = MCPBA | 36 | 10 | 29 | 25 |

reactions and have been attributed to the preference of a diene cation radical for reaction at the terminus of highest hole density.[22] MP-catalyzed epoxidation of **2**, like the hole-catalyzed reaction, is also highly site selective, again preferring the conjugated diene moiety. The regiochemical preference is qualitatively the same as for hole-catalyzed epoxidation, but the preference is now much more modest (3:1). In contrast, *m*-chloroperbenzoic acid (MCPBA) epoxidation of **2** is quite unselective and also produces large amounts of bis(epoxides). While these results are not mechanistically definitive, they demonstrate interesting parallels between both site selectivity and regioselectivity in hole- and MP-catalyzed epoxidation which are consistent with the development of HT character in the transition state of MP-catalyzed epoxidation.

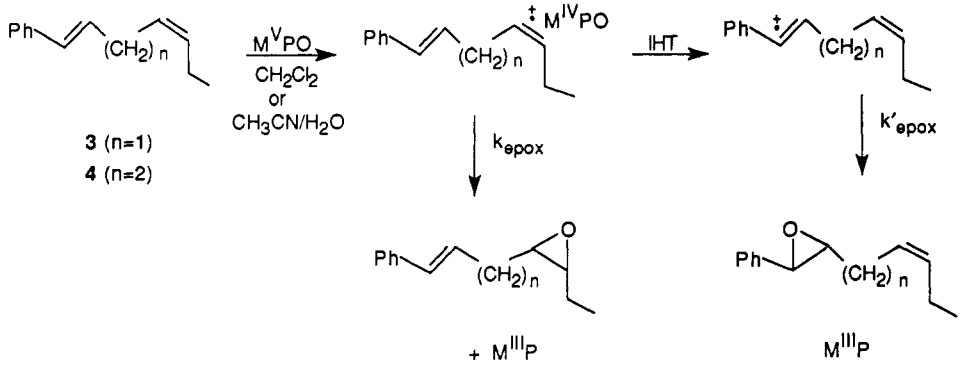
**Intramolecular Hole Transfer (IHT) as a Probe for Cation Radical Intermediates.** The quasi-unimolecular context of MP-catalyzed epoxidation and the unique nature of the oxidant (MPO) differentiate this reaction from the intermolecular oxidation of substrate cation radicals by selenium dioxide or benzeneseleninic anhydride. Inferences concerning the hypothetical HT mechanism of MP-catalyzed epoxidation based on comparative studies, while informative, are necessarily tentative. The most direct and potentially decisive means of investigating the hypothetical HT mechanism would appear to involve the use of cation radical probes. Two basic types of probes have been devised and applied in this work. The first approach is based upon the phenomenon of rapid, exoergic intramolecular hole transfer (IHT). Dienes **3** and **4** (Scheme IV) were selected as the specific probe substrates for this study on the basis of the following strategy. The reactivity of *trans*-alkenes in MP-catalyzed epoxidation is at least roughly correlated with substrate ionization potential, but *cis*-alkenes are typically much more reactive than the corresponding *trans*-alkenes as a result of greater ease of coordination with MPO.[1,5,9] Consequently, simple *cis*-alkenes are often more reactive than much more easily ionizable *trans* substrates.[9] For example, *cis*-2-pentene has been reported to be *ca.* 8 times as reactive as *trans*-β-methylstyrene. In the present study, the relative reactivity of *cis*-2-heptene and *trans*-β-methylstyrene toward MPO was found to be 9:1. These arguments suggest that the *cis*-alkene moieties of **3** and **4** should be much more reactive than the *trans*-β-alkylstyrene moieties. In fact, a more apt comparison is actually provided by the relative epoxidation rates of *cis*-2-octene and *trans*-1-hexenylbenzene (>50:1), since the *trans*-β-alkyl group in **3** and **4** is sterically larger than methyl. If, then, the *cis*-alkene moiety preferentially complexes with MPO and a *cis*-alkene cation radical is formed as an intermediate, IHT to the much more ionizable styrene moiety is possible. This hole transfer is *ca.* 0.4 eV exergonic and should therefore be relatively fast.[23] If IHT is faster than oxygen transfer to the hypothetical cation radical, epoxidation should take place exclusively on the styrene moiety.

The MP-catalyzed epoxidation (M = Mn; P = 5,10,15,20-tetraphenylporphyrin) of **3** in $CH_2Cl_2$ yields a 68:32 mixture of the epoxides, slightly preferring oxidation of the styrene moiety (Figure 1). The possibility that IHT is occurring at a rate competitive with oxygen transfer is rendered unlikely by the observation that **4** also yields a very similar epoxide ratio and that solvent polarity has only a small effect on the epoxide composition in either case. The rate of hole transfer, of course, should be strongly dependent upon hole-transfer distance and solvent polarity.[10] Instead, the data appear to suggest that intramolecular site selectivity may differ markedly from the intermolecular selectivity modeled by *cis*-2-octene and β-alkylstyrenes. The modest preference for the *trans*-β-alkylstyrene moiety in the intramolecular context could, e.g., result from the circumstance that once the bifunctional substrate has coordinated to the MPO *via* the *cis*-alkene moiety, further coordination of the styrene moiety to the MPO is assisted by an entropy effect. Epoxidation could then occur at either double bond and might, because of the ionizability factor, now prefer the styrene moiety. The absence of any substantial dependence of the epoxide composition upon HT distance (increased in **4**) and solvent polarity suggests that HT, if it occurs at all, is slow relative to oxygen transfer under all of the pertinent conditions. Since IHT is not detected by these probes, the presence of cation radical intermediates is not decisively affirmed. However, in order to negate

(22) Bellville, D. J.; Bauld, N. L. *J. Am. Chem. Soc.* **1982**, *104*, 2665–2667.

(23) $E_{1/2}$[(*Z*)-2-octene)] = 2.3 V *vs* SCE: Shono, T. *Electroorganic Chemistry as a New Tool in Organic Synthesis*; Springer-Verlag: New York, 1984; p 9. $E_{1/2}$(β-methylstyrene) = 1.93 V: Arai, T.; Sakurai, H.; Tokumaru, K.; Kobayashi, T. *Denki Kagaku Øyobi Kogyo Butsuri Kagaku* **1982**, *50*, 201.

**Scheme IV.** Intramolecular Hole Transfer Probes: Hypothetical Hole-Transfer Mechanism of MP-Catalyzed Epoxidation[a]




[a] IHT = intramolecular hole transfer (0.4 eV exoergic); $M^{V}PO$ = oxene (from MP + PhIO); $M^{IV}PO$ = reduced oxene; $M^{III}P$ = MP = metalloporphyrin; M = Mn; P = 5,10,15,20-tetraphenylporphine and tetrakis(2,6-dichlorophenyl)porphine.

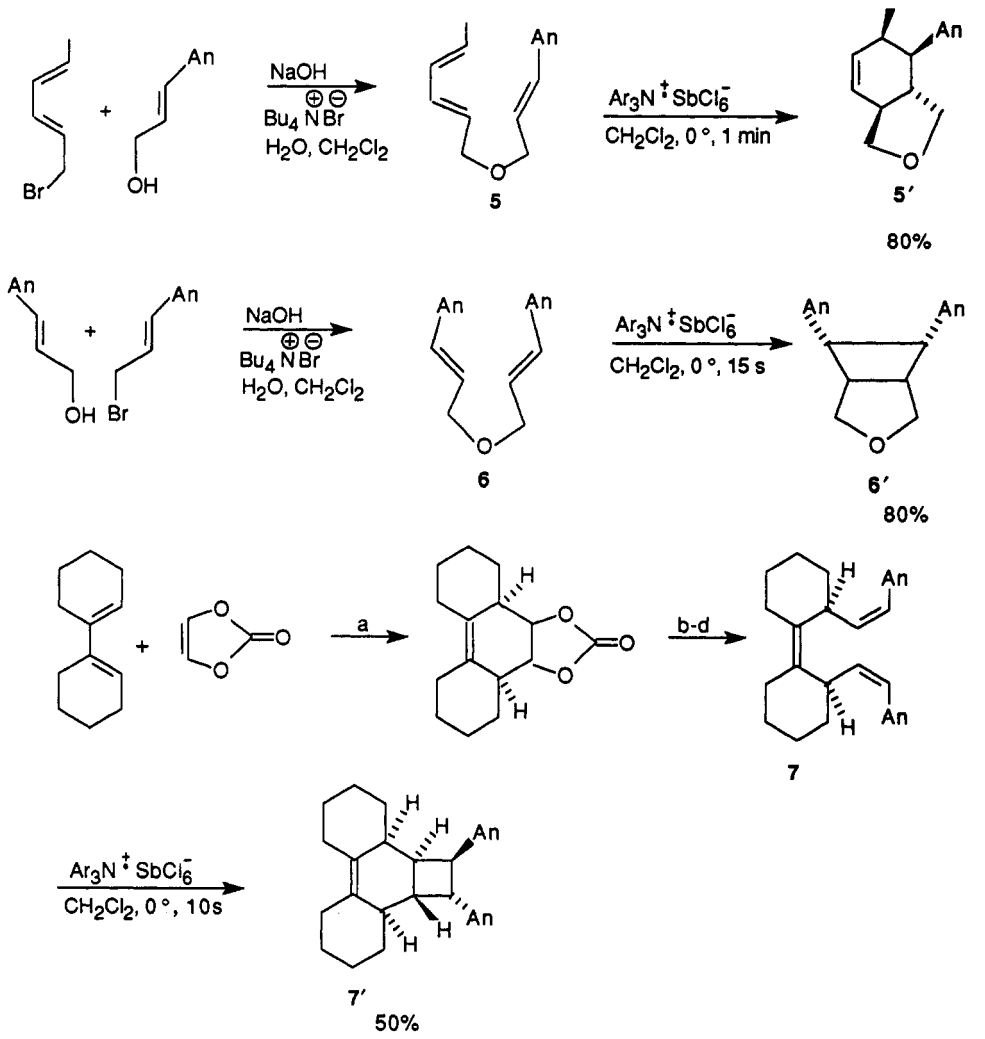
the possibility of a cation radical intermediate the probe reaction (in this case, IHT) would have to be competitive with a hypothetical oxygen-transfer reaction which, *a priori*, could have a maximum rate constant approaching $10^{13}$ $s^{-1}$. Depending upon the sensitivity with which the probe reactions can be detected, this requirement could probably be fulfilled by probe reactions in the $10^{10}$–$10^{12}$-$s^{-1}$ range. In principle, the rate of exoergic hole transfer could be calculated from the Marcus equation if the intrinsic activation energy ($\Delta G_0^*$) and the free energy change ($\Delta G_0'$) of the specific hole transfer were known.[24] Unfortunately, the former quantity is not known for hole transfers similar to that under consideration, and the substantial variability in $\Delta G_0^*$ values from system to system would appear to preclude a reliable estimate of the desired rate constant. Consequently, although cation radicals are not detected, only the existence of relatively long-lived or free cation radicals can be decisively ruled out. It is further suggested by this work that intramolecular selectivities can differ sharply from intermolecular selectivities in metalloporphyrin-catalyzed epoxidations.

**Intramolecular Cycloaddition Probes.** Potentially the most sensitive chemical detection of cation radical intermediates should be provided by probe reactions which are uniquely undergone by cation radicals. The extraordinarily low activation energies of many cation radical/neutral cycloadditions, including both Diels-Alder and cyclobutanation reactions, suggest the possibility that intramolecular versions of these cycloadditions might be exploited as sensitive and versatile cation radical probes.[12,13] The mild conditions of MP-catalyzed epoxidation would, of course, assure that such cycloadditions do not occur thermally. The rate constant for the intermolecular Diels-Alder addition of the 1,3-cyclohexadiene cation radical to neutral 1,3-cyclohexadiene has been found to be $3 \times 10^8$ $M^{-1}$ $s^{-1}$, only a factor of 60 less than the diffusion-controlled rate.[25] Intramolecular versions of both cation radical Diels-Alder[26] and cyclobutanation[27] reactions have also been observed and inferred to be unusually facile. Substrates **5** and **6** were selected for development as cation radical probes on the basis of considerations of synthetic accessibility and reactivity. Both are conveniently prepared by phase-transfer-catalyzed coupling of readily available alcohols and bromides (Scheme V). Although the probe reaction of **6** (cyclobutanation) would appear to be inherently less favorable than that of **5** (Diels-Alder addition), it is significant that the trapping moiety of $\mathbf{6}^{\bullet+}$ (a neutral moiety of the *trans*-anethole type) is expected to be much more reactive toward a cation radical moiety than is the neutral diene moiety of $\mathbf{5}^{\bullet+}$. In both instances the cation radical moiety is of the *trans*-anethole type. Further, $\mathbf{5}^{\bullet+}$ but not $\mathbf{6}^{\bullet+}$ requires prior *s-trans* to *s-cis* conformational isomerization of the diene moiety. The barrier toward this isomerization is undoubtedly greater than the torsional barriers to the other two conformational adjustments required for intramolecular cycloaddition in both $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$, which are *anti* to *gauche* conversions with respect to the two carbon–oxygen single bonds. In order to further minimize conformational contributions to the activation free energy of cyclization the preorganized probe (**7**) was also synthesized (Scheme V). The efficient cyclizations of $\mathbf{5}^{\bullet+}$–$\mathbf{7}^{\bullet+}$ were then characterized synthetically under standard aminium salt conditions [tris(4-bromophenyl)aminium hexachloroantimonate ≡ $\mathbf{1}^{\bullet+}$, $CH_2Cl_2$, 0 °C].[12,13] Finally, the exceptionally fast and well-characterized cyclodimerization of the 1,3-cyclohexadiene cation radical ($\mathbf{8}^{\bullet+}$) was also adopted as a *bimolecular* cation radical probe reaction.

The rate of the intramolecular cycloaddition of $\mathbf{5}^{\bullet+}$ was estimated by means of a quenching study under photosensitized electron-transfer conditions, using 1,4-dicyanobenzene as the sensitizer, 1,2,4-trimethoxybenzene as the quencher, and acetonitrile as the solvent (Scheme VI). These conditions, and in particular this quencher, had previously been used to estimate the rate constant for the cyclodimerization of *trans*-anethole, and it was considered that the cation radical moieties of $\mathbf{5}^{\bullet+}$–$\mathbf{7}^{\bullet+}$ should be modeled quite well by the *trans*-anethole cation radical.[28] It is noted, however, that the rigorous kinetic approach used by Calhoun and Schuster in their study of the cyclohexadiene dimerization[25] could not be readily adapted to the unimolecular reactions of $\mathbf{5}^{\bullet+}$–$\mathbf{7}^{\bullet+}$. Consequently the somewhat less rigorous approach used in the *trans*-anethole study was adopted and buttressed by further studies which indicate the essential independence of the measured rate constant with respect to the quencher concentration. The estimated rate constant for the intramolecular cation radical Diels-Alder cyclization $\mathbf{5}^{\bullet+} \rightarrow \mathbf{5'}^{\bullet+}$, $k_{DA} = 3 \times 10^7$ $s^{-1}$, is a factor of 10 *slower* than the bimolecular rate constant for the cyclohexadiene cyclodimerization, probably as a result of the conformational factors mentioned earlier and the much greater stabilization of the *trans*-anethole type cation radical moiety of $\mathbf{5}^{\bullet+}$ than the diene cation radical moiety of $\mathbf{8}^{\bullet+}$. Since cyclohexadiene can be used in concentrations well above 1 M, it is actually a better probe than **5** in a context, such as the present study, where a bimolecular probe reaction is permissible. The intramolecular cyclobutanation of $\mathbf{6}^{\bullet+}$, however, is considerably faster than the probe reaction of $\mathbf{5}^{\bullet+}$ and even that of $\mathbf{8}^{\bullet+}$. To obtain a lower limit for this rate constant ($k_{CB}$), studies of the reactions of $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$ with a common reagent, ethyl diazoacetate, were carried out under standard aminium salt conditions.[29] Under these conditions $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$ are cyclopropanated (with second-order rate constants $k_{CP}$ and $k_{CP'}$ respectively) in competition with the respective intramolecular probe reactions (rate

(24) Marcus, R. A. *J. Chem. Phys.* **1956**, *24*, 4966.
(25) Calhoun, G. C.; Schuster, G. B. *J. Am. Chem. Soc.* **1984**, *106*, 6870–6871.
(26) Harirchian, B.; Bauld, N. L. *Tetrahedron Lett.* **1987**, *28*, 927–930.
(27) Courtneidge, J. L.; Davies, A. G.; Tollerfield, S. M.; Rideout, J.; Symons, M. C. R. *J. Chem. Soc., Chem. Commun.* **1985**, 1092.
(28) Lewis, F. D.; Kojima, M. *J. Am. Chem. Soc.* **1988**, *110*, 8664–8670. Actually, the electron-withdrawing ether function should render $\mathbf{5}^{\bullet+}$ more easily quenched than the *trans*-anethole cation radical.
(29) Stufflebeme, G.; Lorenz, K. T.; Bauld, N. L. *J. Am. Chem. Soc.* **1986**, *108*, 4234; *J. Phys. Org. Chem.* **1989**, *2*, 585–601.

**Scheme V.** Synthesis of Probe Substrates and Characterization of the Probe Reactions[a]



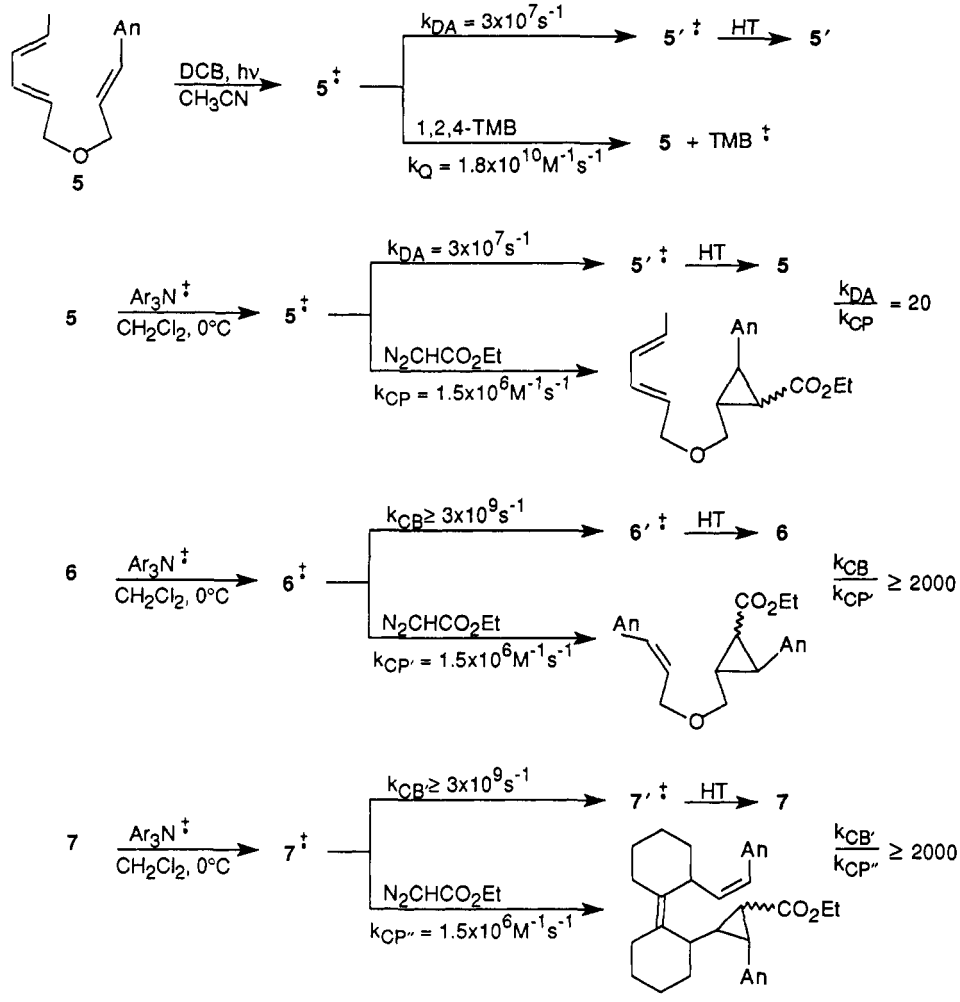

[a] An = 4-$MeOC_6H_4$; Ar = 4-$BrC_6H_4$. (a) Δ, 24 h, 270 °C. (b) LAH, $Et_2O$, 1 h, room temperature. (c) $Pb(OAc)_4$, benzene, 1 h, room temperature. (d) $AnCH_2PPh_3^+$ $Cl^-$, *n*-BuLi, THF, 3 h, room temperature.

constants $k_{DA}$ and $k_{CB}$, respectively). The experimentally determined ratio $k_{DA}/k_{CP} = 20$ affords $k_{CP} = 1.5 \times 10^6$ $M^{-1}$ $s^{-1}$. Assuming $k_{CP} = k_{CP'}$ (the hole sites in $5^{\bullet+}$ and $6^{\bullet+}$ are essentially identical), the experimentally observed minimum ratio $k_{CB}/k_{CP} \geq 2000$ affords $k_{CB} \geq 3 \times 10^9$ $s^{-1}$. The accuracy of this estimate is considered to be primarily limited by the accuracy of the measurement of $k_{DA}$ and by the validity of the assumption that the relative rate ratios $k_{DA}/k_{CP}$ and $k_{CB}/k_{CP'}$ (hence, $k_{DA}/k_{CB}$), which are measured in dichloromethane, are not substantially different in acetonitrile, the solvent in which $k_{DA}$ was measured and to which $k_{CB}$ is referred. This assumption was supported by additional studies of the competitive dimerization ($k_{CB^0}$)/cyclopropanation ($k_{CP^0}$) of *trans*-anethole. The rate ratio $k_{CB^0}/k_{CP^0} = 2$ affords $k_{CB^0} = 3 \times 10^6$ $M^{-1}$ $s^{-1}$, in very reasonable agreement with the value previously derived from quenching studies in acetonitrile ($2 \times 10^6$ $M^{-1}$ $s^{-1}$).[28] Since cyclopropanation of $6^{\bullet+}$ could not be detected in competition with cyclization, the actual rate constant for cyclization may well be greater than $3 \times 10^9$ $s^{-1}$. Similarly, the cyclization of $7^{\bullet+}$ is much too fast to permit the detection of cyclopropanated products, and only a lower limit can presently be estimated for this rate constant ($k_{CB'} \geq 3 \times 10^9$ $s^{-1}$).

**MP-Catalyzed Epoxidation of 5–8.** The ease of ionization of the *trans*-anethole moieties of **5–7** was considered to render them especially amenable to a hole-transfer mechanism of epoxidation if this were operable, and the cation radicals produced ($5^{\bullet+}$–$7^{\bullet+}$) should be relatively long-lived (compared to cation radicals of simple alkenes) and thus especially susceptible to detection. In preparation for studies of the MP-catalyzed epoxidations of **5** and **6**, a series of potentially relevant epoxides was prepared *via* MCPBA epoxidation (Scheme VII). These include the three possible monoepoxides of **5**, the epoxides of the cyclization product of **5**, and the epoxide of **6** (Scheme VII). Further, the hole-catalyzed epoxidations[14] of **5** and **6** were studied for comparison with the MP results (Scheme VIII). Using the less soluble oxidant $SeO_2$, only the cyclization product of **5** and its corresponding epoxides were formed. However, the more soluble and more efficient oxidant benzeneseleninic anhydride (BSA) also produces a single epoxide of uncyclized **5** which, as expected, corresponds to exclusive epoxidation at the *trans*-anethole moiety. The attempted hole-catalyzed epoxidation of **6**, even at high concentrations of BSA, yields only the cyclized product **6′**, as expected for a cyclization which approaches diffusion control.

The MP-catalyzed epoxidations of **5** and **6** were then studied under a variety of conditions, with M = Mn and Fe and P = 5,10,15,20-tetraphenylporphyrin and 5,10,15,20-tetrakis(2,6-dichlorophenyl)porphyrin, and in solvents dichloromethane, acetonitrile, and acetonitrile/water (90:10), with iodosylbenzene as oxidant (Scheme VIII). Reactions were carried out to ≈10% conversions to the monoepoxides, and material balances were >99%. In every instance only the unreacted probe (**5** or **6**) and the corresponding uncyclized epoxide were formed. Specifically, no **5′**, **6′**, any of the other epoxides characterized, nor any other product of epoxidation, dehydrogenation, or oxidation could have been formed in an amount as great as 0.5% of the product epoxide. The reactions are, in other words, extremely clean, and no

**Scheme VI.** Calibration of the Probe Reactions[a]




[a] DCB = 1,4-Dicyanobenzene; 1,2,4-TMB = 1,2,4-trimethoxybenzene (quencher); $k_Q = 1.8 \times 10^{10}$ $M^{-1}$ $s^{-1}$ is the diffusion rate in acetonitrile; HT = hole transfer to **5** or $DCB^{\bullet-}$.

byproducts are formed in detectable quantities. The corresponding metalloporphyrin-catalyzed epoxidation of **7** was also studied. Again, the cyclized product **7'** was not formed, and the reaction exclusively produced a mixture of epoxides corresponding to epoxidation on the *trans*-anethole-like moiety and on the tetrasubstituted double bond. No alcohols or other conceivable oxidation products of **7** were formed, and the recovered **7** had not undergone geometric isomerization. Finally, the MP-catalyzed epoxidation of 1,3-cyclohexadiene (**8**) was carried out on 2 M solutions in dichloromethane and also acetonitrile/dichloromethane (75:25). Neither the hole-catalyzed Diels-Alder cyclodimer[12,13] nor its epoxides or other dimeric materials were formed in detectable quantities.

**Conclusions.** These results decisively negate the possibility of the formation of free cation radicals, i.e., cation radicals which have dissociated from the reduced MPO, since the cyclized products **5'–7'** and the cyclodimer of **8** would then have been sensitively detected. Further, if it can be assumed that the negative charge on the reduced ferryl oxygen is about −1, the rate of separation of the singly charged ion radical pair should be about $5 \times 10^8$ $s^{-1}$ in acetonitrile.[30] Since **5'–7'** can easily be detected at the 0.5% level, dissociation to free cation radicals should be a detectable process in competition with a monoxygen transfer occurring at a rate of $1 \times 10^{11}$ $s^{-1}$. To proceed further with the analysis, it must be assumed that the probe reactions, as characterized, are essentially unperturbed by the reduced MPO moiety with which the substrate cation radical would be associated in the hypothetical hole-transfer mechanism of MP-catalyzed epoxidation. This seems especially likely to be valid in the more polar solvent used in this study. The fact that the probe reactions or products of the subsequent oxidation of the probe reaction products ($5'^{\bullet+}$–$7'^{\bullet+}$) were not detectable under MP catalyzed epoxidation conditions indicates that either cation radicals are not intermediates in these reactions or, if formed, their epoxidation by the reduced MPO is so rapid that neither diffusive separation nor any of the rapid probe reactions are competitive. With **5** as the probe substrate ($k_{DA} = 3 \times 10^7$ $s^{-1}$) and the product detectability level of 0.5%, it is estimated that the rate constant ($k_{ep}$) for monoxygen transfer to the probe cation radical ($5^{\bullet+}$) would have to be $k_{ep} \geq 6 \times 10^9$ $s^{-1}$. With **8** as the probe substrate, $k_{ep} \geq 1.2 \times 10^{11}$ $s^{-1}$ is required. Finally, using either **6** or **7** as the probe substrate, $k_{ep} \geq 6 \times 10^{11}$ $s^{-1}$ is required. Since rate constants up to about $10^{13}$ $s^{-1}$ are theoretically possible, the intervention of very short-lived (less than about 20 vibrations) cation radicals cannot be rigorously excluded by these probe experiments. However, it is again appropriate to recall that the *trans*-anethole type cation radical moieties of $5^{\bullet+}$–$7^{\bullet+}$ are highly stabilized and should be epoxidized much more slowly than cation radicals of simple alkene substrates. Further, the estimates of the rate constants for the cyclizations of $6^{\bullet+}$ and $7^{\bullet+}$ are minimum rate constants. These two probes may actually be significantly more sensitive than can presently be demonstrated. In any case, it is informative to compare the minimum required rate of monoxygen transfer to a stabilized cation radical ($6 \times 10^{11}$ $s^{-1}$)

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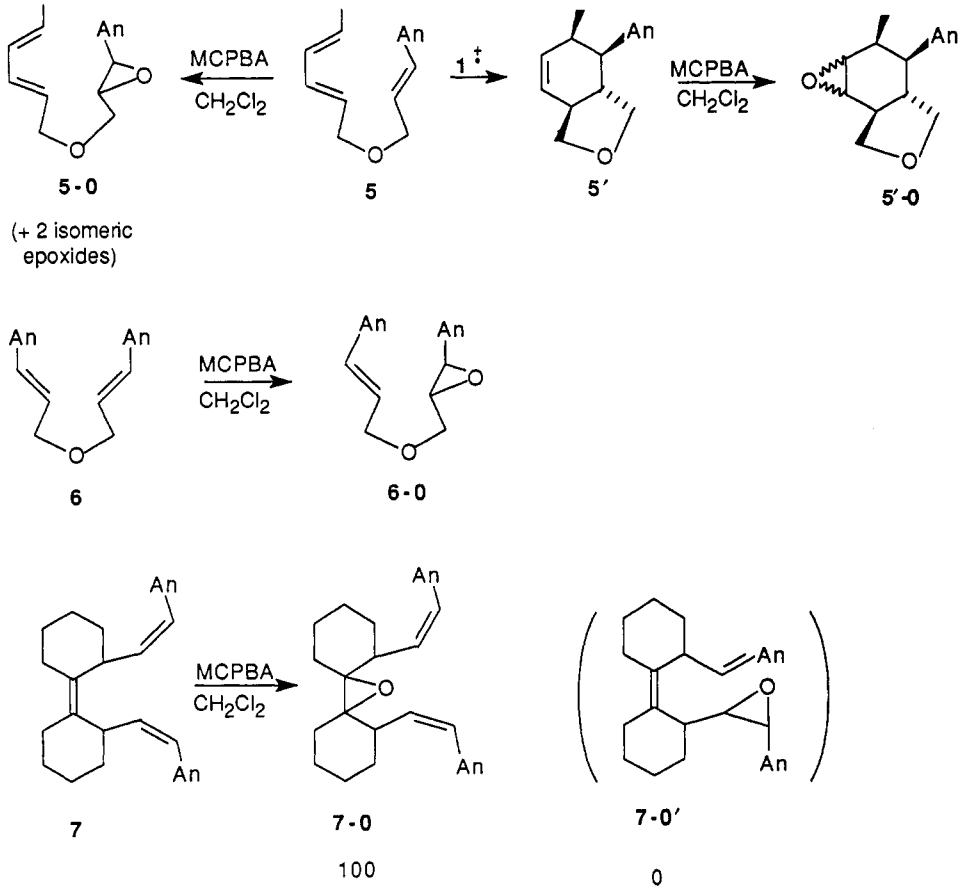
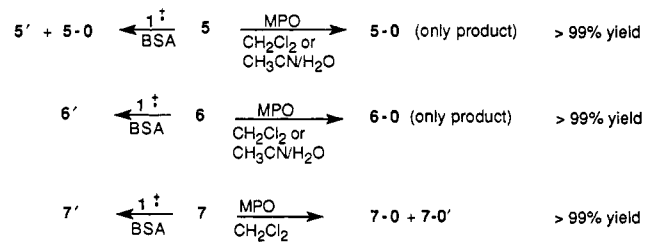
**Scheme VII.** Preparation of Relevant Epoxides[a]




[a] An = 4-methoxyphenyl; MCPBA = 3-chloroperbenzoic acid.

**Scheme VIII.** Hole- and Metalloporphyrin-Catalyzed Epoxidations[a]




[a] MPO = metalloporphyrin oxene; BSA = benzeneseleninic anhydride; yields based upon consumed starting materials.

with the rate of hydroxyl transfer from MP-OH to an alkyl radical (R•) in the rebound mechanism of hydroxylation (only $2 \times 10^{10}$ $s^{-1}$).[18]

**Summary.** The discovery of authentic hole-catalyzed epoxidation establishes that cation radicals can be efficiently and stereospecifically epoxidized. Comparative studies of hole- and metalloporphyrin-catalyzed epoxidation reveal far more contrasts than similarities. Whereas hole-catalyzed epoxidation is essentially free of side reactions, metalloporphyrin-catalyzed epoxidation is typically accompanied by one or more minor reaction channels. Further, whereas the *cis*-stilbene cation radical is configurationally relatively stable on the microsecond time scale and hole-catalyzed epoxidation of the stilbenes is correspondingly stereospecific, the metalloporphyrin-catalyzed epoxidation of these substrates is nonstereospecific, at least where the metal is manganese. A careful search for transient cation radical intermediates in metalloporphyrin-catalyzed epoxidations using newly developed cation radical probe reactions reveals no traces of cation radical intermediates. If such intermediates are involved at all, they must be extremely short-lived ($<2 \times 10^{-12}$ s). The results of this work, taken as a whole, are reasonably construed to suggest that, even for the relatively easily ionizable probe substrates of this study, an HT mechanism is probably not operative. It is noteworthy that, in a recent careful analysis of rates of MP- and enzyme-catalyzed epoxidations, Eberson has concluded that a hole-transfer mechanism, if operative at all, is most probably not the sole mechanism for these epoxidations.[31] A hole-transfer mechanism has also been ruled out for the cytochrome P-450 catalyzed oxidation of phenylethyne.[32] The formation of a cation radical intermediate in the MP-catalyzed (M = chromium) reaction of the extremely readily ionizable substrate 4,4-dimethoxystilbene has been inferred by Bruice, but the reaction does not lead to epoxidation.[33]

## Experimental Section

**Analysis.** Proton magnetic resonance and proton-decoupled carbon-13 NMR spectra were recorded on a General Electric QE-300 or Nicolet NT-360 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. UV–visible spectra were recorded on a Hewlett-Packard 8450A spectrometer. Low-resolution mass spectra (LRMS) were obtained on a Hewlett-Packard 5971A GC–MS spectrometer equipped with an HP-1 cross-linked methyl silicone GVM (12 m × 0.2 mm) capillary column. High-resolution mass spectra (HRMS) were recorded on a Dupont (CEC) 21-110B mass spectrometer. HPLC analyses were done on a Waters system using a Prep Nova-Pak HR silica cartridge column (40 mm × 300 mm). Analytical gas chromatographic (GC) analyses were performed on a Varian Model 3700 equipped with a flame ionization detector and a 12-M BP1 capillary column using nitrogen as a carrier gas. GC yields were calculated with the aid of a Hewlett-Packard 3390A reporting integrator. Internal

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(32) Komives, E. A.; Ortiz de Montellano, P. R. *J. Biol. Chem.* **1987**, *262*, 9793–9802.
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standards (*n*-decane or octadecane) were used for all the quantitative analyses, and detector response factors were calculated for all the products.

**Reagents.** Methylene chloride and HPLC grade acetonitrile were distilled from phosphorus pentoxide and were stored over molecular sieves prior to use. Tetrahydrofuran was distilled from sodium in the presence of benzophenone. Tris(4-bromophenyl)aminium hexachloroantimonate (Aldrich) was washed several times with cold anhydrous ether and dried *in vacuo* prior to use. 1,4-Dicyanobenzene (Aldrich) was twice recrystallized from benzene and dried *in vacuo* prior to use. All the olefins in this study were synthesized and purified as described here with the exception of 1,3-cyclohexadiene and those olefins tested in Table I which were purchased from Aldrich Chemical Company. These olefins were independently passed through a short column of activated neutral alumina immediately prior to reaction to remove trace peroxides. Iodosylbenzene was prepared according to a literature procedure.[34] 5,10,15,20-*meso*-Tetraphenylporphyrin was synthesized by Alder's method[35] and was metalated according to the literature procedures to (*meso*-tetraphenylporphyrinato)manganese(III) chloride[36] and (*meso*-tetraphenylporphyrinato)iron(III) chloride.[37] *meso*-Tetrakis(2,6-dichlorophenyl)-porphyrin was prepared according to the procedure of Lindsey[38] and was metalated using a procedure similar to that used for the metalation of *meso*-tetraphenylporphyrin. (4-Methoxybenzyl)triphenylphosphonium chloride was purchased from Lancaster Chemical Company. Rhodium-(II) acetate, *m*-chloroperbenzoic acid, tetrachloro-1,4-benzoquinone, phosphorus oxychloride, (–)-perillaldehyde, 2(*E*),4(*E*)-hexadien-1-ol, 4-methoxycinnamic acid, ethyl diazoacetate, iodosobenzene diacetate, vinylene carbonate, 1,2,4-trimethoxybenzene, lithium aluminum hydride, *n*-butylammonium chloride, and lead tetraacetate were all purchased from the Aldrich Chemical Company and were used without further purification. Selenium dioxide (MC/B) and benzeneseleninic anhydride (Aldrich or Lancaster) were used as received without further purification. *cis*-4-Heptenol was purchased from Pfaltz & Bauer Chemical Company.

**General Procedure for the Epoxidation of Olefins with Benzeneseleninic Anhydride (BSA) Catalyzed by Tris(*p*-bromophenyl)aminium Hexachloroantimonate ($1^{\cdot+}$).** To a stirred solution of 0.292 mmol of alkene and 0.306 mmol of benzeneseleninic anhydride in 1.7 mL of methylene chloride under an inert nitrogen atmosphere at 0 °C was added 47.7 mg (0.0584 mmol, 20 mol %) of tris(*p*-bromophenyl)aminium hexachloroantimonate. The reaction was stopped after 10–15 min (color change from blue to light red) and quenched with a saturated aqueous solution of potassium carbonate in methanol (1 mL). The product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine solution. The ethereal solution was dried over anhydrous sodium sulfate. After filtration of sodium sulfate and removal of volatile material, the product was purified by flash silica gel column chromatography with hexanes followed by methylene chloride eluent, to give the desired epoxide product. The following epoxides were derived and isolated from their respective precursor olefins in this fashion:

***cis*-Stilbene oxide**: GC yield, 85% (detector response factor, 1.2); isolated yield, 65%; $^1$H NMR ($CDCl_3$) $\delta$ 7.20 (s, 10H, PhH), 4.33 (s, 2H); LRMS *m/e* 196, 167 (base), 152, 139, 115, 89, 51.

***trans*-Stilbene oxide**: GC yield, 85% (detector response factor, 1.2); isolated yield, 66%; $^1$H NMR ($CDCl_3$) $\delta$ 7.35 (s, 10H, PhH), 3.87 (s, 2H); LRMS *m/e* 196, 167 (base), 152, 115, 89, 63.

**1,1-Diphenylethene oxide**: GC yield, 70% (detector response factor, 1.26); isolated yield, 42%; $^1$H NMR ($CDCl_3$) $\delta$ 7.40 (m, 10H, PhH), 3.27 (s, 2H); LRMS *m/e* 196, 167 (base), 139, 115, 91, 63, 51.

***trans*-β-Methylstyrene oxide**: GC yield, 62% (detector response factor, 1.16); isolated yield, 35%; $^1$H NMR ($CDCl_3$) $\delta$ 7.28 (s, 5H, PhH), 3.55 (d, 1H, $J$ = 3 Hz), 3.03 (m, 1H), 1.43 (d, 3H, $J$ = 6 Hz); LRMS *m/e* 134, 119, 105, 91 (base), 77, 65, 51.

**4-Isopropenyl-1-vinylcyclohexene oxide**: GC yield, 72% (detector response factor, 1.22); isolated yield, 56%; $^1$H NMR ($CDCl_3$) $\delta$ 5.95 (m, 1H, endo $\alpha$ exo), 5.35 (dd, 1H, $J$ = 18 Hz), 5.18 (dd, 1H, $J$ = 10 Hz), 4.68 (s, 2H), 3.53 (m, 1H, $J$ = 4 Hz), 2.36–1.16 (m, 7H), 1.66 (s, 3H); LRMS *m/e* 164, 149, 123, 122, 121, 107, 95, 94, 81, 79, 68, 67 (base), 55, 53; HRMS *m/e* calcd for $C_{11}H_{16}O$ 164.120 115, found 164.121 010.

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(36) Fleischer, E. B.; Palmer, J. M.; Srivastava, T. S.; Chatterjee, A. *J. Am. Chem. Soc.* **1971**, *93*, 3162.
(37) Kobayashi, H.; Higuchi, T.; Kaizu, Y.; Osada, H.; Aoki, M. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 3137.
(38) Lindsey, J. S.; Hsu, H. C.; Schreiman, I. C. *Tetrahedron Lett.* **1986**, *27*, 4969.

**Epoxidation of Substrates in Table I with Iodosylbenzene Catalyzed by Metalloporphyrin.** To a solution of 1–2 mmol of the alkene substrate and 0.02 mmol of (5,10,15,20-tetraphenylporphyrinato)manganese(III) chloride in 10 mL of methylene chloride under a nitrogen atmosphere at room temperature was added 0.3 mmol of iodosylbenzene. The solution was stirred for 3 h and then quenched with 5 mL of 2 N sodium sulfite. The products were separated from the aqueous layer by extraction with diethyl ether and analyzed by GC and GC–MS, using decane as an internal standard. The identities of all of the reaction products were confirmed by GC coinjection with authentic samples, as well as by comparison of MS fragmentation patterns.

**Preparation of 4-Isopropenyl-1-vinylcyclohexene (2).** To a dry 250-mL three-necked round-bottomed flask equipped with a stirrer, nitrogen inlet, and an addition funnel were added 18.5 g (0.046 mol) of methyltriphenylphosphonium iodide and 90 mL of anhydrous diethyl ether. The solution was cooled to –10 °C, and with stirring, a solution of 0.045 mol (2.5 M, 18 mL) of *n*-butyllithium in diethyl ether was added (*via* addition funnel) in a dropwise fashion to the reaction mixture while the bath temperature was maintained at 0 °C. Upon formation of the ylide, the mixture turned red. It was then stirred at 0 °C for an additional 30 min. To the resulting ylide, a solution of 4.50 g (0.03 mol) of (–)-perillaldehyde in 30 mL of anhydrous diethyl ether was added in a dropwise fashion through the addition funnel; the reaction was allowed to proceed for an additional 1 h before the orange-red solution was quenched with water. The product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine solution. The ethereal solution was dried over anhydrous magnesium sulfate. After filtration of sodium sulfate and removal of volatile material, the product was purified by flash silica gel column chromatography with hexanes/ethyl acetate (9:1 v/v) eluent, to give a pure sample of **2** upon removal of solvent: yield, 1.75 g, 62%; $^1$H NMR ($CDCl_3$) $\delta$ 6.41 (dd, 1H, $J$ = 18 Hz, 10 Hz), 5.80 (brs, 1H), 5.10 (d, 1H, $J$ = 18 Hz), 4.93 (d, 1H, $J$ = 10 Hz), 4.74 (s, 2H), 2.40–1.20 (m, 7H), 1.76 (s, 3H); LRMS *m/e* 148, 133, 119, 105, 91, 79 (base), 67, 53; HRMS *m/e* calcd for $C_{11}H_{16}$ 148.125 201; found 148.125 307.

**Epoxidation of 4-Isopropenyl-1-vinylcyclohexene (2) with Iodosylbenzene Catalyzed by Metalloporphyrin.** Using the general procedure described above, a 75:25 mixture of epoxides was observed in methylene chloride solvent (Scheme III). Analysis of the major epoxidation product, 4-isopropenyl-1-vinylcyclohexene oxide, revealed the following spectral characteristics: $^1$H NMR ($CDCl_3$) $\delta$ 5.95 (m, 1H, endo $\alpha$ exo), 5.35 (dd, 1H, $J$ = 18 Hz), 5.18 (dd, 1H, $J$ = 10 Hz), 4.68 (s, 2H), 3.53 (m, 1H, $J$ = 4 Hz), 2.36–1.16 (m, 7H), 1.66 (s, 3H); LRMS *m/e* 164, 149, 123, 122, 121, 107, 95, 94, 81, 79, 68, 67 (base), 55, 53; HRMS *m/e* calcd for $C_{11}H_{16}O$ 164.120 115, found 164.121 010. The minor epoxidation product gave the following mass analysis: LRMS *m/e* 164, 149, 136, 121, 107, 93, 91, 79 (base), 77, 67, 55.

**Preparation of 1(*E*),4(*Z*)-1-Phenylheptadiene (3).** To a dry 100-mL three-necked round-bottomed flask equipped with a reflux condenser, stirrer, nitrogen inlet, and addition funnel were added 965 mg (40.2 mmol) of dry magnesium turnings, 10 mL of anhydrous ethyl ether, a few crystals of iodine, and a few drops of the previously measured bromobenzene (5.04 g, 32.16 mmol). The rest of the bromobenzene was dissolved in 30 mL of anhydrous ether, and the solution was added to the addition funnel for later use. After the reaction had begun, as indicated by formation of bubbles and a change of color to cloudy (gray-milky), the remaining bromobenzene solution was slowly added from the addition funnel to the reaction mixture. The mixture was then brought to a gentle reflux in the warm water bath (20 min), and a solution of 3.0 g (26.8 mmol) of *cis*-4-heptenal in 20 mL of anhydrous ether was added dropwise (via the addition funnel) to the Grignard reagent. After all of the *cis*-4-heptenal had been added, the reaction mixture was brought to a gentle reflux for a period of 20 min and then allowed to cool to room temperature, where it was further stirred for an additional 1 h. The alkoxy magnesium 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 20 mL of diethyl ether. The combined ether layers were dried over anhydrous sodium sulfate. After removal of the sodium sulfate and evaporation of the volatile materials under reduced pressure, the product was purified by flash silica gel column chromatography with hexanes followed by ethyl acetate eluent, to give the desired 1-phenyl-*cis*-4-hepten-1-ol product upon removal of solvent: yield, 4.94 g, 97%; $^1$H NMR ($CDCl_3$) $\delta$ 7.31 (s, 5H, PhH), 5.37 (m, 2H), 4.60 (t, 1H, $J$ = 6 Hz), 2.65 (s, 1H), 2.20–1.60 (m, 6H), 0.93 (t, 3H, $J$ = 7.2 Hz); LRMS *m/e* 190, 172, 154, 143, 133, 120, 107 (base), 79, 77, 55; HRMS *m/e* calcd for $C_{13}H_{18}O$ $[M - H]^+$ = 189.127 94, found $[M - H]^+$ = 189.127 872. This alcohol was dehydrated as follows:

To a dry 50-mL two-necked round-bottomed flask equipped with a stirrer and a nitrogen inlet, were added 2.47 g (0.013 mol) of 1-phenyl-*cis*-4-hepten-1-ol and 10.3 g (0.130 mol) of pyridine. With stirring, 3.99 g (0.026 mol) of phosphorus oxychloride was slowly added via syringe through a rubber septum to the reaction mixture. After the addition was completed, the mixture was brought to a gentle reflux for a period of 3 h. To this solution 10 mL of water was slowly added, and the desired product **3** 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 sodium sulfate. After removal of sodium sulfate and evaporation of the volatile material under reduced pressure, compound **3** was purified by flash silica gel column chromatography with hexanes/diethyl ether (1:1 v/v) eluent, to give a pure sample of **3** upon removal of solvent: yield, 2.43 g, 90%; $^1$H NMR ($CDCl_3$) $\delta$ 7.31 (s, 5H, PhH), 6.44 (d, 1H, $J$ = 16.4 Hz), 6.18 (dt, 1H, $J$ = 16.4 Hz, 6 Hz), 5.48 (m, 2H), 2.95 (t, 2H, $J$ = 6 Hz), 2.11 (p, 2H, $J$ = 7.2 Hz), 0.97 (t, 3H, $J$ = 7.2 Hz); LRMS $m/e$ 172, 143, 129 (base), 115, 102, 91, 77, 65; HRMS $m/e$ calcd for $C_{13}H_{16}$ 172.125 201, found 172.125 664.

**Preparation of 1(*E*),5(*Z*)-1-Phenyloctadiene (4).** 1-Phenyl-*cis*-5-octen-2-ol was prepared using an experimental procedure similar to that used in the preparation of the alcohol precursor of compound **3**, except that benzyl chloride was used to prepare the Grignard reagent: yield, 5.25 g, 96%; $^1$H NMR ($CDCl_3$) $\delta$ 7.27 (s, 5H, PhH), 5.38 (m, 2H), 3.81 (p, 1H, $J$ = 6 Hz), 2.77 (m, 2H), 2.33–1.82 (m, 2H), 2.18 (s, 1H), 1.56 (p, 2H, 7.2 Hz), 0.96 (t, 3H, $J$ = 7.2 Hz); LRMS $m/e$ 204, 186, 157, 130, 113, 100, 92 (base), 91, 84, 77, 69; HRMS $m/e$ calcd for $C_{14}H_{20}O$ $[M-H]^+$ = 203.143 590, found $[M-H]^+$ = 203.143 269. This alcohol was converted to **4** as follows:

To a dry 50-mL two-necked round-bottomed flask equipped with a stirrer, nitrogen inlet, and addition funnel were added 2.65 g (0.013 mol) of 1-phenyl-*cis*-5-octen-2-ol, 10.3 g (0.130 mol) of pyridine, and 20 mL of methylene chloride. The flask was cooled to 0 °C in an ice water bath, and with stirring, a solution of 3.99 g (0.026 mol) of phosphorus oxychloride in 10 mL of methylene chloride was slowly added *via* the addition funnel to the reaction mixture. After the addition was completed, the mixture was allowed to warm up to room temperature and stirred for an additional 1 h. To this solution was slowly added 10 mL of water, and the organic 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 sodium sulfate. After removal of sodium sulfate and evaporation of the volatile material under reduced pressure, the product was purified by flash silica gel column chromatography with hexanes/diethyl ether (1:1 v/v) eluent, to give 7-chloro-8-phenyl-*cis*-3-octene as the major product of the reaction: yield, 2.65 g, 92%; LRMS $m/e$ 222, 186, 165, 143, 117, 91 (base), 77, 65, 55; HRMS $m/e$ calcd for $C_{14}H_{19}Cl$ 222.117 528, found 222.118 031.

The direct dehydration procedure used for the dehydration of 1-phenyl-*cis*-4-hepten-1-ol failed for this non-benzylic alcohol. Even in refluxing pyridine, the major product of reaction was still 7-chloro-8-phenyl-*cis*-3-octene. The dehydrohalogenation of the above alkyl chloride was achieved as follows:

To a dry 50-mL one-necked round-bottomed flask equipped with a stirrer, nitrogen inlet, and a reflux condenser were added 10 mL of absolute ethanol and 0.276 g (12 mmol) of sodium. The mixture was stirred under a nitrogen atmosphere until all the sodium was dissolved to give the desired solution of sodium ethoxide. To this solution was slowly added 2.0 g (9 mmol) of 7-chloro-8-phenyl-*cis*-3-octene, and the resulting mixture was brought to a gentle reflux for a period of 2 h. The solution was then allowed to cool to room temperature, and to this was slowly added 10 mL of water. The organic 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 sodium sulfate. After removal of sodium sulfate and evaporation of the volatile material under reduced pressure, product **4** was purified by flash silica gel column chromatography with hexanes followed by hexanes/diethyl ether (1:1 v/v) eluent, to give a pure sample of **4** upon removal of solvent: yield, 1.47 g, 88%; $^1$H NMR ($CDCl_3$) $\delta$ 7.31 (s, 5H, PhH), 6.46 (d, 1H, $J$ = 16.4 Hz), 6.21 (dt, 1H, $J$ = 16.4 Hz, 6 Hz), 5.41 (m, 2H), 2.23 (s, 4H), 2.07 (p, 2H, $J$ = 7.2 Hz), 0.95 (t, 3H, $J$ = 7.2 Hz); LRMS $m/e$ 186, 157, 144, 128, 117 (base), 91, 77, 65; HRMS $m/e$ calcd for $C_{14}H_{18}$ 186.140 851, found 186.139 758.

**Epoxidation of 1(*E*),4(*Z*)-1-Phenylheptadiene (3) with Iodosylbenzene Catalyzed by Metalloporphyrin.** Using the general procedure for metalloporphyrin epoxidations, a 68:32 mixture of epoxides was obtained in methylene chloride solvent. This ratio was 81:19 when the reaction was performed in the acetonitrile/water (3:1 v/v) solvent system (Figure 1). Epoxidation of compound **3** at the *cis* double bond gave a product with the following spectral characteristics: $^1$H NMR ($CDCl_3$) $\delta$ 7.32 (s, 5H, PhH), 6.56 (d, 1H, $J$ = 16.4 Hz), 6.22 (dt, 1H, $J$ = 16.4 Hz, 6 Hz), 2.96 (m, 2H, $J$ = 6 Hz), 2.42 (dt, 2H, $J$ = 6 Hz), 1.55 (p, 2H, $J$ = 7.1 Hz), 1.03 (t, 3H, $J$ = 7.1 Hz); LRMS $m/e$ 188, 173, 145, 129, 117 (base), 115, 91, 51. The product of epoxidation of compound **3** at the *trans* double bond had the following spectral characteristics: $^1$H NMR ($CDCl_3$) $\delta$ 7.23 (s, 5H, PhH), 5.47 (m, 2H), 3.52 (d, 1H, $J$ = 3 Hz), 2.86 (dt, 1H, $J$ = 7.2 Hz, 3 Hz), 2.38 (m, 2H), 2.10 (P, 2H, $J$ = 7.2 Hz), 0.96 (t, 3H, $J$ = 7.2 Hz); LRMS $m/e$ 188, 154, 145, 120, 105, 91 (base), 77, 67.

**Epoxidation of 1(*E*),5(*Z*)-1-Phenyloctadiene (4) with Iodosylbenzene Catalyzed by Metalloporphyrin.** Using the same procedure as that used for the epoxidation of **3**, a 53:47 mixture of epoxides was observed in methylene chloride solvent. When the reaction was performed in the acetonitrile/water (3:1 v/v) solvent system (Figure 1), the ratio found was 75:25.

**Preparation of 2(*E*),4(*E*)-Hexadienyl Bromide.** To a stirred solution of 4.90 g (50 mmol) of 2(*E*),4(*E*)-hexadien-1-ol in 10 mL of methylene chloride under an inert nitrogen atmosphere at −10 °C was slowly added a solution of 4.60 g (17 mmol) of phosphorus tribromide in 10 mL of methylene chloride in a dropwise fashion *via* an additional funnel. After all the phosphorous tribromide was added, the reaction mixture was stirred for an additional 15–20 min before it was quenched with a saturated aqueous solution of sodium bicarbonate. The product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine. The ethereal solution was then dried over anhydrous sodium sulfate. After removal of sodium sulfate by filtration and evaporation of the volatile material under reduced pressure at room temperature, 5.20 g (65%) of 2(*E*),4(*E*)-hexadienyl bromide was obtained. GC–MS analysis showed the presence of only one peak, indicating reasonably high purity: LRMS $m/e$ 162, 160, 82, 81 (base).

**Preparation of 4-Methoxycinnamyl Alcohol.** To a dry 50-mL one-necked round-bottomed flask equipped with a reflux condenser, a stirrer, and a nitrogen inlet were added 7 g (39 mmol) of 4-methoxycinnamic acid, 15 mL of ethanol, and 2 mL of concentrated sulfuric acid. The solution was brought to reflux for a period of 8 h and then allowed to cool to room temperature. Water (30 mL) was added to the reaction mixture, and the product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine solution. The ethereal layer was washed a couple of times with water and a saturated solution of sodium carbonate, before it was allowed to dry over anhydrous sodium sulfate. After removal of sodium sulfate and evaporation of the volatile materials under reduced pressure, the product was purified by flash silica gel column chromatography with hexanes/methylene chloride (1:1 v/v) eluent, to give 6.90 g (86%) of pure ethyl 4-methoxycinnamate upon removal of solvent. GC–MS analysis showed the presence of only one peak, indicating reasonably high purity: LRMS $m/e$ 206, 178, 161 (base), 134, 118, 102. This ester was reduced as follows:[39]

To a dry 100-mL one-necked round-bottomed flask equipped with a stirrer, a nitrogen inlet, and an addition funnel was added a solution (20 mL, 1 M) of lithium aluminum hydride in ether. The flask was placed in an ice bath (0 °C). To this cooled, stirred suspension of lithium aluminum hydride was added a solution of 0.86 g (6.4 mmol) of aluminum chloride in 10 mL of ether. The mixture was then allowed to warm up to room temperature and was stirred for an additional 30 min. Then a solution of 1.50 g (7.30 mmol) of ethyl 4-methoxycinnamate in 20 mL of ether was added dropwise *via* an addition funnel. After the addition was completed, the mixture was stirred for an additional 30 min before it was quenched with a 10% aqueous solution of sodium hydroxide. The resulting mixture was then acidified with dilute hydrochloric acid, and the product was separated by extraction with diethyl ether and the aid of brine. The ethereal solution was dried over anhydrous sodium sulfate. After filtration of sodium sulfate and removal of volatile material, 0.98 g (82%) of a desired white solid 4-methoxycinnamyl alcohol was obtained. GC–MS analysis showed the presence of only one peak, indicating high purity: LRMS $m/e$ 164, 147, 131, 121 (base), 108, 91, 77.

**Preparation of 4-Methoxycinnamyl 2(*E*),4(*E*)-Hexadienyl Ether (5).** To a stirred solution of 1.60 g (9.8 mmol) of 4-methoxycinnamyl alcohol and 1.80 g (11 mmol) of 2(*E*),4(*E*)-hexadienyl bromide in 5 mL of methylene chloride were added 0.1 g (0.3 mmol) of tetrabutylammonium bromide and 1 g of 50% aqueous sodium hydroxide. The reaction mixture was stirred at room temperature for a period of 3–4 h. The reaction mixture was then poured into 15 mL of water. The product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine solution. The ethereal solution was dried over anhydrous sodium sulfate. After filtration of sodium sulfate and removal of volatile material, the product was purified by flash silica gel column chromatography with

(39) Tucker, H. *J. Med. Chem.* **1980**, *23* (10), 1122.

hexanes/ethyl acetate (9:1 v/v) eluent, to give 1.92 g (80%) of pure ether product **5** upon removal of solvents: mp 45–46 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.35 (d, 2H, PhH, $J$ = 9 Hz), 6.86 (d, 2H, PhH, $J$ = 9 Hz), 6.58 (d, 1H, $J$ = 16 Hz), 6.41–6.13 (dt, 1H, $J$ = 16 Hz, 6 Hz), 6.05–5.50 (m, 4H), 4.05 (dd, 4H, $J$ = 6 Hz), 3.75 (s, 3H, $OCH_3$), 1.74 (d, 3H, $CH_3$, $J$ = 6.4 Hz); LRMS $m/e$ 244, 213, 174, 163, 147 (base), 135, 121, 115, 91, 67; HRMS $m/e$ calcd for $C_{16}H_{20}O_2$ 244.146 330, found 244.145 588.

**Tris(4-bromophenyl)aminium Hexachloroantimonate (1$^{\bullet+}$) Catalyzed Intramolecular Cyclization of 4-Methoxycinnamyl 2(*E*),4(*E*)-Hexadienyl Ether (5).** To a stirred solution of 142.5 mg (0.584 mmol) of ether **5** in 3.4 mL of methylene chloride under an inert nitrogen atmosphere at 0 °C was added 95 mg (0.117 mmol, 20 mol %) of catalyst **1**$^{\bullet+}$. After completion of reaction (1–2 min), the reaction mixture was then quenched with a saturated aqueous solution of potassium carbonate in methanol (1 mL). The product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine solution. The ethereal solution was dried over anhydrous sodium sulfate. After filtration of sodium sulfate and removal of volatile material, the cyclized product **5′** was purified by flash silica gel column chromatography with hexanes followed by hexanes/ethyl acetate (5:5 v/v) eluent, to give 114 mg (80%) of pure cyclized product (**5′**) upon removal of solvents: $^1$H NMR ($CDCl_3$) $\delta$ 7.38 (d, 2H, $J$ = 9 Hz), 6.88 (d, 2H, $J$ = 9 Hz), 5.20 (m, 2H, $J$ = 6 Hz), 4.15–3.34 (m, 7H), 3.79 (s, 3H, $OCH_3$), 1.21 (m, 1H), 0.78 (d, 3H, $CH_3$, $J$ = 7 Hz); LRMS $m/e$ 244 (base), 213, 174, 163, 148, 147, 135, 121, 115, 91, 77; HRMS $m/e$ calcd for $C_{16}H_{20}O_2$ 244.146 330, found 244.145679.

**Epoxidation of 4-Methoxycinnamyl 2(*E*),4(*E*)-Hexadienyl Ether (5) with Iodosylbenzene Catalyzed by Metalloporphyrin.** To a solution of 300 mg (1.23 mmol) of ether **5** and 11 mg (0.0154 mmol) of (5,10,-15,20-tetraphenylporphyrinato)manganese(III) chloride in 10 mL of methylene chloride under an inert nitrogen atmosphere at room temperature was added 67.8 mg (0.308 mmol) of iodosylbenzene. The solution was stirred for a period of 3 h and then quenched with 5 mL of a 2 N solution of sodium sulfite. The product(s) were then separated from the aqueous layer by extraction by extraction with diethyl ether and the aid of brine solution and were quantitatively analyzed by GC and GC–MS spectrometry. Using *n*-decane as an internal standard, a ≥99% of material balance was obtained for this reaction. After removal of volatile material under reduced pressure, the crude product was chromatographed on a silica gel column with hexanes/ethyl acetate (9:1 v/v), followed by hexanes/ethyl acetate (5:5 v/v) eluent, to give purified (4-methoxyphenyl)-glycidyl 2(*E*),4(*E*)-hexadienyl ether **5**–O as the only product of monoepoxidation upon removal of solvents. To check the detectability of cyclized product **5′**, a 1:200:1000 mixture of cyclized product **5′**, epoxide **5**–O, and starting material **5** was examined by GC spectrometer. The peak for cyclized product **5′** was successfully detectable: $^1$H NMR ($CDCl_3$) $\delta$ 7.34 (d, 2H, PhH, $J$ = 8.8 Hz), 6.87 (d, 2H, PhH, $J$ = 8.8 Hz), 6.05–5.51 (m, 4H), 4.13 (d, 2H, $J$ = 7.4 Hz), 3.95 (d, 1H, $J$ = 3 Hz), 3.81 (s, 3H, $OCH_3$), 3.46 (d, 2H, $J$ = 7 Hz), 3.28 (dt, 1H, $J$ = 7.2 Hz, 3 Hz), 1.74 (d, 3H, $CH_3$, $J$ = 6.4 Hz); LRMS $m/e$ 260, 244, 207, 163, 148, 147, 136, 121 (base), 91, 81; HRMS $m/e$ calcd for $C_{16}H_{20}O_3$ 260.141 245, found 260.140 953. Analogous results were obtained when the above reaction was carried out in the acetonitrile/water (9:1 v/v) solvent system and also when the catalysts (5,10,15,20-tetraphenylporphyrinato)iron-(III) chloride and (*meso*-tetrakis(2,6-dichlorophenyl)porphyrinato)iron-(III) chloride were used.

**Epoxidation of 4-Methoxycinnamyl 2(*E*),4(*E*)-Hexadienyl Ether (5) with Benzeneseleninic Anhydride (BSA) Catalyzed by Tris(4-bromophenyl)aminium Hexachloroantimonate (1$^{\bullet+}$).** To a solution of 71.2 mg (0.292 mmol) of ether **5** and 0.292 mmol of benzeneseleninic anhydride in 1.7 mL of methylene chloride under an inert nitrogen atmosphere at 0 °C was added 47.7 mg (0.0584 mmol, 20 mol %) of catalyst **1**$^{\bullet+}$. The reaction was stopped after 10–15 min (color change from blue to light red) and quenched with a saturated aqueous solution of potassium carbonate in methanol (1 mL). The product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine solution. The ethereal solution was dried over anhydrous sodium sulfate. GC–MS analysis revealed the formation of two products with the following percent composition: (4-methoxyphenyl)glycidyl 2(*E*),4(*E*)-hexadienyl ether **5**-O (11%) and cyclized intramolecular Diels-Alder product **5′** (89%).

**Cyclopropanation of 4-Methoxycinnamyl 2(*E*),4(*E*)-Hexadienyl Ether (5) with Ethyl Diazoacetate Catalyzed by Rhodium(II) Acetate.**[40] To a stirred solution of 2 g (6.97 mmol) of ether **5** and 62 mg (2 mol %) of rhodium acetate in 5 mL of methylene chloride at room temperature was added a solution of 1.56 g (13.94 mmol) of ethyl diazoacetate in 5 mL of methylene chloride over a period of 2 h. Then 40 mL of a saturated aqueous solution of sodium bicarbonate was added, and the reaction mixture was extracted with diethyl ether. The ethereal solution was dried over anhydrous magnesium sulfate and was analyzed by GC–MS. All six possible cyclopropanated products, corresponding to *syn* and *anti* adducts at each of the three double bonds of triene ether **5**, were observed. The two major products corresponded to cyclopropanation at the anisyl double bond, as indicated by mass spectral fragmentation patterns shown below and with the comparison to aminium salt catalyzed cyclopropanation of this triene **5**: LRMS $m/e$ 330, 257, 233, 163, 159, 147, 135, 121 (base), 91; HRMS $m/e$ calcd for $C_{20}H_{26}O_4$ 330.183 110, found 330.183 561.

**Cyclopropanation of 4-Methoxycinnamyl 2(*E*),4(*E*)-Hexadienyl Ether (5) with Ethyl Diazoacetate Catalyzed by Tris(4-bromophenyl)aminium Hexachloroantimonate (1$^{\bullet+}$).**[41] To a stirred solution of 48.8 mg (0.2 mmol) of ether **5** and 114 mg (1 mmol) of ethyl diazoacetate in 1 mL of methylene chloride at 0 °C was added 82.0 mg (0.1 mmol) of catalyst **1**$^{\bullet+}$. After 6 s, the reaction mixture was quenched by 3 mL of a saturated solution of potassium bicarbonate in methanol. The product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine solution. GC analysis of the ethereal solution showed an 18:1 ratio of intramolecular cyclized product **5′** and monocyclopropanation at the anisyl double bond of triene **5**. At different concentrations of ethyl diazoacetate (2 M, 0.5 M), the ratios of **5** and **5′** were 27:1 and 9:1, respectively, as demanded by a competition between unimolecular cyclization of triene cation radical **5**$^{\bullet+}$ and bimolecular reaction of triene cation radical **5**$^{\bullet+}$ with ethyl diazoacetate. In the reactions above, less than 10% of the triene **5** was converted to the products by limiting the reaction times.

**Determination of the Rate Constant for the Diels–Alder Reaction of 5$^{\bullet+}$ + 5 by Quenching.**[42] This study was based on the pioneering quenching studies of Calhoun and Schuster on the cation radical Diels–Alder cyclodimerization of 1,3-cyclohexadiene **8** and of Lewis and Kojima on the cyclobutadimerization of *trans*-anethole, a substrate to which the more ionizable moieties of **5**–**7** are structurally quite closely related. The kinetic scheme on which the studies of **8** were based was quite comprehensive, taking into account the possible quenching of **8**$^{\bullet+}$ by the quencher (Q; rate constant $k_3$ in the notation of Calhoun and Schuster) as well as by the sensitizer anion radical ($S^{\bullet-}$; rate constant $k_5$ and assumed to be diffusion controlled) and of $Q^{\bullet+}$ by $S^{\bullet-}$ ($k_5$; also assumed to be diffusion controlled). The chain nature of the reaction is accounted for by $k_4$, the rate constant for the hole transfer between the dimer cation radical and **8**. On the basis of the foregoing detailed kinetic scheme and the indicated assumptions concerning diffusion-controlled steps, the quantum yield relation given in eq 1 was obtained, where $k_2$ is the rate constant for the Diels–Alder reaction **8**$^{\bullet+}$ + **8**, $\Phi^\circ$ is the quantum yield in the absence of quencher, and $\Phi$ is the quantum yield in the presence of quencher, and $\Phi$ is the quantum yield in the presence of quencher.

$$\Phi/(\Phi^\circ - \Phi) = k_5[S^{\bullet-}]/k_3[Q] + k_2[\mathbf{4}]/k_3[Q] \qquad (1)$$

Maintaining both [Q] and [$S^{\bullet-}$] constant (the latter by keeping [S] constant), the quantum yield ratio was measured as a function of [**8**]. The slope of the latter plot, assuming $k_3$ has the diffusion-controlled value 1.8 × $10^{10}$, affords $k_2$ = 3 × $10^8$ $M^{-1}$ $s^{-1}$. Under the conditions of the experiment, light absorption by Q is negligible, and the relative concentrations of Q and **8** were such that quenching of S* by Q is negligible. The same kinetic scheme was adopted in this work except that the cyclization step (**5**$^{\bullet+}$ → **5′** $^{\bullet+}$) is intramolecular. The treatment of this revised kinetic scheme using steady-state assumptions provides the revised quantum yield expression in the way expected intuitively. The disappearance of the substrate concentration from the quantum yield expression unfortunately precludes the more rigorous experimental approach of varying the substrate concentration. As an alternative, we chose to adopt the approximate method used by Lewis and Kojima, *viz.*, variation of [Q]. However, we took the additional precaution of measuring $k_{CD}$ at different sensitizer concentrations and thus, almost certainly, at different [$S^{\bullet-}$]. The values of $k_{DA}$ are identical even when [S] is varied rather widely (*vide infra*). It is thus considered that the first term in eq 2 is quite small relative to the second term, and that the approximate method yields the approximate rate constant ($k_{DA}$) within the approximate

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(42) (a) Calhoun, G. C.; Schuster, G. B. *J. Am. Chem. Soc.* **1984**, *106*, 6870. (b) Lewis, F. D.; Kijima, M. *J. Am. Chem. Soc.* **1988**, *110*, 8664.

accuracy of a typical quenching study.

$$\Phi/(\Phi^\circ - \Phi) = k_5[S^{\bullet-}]/k_3[Q] + k_{DA}/k_3[Q] \quad (2)$$

The Pyrex reaction tubes were all dried in the oven overnight and further flame dried before reaction. HPLC grade acetonitrile and dicyanobenzene were purified and dried as mentioned previously. 4-Methoxycinnamyl 2(*E*),4(*E*)-hexadienyl ether (**5**), 1,2,4-trimethoxybenzene (the quenching agent), dicyanobenzene, and acetonitrile were added, and the reaction tubes were all degassed by nitrogen flow and placed in a cool water bath against the outside of the cooling jacket of a medium-pressure mercury vapor lamp and irradiated for 10 min. The conversion to product **5′** was less than 15% in all cases. Each tube in this experiment contained 1 mL of acetonitrile, 12.8 mg (0.1 M) of 1,4-dicyanobenzene, and 12.2 mg (0.05 M) of 4-methoxycinnamyl 2(*E*),4-(*E*)-hexadienyl ether (**5**), and concentrations of 1,2,4-trimethoxybenzene (quencher) were as listed below. The products were analyzed by GC compared to the internal standard (octadecane) which was added after reaction.

| tube | 1,2,4-trimethoxybenzene | $[5']/([5']_0 - [5'])$ |
|---|---|---|
| 1 | $1 \times 10^{-3}$ M | 1.97 |
| 2 | $2 \times 10^{-3}$ M | 1.22 |
| 3 | $3 \times 10^{-3}$ M | 0.930 |
| 4 | $4 \times 10^{-3}$ M | 0.686 |
| 5 | $5 \times 10^{-3}$ M | 0.468 |
| 6 | $6 \times 10^{-3}$ M | 0.430 |

[5′] is the concentration of the cyclization product in the tube with quenching agent, and $[5']_0$ is the concentration of the product in the tube without quenching agent. Linear regression analysis of this data gives slope = $1.85 \times 10^{-3}$, with $r = 0.987$. This affords a rate constant of $3.32 \times 10^7$ $M^{-1}$ $s^{-1}$.

**Cyclopropanation of *trans*-Anethole with Ethyl Diazoacetate Catalyzed by Tris(4-bromophenyl)aminium Hexachloroantimonate (1$^{\bullet+}$).**[41] To a stirred solution of *trans*-anethole and ethyl diazoacetate in 1 mL of methylene chloride at 0 °C was added 82 mg (0.1 mmol) of catalyst **1**$^{\bullet+}$. After 1 min, the reaction mixture was quenched with 2 mL of saturated solution of potassium carbonate in methanol. After extraction with diethyl ether and the aid of brine solution, the ethereal solution was analyzed by GC, showing the following ratios between cycloaddition products **9** and cyclopropanated products **10**:

| *trans*-anethole/ ethyl diazoacetate | [9]/[10] |
|---|---|
| 1:1 | 0.47 |
| 1:0.5 | 0.987 |
| 0.5:1 | 0.23 |

**Preparation of 4-Methoxycinnamyl Bromide.** This compound was prepared using an experimental procedure similar to that used for the preparation of 2(*E*),4(*E*)-hexadienyl bromide, but using 4-methoxycinnamyl alcohol: yield, 60%; LRMS *m/e* 228, 226, 147(base), 135, 121, 91.

**Preparation of Bis(4-methoxycinnamyl) Ether (6).** To a stirred solution of 0.53 g (3.2 mmol) of 4-methoxycinnamyl alcohol and 0.83 g (3.7 mmol) of 4-methoxycinnamyl bromide in 3.5 mL of methylene chloride were added 100 mg (0.31 mmol) of tetra-*n*-butylammonium chloride and 2.8 mL of 37% aqueous sodium hydroxide. The reaction mixture was stirred at room temperature for a period of 4 h. The mixture was then poured into 10 mL of water. The product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine solution. The organic layer was then dried over anhydrous magnesium sulfate. After filtration of magnesium sulfate and removal of volatile material, the product was purified by flash silica gel column chromatography with hexanes/ethyl acetate (6:1 v/v) eluent, to give 0.61 g (60.9%) of pure ether **6** upon removal of solvents: $^1$H NMR ($CDCl_3$) $\delta$ 7.32 (d, 2H, $J$ = 9 Hz), 6.87 (d, 2H, $J$ = 9 Hz), 6.63 (d, 1H, $J$ = 15 Hz), 6.20 (dt, 1H, $J$ = 15 Hz, 6 Hz), 4.07 (d, 2H, $J$ = 6 Hz), 3.78 (s, 3H); $^{13}$C NMR $\delta$ 159.263, 132.148, 129.470, 127.651, 123.802, 113.933, 70.791, 55.123; LRMS *m/e* 310, 240, 161, 148, 135, 121 (base), 91, 78; HRMS *m/e* calcd for $C_{20}H_{22}O_3$ 310.156 895, found 310.156 322.

**Tris(4-bromophenyl)aminium Hexachloroantimonate (1$^{\bullet+}$) Catalyzed Intramolecular Cyclization of Bis(4-methoxycinnamyl) Ether (6).** To a stirred solution of 200 mg (0.65 mmol) of ether **6** in 18 mL of methylene chloride under an inert nitrogen atmosphere 0 °C was added 107 mg (0.13 mmol, 20 mol %) of catalyst **1**$^{\bullet+}$. After completion of reaction (~20 s), the reaction mixture was quenched with a saturated aqueous solution of potassium carbonate in methanol (5 mL). The product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine solution. The ethereal solution was dried over anhydrous sodium sulfate. After filtration of sodium sulfate and removal of volatile material, the cyclized product (**6′**) was purified by flash silica gel column chromatography with hexanes/ethyl acetate (4:1 v/v) eluent, to give 105 mg (52.5%) of pure cyclized product upon removal of solvents: $^1$H NMR ($CDCl_3$) $\delta$ 6.84 (d, 4H, $J$ = 8.7 Hz), 6.63 (d, 4H, $J$ = 8.7 Hz), 4.07 (d, 2H, $J$ = 9.3 Hz), 3.68 (s, 6H), 3.66 (m, 2H), 3.64 (d, 2H, $J$ = 5.1 Hz), 3.198 (m, 2H); $^{13}$C NMR $\delta$ 157.440, 133.081, 129.039, 113.155, 73.948, 55.058, 46.490, 42.464; LRMS *m/e* 310, 279, 240, 148 (base), 135, 115, 91, 77; HRMS *m/e* calcd for $C_{20}H_{22}O_3$ 310.156 895, found 310.159 124.

**Epoxidation of Bis(4-methoxycinnamyl) Ether (6) with *m*-Chloroperbenzoic Acid.**[43] To a stirred solution of 300 mg (0.96 mmol) of ether **6** in 18 mL of methylene chloride at 0 °C was added a solution of 220 mg (0.76 mmol) of *m*-chloroperbenzoic acid. The reaction mixture was stirred for 1 h at 0 °C and for 24 h at room temperature. The mixture was then diluted with 50 mL of diethyl ether and washed with an aqueous solution of sodium hydroxide. The organic layer was further washed with 50 mL of water and dried over anhydrous magnesium sulfate. After removal of magnesium sulfate and evaporation of volatile material under reduced pressure, the crude product was chromatographed on a silica gel column with hexanes/ethyl acetate (4:1 v/v) eluent, to give 169 mg (67.5%) of purified monoepoxidized bis(4-methoxycinnamyl) ether **6–O**, upon removal of solvents: $^1$H NMR ($CDCl_3$) $\delta$ 7.380 (d, 2H, $J$ = 8.1 Hz), 6.875 (d, 2H, $J$ = 8.7 Hz), 6.846 (d, 2H, $J$ = 8.7 Hz), 6.475 (d, 1H, $J$ = 15.9 Hz), 6.608 (dt, 1H, $J$ = 15.9 Hz, 6.3 Hz), 4.160 (m, 2H), 4.097 (d, 2H, $J$ = 6.3 Hz), 3.807 (s, 3H), 3.773 (s, 3H), 3.491 (dd, 1H, $J$ = 9.6 Hz, 3.9 Hz), 3.325 (dd, 1H, $J$ = 9.6 Hz, 5.1 Hz); $^{13}$C NMR $\delta$ 159.673, 159.317, 132.946, 132.531, 129.652, 128.520, 127.648, 123.118, 113.997, 113.932, 77.509, 73.268, 72.073, 70.156, 55.182; LRMS *m/e* calcd for $C_{20}H_{22}O_4$ 326.151 809, found: 326.150 907.

**Epoxidation of Bis(4-methoxycinnamyl) Ether (6) with Iodosylbenzene Catalyzed by Metalloporphyrin.** Using the same procedure as that used for epoxidation of ether **5** afforded monoepoxidized bis(4-methoxycinnamyl) ether **6–O** as the only product of reaction with analytical data similar to those found for authentic monoepoxide sample **6–O** made by MCPBA reaction. Using octadecane as an internal standard, ≥99% of material balance was obtained for epoxidation of ether **6** under metalloporphyrin conditions. To set the detectability limits, a 1:200:1000 mixture of cyclized product **6′**, epoxide **6–O**, and starting material **6** was checked by GC. The cyclized product **6′** was successfully detectable. Analogous results were obtained when the above reaction was carried out with (5,10,15,20-tetraphenylporphyrinato)iron(III) chloride and with (5,10,15,20-tetrakis(2,6-dichlorophenyl)porphyrinato)manganese(III) and -iron(III) chlorides as the catalyst.

**Cyclopropanation of Bis(4-methoxycinnamyl) Ether (6) with Ethyl Diazoacetate Catalyzed by Rhodium(II) Acetate.**[40] To a stirred solution of 100 mg (0.32 mmol) of ether **6**, a trace amount of anhydrous potassium carbonate, and 2.6 mg (5 mol %) of rhodium acetate in 1 mL of methylene chloride at room temperature was added a solution of 112 mg (1 mmol) of ethyl diazoacetate in 1 mL of methylene chloride over a period of 6 h. Then 10 mL of a saturated aqueous solution of sodium bicarbonate was added, and the reaction mixture was extracted with diethyl ether. The ethereal solution was dried over anhydrous magnesium sulfate. After filtration of magnesium sulfate and removal of volatile material under reduced pressure, the crude product was chromatographed on a silica gel column with hexanes/ethyl acetate (4:1 v/v) eluent to give 62 mg (49%) of the desired mixture of *syn* and *anti* monocyclopropanated products upon removal of solvents: LRMS *m/e* 396, 335, 233, 189, 165, 159, 147 (base), 121, 115, 91; HRMS *m/e* calcd for $C_{24}H_{28}O_5$ 396.193 674, found 396.193 147.

**Cyclopropanation of Bis(4-methoxycinnamyl) Ether (6) with Ethyl Diazoacetate Catalyzed by Tris(4-bromophenyl)aminium Hexachloroantimonate (1$^{\bullet+}$).**[41] To a stirred solution of 62 mg (0.2 mmol) of ether **6** and 114 mg (1 mmol) of ethyl diazoacetate in 1 mL of methylene chloride at 0 °C was added 82 mg (0.1 mmol) of catalyst **1**$^{\bullet+}$. After 3 s, the reaction mixture was quenched by 2 mL of a saturated solution of potassium bicarbonate in methanol. The product was separated from the aqueous layer by extraction with diethyl ether and the aid of brine. GC analysis of the ethereal solution showed that the only product of reaction is intramolecular cyclized product **6′**, and no monocyclopropanated product **11** was detected. The peak of monocyclopropanated product **11** was detectable by GC when a standard solution of a 2000:1 mole ratio mixture of **6′** and **11** was analyzed.

(43) Schwartz, L. N.; Blumberg, J. H. *J. Org. Chem.* **1964**, *29*, 1976.

**Diels–Alder Reaction of 1,1′-Bicyclohexenyl (12) and Vinylene Carbonate.** A mixture of 12.9 g (0.08 mol) of the diene **12** and 5.7 g (0.066 mol) of vinylene carbonate was heated to reflux with vigorous stirring under nitrogen until the amount of refluxing vinylene carbonate became minimal (1 day). After cooling down, the crude product was column chromatographed to give 2 g of Diels–Alder product **13** (72.9%) as a white solid: $^1$H NMR ($CDCl_3$) $\delta$ 4.77 (m, 1H), 4.69 (m, 1H), 1.3–2.3 (m, 18H); LRMS *m/e* 248 (base), 204, 186, 162, 91, 79; HRMS *m/e* calcd for $C_{15}H_{20}O_3$ 248.1412, found 248.1405.

**$\Delta^{4a,5a}$-*cis*-9,10-Dihydroxydodecahydrophenanthrene (14).** A solution of 4.0 g (16.1 mmol) of carbonate **13** in 15 mL of diethyl ether was added slowly to a solution of 0.61 g (16.1 mmol) of lithium aluminum hydride in 20 mL of diethyl ether. After 30 min, the solution was slowly neutralized with 3 N HCl solution and the ether layer was separated. The aqueous phase was extracted once with 20 mL of ether, the combined organic layer was washed with three 10-mL portions of water and dried over anhydrous magnesium sulfate, and the ether was evaporated to give 3.3 g of diol **14** (92%): $^1$H NMR ($CDCl_3$) $\delta$ 3.93 (d, 2H, $J$ = 6 Hz), 2.83 (m, 2H), 1.33–2.4 (m, 16H); LRMS *m/e* 222, 204, 186, 162 (base).

**Cyclohexylidenecyclohexane-*cis*-2,2′-dicarboxaldehyde (15).** To a stirred solution of 1 g (4.5 mmol) of diol **14** in 10 mL of benzene was added 2.2 g (4.73 mmol) of lead tetraacetate in portions. The resulting solution was stirred for 2 h. The crude mixture was filtered under vacuum, and the solid was washed with 50 mL of ether. The filtrate was washed with 50 mL of saturated sodium bicarbonate solution and 50 mL of saturated sodium chloride solution and dried over anhydrous magnesium sulfate, and the solvent was evaporated to give 0.99 g of crude product **15** (99%) as a pale yellow solid, which is pure enough for the next reaction: $^1$H NMR ($CDCl_3$) $\delta$ 9.73 (s, 2H), 3.53 (m, 2H), 2.78 (m, 2H), 2.32 (m, 2H), 1.40–1.82 (m, 12H); LRMS *m/e* 220, 202 (base), 191, 163; HRMS *m/e* calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1460.

**Wittig Reaction of Dialdehyde 15 with (4-Methoxybenzylidene)-triphenylphosphorane (16).** A solution of 0.99 g (4.5 mmol) of dialdehyde **15** in 20 mL of dry THF was added dropwise over 30 min to 9 mmol of **16** in THF, which was prepared from 3.6 mL of 2.5 M *n*-butyllithium and 3.77 g (9 mmol) of (4-methoxybenzyl)triphenylphosphonium chloride in 80 mL of dry THF. After 2 h, the solvent was evaporated under vacuum to give a viscous liquid. All crude product was slurried in 100 mL of hexane, and the solid was filtered and washed with 3 × 100 mL of hexane. After evaporation of hexane, the yellow viscous liquid was filtered through a 10-cm alumina column and the solvent evaporated to give 840 mg of crude product as a white solid. The separation of three products was done by HPLC with hexanes/ethyl acetate (15:1 v/v) and gave 302 mg (0.7 mmol, 15.7%) of the *Z,Z* product (**7**) as a white solid and 192 mg (0.45 mmol, 10%) of a mixture of the *Z,E* and *E,E* isomers as a colorless gum-like solid. Spectral data for (*Z,Z*)-triene **7**: $^1$H NMR ($CDCl_3$) $\delta$ 7.15 (d, 4H, $J$ = 8.7 Hz), 6.727 (d, 4H, $J$ = 8.7 Hz), 6.18–6.34 (m, 4H), 3.77 (bs, 2H), 3.70 (s, 6H), 2.60–2.65 (m, 2H), 1.55–2.03 (m, 14H), 1.20–1.38 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 158.541, 132.468, 131.401, 130.851, 129.298, 127.001, 113.732, 55.122, 39.725, 33.118, 28.475, 25.944, 22.291; LRMS *m/e* 428, 307, 294, 240, 225, 165, 121 (base); HRMS *m/e* calcd for $C_{30}H_{36}O_2$ 428.271 472, found: 428.271 531.

**Tris(4-bromophenyl)aminium Hexachloroantimonate (1$^{\bullet+}$) Catalyzed Intramolecular Cyclization of (*Z,Z*)-Triene 7.** To a stirred solution of 86 mg (0.2 mmol) of triene **7** in 2 mL of methylene chloride was added 33 mg (0.04 mmol, 20 mol %) of catalyst **1**$^{\bullet+}$ at 0 °C. After 7 s, the reaction mixture was quenched with 2 mL of saturated potassium carbonate solution in methanol and extracted with 2 × 20 mL of ether. The combined organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under vacuum. Crude product was purified by HPLC (hexanes/ethyl acetate = 15:1 v/v) to give 24 mg (0.056 mmol, 50% yield based on the consumed starting material) of cyclized product **7′**: $^1$H NMR ($CDCl_3$) $\delta$ 7.17 (d, 2H, $J$ = 8.4 Hz), 7.08 (d, 2H, $J$ = 8.4 Hz), 6.81 (d, 2H, $J$ = 8.4 Hz), 6.75 (d, 2H, $J$ = 8.4 Hz), 3.775 (s, 3H), 3.761 (s, 3H), 3.12 (t, 1H, $J$ = 9 Hz), 3.00 (t, 1 H, $J$ = 9 Hz), 2.77 (m, 2H), 2.16 (m, 2H), 0.9–2.0 (m, 16H); $^{13}$C NMR ($CDCl_3$) $\delta$ 55.190, 55.127, 53.828, 49.626, 45.061, 44.610, 44.445, 41.738, 34.262, 31.578, 29.825, 29.727, 29.242, 27.524, 26.752, 25.712; LRMS *m/e* 428, 307, 294, 240, 227, 198, 173, 149, 121 (base), 84, 73; HRMS *m/e* calcd for $C_{30}H_{36}O_2$ 428.271 531; found 428.270 381.

**Epoxidation of 1,3-Cyclohexadiene (8) with Iodosylbenzene Catalyzed by Metalloporphyrin.** Using the same procedure as that used for epoxidation of ether **5**, epoxidation of a 2.0 M solution of **8** in methylene chloride yielded only 3,4-oxidocyclohexene and none of the Diels–Alder dimer of **8** or the epoxide of the latter. $^1$H NMR ($CDCl_3$): $\delta$ 5.97 (d, 2H), 3.51 (dd, 1H), 3.23 (dt, 1H), 2.40–1.50 (m, 4H). Similar results were obtained when the above reaction was carried out in a 2.0 M solution of **8** in the acetonitrile/dichloromethane (1:1 v/v) solvent system, and also when the catalysts (5,10,15,20-tetraphenylporphyrinato)iron(III) chloride and (*meso*-tetrakis(2,6-dichlorophenyl)porphyrinato)iron(III) chloride were used.

**Epoxidation of (*Z,Z*)-Triene 7 with *m*-Chloroperbenzoic Acid.** To a solution of (*Z,Z*)-triene **7** (86 mg, 0.2 mmol) in 5 mL of methylene chloride was added *m*-chloroperbenzoic acid (43 mg, 0.2 mmol, 80% pure) in 4 mL of methylene chloride at 0 °C for 5 min. After 1 h, TLC analysis (hexanes/ethyl acetate = 10:1) showed that the reaction was complete. The mixture was diluted with 50 mL of diethyl ether, washed with 2 × 20 mL of a 10% sodium hydroxide solution, and dried over anhydrous magnesium sulfate. Evaporation of volatile material gave 118 mg of crude product, which was chromatographed on a silica gel column (hexanes/ethyl acetate = 10:1) to give the (*Z,Z*)-triene oxide **7-O** in quantitative yield. The NMR analysis showed that a single product (corresponding to epoxidation at the tetrasubstituted double bond) was obtained: $^1$H NMR ($CDCl_3$) $\delta$ 7.072 (d, 4H, $J$ = 8.7 Hz), 6.652 (d, 4H, $J$ = 8.7 Hz), 6.304 (d, 2H, $J$ = 16.2 Hz), 6.216 (dd, 2H, $J$ = 16.2 Hz, 6 Hz), 3.744 (s, 6H), 2.632 (bs, 2H), 1.919–1.512 (m, 16 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 158.733, 130.462, 130.267, 128.214, 127.162, 113.705, 70.067, 55.154, 40.762, 29.437, 25.685, 24.069, 20.769; LRMS *m/e* 444, 426, 323, 292, 240, 230, 214, 186, 171, 121 (base), 91; HRMS *m/e* calcd for $C_{30}H_{36}O_3$ 444.266 445, found 444.266 134.

**Epoxidation of (*Z,Z*)-Triene 7 with Iodosylbenzene Catalyzed by Metalloporphyrin.** To a stirred solution of (*Z,Z*)-triene **7** (428 mg, 1 mmol) and (5,10,15,20-tetraphenylporphyrinato)manganese(III) chloride (8.8 mg, 0.0124 mmol) in 10 mL of dichloromethane was added iodosylbenzene (66 mg, 0.3 mmol). The mixture was stirred for 3 h and quenched with saturated potassium carbonate solution in methanol. After evaporation of volatile material *in vacuo*, the crude product was separated by flash silica gel column chromatography. Further separation was done by HPLC (hexanes/ethyl acetate = 4:1) to give 23 mg (18% yield) of (*Z,Z*)-triene oxide (epoxidation at a bridge double bond), 46 mg (35.8% yield) of an isomeric (*Z,Z*)-triene oxide (epoxidation at a side chain) was obtained, and remaining starting material was recovered: LRMS *m/e* 444, 426, 305, 292, 171, 135, 121 (base), 91; HRMS *m/e* calcd for $C_{30}H_{36}O_3$ 444.266 445, found 444.265 864. Analogous results were obtained when the above reaction was carried out with (5,10,15,20-tetraphenylporphyrinato)iron(III) chloride as the catalyst.

**Cyclopropanation of (*Z,Z*)-Triene 7 Catalyzed by Rhodium(II) Acetate.** To a stirred solution of (*Z,Z*)-triene **7** (92 mg, 0.215 mmol) and 1 mg of rhodium acetate in 1 mL of methylene chloride was added dropwise over 6 h 24.5 mg (0.215 mmol) of ethyl diazoacetate. The reaction mixture was diluted with 30 mL of diethyl ether and washed with saturated sodium bicarbonate solution. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under vacuum. The crude product (30%) was chromatographed on a flash silica gel column (hexanes/ethyl acetate = 4:1) to give a mixture of cyclopropanated products: LRMS *m/e* 514, 441, 393, 380, 352, 307, 294, 279, 219, 187, 174, 145, 121 (base); HRMS *m/e* calcd for $C_{34}H_{42}O_4$ 514.308 310, found 514.307 872.

**Cyclopropanation of (*Z,Z*)-Triene 7 with Ethyl Diazoacetate Catalyzed by Tris(4-bromophenyl)aminium Hexachloroantimonate (1$^{\bullet+}$).** A stirred solution of (*Z,Z*)-triene **7** (103 mg, 0.24 mmol) and ethyl diazoacetate (118 mg, 1 mmol, 1 M) in 1 mL of dichloromethane was cooled to 0 °C in an ice water bath. Aminium salt (78 mg, 0.1 mmol, 42 mol %) was added, and the solution was quenched with 1 N sodium hydroxide solution after 10 s. GC analysis indicated that **7′** was the exclusive product. Cyclopropanated products could not be detected. A known mixture of **7′** and the cyclopropanated products was prepared and analyzed to investigate the detectability limits on measurement of GC. The cyclopronated products were successfully detected up to 1/1000 of the concentration of the **7′** product.

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