Intermediates in the Epoxidation of Alkenes by Cytochrome P-450 Models. 1. *cis*-Stilbene as a Mechanistic Probe

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Abstract: Product yields were determined for the reactions of *cis*-stilbene with C_6F_5IO in CH_2Cl_2 with (*meso*-tetrakis(pentafluorophenyl)porphinato)iron(III) chloride [$(F_{20}TPP)Fe^{III}(Cl)$], (*meso*-tetrakis(2,6-dichlorophenyl)porphinato)iron(III) chloride [$(Cl_8TPP)Fe^{III}(Cl)$], and (*meso*-tetrakis(2,6-dichlorophenyl)porphinato)manganese(III) chloride [$(Cl_8TPP)Mn^{III}(Cl)$] as catalysts. Because they provided less *cis*-stilbene destruction and best yields of *cis*-stilbene oxide, the above catalysts and solvent were chosen from a number of systems investigated. *cis*-Stilbene destruction was found to exceed the C_6F_5IO oxidant employed. Aside from *cis*-stilbene, the products *cis*-stilbene oxide, *trans*-stilbene, *trans*-stilbene oxide, diphenylacetaldehyde (DPhA), deoxybenzoin (DEB), and PhCHO were quantified. These products do not arise from *cis*-stilbene oxide. In the absence of O_2, yields of PhCHO decreased, yields of *trans*-stilbene and *cis*-stilbene oxide increased, and destruction of *cis*-stilbene (to unaccountable products) decreased. Formation of PhCHO and destruction of *cis*-stilbene are explained by $1e^-$ oxidation of *cis*-stilbene to a carbocation radical (**1**). Reaction of **1** with O_2 results in the formation of PhCHO and radical polymerization of the alkene. In the absence of O_2, electron capture by **1** yields *cis*- and *trans*-stilbene. The products DPhA, DEB, and *cis*-stilbene oxide are proposed to be formed from the acyclic carbocation **2**. From **2**, phenyl migration provides DPhA, proton migration yields DEB, and cyclization yields epoxide. The observation that DPhA is produced in greater yield compared to DEB is explained in terms of an intrinsically greater migratory aptitude for phenyl versus hydrogen in the cationic intermediate **2b**. We conclude that the acyclic carbocation **2** is a pivotal structure in the epoxidation reaction and the formation of other side products.

Cytochrome P-450, peroxidase, and catalase enzymes share in common iron(III) protoporphyrin IX as a cofactor. The formation of the oxidizing species of cytochrome P-450 involves the complexing of enzyme with substrate, $1e^-$ reduction, addition of O_2, and a second $1e^-$ reduction. The last step is rate-determining, so that the structure of the oxidizing species cannot be directly probed.[1] Reaction of cytochrome P-450 enzymes with various oxygen transfer agents (peroxide shunt mechanism) leads to an enzyme oxidant having characteristics similar to the oxidant produced via the biochemical pathway.[1] HR-peroxidase and catalase enzymes react with hydroperoxides to provide compound I species whose structures have been established as Fe(IV)–oxo porphyrin π-cation radicals.[1,2] A considerable similarity exists between the products obtained via the peroxide shunt mechanism with cytochrome P-450 and oxidation reactions carried out with metallo(III) porphyrins and oxygen atom transfer agents which include percarboxylic acids, persulfates, hydroperoxides, iodosylarenes, hypochlorites, and aniline *N*-oxides.[3] Presumably the oxidizing species in these model reactions possess compound I structures.

There is strong support for a radical mechanism for insertion of oxygen into an alkane C–H bond catalyzed by both cytochrome P-450 and the metallo(III) porphyrin models;[4] however, the mechanism of alkene epoxidation remains unsolved. The following electron-deficient tetraphenylporphinato metallo(III) species have received considerable attention as epoxidation catalysts with iodosylarene oxidants: (5,10,15,20-tetrakis(pentafluorophenyl)porphinato)iron(III) chloride [$(F_{20}TPP)Fe^{III}(Cl)$], (5,10,15,20-tetrakis(2,6-dichlorophenyl)porphinato)iron(III) chloride [$(Cl_8TPP)Fe^{III}(Cl)$], and 5,10,15,20-tetrakis(2,6-dichlorophenyl)porphinato)manganese(III) chloride [$(Cl_8TPP)Mn^{III}(Cl)$].[5] Perfluoroiodosylbenzene has been offered as the ideal oxidant in these systems.[6] In this study we describe the oxidation of *cis*-stilbene using C_6F_5IO with $(F_{20}TPP)Fe^{III}(X)$, $(Cl_8TPP)Fe^{III}(X)$ (where $X = Cl^-$ or HO^-), and $(Cl_8TPP)Mn^{III}(OH)$ as catalysts in CH_2Cl_2 or a mixed protic solvent. The products that are formed provide an insight into the mechanisms of epoxidation.

Methods and Materials

HPLC–GC standards (Aldrich) were purified to homogeneity as established by HPLC. *cis*-Stilbene oxide was synthesized from *cis*-stilbene with *m*-chloroperbenzoic acid and Na_2HPO_4 in CH_2Cl_2. Analysis by HPLC of *cis*-stilbene showed 1.1% *trans*-stilbene contamination, which did not vary throughout the course of the study. Perfluoroiodosylbenzene was obtained by a literature procedure.[7] Spectrophotometric[8a] and titrimetric[8b] assays of the oxidant showed 98% purity, which did not vary on storage (−10 °C). Purification of CH_2Cl_2 was according to literature procedures.[9b] Chromatography of $(F_{20}TPP)Fe^{III}(Cl)$ (Aldrich) over alumina (neutral, activity I) eluting with $C_6H_6/CHCl_3$ (50:50) gave $(F_{20}TPP)Fe^{III}(OH)$, which was reconverted to $(F_{20}TPP)Fe^{III}(Cl)$ with HCl(g). Literature procedures were used to prepare $(Cl_8TPP)H_2$.[5a,c] The metals Fe(III) and Mn(III) were inserted into the porphyrin by the method of Kobayashi.[10] Purification, as above, provided $(Cl_8TPP)Fe^{III}(OH)$ and $(Cl_8TPP)Mn^{III}(OH)$. With $(Cl_8TPP)Mn^{III}(OH)$ treatment with HCl(g) did not generate $(Cl_8TPP)Mn^{III}(Cl)$. $(Cl_8TPP)Mn^{III}(OH)$ is partly characterized by a broad band in its UV–vis spec-

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(8) (a) Addition of C_6F_5IO to a buffered KI solution generates I_3^-, which is quantified by its absorbance at 358 nm. (b) Titrimetric assay quantifies I_3^- by Na_2SO_3(aq) titration.

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Table I. Relative Substrate Destruction and Epoxide Yields for *cis*-Stilbene Oxidation with Electron-Deficient Porphyrins in CH_2Cl_2 and $CH_2Cl_2/CH_3OH/H_2O$ (80:18:2) Mixed Protic Solvent under Partial Aerobic Conditions[a]

system	rel substrate destruction	rel *cis*-stilbene oxide yield
$(F_{20}TPP)Fe^{III}(Cl)/CH_2Cl_2$[b]	1.00	1.00
$(F_{20}TPP)Fe^{III}(OH)$/mixed	1.07	0.62
$(Cl_8TPP)Fe^{III}(Cl)/CH_2Cl_2$[c]	1.40	0.44
$(Cl_8TPP)Fe^{III}(OH)/CH_2Cl_2$	1.56	0.40
$(Cl_8TPP)Mn^{III}(OH)/CH_2Cl_2$[d]	1.34	0.34
$(Cl_8TPP)Mn^{III}(OH)$/mixed	2.07	0.24
$(Cl_8TPP)Fe^{III}(Cl)$/mixed	1.95	0.26
$(Cl_8TPP)Fe^{III}(OH)$/mixed	2.51	0.14

[a] Partially aerobic conditions are described in the Methods and Materials section. [b] System A. [c] System B. [d] System C.

trum centered at 371 nm with multiple shoulders. Addition of concentrated HCl to a CH_2Cl_2 solution of $(Cl_8TPP)Mn^{III}(OH)$ provides absorbances at 370 and 395 nm due to $(Cl_8TPP)Mn^{III}(Cl)$; upon washing with water, the spectrum of $(Cl_8TPP)Mn^{III}(OH)$ reappears.

Reaction Conditions and Product Separations. Reactions designated mixed protic were conducted in a 80:18:2 CH_2Cl_2:methanol:water solvent system.[6] Reactions defined as strictly anaerobic were conducted in a N_2 glovebox. Reactions defined as partially aerobic were conducted by exposing an anaerobic mixture of catalyst and alkene in CH_2Cl_2 to air during the addition of the oxidant. In a typical oxidation run, C_6F_5IO (0.10 mmol) was added in one portion to a 1.0 mL CH_2Cl_2 solution of catalyst (10^{-3} M) and *cis*-stilbene (0.25 M). After 30 min the reaction was quenched with aqueous Na_2SO_3. The organic layer was then analyzed for *cis*-stilbene, *trans*-stilbene, *cis*-stilbene oxide, *trans*-stilbene oxide, diphenylacetaldehyde (DPhA), benzaldehyde, and deoxybenzoin (DEB). Identification of reaction products was by coinjection of reaction mixtures with standards onto HPLC or GC columns. Coelution on two different HPLC systems described below or on one HPLC system and on GC was required before structural assignments were made. HPLC analysis was performed with a 5 μm Lichrosorb SiO_2 column (4.6 × 250 mm) eluted with either 100% hexanes or 99:1 hexanes:ethyl acetate at 1.0 mL/min and with a 5 μm Spherisorb Alumina column (4.6 × 250 mm) eluted with 48:1 hexanes:ethyl acetate at 1.5 mL/min. For HPLC, two Perkin-Elmer Series 10 pumps, a Perkin-Elmer Series 10 LC Controller, a Schoeffel Spectroflow Monitor (Model SF770) at 254 nm, and a Hewlett Packard Integrator (Model 3392A) were used. For GC, a Varian Model 3700 with flame ionization detection using a 0.2 mm × 25 m WCOT Vitreous SiO_2 capillary column operated at either 200 or 175 °C was employed. Product quantitation was determined from HPLC analysis by integration after determining response factors for authenic standards. Quantitation must proceed immediately after workup for consistent results. The detection limit was 0.05%. Reaction yields, especially of *cis*-stilbene oxide, are very dependent on the batch of C_6F_5IO used, although all batches assay identically.[11] Therefore, quantitative data presented in this paper are derived from a single batch of C_6F_5IO.

Results

Exploratory epoxidation studies were carried out with *cis*-stilbene and C_6F_5IO with the catalysts $(F_{20}TPP)Fe^{III}(X)$, $(Cl_8TPP)F^{III}(X)$ (where X = Cl^- or HO^-), and $(Cl_8TPP)Mn^{III}(OH)$ in both CH_2Cl_2 and the mixed protic solvent $CH_2Cl_2/CH_3OH/H_2O$ (80:18:2).[6] Spectrophotometric examination shows that in mixed protic solvent $(F_{20}TPP)Fe^{III}(Cl)$ exists as $(F_{20}TPP)Fe^{III}(OH)$ whereas $(Cl_8TPP)Fe^{III}(Cl)$ is a mixture of $(Cl_8TPP)Fe^{III}(Cl)$ and $(Cl_8TPP)Fe^{III}(OH)$. After accounting for all identifiable products there is found to be more alkene consumed than C_6F_5IO used. This discrepancy is defined as substrate destruction (to unidentifiable and presumably polymeric products). As a means of assessing *cis*-stilbene destruction for a selection of oxidizing systems, yields of *cis*-stilbene oxide and the amount of lost *cis*-stilbene were determined relative to that obtained from the $(F_{20}TPP)Fe^{III}(Cl)/CH_2Cl_2$ catalytic system (Table I), since this system provided the highest yields of *cis*-stilbene oxide and the least substrate destruction. With HO^- ligated catalysts in the mixed protic solvent, substrate destruction increases in the order $(Cl_8TPP)Fe^{III}(OH) > (Cl_8TPP)Mn^{III}(OH) > (F_{20}TPP)Fe^{III}(OH)$. Also from Table I, there is more substrate destruction (for a given ligated metalloporphyrin) in the mixed protic solvent compared to that in the CH_2Cl_2 solvent. In all cases the yield of *cis*-stilbene oxide decreases as substrate destruction increases.

The catalytic systems that exhibited the lowest substrate destruction were chosen for further study. These are the following: system A, $(F_{20}TPP)Fe^{III}(Cl)/CH_2Cl_2$; system B, $(Cl_8TPP)Fe^{III}(Cl)/CH_2Cl_2$; and system C, $(Cl_8TPP)Mn^{III}(OH)/CH_2Cl_2$ (Table II). The data provided in Table II are for a representative set of reaction runs. Error analyses from each reaction run show that the product yields are accurate to 0.1%. Repetitions of each reaction run give the same product ratios. Also, the same trends in product yields are seen when comparing strictly anaerobic to partially aerobic reactions; e.g., the yield of *trans*-stilbene always doubles on going from a partially aerobic to a strictly anaerobic reaction with system A. The integrity of the catalyst at the end of each run was checked spectrophotometrically. All catalysts were recovered with hydroxide ligation with only system C showing any catalyst destruction (25%). Of significance is the amount of *trans*-stilbene formed with *cis*-stilbene as substrate in systems A and B and *trans*-stilbene oxide formed in systems A, B, and C which indicate loss of stereochemical control over epoxidation by the catalyst. In contrast, *m*-chloroperbenzoic acid oxidation of *cis*-stilbene gives no *trans*-stilbene or *trans*-stilbene oxide as determined by HPLC.

The following control reactions were carried out with each metallo(III) porphyrin (where applicable): (i) *cis*-stilbene + C_6F_5IO; (ii) metallo(III) porphyrin + *cis*-stilbene; (iii) metallo(III) porphyrin + *cis*-stilbene oxide; and (iv) metallo(III) porphyrin + C_6F_5IO + *cis*-stilbene oxide. *trans*-Stilbene, *trans*-stilbene oxide, diphenylacetaldhyde (DPhA), and deoxybenzoin (DEB) are not formed in experiments i–iv. Rearrangement of *cis*-stilbene oxide to DPhA or DEB is ruled out by their absence in control reactions iii and iv. Thus, all the above products must arise from *cis*-stilbene in the presence of metalloporphyrin and C_6F_5IO.

In contrast to the epoxidation reactions, the control reaction iv gives only 1% and 0% yields of PhCHO when $(F_{20}TPP)Fe^{III}(Cl)/CH_2Cl_2$ and $(Cl_8TPP)Fe^{III}(Cl)/CH_2Cl_2$ are used, respectively. Therefore, the major fraction of PhCHO seen in the oxidation of *cis*-stilbene with these systems does not result from subsequent oxidation of *cis*-stilbene oxide. When *cis*-stilbene is epoxidized with either system under strict anaerobic conditions there is less *cis*-stilbene destruction, PhCHO is detected only at control levels, and a concomitant increase in yields of *cis*-stilbene oxide and *trans*-stilbene is seen.

Oxidation of *trans*-stilbene (Table III) with systems A, B, and C gives low yields of *trans*-stilbene oxide and no *cis*-stilbene oxide. Also, little or no rearrangement products (DPhA and DEB) are found. The low product yields from oxidation of *trans*-stilbene as compared to *cis*-stilbene probably reflect the lower reactivity of the former.[12]

Discussion

cis-Stilbene is a simple mechanistic probe for a stepwise reaction pathway for epoxidation. Destruction of the π-system with formation of an acyclic intermediate can result in loss of stereochemical information and formation of rearrangement products peculiar to the intermediate. Plausible stepwise mechanisms for epoxidation are given in Figure 1. In pathway a electrophilic attack upon the alkene provides an acyclic carbocation (**2**) that partitions between epoxide and rearrangement products. In pathway b a caged pair consisting of an alkene-derived carbocation radical (**1**) and $(Porph)M^{IV}(O)$ is formed by outersphere $1e^-$ transfer from the alkene to the hypervalent metallo–oxo porphyrin $[(^{+\bullet}Porp)M^{IV}(O)]$. Collapse of the caged pair containing **1** provides **2**. This mechanism has been expounded to explain the formation of both endo and exo epoxides as well as cationic rearrangement products in the oxidation of norbornene with

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Table II. Product Yields[a] and Material Balances[b] for the Oxidation of *cis*-Stilbene Catalyzed by Metalloporphyrins

system[c]	percent yield						material balance (%)
	trans-stilbene[d]	*cis*-oxide	*trans*-oxide	DPhA	DEB	PhCHO	
A[e]	1.1	42.4	1.5	13.8	1.5	5.0	75
A[f]	2.0	51.2	0.3	6.9	1.3	1.5	81
B[e]	1.4	36.1	0.5	3.3	0.7	0.5	72
B[f]	1.6	40.0	0.4	5.7	0.5	0	75
C[e]	0.0	33.7	1.8	6.3	1.5	0	55

[a] Reactions employed 0.25 mmol of *cis*-stilbene, 0.1 mmol of C_6F_5IO, and 10^{-3} mmol of catalyst in CH_2Cl_2. Yields are based on oxidant. [b] Material balance is defined as (mmole of products + mmole of recovered substrate)/0.25 mmol × 100%. [c] Systems are defined in Table I. [d] Values reflect correction for *trans*-stilbene contamination in substrate. [e] Reaction conducted under partially aerobic conditions. [f] Reaction conducted under strict anaerobic conditions.

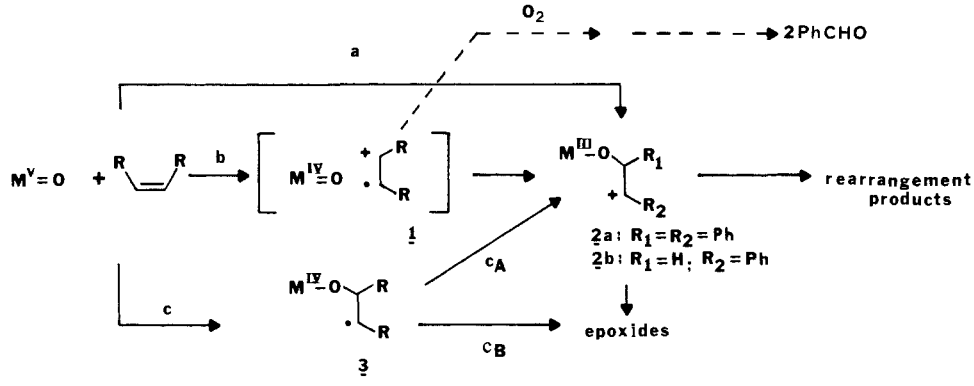

Figure 1. Stepwise mechanisms for oxygen insertion into alkenes. M^V=O symbolically represents the formal oxidation state of the metalloporphyrin catalyst after oxidation by C_6F_5IO. No structural inference is to be made from this representation.

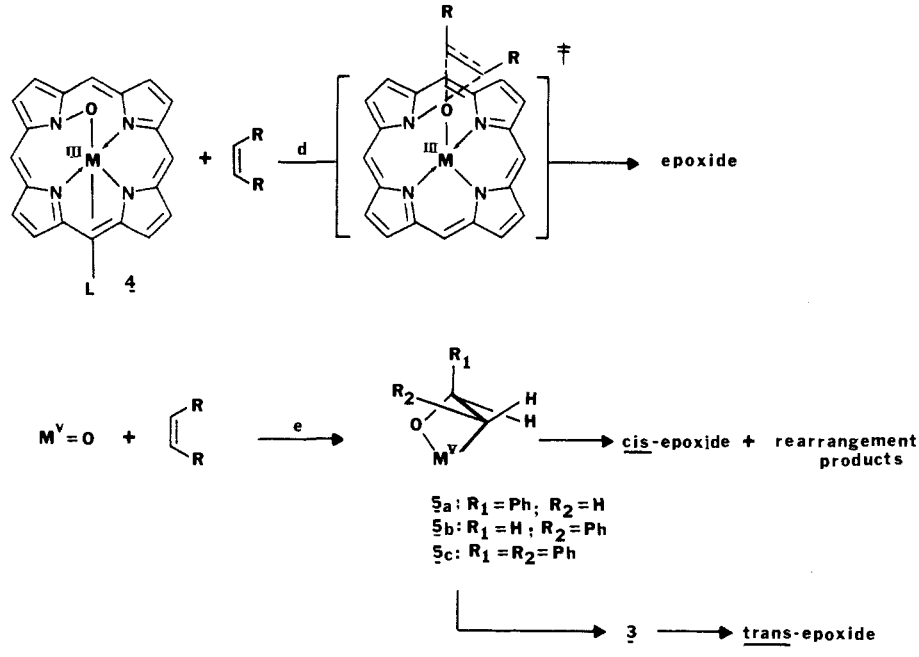

Figure 2. Two concerted mechanisms for oxygen insertion into alkenes. M^V=O in the metallaoxetane intermediate of pathway e represents the overall oxidation level of the porphinato–metal moiety.

$(Cl_8TPP)Fe^{III}(Cl)$ + C_6F_5IO.[13] Since "...addition of electrophiles or radicals to norbornene,..occur exclusively on the *exo*-side...",[13] the lack of stereospecificity seen in the epoxidation of norbornene was used to rule out the direct formation of the acyclic cationic intermediate **2** as in pathway a.[13] However, the eventual formation of **2** is required to explain the observed rearranged products (vide infra). The formation of **1** would not be inconsistent with known $1e^-$ oxidation potentials of $(Porp)Fe^{III}(OH)$ and alkenes.[14,15]

Pathway c of Figure 1 is consistent with the proposed[4] radical character of the M=O π-bond in $(^{+\bullet}Porp)M^{IV}(O)$. This radical character was suggested to explain the formation of *trans*-stilbene oxide from *cis*-stilbene through **3** when Mn(III) porphyrins are used.[16,17] Formation of *trans*-stilbene oxide could equally well

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Table III. Product Yields[a] and Material Balances[b] for the Oxidation of *trans*-Stilbene Catalyzed by Metalloporphyrins under Partially Aerobic Conditions[c]

system[d]	percent yield			material balance (%)
	trans-oxide	DPhA	DEB	
A	5.3	2.4	0.1	85
B	2.0	0	0	68
C	2.5	0	0	84

[a] Reactions employed 0.25 mmol of *trans*-stilbene, 0.1 mmol of C_6F_5IO, and 10^{-3} mmol of catalyst in CH_2Cl_2. Yields are based on oxidant. [b] Material balance is defined as (mmole of products + mmole of recovered substrate)/0.25 mmol × 100%. [c] Partially aerobic reaction conditions are described in the Methods and Materials section. [d] Systems are defined in Table I.

occur through **2**. After its generation, intermediate **3** may undergo direct collapse to give epoxide (pathway c_B) or it may undergo an innersphere electron transfer to give **2** which then collapses to epoxide or rearranges (pathway c_A).[18] The formation of rearranged products from **2** would explain the consistent finding of aldehydes and not ketones from the oxidation of terminal alkenes.[5e,18,19a,c,22] Additional support for a stepwise mechanism passing through **2** was offered on the basis of the observation that rate constants for epoxidation of substituted styrenes correlate well with $\sigma(+)$ and give $-\rho$ values. This was interpreted in terms of positive charge buildup in the transition state for the alkene epoxidation.[16]

In addition to direct oxene insertion into the C=C bond by hypervalent metallo–oxo porphyrin, two mechanisms (Figure 2), which involve concerted steps, have been proposed. In pathway d the oxygen insertion agent is a bridged metallo–oxo porphyrin (**4**). This mechanism has been favored on theoretical grounds.[20] Pathway e involves a hypervalent metallo–oxo species which undergoes a 2a + 2s cycloaddition with alkene to give a metallaoxetane (**5**).[5f,21] Breakdown of **5** provides epoxide by reductive elimination. Because both formation and breakdown of **5** are concerted processes, any loss of stereochemical control has been relegated[21] to a minor parallel reaction involving ring opening of **5** to give **3**. This proposal may be questioned on the basis that *trans*-stilbene oxide is sometimes the major product in the epoxidation of *cis*-stilbene with manganese(III) porphyrins,[16,17] With styrene as substrate, phenylacetaldehyde is obtained as a product. Phenylacetaldehyde has been postulated to result from a metallaoxetane, **5b**, which is regioisomeric with the metallaoxetane, **5a**, responsible for epoxide formation.[22] Rearrangement of **5b** to aldehyde is proposed to occur by preferential migration of the *cis*-hydrogen because "...the conformational preference of the four-membered ring results in the *cis* C–H bond being better aligned for a rearrangement...".[22] These conclusions were based on the distribution of label in phenylacetaldehyde derived from the oxidation of deuterium-labeled styrenes and the lack of phenyl migration to give acetophenone.

With *cis*-stilbene only one metallaoxetane (**5c**) can be formed. Explicit in the metallaoxetane hypothesis is a much faster collapse of **5a** to epoxide compared to phenyl migration.[22] With **5c** the situation should be no different, since the metal–carbon bond in **5c** should have nearly the same polarization as in **5a**. Therefore, *cis*-stilbene should behave in an analogous manner to styrene, and no phenyl migration should occur.[22] Since no hydrogens are in the proper spatial arrangement for their migration, no rearrangement products should be seen. As shown in Table II this predicted outcome is not realized, and all catalytic systems give substantial amounts of diphenylacetaldehyde (DPhA) resulting

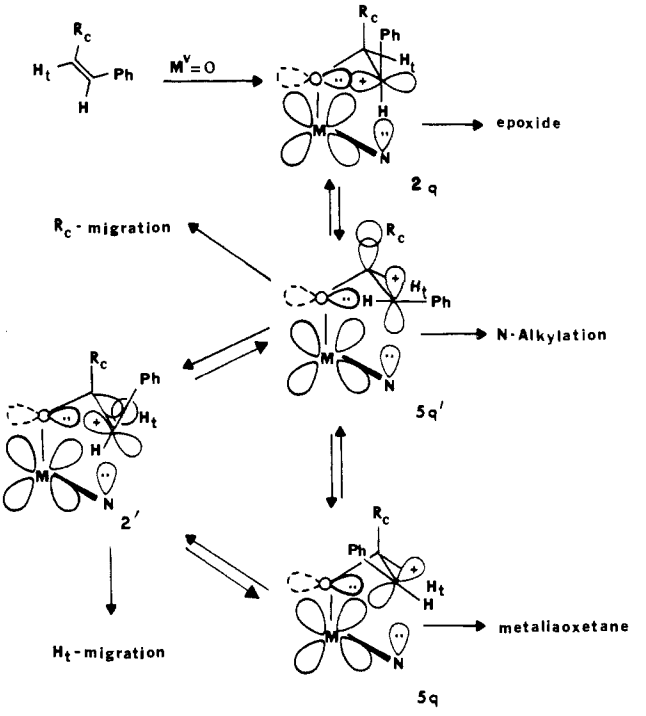

Figure 3. Stereoorbital diagram depicting acyclic intermediates as possible intermediates in epoxidation, rearrangement to aldehydes from preferential substituent migration, porphyrin N-alkylation, and metallaoxetane formation.

from phenyl migration and deoxybenzoin (DEB) resulting from hydrogen migration. Significantly, the product yield from phenyl migration (DPhA) is always much greater than the product yield from hydrogen migration (DEB). This is in accord with formation of a cationic intermediate **2a**, if phenyl migration to the carbocation center is favored over hydrogen migration.

If acyclic cationic intermediates (**2**) are involved in alkene epoxidation, then the intermediate formed from styrene (**2b**) would be a substituted benzyl carbocation so that phenyl migration could not take place. This would explain why phenyl migration to provide acetophenone does not occur during styrene epoxidation.[22] One argument used against **2** as an intermediate is based on the lack of substituent effects on the ratio of epoxide to $PhCH_2CHO$ obtained by hydrogen migration.[22] Although substituent effects would control the rate of formation of **2b**, these would have a questionable effect on the partitioning of **2b** to epoxide and $PhCH_2CHO$. A second argument against **2**, and in favor of a metallaoxetane, is based on the preferential migration of *cis*-H(D) in *cis*- and *trans*-styrene-β-*d* to give the deuteriated phenylacetaldehydes. The stereoelectronic control required for preferred migration of *cis*-H(D) is not present in a rotationally unrestricted acyclic intermediate. However, a quasiclosed intermediate[23] with positive charge on the benzylic center can be used as well as a metallaoxetane (**5b**) to explain the *1-d*/*2-d* phenylacetaldehyde product ratios (Figure 3).

The initial acyclic intermediate **2**, formed either directly or by intramolecular transfer in **3**, may exist in several conformations as shown in Figure 3. Conformers **2q**, **5q'**, and **5q** are quasiclosed forms and are stabilized by interaction of the empty p orbital with an oxygen lone pair, a nitrogen lone pair, or a metal d orbital, respectively. Epoxide would proceed from collapse of **2q** while rearrangement would proceed from R_c migration in **5q'** or **5q**. Collapse of **5q'** may explain porphyrin N-alkylation that is seen in cytochrome P-450[24] and model systems[25] while collapse of **5q**

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would give a metallaoxetane. For H_t migration conformer **2'** is required, which lacks the stabilization of **2q**, **5q'**, or **5q**. Thus, preferential migration of the *cis*-hydrogen ($R_c = H_c$ in Figure 3) during styrene oxidation is successfully predicted. Figure 3 also successfully predicts preferential migration of phenyl over hydrogen which is seen during the oxidation of *cis*-stilbene (R_c = Ph). From these arguments, and the results of this and other investigations (loc. cit.), we conclude that viable reaction schemes for epoxidation by metalloporphyrin model systems must allow **2** as an intermediate.

Along with the rearrangement products DPhA and DEB, oxidation of *cis*-stilbene gives *trans*-stilbene oxide and *trans*-stilbene. *trans*-Stilbene oxide is produced in comparable amounts in systems A, B, and C. In CH_2Cl_2 solvent $(Cl_8TPP)Mn^{III}(OH)$, $(Cl_8TPP)Fe^{III}(OH)$, and $(TPP)Fe^{III}(Cl)$[12] give similar stereochemical control with respect to *trans*-stilbene oxide formation. This is in contrast to $(TPP)Mn^{III}(Cl)$, which gives considerable amounts of *trans*-stilbene oxide.[16,17] Although the amounts of *trans*-stilbene oxide are small, this is the first report of a *trans*-epoxide being generated from a *cis*-alkene with an iron(III) porphyrin catalyst.

Isomerization of *cis*- to *trans*-stilbene and formation of benzaldehyde have been observed during oxidations of *cis*-stilbene by bleomycin–Fe^{III} + H_2O_2, $NaIO_4$, or cumene hydroperoxide in methanol/water[26] and the heteropolytungstate $MnHPW_{11}O_{59}^{5-}$ + C_6F_5IO in acetonitrile.[27] In the former study, it was shown that formation of PhCHO is favored under aerobic conditions and that the PhCHO incorporates molecular oxygen. On the other hand, isomerization of *cis*- to *trans*-stilbene is favored under anaerobic conditions. These results were explained by assuming a reaction pathway that is independent of epoxide formation and which results from an outersphere electron transfer to give the carbocation radical **1** (as in pathway b).[26] Thus, formation of *trans*-stilbene in the present study cannot be assumed to share the same reaction pathway as *cis*-stilbene oxide. It was further proposed that **1** reacts with O_2 in such a manner that a dioxetane is formed. The proposed dioxetane then decomposes to PhCHO.[26] In the present study $(Cl_8TPP)Fe^{III}(Cl)/CH_2Cl_2$ and $(F_{20}TPP)Fe^{III}(Cl)/CH_2Cl_2$ are the only systems that give both *trans*-stilbene and PhCHO. By conducting these epoxidations under strictly anaerobic conditions, isomerization of *cis*- to *trans*-stilbene is increased at the expense of the formation of PhCHO (Table II systems A[f] and B[f]). Also, product inventory now gives improved material balances due to an increase in *cis*-stilbene oxide production and less substrate destruction. These changes are more pronounced with system A, but for system B only changes in *cis*-stilbene oxide and PhCHO yields can be regarded as significant. It is thus consistent with available data to suggest that substrate destruction proceeds through interaction of **1** with molecular oxygen (Figure 1) to generate free radicals which then initiate chain processes. Alternatively, O_2 may combine with **3** to form a peroxy radical which is responsible for alkene destruction and eventually decomposes to PhCHO. Such a scheme has been postulated to explain PhCHO formation during the oxidation of styrene with $(TPP)Fe^{III}Cl$ + C_6H_5IO in benzene.[19c] These mechanisms would obtain how more substrate is consumed in systems of the present study than would be expected on the basis of a simple molar relationship with oxidant. Shutting down such pathways would also increase the likelihood of the carbocation radical **1** regaining its electron in intermediate **1** or **3** reverting back to alkene and metallo–oxo porphyrin after carbon–carbon bond rotation.[28] Either outcome would result in greater substrate isomerization as we have observed. Higher yields of *cis*-stilbene oxide are also expected due to decreased destruction of the alkene precursor. Therefore, the postulation that *endo*-norbornene oxide is formed from norbornene by the latter's conversion to a carbocation radical on reaction with $(Cl_8TPP)Fe^{III}(Cl)$ and C_6F_5IO[13] is reasonable. If pathways a (or c) and b are competitive in epoxide formation, then pathway b would give both *endo*- and *exo*-norbornene oxide while pathway a (or c) would give only *exo*-norbornene oxide. With *cis*-stilbene as substrate, leakage of **1** from pathway b results in alkene destruction and formation of PhCHO (in the presence of O_2) as well as alkene isomerization. Pathways a and c are consistent with available data and presently cannot be distinguished. In order to make this distinction and to determine if radical species (**1** and **3**) are obligate intermediates to epoxide formation, the design of special substrate molecules is required. Such efforts are now in place in this laboratory.

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