and 20 mL of absolute ethanol was added to it. Palladium on carbon (0.005 g of 10% Pd/C) was added to the above solution, and the reaction mixture was hydrogenated in a Parr apparatus (40 psi H_2 pressure). After 5 h the reaction mixture was filtered and concentrated to obtain a gum which was passed through a short column of silica gel eluting with hexane/EtOAc (1:1) to give 0.035 g (68%) of the cyclized product **12**: IR (CH_2Cl_2, cm^{-1}) 2930, 2860, 2800–2500, 1590, 1470, 1410, 1345, 1110, 1075, 920, 860, 810; ^1H NMR (360 MHz, $CDCl_3$, δ) 4.29 (q, 1 H, $J = 6.7$ Hz), 3.81 (s, 3 H), 3.78 (s, 3 H), 3.66 (s, 3 H), 3.15–3.05 (m, 2 H), 2.75–2.6 (m, 2 H), 2.17 (s, 3 H), 1.44 (d, 3 H, $J = 6.63$ Hz).

(**b**) **Dehydrogenation of 12.** Tetrahydroisoquinoline **12** (0.025 g, 0.1 mmol) was taken in a 10-mL, round-bottomed flask equipped with a magnetic stirrer bar and a reflux condenser, and 1 mL of decalin was added to it. The mixture was placed in an oil bath maintained at 160 °C, and after 3 h the reaction mixture was cooled, and the product was purified by flash chromatography over a column of silica gel (230–400 mesh, hexane/EtOAc, 10%) to give 0.015 g (60%) of **13**: IR (CH_2Cl_2, cm^{-1}) 2940, 2860, 1460, 1410, 1330, 980; ^1H NMR (360 MHz, $CDCl_3$, δ) 8.3 (d, 1 H, $J = 5.95$ Hz), 7.65 (d, 1 H, $J = 5.92$ Hz), 3.94 (s, 3 H), 3.85 (s, 3 H), 3.1 (s, 3 H), 2.4 (s, 3 H); mass spectral M_r calcd for $C_{14}H_{17}NO_3$ 247.1208, found 247.1211.

Oxidation of 13. The trimethoxyisoquinoline **13** (0.03 g, 0.12 mmol) and 0.06 g (0.48 mmol) of Ag_2O was taken in a flask containing 1 mL of dioxane. Nitric acid (0.1 mL, 6 M) was added to the mixture, and after having been stirred at room temperature for 15 min, the reaction mixture was diluted with water and extracted with $CHCl_3$. The chloroform extract was washed with water, dried, and concentrated to obtain a yellow solid which was purified by flash chromatography over silica gel (230–400 mesh, hexane/EtOAc, 10%) to give 0.012 g (50%) of the known compound[6] **1,6-dimethyl-7-methoxy-5,8-dihydroisoquinoline-5,8-dione, 8**: mp 188–190 °C; IR (CH_2Cl_2, cm^{-1}) 2920, 2850, 1670, 1615, 1570, 1400, 1380, 1340, 1300, 1205, 905; ^1H NMR (360 MHz, $CDCl_3$, δ) 8.85 (d, 1 H, $J = 4.45$ Hz), 7.81 (d, 1 H, $J = 4.96$ Hz), 4.14 (s, 3 H), 2.99 (s, 3 H), 2.08 (s, 3 H).

Acknowledgment. This investigation was supported by PHS Grant number CA-40157 awarded by the National Cancer Institute, DHHS. We are grateful to Professor Rick Danheiser of MIT for an insightful discussion on the origins of the regioselection of the quinone formation.

Registry No. 1, 92421-26-6; **2** (R = Me; R′ = CO_2Et), 92421-38-0; **2** (R = CO_2Et; R′ = Me), 92421-39-1; **2** (R = Me; R′ = CO_2Et, hydroquinone), 107301-78-0; **2** (R = CO_2Et; R′ = Me, hydroquinone), 107301-79-1; **2** (R = Et; R′ = COMe), 107301-67-7; **2** (R = COMe; R′ = Et), 107301-68-8; **2** (R = CH_2SiMe_3; R′ = Me), 107301-69-9; **2** (R = Me; R′ = CH_2SiMe_3), 107301-70-2; **2** (R = CH_2SiMe_2Bu-*t*; R′ = Me), 107301-71-3; **2** (R = Me; R′ = CH_2SiMe_2Bu-*t*), 107301-72-4; **2** (R = OEt; R′ = Me), 92421-48-2; **2** (R = Me; R′ = OEt), 92421-49-3; **2** (R = R′ = Me, hydroquinone), 107301-80-4; **3** (R = Bu), 92421-34-6; **3** (R = CH_2SiMe_2Bu-*t*), 107301-73-5; **3** (K = CH=CHOMe-(*Z*)), 107301-75-7; **3** (R = $(CH_2)_2NPhth$), 107301-85-9; **3** (R = $(CH_2)_2NCbz(Bn)$), 107301-87-1; **3** (R = $(CH_2)_2NCOCF_3(Bn)$), 107301-89-3; **3** (R = $(CH_2)_2NSO_2CF_3(Bn)$), 107301-91-7; **3** (R = $(CH_2)_2NCOCO_2Et(Bn)$), 107301-93-9; **4** (R = Bu), 92421-35-7; **4** (R = CH_2SiMe_2Bu-*t*), 107301-74-6; **4** (R = (*Z*)-CH=CHOMe), 107301-76-8; **4** (R = $(CH_2)_2NPhth$), 107301-86-0; **4** (R = $(CH_2)_2NCbz(Bn)$), 107301-88-2; **4** (R = $(CH_2)_2NCOCF_3(Bn)$), 107301-90-6; **4** (R = $(CH_2)_2NSO_2CF_3(Bn)$), 107301-92-8; **4** (R = $(CH_2)_2NCOCO_2Et(Bn)$), 107301-94-0; **7**, 107302-04-5; **8**, 79664-58-7; **9**, 107301-97-3; **10** (major isomer), 107301-98-4; **10** (minor isomer), 107301-99-5; **10** (major isomer, hydroquinone), 107302-00-1; **10** (minor isomer, hydroquinone), 107302-01-2; **11**, 107302-03-4; **12**, 107302-02-3; **13**, 98498-39-6; MeBrMg, 75-16-1; $ClCo(PPh_3)_3$, 26305-75-9; $Me_3SiC{\equiv}CMe$, 6224-91-5; *t*-$BuMe_2SiCl$, 18162-48-6; *t*-$BuMe_2SiCH_2C{\equiv}CH$, 107301-60-0; $HO(CH_2)_2C{\equiv}CH$, 927-74-2; $HC{\equiv}C(CH_2)_2NPhth$, 14396-90-8; 4-$MeC_6H_4SO_2(CH_2)_2C{\equiv}CH$, 36832-51-6; $PhCH_2NH_2$, 100-46-9; $PhCH_2NH(CH_2)_2C{\equiv}CH$, 107301-61-1; $PhCH_2CO_2Cl$, 501-53-1; $PhCH_2N(Cbz)(CH_2)_2C{\equiv}CH$, 107301-62-2; $F_3CCO_2OCF_3$, 407-25-0; $PhCH_2N(COCF_3)(CH_2)_2C{\equiv}CH$, 107301-63-3; $F_3CSO_2N(CH_2Ph)(CH_2)_2C{\equiv}CH$, 107301-64-4; $PhCH_2N(COCO_2Et)(CH_2)_2C{\equiv}CH$, 107301-65-5; $HC{\equiv}C(CH_2)_3CH_3$, 693-02-7; $MeCH_2C{\equiv}CCOMe$, 1679-36-3; $MeOCH{=}CHC{\equiv}CH$, 2798-73-4; $EtOC{\equiv}CMC$, 14273-06-4; *t*-$BuMe_2SiCH_2C{\equiv}CMe$, 107301-66-6; Cl_2CHOMe, 4885-02-3; $ClCH_2OMe$, 107-30-2; $Me_3SiSiMe_3$, 1450-14-2; MeCHO, 75-07-0; $Me_3SiC{\equiv}CCH_2SiMeBu$-*t*, 78978-51-5; $PhCH_2NH(CH_2)_2C{\equiv}CCH(OH)Me$, 107301-95-1; $PhCH_2N(Cbz)(CH_2)_2C{\equiv}CCH(OH)Me$, 107301-96-2; $Me_3SiCH_2C{\equiv}CMe$, 18825-29-1; squaric acid, 2892-51-5; diethyl squarate, 5231-87-8; 3-hydroxy-4-methylcyclobutenedione, 29769-75-3; 3-methoxy-4-methylcyclobutenedione, 29769-77-5; dimethylglyoxime, 95-45-4; silver trifluoroacetate, 2966-50-9; phthalimide, 85-41-6; triflic anhydride, 358-23-6; ethyloxachloride, 4755-77-5; ethyl tetrolate, 4341-76-8; 2,4-dimethyl-3,5,6-(trimethoxy)benzyl alcohol, 107301-77-9; 2,5-dimethyl-3,4,6-(trimethoxy)benzyl alcohol, 92421-45-9; 2,4-dimethyl-3,5,6-(trimethoxy)ethyl benzoate, 92421-40-4; 1,3-dimethoxy-2,4,5-triacetoxybenzene, 41168-76-7; 1,3-dimethyl-2,4,5-trimethoxybenzene, 92421-42-6; 2,4-dimethyl-3,5,6-trimethoxybenzaldehyde, 92421-43-7; ethyl 2,5-dimethyl-3,4,6-trimethoxybenzoate, 92421-44-8; 2,5-dimethyl-3,4,6-trimethoxybenzyl alcohol, 92421-45-9; 4,4-dimethyl-2,3,6-triacetoxybenzene, 40853-36-9; 1,4-dimethyl-2,3,6-trimethoxybenzene, 92421-46-0; 2,5-dimethyl-3,4,6-trimethoxybenzaldehyde, 92421-47-1; 2,4,5-trimethoxy-3,6-(dimethylbenzyl)trimethyl)silane, 107301-81-5; 2,4-dimethyl-3,5,6-trimethoxybenzyl chloride, 107301-82-6; 2,3,5-trimethoxy-1,4-dimethylbenzene, 92421-46-0; 2,5-dimethyl-3,4,6-(trimethoxy)benzyl chloride, 107301-83-7; 2,3,5-trimethoxy-4,6-dimethylbenzyl(trimethyl)silane, 107301-84-8; chlorobis(triphenylphosphine)maleoylcobalt complex, 92421-25-5; *p*-quinone, 106-51-4; 2-butyne, 503-17-3.

Mechanisms of Hemin-Catalyzed Epoxidations: Electron Transfer from Alkenes

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Abstract: Two rearrangements of alkenes, known to proceed through the intermediacy of the alkene cation radical, have been observed to accompany the hemin-catalyzed epoxidations of these alkenes. Hexamethyl(Dewar benzene) partially rearranged to hexamethylbenzene during its epoxidation using (tetraphenylporphyrinato)iron(III) chloride and *m*-chloroperbenzoic acid, but not with either of the reagents separately. In a similar manner the diene, 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*endo,endo*-dimethanonaphthalene, closed to the known "birdcage hydrocarbon" under these conditions. This diene also brought about some N-alkylation of the catalyst during the reaction. These observations are interpreted in terms of an electron transfer from alkene to the high-valent iron intermediate, leading to both rearrangement and epoxidation.

It is generally agreed that an iron(IV) porphyrin cation radical ($Fe^+{=}O$, oxene) is an intermediate in epoxidation and hydroxylation reactions catalyzed by cytochromes P-450 or by model iron(III) porphyrins.[1-5] The first step in the reaction of the oxene

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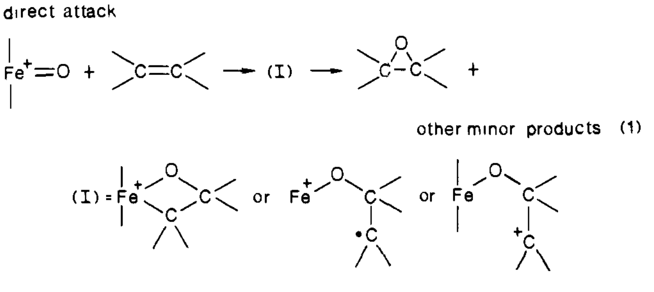
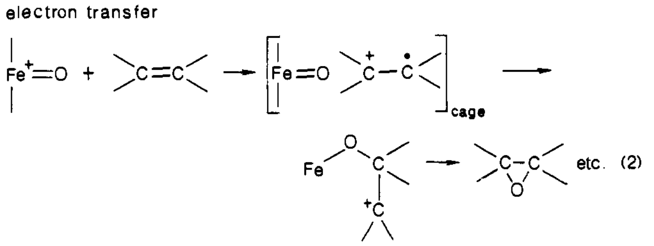
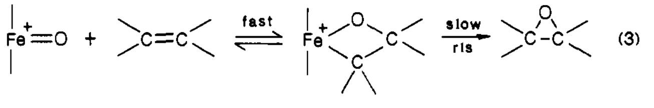
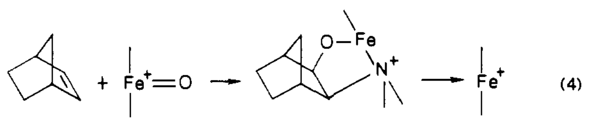
with alkenes has been postulated to be either direct attack to produce a radical, carbocation, or a metallacycle (eq 1) or electron transfer to produce a caged pair which collapses[6,7] to one of these intermediates[5] (eq 2). Rearrangements which accompany epoxidation suggest an intermediate carbocation arising from caged pair collapse or metallacycle opening.[3,5]



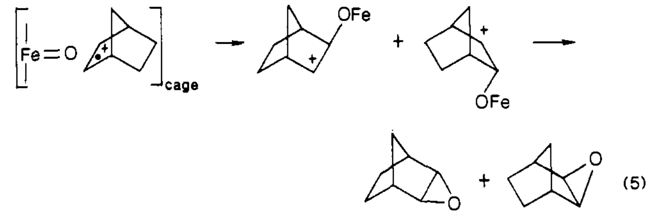


Kinetic evidence seemed to support the accumulation of an intermediate metallacycle which decomposes in a rate-limiting step (rls) to epoxide (eq 3).[3] This proposal requires the buildup of an intermediate. In searching for spectroscopic evidence for an intermediate, which we had observed as a transient green color, we discovered evidence for the transient accumulation of an *N*-alkylhemin (eq 4), a process which we have studied further.[5e] Since this is the only transient formed and since it can be shown *not* to be an intermediate, the proposed metallacycle accumulation seems to be excluded.

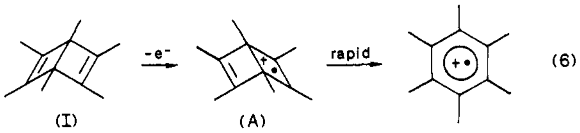


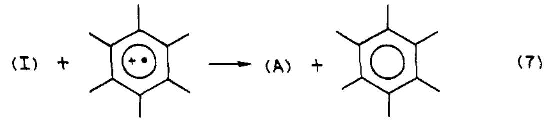


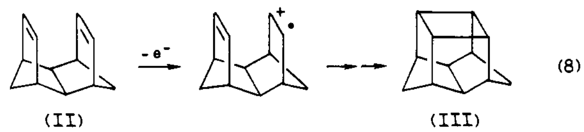
The mixtures of exo and endo epoxides having exo/endo ratios as low as 3.5 observed in these reactions contrast the results with hundreds of other norbornene additions in which the exo/endo ratio exceeds 100.[5c] These results are consistent with formation of a cation radical which collapsed by free-radical interaction to a carbocation (eq 5). Such reactions of 2-norbornyl radicals give low exo/endo ratios.



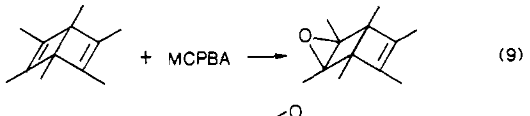
In order to test the viability of an electron-transfer mechanism, we have sought for methods to show that the intermediate "oxene" is capable of electron transfer from alkenes. A logical way to accomplish this is to discover some internal reaction of an alkyl cation radical which is competitive with cage collapse. Molecular rearrangements of cationic systems are known to occur at such rates. We have chosen two well-documented cation-radical rearrangements for this test. Jones,[8,9] Bauld,[10] their co-workers, and others have shown that reactions 6–8 occur rapidly upon one-electron oxidation by photochemical or electrochemical means.

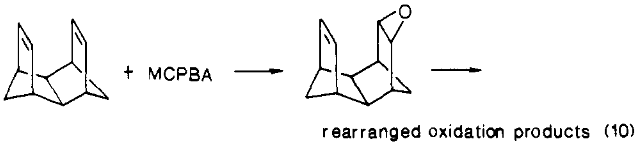






In both cases, a chain electron-transfer process occurs.[8-10] As we demonstrate here, chemical one-electron oxidation gives the same result. These same alkenes are epoxidized without these rearrangements when treated with *m*-chloroperbenzoic acid (MCPBA), eq 9 and 10.





We have therefore carried out hemin-catalyzed epoxidations of these alkenes in the hope that, if radical cations occur in the cage as in eq 2, there would be some leakage from the cage and therefore some rearrangement. This turns out to be the case.

Experimental Section

Materials. Hexamethyl(Dewar benzene) (Aldrich, HMDB) was purified by passage through alumina and used immediately for oxidation reactions. Diene, 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*endo,endo*-dimethanonaphthalene, was prepared by the reductive dechlorination of isodrin.[11] Birdcage hydrocarbon, hexacyclo$[6.2.1.1^{3,6}.0^{2,7}.0^{4,10}.0^{5,9}]$dodecane,[9] was prepared by isomerization of diene in two ways. An acetone solution of diene was photolyzed with UV light in a Rayonet reactor for 1 h to afford complete conversion to the birdcage hydrocarbon. The

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(6) Several authors[1,2] have considered electron transfer to high-valent iron porphyrins in or out of the P-450 enzymes as being limited only by oxidation potentials and not by reaction type.

(7) Groves and Myers[4] suggested carbocation intermediates for the formation of phenylacetaldehyde during styrene epoxidation, and Stearns and Ortiz de Montellano[2b] suggested analogous intermediates for the P-450-catalyzed oxidation of quadricyclene to a rearranged aldehyde. See Also ref 1.

(8) (a) Jones, G., II; Chiang, S. H. *J. Am. Chem. Soc.* **1979**, **101**, 7421. (b) Jones, G., II; Becker, W. G. *J. Am. Chem. Soc.* **1983**, *105*, 1276.

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(11) Howe, R. K.; Winstein, S. *J. Org. Chem.* **1973**, *38*, 2797.

solvent was evaporated to dryness under vacuum, and the solid was sublimed at 1 torr at 50 °C to give a white, waxy solid. The second approach involved treating a methylene chloride solution of the diene with 5% by mole weight tris(*p*-bromophenyl)aminium hexachloroantimonate for 10 min. The product was isolated by evaporation of solvent and sublimed. The NMR and IR of the birdcage hydrocarbon prepared by routes 1 and 2 were identical with the published spectra.[9,12] *m*-Chloroperbenzoic acid (technical grade, Aldrich, MCPBA) was purified by literature methods[13] and recrystallized from CH_2Cl_2. Titration by iodometric assay indicated >99% purity. Pentafluoroiodosylbenzene (PFIB) was prepared from perfluoroiodosobenzene–bis(trifluoroacetate)[14] in a manner similar to that for iodosylbenzene[15] and was dried over P_2O_5 under vacuum (<1 torr). (EXPLODES![15b]) (Tetraphenylporphyrinato)iron chloride was prepared and purified by literature methods.[16] Hexamethylbenzene (99+%, Aldrich), tris(*p*-bromophenyl)aminium hexachloroantimonate (Aldrich), and *n*-tetradecane (Eastman Organic Chemicals) were used as received. Methylene chloride and acetonitrile (Analytical reagent grade, Mallinckrodt) were stirred over and distilled from CaH_2.

Instrumental. Samples were analyzed on a Varian 3700 gas–liquid chromatograph equipped with a 10% Carbowax 20M 80/100 Suppelcoport column. Infrared spectra were obtained as KBr pellets on a Perkin-Elmer 1330 infrared spectrophotometer. ^1H NMR were recorded on a Varian EM-390 90-MHz spectrometer in CCl_4 or $CDCl_3$ with Me_4Si as an internal standard. UV–visible spectra were recorded on a Kontron Uvikon 810 spectrophotometer.

Procedures. The conditions for a typical HMDB oxidation reaction using the complete reaction mixture were as follows. Into a small test tube were placed 0.040 mL of HMDB (4.7 M, 0.19 mmol), 0.040 mL of tetradecane standard in CH_2Cl_2 (0.27 M, 0.011 mmol), 0.080 mL of a CH_2Cl_2 solution of FeTPPCl (5.0 mM, 4.0×10^{-4} mmol), and 0.240 mL of solvent (CH_2Cl_2/CH_3CN). The test tube was sealed with a silicon septum, and the contents were thoroughly mixed. MCPBA (4.0 mg, 0.023 mmol) was added, and the test tube was shaken for 5 min; then an aliquot was removed and injected into the GLC for analysis.

The conditions for the oxidation of HMDB in the presence of tetrabutylammonium perchlorate (TBAP) using the complete reaction mixture were as follows. Into a small test tube were added 0.040 mL of HMDB (4.7 M, 0.19 mmol), 0.040 mL of tetradecane standard in CH_2Cl_2 (0.28 M, 0.011 mmol), 0.080 mL of a CH_2Cl_2 solution of FeTPPCl (5.0 mM, 4.0×10^{-4} mmol), 65 mg of TBAP (0.19 mmol), and 0.240 mL of solvent (CH_2Cl_2/CH_3CN). The test tube was stoppered and shaken. To the solution was added MCPBA (4.0 mg, 0.023 mmol) and the test tube shaken for 5 min; then an aliquot was removed and analyzed by GLC.

The conditions for the oxidation of HMDB in which the initial concentration of HMDB was varied using the complete reaction mixture were as follows. Into a small test tube were added 0.040 mL of tetradecane standard in CH_2Cl_2 (0.28 M, 0.011 mmol), 0.080 mL of a CH_2Cl_2 solution of FeTPPCl (5.0 mM, 4.0×10^{-4} mmol), 0.120 mL of CH_3CN, 0.060 mL CH_2Cl_2, and either 0.100, 0.040, or 0.020 mL of HMDB (4.7 M). The amount of CH_2Cl_2 was also varied so that the total volume of solvent was always 0.400 mL. MCPBA (4.0 mg, 0.023 mmol) was added to the solution and the test tube shaken for 5 min; then an aliquot was removed and analyzed by GLC.

The conditions for a typical diene oxidation reaction using MCPBA and the complete reaction mixture were as follows. Into a small test tube were placed 7.6 mg of diene (0.048 mmol), 0.020 mL of tetradecane standard in CH_2Cl_2 (0.61 M, 0.012 mmol), 0.140 mL of a CH_2Cl_2 solution in FeTPPCl (5.7 mM, 8.0×10^{-4} mmol), and 0.240 mL of solvent (CH_2Cl_2/CH_3CN). The test tube was sealed, and the contents were thoroughly mixed. MCPBA (4.1 mg, 0.024 mmol) was added to the solution, and the test tube was shaken for 5 min in the dark; then an aliquot was removed and injected for GLC analysis.

The conditions for a typical diene oxidation reaction using pentafluoroiodosylbenzene and the complete reaction mixture were as follows. Into a small test tube were placed 3.8 mg of diene (0.024 mmol), 0.020 mL of tetradecane standard in CH_2Cl_2 (0.30 M, 0.0060 mmol), 0.040 mL of a CH_2Cl_2 solution of FeTPPCl (9.9 mM, 4.0×10^{-4} mmol), and 0.140 mL of solvent (CH_2Cl_2/CH_3CN). The test tube was sealed with a septum, and the contents were thoroughly mixed. Pentafluoroiodosylbenzene (3.7 mg, 0.012 mmol) was added all at once to the test tube, and it was shaken for 5 min in the dark; then an aliquot was removed and injected for analysis. The oxidant (MCPBA or PFIB) dissolved in less than 1 min, and nothing precipitated from the solutions at the end of all the above reactions.

Table I. Yields of Hexamethylbenzene and Hexamethyl(Dewar benzene) Epoxide in Uncatalyzed and Hemin-Catalyzed Epoxidations of Hexamethyl(Dewar benzene) Using *m*-Chloroperbenzoic Acid[a]

	products					
	complete reaction mixture		without FeTPPCl		without MCPBA	
solvent % CH_3CN in CH_2Cl_2	HMB,[b] μmol	epoxide,[b] μmol	HMB,[b] μmol	epoxide,[b] μmol	HMB,[b] μmol	epoxide,[b] μmol
60	47[c]	11	0.0	10	2.2	0.0
30	21	10	0.0	10	1.1	0.0
0	5.6	13	0.0	12	0.0	0.0
0[d]	6.7	11	0.0	12	0.0	0.0
0[e]					48	0.0

[a] Conditions: For the complete reaction mixture (0.4 mL), solutions were made 0.47 M in HMDB, 0.028 M in the tetradecane standard, 0.001 M in iron(III) tetraphenylporphyrin chloride, and 0.058 M in MCPBA. In the other mixtures the indicated reagent was omitted and the reaction treated in the same way. [b] Total amount of product as determined by comparing peak areas with that of an internal standard and correcting for detector responses. Yields were also corrected for the small amounts (1 μmol) of epoxide and HMB in the starting HMDB. [c] This corresponds to 120 mol/mol of Hm^+Cl^- catalyst. [d] The concentration of FeTPPCl was 0.008 M. [e] In this experiment, 0.47 M HMDB in CH_2Cl_2 was made 0.001 M in tris(*p*-bromophenyl)aminium hexachloroantiomonate for 5 min without any other reagent except the GLC standard.

Table II. Yields of Birdcage Hydrocarbon (III) and Diene (II) Oxidation Products in Uncatalyzed and Hemin-Catalyzed Epoxidations of Diene (II) Using *m*-Chloroperbenzoic Acid[a]

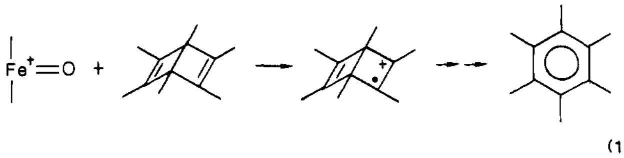
	products					
	complete reaction mixture		without FeTPPCl		without MCPBA	
solvent % CH_3CN in CH_2Cl_2	III, μmol	oxidation,[b] μmol	III, μmol	oxidation,[b] μmol	III, μmol	oxidation,[b] μmol
60	17[c]	9.6	0.0	12	0.0	0.0
30	7.2	8.4	0.0	13	0.0	0.0
0	2.4	9.6	0.0	14	0.0	0.0
0[d]					54.0	

[a] Conditions: For the complete reaction mixture (0.4 mL), solutions were made 0.12 M in diene (II), 0.030 M in the tetradecane standard, 0.002 M in FeTPPCl, and 0.060 M in MCPBA. In all other respects the reactions were treated as in Table I. [b] There were three oxidation products with or without catalyst. [c] This corresponds to 21 mol/mol of Hm^+Cl^- catalyst. [d] See footnote *e* of Table I for conditions.

Results and Discussion

The products of the reaction of hexamethyl(Dewar benzene) with the hemin catalyst alone, with MCPBA alone, and with both reagents are shown in Table I. This table shows that both MCPBA and the catalyst are required to obtain ring opening to hexamethyl(Dewar benzene). The last entry also shows that the one-electron oxidant, tris(*p*-bromophenyl)aminium hexachloroantimonate, brings about efficient isomerization to HMB.

Epoxidation with MCPBA alone is fast and complete. Therefore, uncatalyzed epoxidation cannot be separated from catalyzed epoxidation in these systems. However, these conditions are known to bring about rapid formation of the high-valent iron intermediate ($Hm^+{=}O$) which rapidly epoxidizes alkenes. Therefore, the rearrangement results from reaction of this intermediate (eq 11). It is also likely that a chain electron transfer like that shown in eq 6 and 7 is involved. There are 15–120



(11)

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Table III. Yields of Hexamethylbenzene and Hexamethyl(Dewar benzene) Epoxide in Uncatalyzed and FeTPPCl-Catalyzed Epoxidations of HMDB Using MCPBA in the Presence of 0.5 M Tetrabutylammonium Perchlorate[a]

	products[b]					
	complete reaction mixture		without FeTPPCl		without MCPBA	
solvent % CH_3CN in CH_2Cl_2	HMB, μmol	epoxide, μmol	HMB, μmol	epoxide, μmol	HMB, μmol	epoxide, μmol
60	47	11	0.0	11	3.4	1.1
30	44	5.6	0.0	10	3.4	1.1
0	45	6.7	0.0	6.7	3.4	0.0

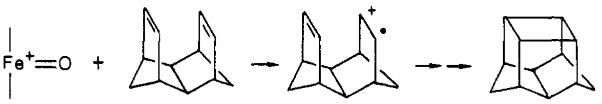
[a] All conditions are as in Table I except for added TBAP. [b] Values calculated as in Table I.

Table IV. Ratio of Hexamethylbenzene to Hexamethyl(Dewar benzene) Epoxide Formed as a Function of the Initial Concentration of Hexamethyl(Dewar benzene) in the FeTPPCl-Catalyzed Epoxidation of Hexamethyl(Dewar benzene) Using MCPBA[a]

	HMB/HMDB epoxide[b]	
initial [HMDB], M	complete reaction mixture	without FeTPPCl
1.18	7.9	0.0
0.47	4.2	0.0
0.24	2.4	0.0

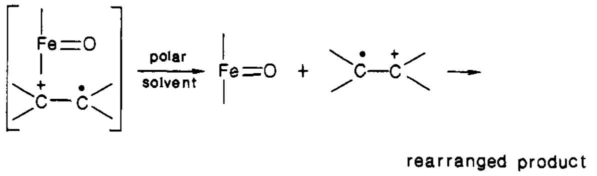
[a] The conditions are as in Table I except for HMDB. [b] The ratio of formed HMB to HMDB epoxide was corrected for the small (0.1) relative areas of HMB and HMDB epoxide in the starting HMDB.

rearrangement products per catalyst molecule. Similarly, Table II demonstrates the ring closure which is known to occur upon one electron oxidation of diene II (eq 12).



(12)

These tables also demonstrate a marked solvent effect on the isomerizations, increasing as polarity increases. This is consistent with solvent-induced separation of a charged cage pair. Indeed, that portion of radical cation which goes to rearranged hydrocarbon might come entirely from diffusion before rearrangement. It is also possible that the polar solvent increases electron-transfer rates since the alkene radical cation is less delocalized and thus better solvated than the porphyrin radical cation (eq 13).



(13)

Table III shows the effect of adding the salt, tetrabutylammonium perchlorate, to the reaction mixture of MCPBA, catalyst, and HMDB. The salt has about the same effect upon isomerization as does the addition of acetonitrile. This result supports the conclusion reached above. In this case, the caged pair could exchange with the salt,[17] essentially removing the cation radical from the cage.

The extent of rearrangement to hexamethylbenzene, if it proceeds through the proposed[8,10] radical cation chain process, should increase with increasing concentration of HMB. This is shown to be the case in Table IV. This is strong evidence for the radical cation mechanism since simple electrophilic attack should show the same order in alkene toward both epoxidation and rearrangement.

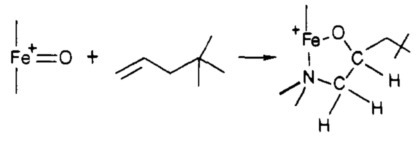
In order to demonstrate that the oxene leads to both alkene isomerization and epoxidation under the same conditions, we have carried out catalyzed epoxidations using pentafluoroiodosylbenzene (PFIB), shown in Table V. Although PFIB slowly isomerizes and epoxidizes this alkene without catalyst, the extent of rearrangement is small. Again, the oxene causes isomerization and, in this case, we document catalyzed epoxidation. Since epoxidation is complete in each case, no solvent effect is seen. But the solvent effect on the isomerization is apparent.

Table V. Yields of Birdcage Hydrocarbon (III) and Diene (II) Oxidation Products in Uncatalyzed and Hemin-Catalyzed Epoxidations of Diene (II) Using Perfluoroiodosylbenzene[a]

	products					
	complete reaction mixture		without FeTPPCl		without PFIB	
solvent % CH_3CN in CH_2Cl_2	III, μmol	oxidation,[b] μmol	III, μmol	oxidation,[b] μmol	III, μmol	oxidation,[b] μmol
60	6.6	4.2	0.6	0.6	0.0	0.0
30	3.0	3.0	0.6	0.6	0.0	0.0
0	0.6	3.6	0.0	0.6	0.0	0.0

[a] Conditions: For the complete reaction mixture (0.2 mL), solutions contained 0.12 M diene (II), 0.06 M PFIB, 0.030 M tetradecane standard, and 0.002 M FeTPPCl. The reaction mixture was shaken for 5 min in the dark and analyzed by GLC as previously described. In all other respects, the reactions were treated as in Table I. [b] There were three oxidation products with or without catalyst.

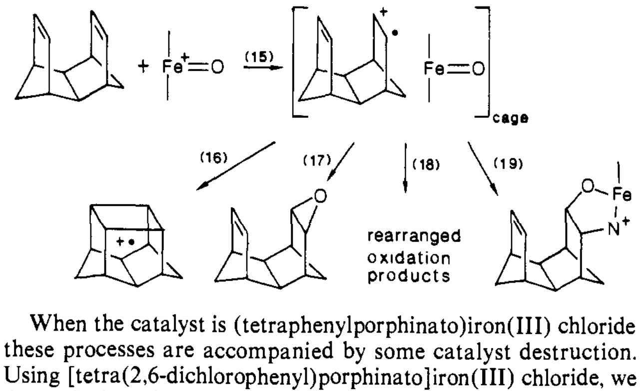
***N*-Alkylhemin Formation.** We have previously observed the formation of a stable *N*-alkylhemin during the catalyzed epoxidation of a terminal alkene using [tetra(2,6-dichlorophenyl)porphinato]iron(III) chloride as catalyst[18] (eq 14). More recently



(14)

similar N-alkylation has been observed with other alkenes[5e] (see eq 4). However, the *N*-alkylhemin tends to revert to the original hemin at rates which depend upon the alkene and hemin structures.

During the catalyzed epoxidation of diene II using iron(III) tetraphenylporphyrin chloride as catalyst, we also observed a species whose spectrum is very similar (λ_{max} = 439 nm) to that observed in a documented *N*-alkylhemin formation. Interestingly the extent of formation of this species increases as the solvent is made more polar by the addition of acetonitrile. Thus, *N*-alkylhemin formation responds to solvent polarity in the same way as does the formation of the birdcage hydrocarbon shown in Tables II and V. This suggests a common intermediate in these two processes. The simultaneous epoxidation, alkene isomerization, formation of rearranged oxidation products, and *N*-alkylhemin formation with this diene are consistent with the formation of a cation-radical pair which reacts in four different ways (eq 15–19).



When the catalyst is (tetraphenylporphinato)iron(III) chloride these processes are accompanied by some catalyst destruction. Using [tetra(2,6-dichlorophenyl)porphinato]iron(III) chloride, we do not find catalyst destruction, but the *N*-alkylhemin decomposes to hemin rapidly, making its observation more difficult. Details

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of the N-alkylation processes will be discussed elsewhere.[5e] It suffices to point out here that most of the various reaction paths in the catalyzed epoxidation of diene II have been observed with other alkenes such as norbornene and cyclohexene, indicating that this diene is not special with regard to its reaction with the high-valent iron intermediate.

The present results demonstrate that the high-valent iron intermediate can remove an electron from these two alkenes. However, the conclusions we reach with regard to other alkenes must include effect of ionization potentials. The gas-phase ionization potentials of I[19] and II[20] are 7.8 and 8.1 eV, respectively, compared to 9.0 eV for norbornene[21] and 9.1 eV for cyclohexene.[21] It seems unlikely that alkenes bearing very electronegative substituents would be epoxidized through radical cations. Therefore, a change in mechanism might occur at some higher ionization potential. We believe that the exo/endo ratios in epoxidation[5c] of norbornene are consistent with a radical cation intermediate even though the ionization potential is somewhat higher than are those of I and II.

Since alkenes I and II are known to undergo radical cation chain rearrangements, it is possible that the rearrangement represents a minor pathway unrelated to epoxidation. However, the observation of simultaneous alkene isomerization, epoxidation, production of rearranged oxidation products, and formation of *N*-alkylhemin, the last three reactions also occurring with other alkenes, encourages us to conclude that all of these processes are related, very probably through radical cation. Thus, all of our results to date are consistent with an electron transfer from alkene to the "oxene" followed by one of the processes discussed above. With most alkenes the dominant process is formation of epoxide.

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Kinetics and Mechanism of Hydration of Alkylketenes

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Abstract: The hydration reactivities of $CH_2{=}C{=}O$ (**1**), $t\text{-}Bu_2C{=}C{=}O$ (**5**), $Et_2C{=}C{=}O$ (**7**), $(CH_2)_4C{=}C{=}O$ (**8**), $(CH_2)_5C{=}C{=}O$ (**9**), and $t\text{-}BuCH{=}C{=}O$ (**10**) in H_2O or H_2O/CH_3CN mixtures have been examined, including acid and base catalysis and solvent and structural isotope effects. These results provide the first systematic comparison of structural effects on the hydration of aliphatic ketenes, as well as the first measurements of base-induced hydration and pH-rate profiles for this process. The significant steric and electronic effects of the substituents observed lead to the interpretation that the acid-catalyzed reaction involves rate-limiting proton transfer to C_β perpendicular to the ketene plane, while the H_2O- and OH^--induced reactions involve nucleophilic attack in the ketene plane. These results resolve the many conflicting previous reports and interpretations regarding ketene hydration.

Ketenes have long been the topic of chemical study, the results of which have been frequently reviewed.[1,2] There has been intense recent interest in ketene addition reactions, including both cycloadditions[3] and other additions,[2c,4] and prevalent views that both of these processes proceed through cyclic as opposed to open transition states have been challenged.[2c,3e] This report deals with the prototypical but controversial hydration of ketenes.

The mechanism of ketene hydration has been the object of several experimental studies, including the reactions of ketene (**1**)[5a] and arylketenes (**2**)[5b] in H_2O, diphenylketene (**3**) and dimethylketene (**4**) in ether containing up to 0.351 M H_2O,[6a,b] di-*tert*-butylketene (**5**)[7] in 50% acetonitrile/H_2O, and ketene (**1**) in the gas phase.[6c] Theoretical studies of ketene hydration have also been presented.[8]

$CH_2{=}C{=}O$ **1** $ArCH{=}C{=}O$ **2** $Ph_2C{=}C{=}O$ **3**

$Me_2C{=}C{=}O$ **4** $t\text{-}Bu_2C{=}C{=}O$ **5**

Several rather different mechanisms for the hydration of ketenes have been presented and reviewed.[2c] For the uncatalyzed reaction these include rate-limiting H_2O attack on C_α of the ketene followed by rearrangement to a carboxylic acid (eq 1),[5a] reaction of **3** with water trimer and **4** with water dimer via cyclic transition states (eq 2),[6a,b] and in theoretical studies attack of water monomer or dimer on the C=C or C=O double bonds of the ketene via cyclic transition states.[8] Additions to the C=C bond were depicted with

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