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Invited Paper

Manganese "Picnic Basket" Porphyrins: Cytochrome P-450 Active Site Analogues

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This paper describes studies of a new class of cytochrome P-450 model compounds called the "picnic basket porphyrins." The picnic basket porphyrins are unsymmetrical porphyrins with one face sterically protected by a superstructure and the other unhindered. The manganese(III) porphyrins have been investigated as shape selective catalysts using oxygen atom donors in the presence of a sterically bulky imidazole. This paper presents ligand binding studies and competitive olefin epoxidations which lead to the surprising conclusion that catalysis by the manganese picnic basket porphyrins occurs exclusively on the sterically unhindered face indicating reaction by the minor catalyst component and not the selective major catalyst component.

Synthetic metalloporphyrins have received considerable attention as olefin epoxidation and alkane hydroxylation catalysts, and, thus, as models of the enzyme cytochrome P-450.[1,2,11,26,28] As catalysts metalloporphyrins are sometimes limited by their low turnover numbers and difficult syntheses, yet some have shown good shape selectivity (cis versus trans olefins) and modest asymmetric induction in olefin epoxidation.[2]

Most studies of catalysis have utilized oxygen atom donors including iodosylbenzene, hypochlorite, hydrogen peroxide, alkyl hydroperoxides, or amine *N*-oxides to generate the metalloporphyrin-based oxidant. In addition, several examples of apparent activation of dioxygen to oxidize substrates employing reducing agents and metalloporphyrins have been reported.[3] In most of these examples, however, it is not clear if metal-bound dioxygen is actually being activated or if catalysis is mediated by free hydrogen peroxide or peracids formed under these conditions.

While metalloporphyrins have limited practical applications, studies of oxygenations by metalloporphyrins and their selectivity have been useful in understanding the mechanism of cytochrome P-450 activity. This family of heme containing monooxygenases catalyze the oxygenation of organic substrates using dioxygen and NADH. Many key steps in the activation of oxygen by cytochrome P-450 and the subsequent oxidation of substrates are still not well-understood.

In an attempt to learn more about this important enzyme, we have prepared a new family of porphyrins called the "picnic basket" porphyrins, which are designed to exclude bulky axial ligands and yet allow small molecules like dioxygen to bind within the pocket.

In our investigation of these porphyrins we were particularly interested in probing the selectivity of the pocket toward axial ligands and olefin structure in catalytic epoxidations. Since we hope eventually to use the picnic basket porphyrins to activate dioxygen, information about the substrate selectivity within the pocket would allow us to determine whether bound dioxygen was activated in this cavity or whether catalysis was mediated by a free oxygen atom donor as discussed earlier. This paper describes the synthesis of the picnic basket porphyrins, ligand binding studies, and results from competitive olefin epoxidation. These studies led to unexpected conclusions about catalysis by manganese derivatives of the picnic basket porphyrins.

Experimental

Materials: Methylene dichloride, chloroform, tetrahydrofuran, 30% hydrogen peroxide and basic alumina (activity I) were purchased from J. T. Baker Chemical Company and used without further purification. Anhydrous manganese(II) bromide, 1-methylimidazole, (diacetoxyiodo)benzene, and *N,N*-dimethylformamide were purchased from Aldrich Chemical Co. and used as received. 2,6-Lutidine was purchased from Aldrich Chemical Co. and was dried by stirring over KOH and distilling from BaO. Manganese tetraphenylporphyrin (TPP) and tetramesitylporphyrin (TMP) were prepared as described in the literature. Iodosylbenzene was prepared from the diacetate by basic hydrolysis. 1,5-Diphenylimidazole was prepared by a modified literature procedure.[4] $\alpha,\alpha,\alpha,\alpha$-Tetrakis(*o*-aminophenyl)porphyrin was prepared as reported in the literature.[5] Manganese(III) porphyrin salts of various counterions were prepared from the corresponding bromide using the method of Bruice et al.[25]

Methods: Visible spectra were recorded either on a Varian Cary 219 Spectrometer or with a Hewlett Packard 8450A Diode Array Spectrometer with 7470A Plotter. In order to obtain reproducible spectral titrations, all glassware was treated with 5% aqueous NaOH for 12 h, rinsed, and then soaked in dilute aqueous HBr for 12 h. Spectra were recorded of CH_2Cl_2 solutions, at 25.0±0.5 °C, from 700 to

300 nm in a 1 cm pathlength cell. The concentration of Mn(PBP)Br was approximately 2×10^{-5} M and the imidazole concentration ranged from 0 to 20 mM. *N*-Substituted imidazoles were added to the cuvette from standard stock solutions via microliter syringe. Data were analyzed by the method of Dolphin and James.⁶⁾ Cyclic voltammograms were obtained using a Princeton Applied Research wave generator and a Hewlett Packard x–y recorder. $E_{1/2}$ values were measured for CH_2Cl_2 solutions containing 0.2 M tetrabutylammonium perchlorate (TBAP) as electrolyte at a glassy carbon electrode and are referenced to SSCE. All measured $E_{1/2}$ values are for reversible (ΔE_p=60—80 mV) or quasireversible waves (ΔE_p=80—110 mV). Epoxide production was monitored on a Hewlett Packard Model 5880A gas chromatograph fitted with a 15′×1/8″ column of OV-101 on Supelcoport. Chiral shift ^{1}H NMR was accomplished by adding Tris[3-(heptafluoropropylhydroxymethylene) (+)-camphorato]europium(III) [Eu(hfc)$_3$] (Aldrich) to a NMR sample of the isolated epoxide until the epoxide signals were resolved.²ᵃ⁾

Synthesis: Bis(5-nitroisophthalamido)-*α,α,α,α*-tetrakis(*o*-aminophenyl)porphyrin (2). The reaction was carried out under a rigorously dry nitrogen atmosphere using oven-dried glassware. 5-Nitroisophthaloyl chloride (3.968 g, 16.0 mmol) in dry CH_2Cl_2 (100 mL distilled from P_2O_5) was slowly added, with stirring, to a solution of *α,α,α,α*-TAMPP (340 mg, 0.50 mmol) in CH_2Cl_2 (1.0 L) containing pyridine (10 mL) in an ice bath. After stirring for 12 h at 0 °C the solution was treated with aqueous $NaHCO_3$ solution. The solution was filtered through a celite pad and the pad was washed with 9:1 EtOH–$CHCl_3$. After separation of the organic layer, the aqueous layer was extracted with two 100 mL portions of $CHCl_3$. The combined organic layers were washed with two 100 mL portions of saturated $NaHCO_3$ and with two 100 mL portions of water, reduced to a small volume, and purified by chromatography on a silica-gel column, eluting with $CHCl_3$ to 20:1 EtOH–$CHCl_3$. A purple band was cleanly separated. The product was crystallized by addition of EtOH and slow evaporation of the solvent and dried in vacuo (10^{-6} Torr) to yield 500 mg (24.4%) of purple crystals. ^{1}H NMR (CF_3CO_2D–$CDCl_3$) δ=9.06 (s, 4H), 8.81 (s, 4H), 8.57 (d, 4H), 8.43 (d, 4H), 8.16 (m, 4H), 7.97 (t, 4H), 7.72 (d, 4H), 7.01 (s, 2H). UV-vis (5% EtOH–$CHCl_3$) λ 449, 512 (sh), 545, 582, 618, 674 nm. IR (KBr) 3411 (vs), 1690 (vs), 1582 (s), 1526 (vs), 1449 (s), 1347 (m), 1313 (s), 967 (m), 812 (m), 800 (m), 759 (s), 723 (s) cm^{-1}. MS *m/z* 1025 (M+H).

Bis(5-aminoisophthalamido)-*α,α,α,α*-tetrakis(*o*-aminophenyl)porphyrin (3). The dinitro compound **2** (1.375 g, 1.34 mmol) was dissolved in a mixture of trifluoroacetic acid (20 mL) and acetic acid (50 mL) cooled in an ice bath. To this solution was added a concentrated hydrochloric acid solution (7.5 mL) of $SnCl_2\cdot2H_2O$ (9.07 g, 40.2 mmol); the mixture was then stirred for 6 h in an ice bath. The reaction mixture was slowly poured into aqueous $NaHCO_3$ in an ice bath. The resulting mixture was filtered through a celite pad. After removal of the water the celite pad was washed with 40% EtOH–$CHCl_3$ (about 500 mL) until the filtrate was nearly colorless. The organic solution was washed with saturated aqueous $NaHCO_3$ and then with water and dried over $MgSO_4$. The solution was concentrated in vacuo and the fine purple crystals which precipitated were centrifuged and washed with EtOH. After drying (10^{-6} Torr, 60—70 °C, 12 h) solvent-free diamine was obtained in 68% yield (884 mg). ^{1}H NMR (CF_3CO_2D–$CDCl_3$) δ=8.89 (s, 4H), 8.58 (s, 4H), 8.39 (d, 4H), 8.14 (m, 8H), 8.01 (t, 4H), 6.94 (s, 2H). UV-vis (5% EtOH–$CHCl_3$) λ 428, 490 (sh), 524, 563, 598, 653 nm. IR (KBr) 3453 (m), 3411 (s), 1681 (vs), 1579 (vs), 1520 (vs), 1446 (vs), 1341 (s), 1298 (s), 1239 (m), 964 (s), 884 (m), 806 (s), 791 (s), 757 (vs) cm^{-1}. MS *m/z* 964 (M−1).

General Method for the Synthesis of Amide-Strapped "Picnic Basket" Porphyrins 4a—e. The following reaction was carried out under a rigorously dry nitrogen atmosphere. To a dry $CHCl_3$ solution (50 mL) containing dry pyridine (0.5 mL), both a DMF solution (3 mL) of the diamine **3** (20 mg, 0.0207 mmol) and a CH_2Cl_2 solution (3 mL) of the diacid chloride (0.03 mmol) were added at the rate of about 10^{-2} mL min^{-1} by means of a syringe pump. After the addition was complete the mixture was stirred for an additional two hours. The reaction mixture was washed with two 20 mL portions of saturated $NaHCO_3$ and with two 20 mL portions of water. After the solvent was evaporated in vacuo, the residue was chromatographed on silica gel, eluting with 5% MeOH–CH_2Cl_2 (or EtOH–$CHCl_3$). A bright purple band was cleanly isolated. The fine red-purple crystals obtained on slow evaporation of the solvent were washed with EtOH and dried in vacuo (10^{-6} Torr, 60 °C, 12 h) to give the amide-strapped picnic basket porphyrins (**4a—e**).

***n*-C8-PBP (4a).** ^{1}H NMR (CF_3CO_2D–$CDCl_3$) δ=9.08 (s, 4H), 8.76 (s, 4H), 8.55 (d, 4H, *J*=7.8 Hz), 8.41 (d, 4H, *J*=7.5 Hz), 8.13 (t, 4H, *J*=7.8 Hz), 7.94 (t, 4H, *J*=7.5 Hz), 7.44 (s, 4H), 6.60 (s, 2H), 2.03 (br, t, 4H, *J*=6.7 Hz), 1.05 (br, t, 4H), 0.72 (br, 4H). UV-vis (5% EtOH–$CHCl_3$) λ 425, 487 (sh), 521, 556, 594, 648 nm. IR (KBr) 3411 (s), 2927 (m), 2857 (w), 1690 (vs), 1678 (vs), 1579 (s), 1520 (vs), 1462 (sh), 1449 (vs), 1338 (s), 1239 (s), 964 (s), 890, 797 (s), 757 (s) cm^{-1}. MS *m/z* 1102 (M).

***n*-C9-PBP (4b).** ^{1}H NMR (CF_3CO_2D–$CDCl_3$) δ=9.05 (s, 4H), 8.78 (s, 4H), 8.51 (d, 4H, *J*=7.9 Hz), 8.41 (d, 4H, *J*=7.3 Hz), 8.14 (t, 4H, *J*=7.9 Hz), 7.96 (t, 4H, *J*=7.3 Hz), 7.47 (s, 4H), 6.48 (s, 2H), 2.12 (br, t, 4H, *J*=5 Hz), 1.26 (br, s, 4H), 0.63 (br, 2H), 0.62 (br, 4H). UV-vis (5% EtOH–$CHCl_3$) λ 427, 523, 562, 596, 652 nm. IR (KBr) 3411 (s), 2927 (m), 2857 (m), 1687 (vs), 1672 (vs), 1579 (s), 1520 (vs), 1462 (sh), 1446 (vs), 1341 (m), 1319 (sh), 1242 (m), 964 (m), 806, 797 (m), 757 (m) cm^{-1}. MS *m/z* 1116 (M).

***n*-C10-PBP (4c).** ^{1}H NMR (CF_3CO_2D–$CDCl_3$) δ=9.02 (s, 4H), 8.79 (s, 4H), 8.50 (d, 4H, *J*=7.9 Hz), 8.39 (d, 4H, *J*=7.6 Hz), 8.15 (t, 4H, *J*=7.9 Hz), 7.97 (t, 4H, *J*=7.6 Hz), 7.51 (s, 4H), 6.54 (s, 2H), 2.13 (br, 4H), 1.27 (br, 4H), 0.78 (br, 8H). UV-vis (5% EtOH–$CHCl_3$) λ 428, 525, 563, 597, 653 nm. IR (KBr) 3411 (s), 2927 (m), 2850 (m), 1690 (vs), 1672 (sh), 1579 (vs), 1520 (vs), 1462 (sh), 1446 (vs), 1341 (s), 1316 (s), 1242 (s), 964 (s), 800 (m), 757 (s) cm^{-1}. MS *m/z* 1130 (M).

***n*-C11-PBP (4d).** ^{1}H NMR (CF_3CO_2D–$CDCl_3$) δ=9.05 (s, 4H), 8.77 (s, 4H), 8.56 (d, 4H, *J*=7.9 Hz), 8.39 (d, 4H, *J*=7.6 Hz), 8.15 (t, 4H, *J*=7.9 Hz), 7.96 (t, 4H, *J*=7.6 Hz), 7.56 (s, 4H), 6.53 (s, 2H), 2.16 (bt, 4H), 1.30 (br, 4H), 0.85 (br, 8H), 0.69 (br, 2H). UV-vis (5% EtOH–$CHCl_3$) λ 429, 488 (sh), 523, 561, 597, 642 nm.

General Procedure for Metallation of H_2(PBP) with Mn. Unmetallated picnic basket porphyrin (100 μmol), anhydrous $MnBr_2$ (215 mg, 1 mmol) and 20 drops of 2,6-lutidene were heated at reflux in 25 mL DMF under air in a 50 mL round bottom flask fitted with a magnetic stirrer and a condenser. After 5 h at reflux, UV-vis spectral analysis indicated complete metallation. The reaction mixture was cooled to room temperature and poured into 600 mL deionized water. The precipitate was collected by filtration through a Celite pad and washed liberally with deionized water. The crude product was extracted from the Celite with $CHCl_3$ and the filtrate reduced on a rotovap. The green residue was dissolved in 20 mL CH_2Cl_2 and loaded onto a basic activity I Al_2O_3 column (3.5 cm diameter×8 cm) prepared from CH_2Cl_2 slurry. The desired green band was obtained by elution with $CHCl_3$. The $CHCl_3$ layer was washed three times with 100 mL saturated aqueous KBr in a separatory funnel and passed through crystalline KBr. Removal of solvent and drying the residue provided the desired Mn(PBP)Br in 80—85% yield.

Mn(C10-PBP)Br, 5. UV-vis (CH_2Cl_2) λ 376, 400 (sh), 420 (sh), 489 (Soret), 534, 591, 628. MS m/z=1158 (M+1−Br) for $C_{70}H_{54}N_8O_6MnBr$ (LSIMS$^+$). Calcd for $C_{70}H_{54}N_8O_6MnBr$: C, 67.90; H, 4.40; N, 9.05%. Found: C, 67.65; H, 4.63; N, 8.72%.

Mn(C8-PBP)Br, 6. UV-vis (CH_2Cl_2) λ 377, 400 (sh), 489 (Soret), 534, 592, 628. MS m/z 1130 (M+1−Br) for $C_{68}H_{50}N_8O_6MnBr$ (LSIMS$^+$). Calcd for $C_{68}H_{50}N_8O_6MnBr$: C, 67.49; H, 4.17; N, 9.26%. Found: C, 66.32; H, 4.19; N, 8.71%.

Mn(C6-PBP)Br, 7. UV-vis (CH_2Cl_2) λ 376, 404 (sh), 489 (Soret), 532, 590, 628. MS m/z 1102 (M+1−Br) for $C_{66}H_{46}N_8O_6MnBr$ (LSIMS$^+$). Calcd for $C_{66}H_{46}N_8O_6MnBr$: C, 67.06; H, 3.93; N, 9.48%. Found: C, 66.99; H, 3.67; N, 9.28%.

Mn(PXY-PBP)Br, 8. UV-vis (CH_2Cl_2) λ 376, 400 (sh), 488 (Soret), 532, 590, 628. MS m/z 1121 (M+1−Br) for $C_{68}H_{42}N_8O_6MnBr$ (LSIMS$^+$). Calcd for $C_{68}H_{42}N_8O_6MnBr$: C, 67.94; H, 3.53; N, 9.32%. Found: C, 65.33; H, 3.55; N, 8.85%.

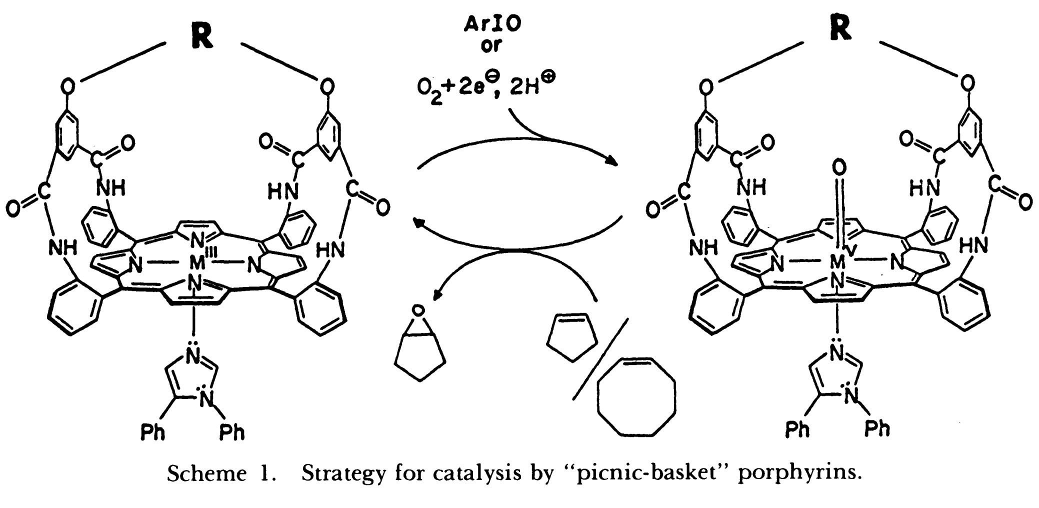
Mn(BN-PBP)Br, 9. UV-vis (CH_2Cl_2) λ 377, 396 (sh), 490 (Soret), 524, 590, 628. CD(CH_2Cl_2) λ 380, 400, 495, 600, 630.

Results and Discussion

The "Picnic Basket" Approach: Our approach to a new cytochrome P-450 model compound is illustrated in Scheme 1. This approach utilizes synthetic porphyrins that are sterically protected on one face of the porphyrin macrocycle. A bulky ligand, which cannot fit into the pocket should block the axial site on the unhindered side of the porphyrin and force molecules such as O_2 or oxygen atom donors to bind within the cavity. Activation of bound dioxygen or O-atom transfer would then generate the metal oxo inside the pocket. A smaller (or cis) olefin, which has greater access to the sterically hindered metal oxo moiety, should then be epoxidized in preference to a larger (or trans) olefin. If R were made chiral catalytic, asymmetric epoxidation might be realized.

In the design of a sterically protected oxidation catalyst several factors must be considered. The cavity must be sufficiently hindered to prevent coordination of the bulky axial ligand but not so hindered as to exclude the oxidant or substrate. Since most of the sterically protected porphyrins reported to date were prepared as hemoglobin or myoglobin active site analogues, they were designed to bind dioxygen within very tight cavities. The cavities hinder coordination of ligands as small as 1-methylimidazole and even carbon monoxide. A crystal structure of Baldwin's capped porphyrin, for example, shows a separation of less than 4 Å between the phenyl "cap" and the porphyrin ring.7) Porphyrins containing hindered pockets have also been prepared by Momenteau8a) and Traylor.8b) While the cavities in these porphyrins can control axial ligand coordination they can also restrict access of a substrate to the active site. In addition, several groups have observed the oxidation of alkyl groups on a porphyrin that are accessible to the metal oxo. Thus a sterically protected porphyrin was needed which had a large, permanent cavity within which O_2 could be bound and activated without oxidation of the superstructure.

We previously reported9) good yields for the high dilution coupling of two equivalents of isophthaloyl chloride and the 4:0 atropisomer of tetrakis(*o*-aminophenyl)porphyrin (TAMPP) (Scheme 2). The

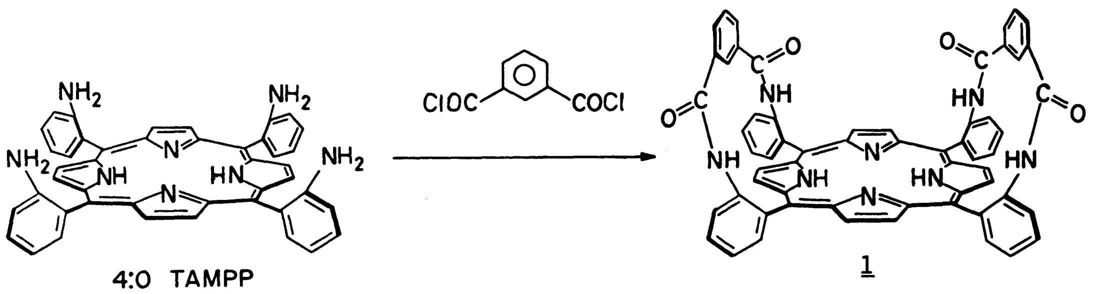


Scheme 1. Strategy for catalysis by "picnic-basket" porphyrins.

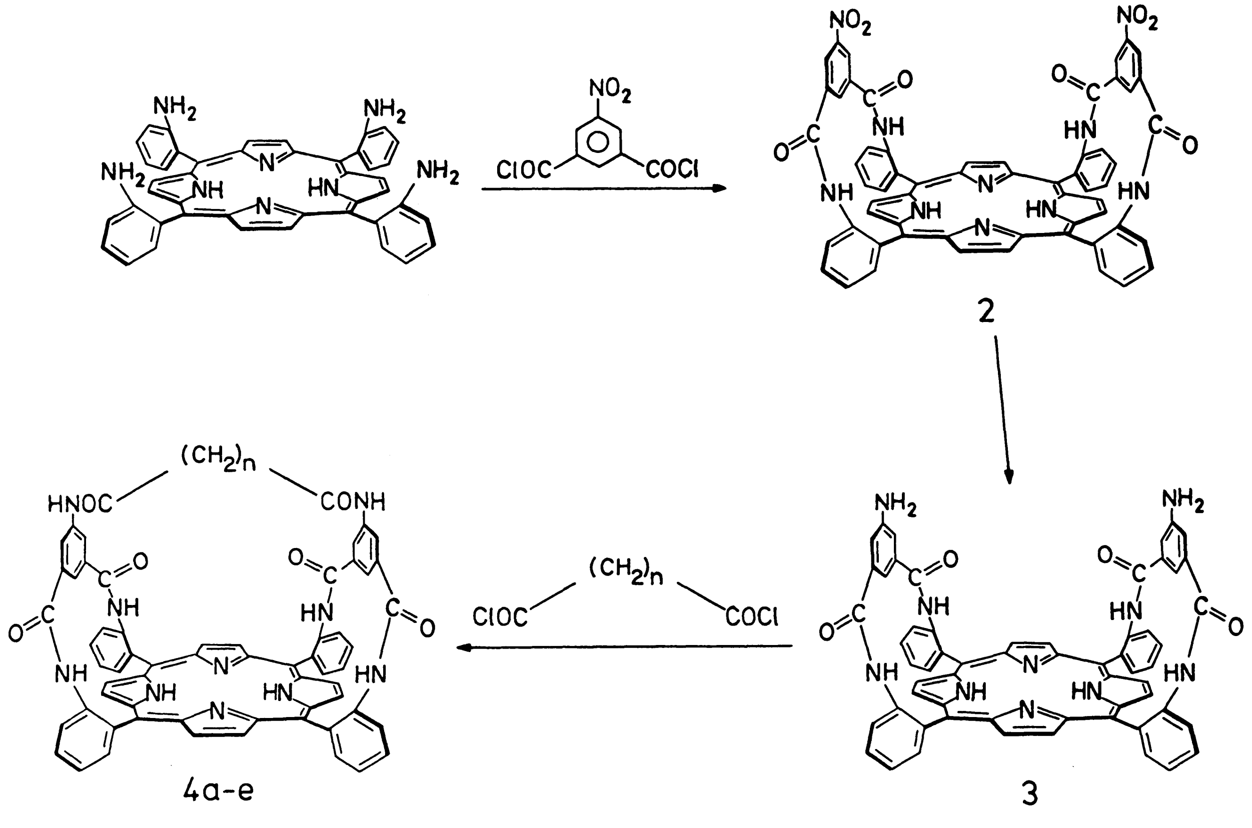
high yield was attributed to the complementary geometries of the isophthaloyl bridge and the aminophenyl groups on adjacent meso positions. No trans aminophenyl-bridged species were detected. Although the iron(II) derivative of **1** proved to be unsuccessful as a hemoglobin or myoglobin model it satisfied the above criteria since the rigid isophthalamido walls extend away from the porphyrin, forming a molecular cleft of large volume. By linking the 5 and 5′ positions the size of the cavity can be varied. Because of their shape we have given this class of molecules the trivial name "picnic basket" porphyrins.

Ligand Synthesis. The first picnic basket porphyrins were synthesized via the route outlined in Scheme 3. High dilution coupling of the 4:0 atropisomer of tetrakis(*o*-aminophenyl)porphyrin with 5-nitroisophthaloyl chloride yielded **2**, the 5,5′-dinitro derivative of **1**. Tin(II) chloride reduction to the 5,5′-diamino derivative **3** followed by high dilution coupling with a series of α,ω-diacid chlorides produced a family of porphyrins of general structure **4**. Derivatives with eight to twelve carbon atoms in the strap were synthesized in overall yields ranging from 10 to 22% based on the amount of 4:0 TAMPP used.

The solubility of these amide-strapped picnic basket porphyrins is very poor in nonprotic polar solvents such as methylene dichloride. This low solubility appears to result from intermolecular hydrogen bonding involving the amides in the strap. In addition to the solubility problem, this synthesis requires two high dilution reactions which severely limit reaction scale and introduce the most expensive

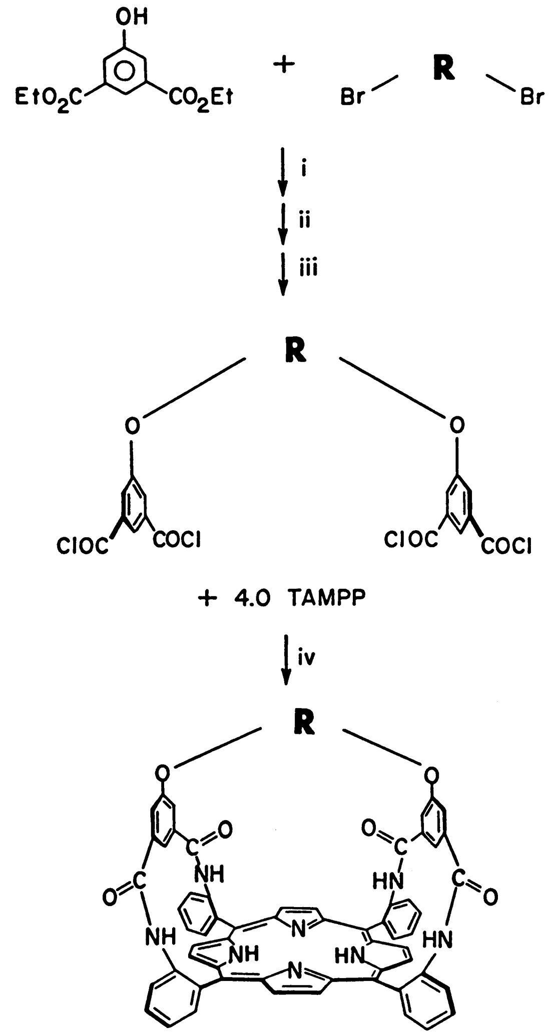


Scheme 2. Picnic basket precursor demonstrating complementary geometries between 4:0 TAMPP and isophthaloyl chloride.



Scheme 3. Synthesis of amide-strapped porphyrins **4a**—**e**.

reagent, the 4:0 TAMPP, three steps from the final product. In spite of these difficulties, the synthesis outlined in Scheme 3 has proven to be a viable route to this class of porphyrins.



Scheme 4. Synthesis of ether-strapped porphyrins **5**—**9**.

Both of these problems were solved by replacing the amide linkages with ether linkages and through the use of a convergent synthesis as outlined in Scheme 4. This general synthesis has several advantages over that outlined in Scheme 3 in that it contains only one high dilution step and introduces the 4:0 TAMPP in the final step. The eight compounds depicted in Fig. 1 are available by this route. All of the following studies were performed on the ether strapped porphyrins whose synthesis and characterization have been described in detail.[10b] The various complexes of these ligands are specified by the following notation in this paper:

$$\mathrm{Mn(R\text{-}PBP)(L)_{in}(L')_{out}}$$

where R=bridging group
C_n=normal alkane
PXY=*p*-xylene
DMB=2,6-dimethylbenzoate
BN=binaphthyl
PBP=picnic basket porphyrin
$(L)_{in}$=ligand coordinated within protected cavity
$(L)_{out}$=ligand bound on unencumbered porphyrin face

Manganese(III) Picnic Basket Porphyrins. Several recent studies have documented the beneficial effects of nitrogenous axial ligands in both Fe(III) and Mn(III) metalloporphyrin catalysts. Meunier[11a] and our group[11b] have observed dramatic increases in reaction rate, catalyst stability, epoxide yield, and stereospecificity in the epoxidation of alkenes by hypochlorite ion catalyzed by Mn(III) porphyrins with imidazoles and pyridine. Although the origin of these effects is not fully understood, they have been shown to result from nitrogenous base ligation.[12] Manganese porphyrin catalyzed epoxidations using

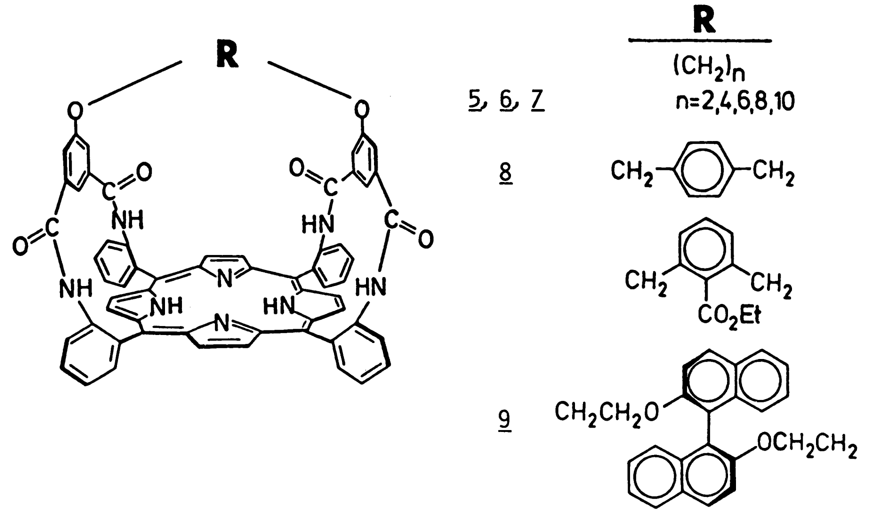


Fig. 1. Structures of ether-strapped porphyrins **5**—**9**.

other oxygen atom sources, such as iodosylbenzene[12] and peroxides,[13] are similarly affected by nitrogenous axial ligands. Since manganese porphyrins are well-behaved catalysts in the presence of nitrogenous ligands, we decided to investigate the selectivity of Mn(III) picnic basket porphyrins.

Metallation was accomplished by heating a DMF solution of the unmetallated picnic basket porphyrin with manganese bromide and the noncoordinating base, 2,6-lutidene, to give a compound with a visible spectrum similar to Mn(TPP)Br. The ^{1}H NMR spectrum shows severe paramagnetic broadening as is expected for a high spin d^4 system. Mass spectral analysis shows a molecular ion peak for Mn(PBP)$^+$. Loss of bromide ion is a result of the ionization method. Thus, the presence of a bromide counterion was inferred from the visible spectrum which is known to be counterion dependent.[24]

Ligand Binding. Since the picnic basket approach requires that the sterically unencumbered face of the porphyrin be made catalytically inactive by blocking that side of the porphyrin with a coordinated nitrogenous base, it is important to understand the thermodynamics and regiochemistry of nitrogenous base ligation. Unlike Mn(II) porphyrins, where crystallographic[14a] and solution[14b] studies have shown formation of only the mono-ligated complex, axial ligation to Mn(III) porphyrins is more complicated. Treatment of a five-coordinate Mn(III) porphyrin with an exogenous neutral ligand, L, can be expected to produce either a mono-L complex or a six coordinate bis-L complex, depending on the concentration of L and the relative magnitudes of the equilibrium binding constants K_L and K_L^L. The mono-ligated complex may be overall five or six-coordinate depending on the coordination properties of the counterion, X$^-$. This situation is depicted in Fig. 2. As the scheme in Fig. 2 suggests, equilibrium binding constants for neutral ligands will depend on the nature of the counterion. This has been demonstrated by isolation and structure determination of six-coordinate Mn(III) mono-L adducts with tightly coordinating anions such as azide[15a] or chloride,[15b] but only bis-L complexes have been isolated when a poorly coordinating counterion, perchlorate,[16] is present. Gravimetric analysis also indicates that a single pyridine binds to Mn(etioporphyrin)OAc.[17]

The spectral changes observed when a CH$_2$Cl$_2$ solution of Mn(PXY-PBP)Br is titrated with 1-methylimidazole are illustrated in Fig. 3. Six sharp isosbestic points indicate only two species, one of which is the starting material, are present over the course of the titration. The spectral changes are linear with the concentration of imidazole to the first power indicating that only one imidazole binds to each Mn(PXY-PBP)Br with an equilibrium constant of 2.7×10^3 M^{-1}. No evidence was found for binding of a

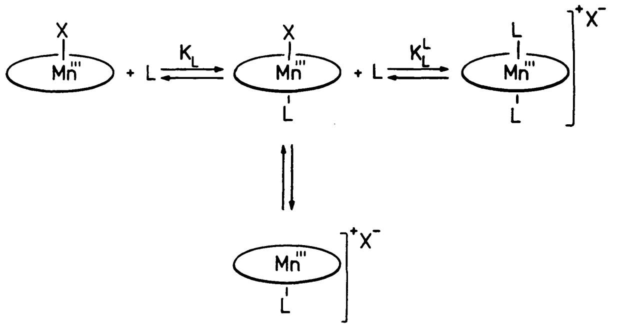


Fig. 2. Ligand binding to Mn(III) porphyrins.

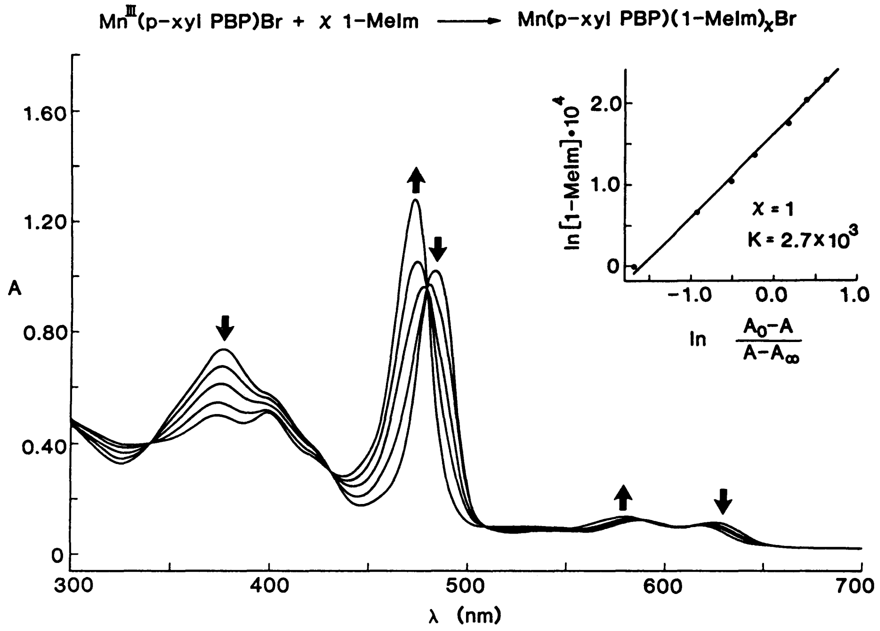


Fig. 3. Spectral titration of Mn(PXY-PBP)Br (**8**) with 1-methylimidazole.

second imidazole.

Similar changes are observed for a spectral titration using the bulky 1,5-diphenylimidazole but are complicated by two factors, that the ligand absorbs below 450 nm and, at high ligand concentrations, slow reduction to Mn(II) occurs. Reduction of Fe(III) porphyrins by excess nitrogenous ligand is well recognized. Despite these complications, the above analysis shows that a single 1,5-diphenylimidazole binds to each Mn(PXY-PBP)Br with an equilibrium constant estimated at $1.2\times10^3\ M^{-1}$.

In order to obtain spectral titrations which maintained sharp isosbestic points and did not change with time, all glassware had to be treated as described in the Experimental Section. Titrations performed in untreated glassware maintained isosbestic points only for the early part of the titration and showed spectral changes over time without addition of imidazole. As mentioned above, the visible spectrum of Mn(III) porphyrins depends strongly on the counterion. The behavior observed in untreated glassware is attributed to exchange of the bromide counterion for another counterion (probably chloride) adsorbed on the cuvette walls. Thus, the treatment described in the Experimental Section was designed to replace any anions which had leached into the glass with bromide.

Boucher studied the visible spectroscopy of Mn(III) porphyrins but reported no quantitative measure of equilibrium binding constants.[18] He does report that in the presence of excess ligand, Mn(III) porphyrins have the same visible spectrum, independent of the counterion in the starting material. Since the spectra of the starting materials do depend on the counterion, Boucher concludes a reaction with the neutral ligand has occurred and the anion is no longer coordinated. The product could be either the five-coordinate mono-L complex or the six-coordinate bis-L species.

La Mar has reported nonisosbestic spectral changes when Mn(III) porphyrins are treated with pyridine or 1-methylimidazole, and concluded that more than two species were present.[19]

Recently, Bruice has derived consecutive binding constants for 1-methylimidazole coordination to Mn(tpp)Cl from a spectral titration.[20] The lack of rigorous isosbestic points was considered evidence for the simultaneous presence of unligated, mono-L and bis-L species. K_L was determined to be $96.3\pm8.4\ M^{-1}$ and $K_LK_L^L$ to be $8530\pm330\ M^{-2}$ using Walker's method of analysis.[21] This analytical method, however, rests upon an unwarranted assumption — that the absorption coefficients of the mono-L and bis-L species are the same at the wavelength chosen for analysis. Several authors[22] have questioned this assumption in Walker's analysis. Thus, the results of Bruice, although consistent with those reported herein, must be considered questionable.

The present spectral study demonstrates that a single imidazole coordinates to Mn(PBP)Br and allows determination of the equilibrium binding constant but does not establish the site of ligation. To show that the hindered face of the picnic basket porphyrin can exclude a bulky axial ligand, an electrochemical study similar to that of Kadish[23] was undertaken.

Kadish examined nitrogenous base ligation to Mn(TPP)X complexes ($X=N_3$, Cl, ClO_4) by monitoring the Mn(II/III) half wave potential as a function of ligand concentration. For X=Cl or ClO_4, a cathodic shift in the half wave potential was observed as the concentration of pyridine increased. The magnitude of the shift, 53 mV per tenfold increase in pyridine concentration, is consistent with loss of a coordinated pyridine on reduction of Mn(III) to Mn(II), as shown in Eq. 1.

$$(1)\quad Mn^{III}(Por)(L)_n \xrightarrow{e^-} Mn^{II}(Por)(L)_{n-1} + L$$

Kadish concluded that the Mn(III) porphyrin is a bis(pyridine) adduct which, on reduction, becomes a monopyridine complex. The alternative explanation, that Mn(III) binds a single pyridine which is lost upon reduction to Mn(II), can be ruled out since Mn(II) porphyrins are known to exist as monopyridine complexes at these concentrations.[14b,24]

We repeated this experiment using Mn(TPP)Br or Mn(C8PBP)Br and varying concentrations of 1-methylimidazole or 1,5-diphenylimidazole. The results are plotted in Fig. 4. For two porphyrin/imidazole combinations, Mn(TPP)Br with the bulky 1,5-diphenylimidazole and the hindered Mn(C8PBP)Br with 1-methylimidazole, no steric hindrance to imidazole coordination is expected by molecular models. For these combinations the Mn(II/III) half wave potential shifts cathodically 65 mV per tenfold increase in the imidazole concentration. This is consistent with the loss of a coordinated imidazole on reduction as observed by Kadish.[23]

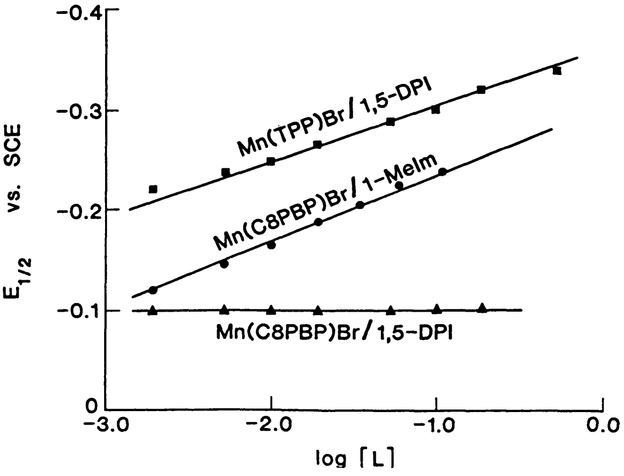


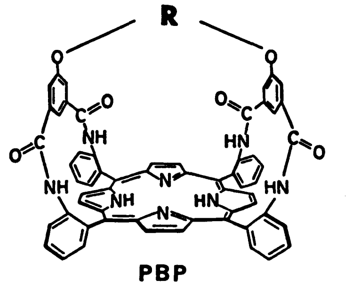
Fig. 4. Electrochemical study of Mn(III/II) half wave potential as a function of log[L].

For the porphyrin/imidazole combination where binding of a second imidazole is sterically disfavored, Mn(C8-PBP) with 1,5-diphenylimidazole, the Mn(II/III) half wave potential is independent of the imidazole concentration. Thus both the Mn(III) and the Mn(II) picnic basket porphyrins bind a single imidazole. This is direct evidence that the cavity in the picnic basket porphyrins will not accommodate 1,5-diphenylimidazole.

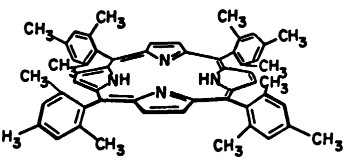
The electrochemical results indicate the binding of two imidazoles to Mn(III) in the unhindered cases while the spectral titrations indicate only one imidazole is bound. This apparent inconsistency can be explained by the fact that the electrochemical titration requires a supporting electrolyte, in this case tetrabutylammonium perchlorate, which supplies the perchlorate anion in concentrations 200 times that of the Mn(III) porphyrin. Under these conditions Bruice[25)] and Kadish[23)] have observed exchange of perchlorate for the counterion in the starting material. Thus, the manganese complex in the electrochemical titration is the perchlorate salt not the bromide salt used in the spectral titration. Since perchlorate is a weakly coordinating anion, perchlorate salts of Mn(III) porphyrins will bind two imidazoles unless sterically prevented from doing so.

Competitive Epoxidations. With knowledge of the regiochemistry and binding constant for imidazole ligation, we examined the substrate selectivity of the picnic basket porphyrin. Examination of molecular models showed that the unhindered face of the picnic basket porphyrin should be like TPP and the hindered pocket should resemble the sterically hindered TMP. As we have reported earlier,[26)] Mn(TMP)Br is very selective for the epoxidation of cis olefins versus trans olefins. Mn(TPP)Br exhibits equal reactivity with cis and trans olefins. Table 1 shows the observed epoxide ratios for the hypochlorite oxidation of 1:1 olefin mixtures when catalyzed by Mn(TPP)Cl and Mn-(TMP)Cl.[26)] Thus, epoxidations of 1:1 mixtures of a cis and trans olefin, for example *cis*-2-octene and *trans*-*β*-methylstyrene, could be used to assay the

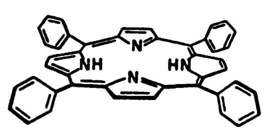
Table 1. Cis/Trans Olefin Selectivity of Mn(TMP)Cl vs. Mn(TPP)Cl in 1:1 Competitions



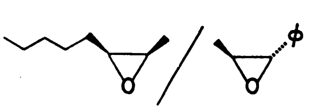
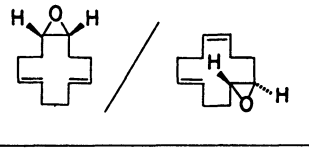
PBP



TMP



TPP

	epoxide ratio from 1:1 competition	
	Mn(TMP)Cl	Mn(TPP)Cl
	>20	1.3
	15	1.4

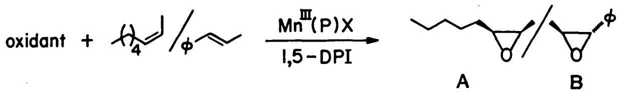
amount of catalytic oxygen atom transfer that occurs inside the pocket of the picnic basket porphyrin.

The epoxide ratios for several competitive oxygenations are listed in Table 2. Despite changes in the pocket size, counter-ion, the 1,5-diphenylimidazole concentration, and the nature of the oxidant, the ratio of epoxides was similar to Mn(TPP)Cl. Control experiments with each oxidant catalyzed by Mn(TPP)Cl and Mn(TMP)Cl showed dramatic changes in epoxide ratios as discussed above. In all cases the yield of total epoxide or the conversion of olefin to epoxide was in the range reported in the literature. Rates of Mn(PBP)Br catalyzed reactions were never less than 60% of the rate for the Mn(TPP)Br catalyzed reaction. The epoxide ratio did not vary significantly over the course of the catalytic reaction. The Mn(PBP)Br was also more stable than Mn(TPP)Br under the same reaction conditions as determined by decay of their visible bands.

These observations all indicate that catalytic reaction is occurring on the unhindered, sterically nonselective face of the porphyrin despite the presence of a large excess of nitrogenous base. The alternative explanation, that all or some fraction of the catalytic reaction is occurring inside the pocket and the pocket is sterically unselective, seems unlikely given the demonstrated steric sensitivity of competitive oxygenation by Mn(TMP)Cl. Similar results were obtained for the competitive oxygenation of *cis,trans,trans*-cyclododecatriene supporting this conclusion. We have attributed the lack of shape selectivity to failure to control the regiochemistry of high-valent metal-oxo formation, as illustrated in Fig. 5.

Studies of the kinetics of ligand exchange on Mn(III) porphyrins, although limited, show extremely fast exchange rates. Jordan has determined rate constants of 1.5×10^7 and 6.4×10^7 s^{-1} respectively for the exchange of free methanol or *N,N*-dimethylformamide for ligand coordinated to Mn(III)(protoporphyrin IX dimethyl ester)(ClO_4).[27] Bruice has also shown rapid exchange of anionic ligands.[25]

Table 2. Cis/Trans Olefin Selectivity of Mn(PBP)X Under a Variety of Reaction Conditions



Oxidant	P	X⁻	[1,5-DPI]	A/B
C_6H_5IO	TPP	Br	50 mM	1.0
C_6H_5IO	TMP	Br	50 mM	25.0
C_6H_5IO	C6-PBP	Br	50 mM	1.9
NaOBr	C6-PBP	Br	50 mM	1.1
H_2O_2	C6-PBP	Br	50 mM	0.9
H_2O_2	PXY-PBP	Br	50 mM	0.8
H_2O_2	PXY-PBP	ClO_4	50 mM	0.8
H_2O_2	PXY-PBP	ClO_4	500 mM	0.8
C_6H_5IO	C8-PBP	Ph_3CCO_2	0 mM	1.6

In contrast, oxygen atom transfer to manganese porphyrins appears to be a much slower process.[28] Bimolecular rate constants for oxygen atom transfer from alkyl hydroperoxides to Mn(TPP)Cl, in the presence of 1-methylimidazole, are reported in the range of 200—300 M^{-1} s^{-1}.[20] Thus, interconversion of the Mn(III) porphyrins, **I** and **II** (Fig. 5), is probably rapid relative to conversion to the postulated oxo complexes, **III** and **IV**. The Mn(III) species, **I** and **II**, are therefore always in equilibrium; the ratio being given by the concentration of 1,5-diphenylimidazole and the equilibrium binding constant, which was determined spectrally. For the competitive alkene epoxidations, the ratio of species **II** to **I** is calculated to be 60:1.

The lack of shape selectivity in the competitive oxygenations must be due to the relative rates of formation of the high-valent manganese species, **III** and **IV**. Perhaps oxygen atom transfer to the minor Mn(III) component, **I**, is so much faster than transfer to the major component, **II**, as to outweigh the concentration difference. This rate difference may arise from the larger steric hindrance of the pocket encountered by the oxygen atom donor in reacting with **II**. As we have previously reported,[10] we have observed rate constants which differ by at least two orders of magnitude for reactions occurring inside versus outside the picnic basket porphyrin cavity. The possibility that species **IV**, which has the oxo ligand bound within the cavity, is formed but reacts with olefin much more slowly than does **III** is inconsistent with the constant rate of epoxidation by Mn(PBP)Br, which is similar to that of Mn(TPP)Br. Under these conditions **IV** should accumulate with time and the

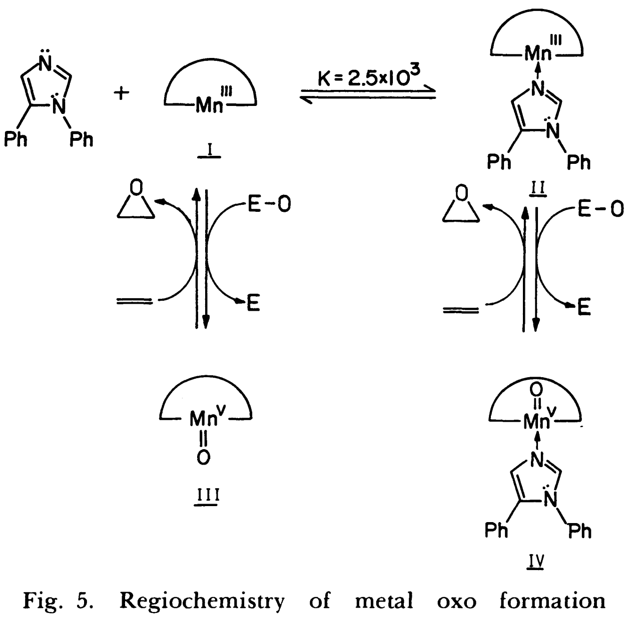


Fig. 5. Regiochemistry of metal oxo formation with Mn(PBP)X.

catalyst should exhibit reduced activity. Thus **IV**, if it is formed, must be able to revert to **II** at a fairly rapid rate. Thus, the lack of shape selectivity is probably due to the minor, unselective component in the catalyst mixture being the more active catalyst.

Studies of the Chiral Picnic Basket Mn(BN-PBP)Br, 9. The chiral binaphthyl picnic basket porphyrin **9** was studied under conditions similar to those reported above with 1-octene or styrene as substrates and LiOCl/phase transfer agent or hydrogen peroxide as the oxygen atom donors in the presence of 1,5-diphenylimidazole. Since circular dichroism spectra of **9** showed bands in the 300—700 nm region the synthesis and Mn metallation did not racemize the porphyrin. Within experimental error no asymmetric induction was observed in the product epoxides by chiral shift ^{1}H NMR using Eu(hfc)$_3$; this result is consistent with oxo formation occurring on the unhindered, achiral face of the porphyrin as observed above and not within the chiral pocket.

Conclusion

While modest regio and enantioselectivities have previously been observed for oxygenations catalyzed by Mn(III) and Fe(III) porphyrins, the porpyrins used in these studies are symmetric with respect to the porphyrin plane. No attempts to observe reaction within the pocket of an unsymmetrical porphyrin have been reported. Studies on the unsymmetrical Mn(PBP)X have shown that metal oxo formation appears to occur only on the unhindered and unselective porphyrin face. Metal oxo formation must occur inside the cavity before shape selective oxygenations can be observed with the picnic basket porphyrins.

While we were unable to observed any olefin selectivity with oxygen atom donors that would indicate epoxidation within the pocket, we felt that dioxygen could still be bound and activated within the pocket. Both ruthenium(II)[10a)] and iron(II) picnic basket porphyrins and similar iron(II) pocket porphyrins[29)] exhibit reversible binding of dioxygen in the presence of a bulky axial ligand, but preliminary attempts to activate dioxygen using two reducing agent/metalloporphyrin systems provided no evidence for oxygen activation.[3a,e)]

We are continuing to study other routes to dioxygen activation including a well-characterized ruthenium(II) picnic basket porphyrin O$_2$ adduct.[10a)] Another possibility is to use oxygen atom donors with a kinetically less labile combination of metalloporphyrin and bulky ligand. One promising candidate is a ruthenium picnic basket porphyrin phosphine complex.

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