Asymmetric Hydroxylation, Epoxidation, and Sulfoxidation Catalyzed by Vaulted Binaphthyl Metalloporphyrins

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A chiral, vaulted binaphthyl porphyrin (1) has been prepared from 5α,10β,15α,20β-tetrakis(*o*-aminophenyl)porphyrin and (*R*)-(+)-2,2′-dimethoxy-1,1′-bi-6-naphthoyl chloride in 79% yield. Asymmetric oxygenations of alkanes, alkenes, and alkyl sulfides were catalyzed with the chloroiron(III) and chloromanganese(III) complexes of 1 with good yields and high stereoselectivities. The first catalytic asymmetric hydroxylations are reported for 1-$Fe^{III}Cl$ with enantiomeric excesses in the range of 40–72%. The corresponding manganese catalyst, 1-$Mn^{III}Cl$, gave much lower enantiomeric excesses. For catalytic asymmetric epoxidations, enantiomeric excesses were in the range of 20–72%. Prochiral alkyl sulfides gave sulfoxides with 14–48% ee with 1-$Fe^{III}Cl$.

Introduction

Asymmetric synthesis has emerged as a rich and rapidly developing area of chemistry, combining elements of organic synthesis, molecular recognition, metal coordination chemistry, and catalysis. Of the various strategies for exploiting the available pool of chiral compounds, catalytic asymmetric induction offers the distinct advantage of chemical amplification of the asymmetry of the catalyst. The rhodium-catalyzed asymmetric hydrogenation of olefins,[1,2] the titanium-catalyzed epoxidation of allylic olefins,[3] the copper-catalyzed cyclopropanation of olefins,[4-7] and, most recently, the osmium-catalyzed dihydroxylation of olefins[8] are the most significant successes of this approach.

The asymmetric epoxidation of simple olefins has been only moderately successful. The epoxidation of styrene with monoperoxycamphoric acid affords less than an 8% enantiomeric excess (ee).[9] Some very high ee's have been reported[10] for a stoichiometric chiral peroxomolybdenum(IV) reagent. The epoxidation of α,β-unsaturated ketones with basic hydrogen peroxide and a chiral phase-transfer catalyst has been reported to afford enantiomeric excesses of 25%[11] and up to 96% in the presence of a chiral polyamino acid template.[12] The enzymic epoxidation of simple olefins such as 1-octene has been shown to proceed with very high enantiomeric excesses, 80–100%.[13-17] In such cases there can be no auxiliary, bonded interactions between the catalytic center and the substrate. Accordingly, it must be possible to develop synthetic catalysts with chirotropic cavities that can mimic this high enantioselectivity.

There are no reports of the catalytic asymmetric hydroxylation of simple alkanes. Asymmetric hydroxylations of ketone enolates have been achieved with chiral oxaziridines[18] with enantiomeric excesses varying from 2 to 95%.[19] Chiral sulfoxides can be prepared by oxidation of prochiral sulfides with a number of chiral reagents. For example, the Sharpless titanium(IV) reagent provides ee's as high as 93%.[20]

The discovery that iron porphyrins will catalyze alkane hydroxylation and olefin epoxidation in the presence of oxygen donors such as iodosylbenzene[21] has provided an opportunity to use synthetic porphyrins for modeling the oxygen transfer reaction of cytochrome P-450.[22] Chiral metalloporphyrins have been shown to mediate catalytic asymmetric oxygen transfer to afford optically active epoxides from prochiral olefins.[23] The largest enantiomeric excess (ee = 51%) was provided by chloro[5α,10β,15α,15β-tetrakis[(*S*)-2′-(carboxymethyl)-1,1′-binaphthyl-2-carboxamidophenyl]porphyrinato]iron(III)[23] with *p*-chlorostyrene as the substrate. Similar ee's have been reported for a chiral "basket handle" porphyrin.[24,25]

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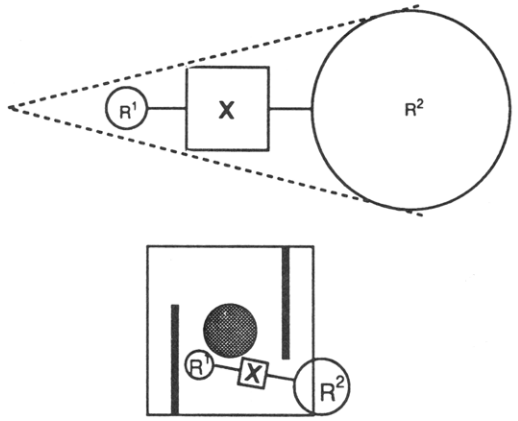


Figure 1. Idealized molecular geometry of a prochiral substrate (above) and its interaction with a porphyrin of D_2 symmetry (below).

The regioselectivity of hydroxylation catalyzed by tetraphenylporphyrin derivatives has been shown to be a sensitive function of the ortho substituent on the *meso*-aryl group.[26-28] Regioselective epoxidation[29a] and hydroxylations[29b] have also been achieved recently with membrane spanning metalloporphyrins, encapsulated in synthetic vesicles.

We describe here the synthesis and characterization of a new, vaulted porphyrin with a chirotropic binaphthyl bridge. The iron(III) and manganese(III) derivatives of this porphyrin have proven to be robust catalysts for olefin epoxidation and sulfoxidation. Most significantly, the first catalytic asymmetric hydroxylations have been observed with this catalyst.

Results and Discussion

We sought to prepare a chirotropic metalloporphyrin that would provide strong asymmetric interactions with substrates and be robust enough to endure the course of catalytic oxygenation reactions. The shape of the active site should also take into consideration the stereoelectronic aspects of oxygen transfer from the metal center to the approaching substrate.[21b] The shape of a typical prochiral substrate can be idealized as shown in Figure 1. If the two substituent groups (R^1 and R^2) are different in size, the reactive functional group (X) can be considered to lie at the midsection of a cone. The cone angle is determined by the difference in size between the two substituents R^1 and R^2.

A chirotropic porphyrin designed for the purposes of asymmetric induction must differentiate the enantiotropic *si* and *re* faces[30c] of an approaching substrate by recognizing the slope of this cone. In order to fulfill this requirement, we sought a bridged porphyrin with the idealized geometry represented in Figure 2. Inspection of space filling models indicated that a 1,1′-binaphthyl group could provide the required shape and that 6,6′-functionality would allow a strain-free vaulting of trans-

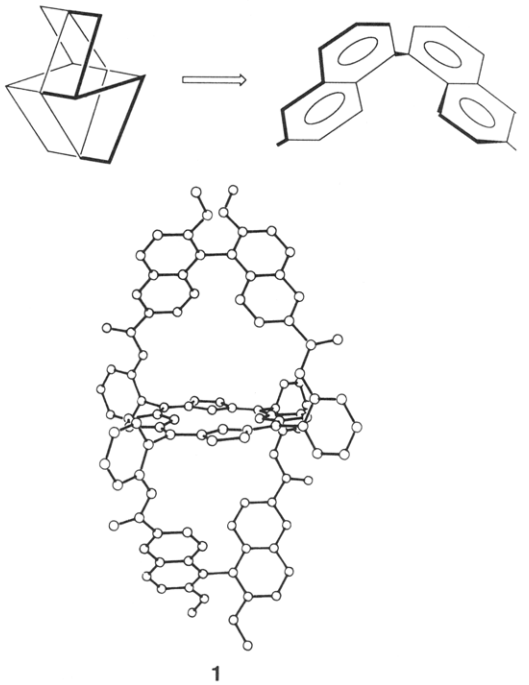
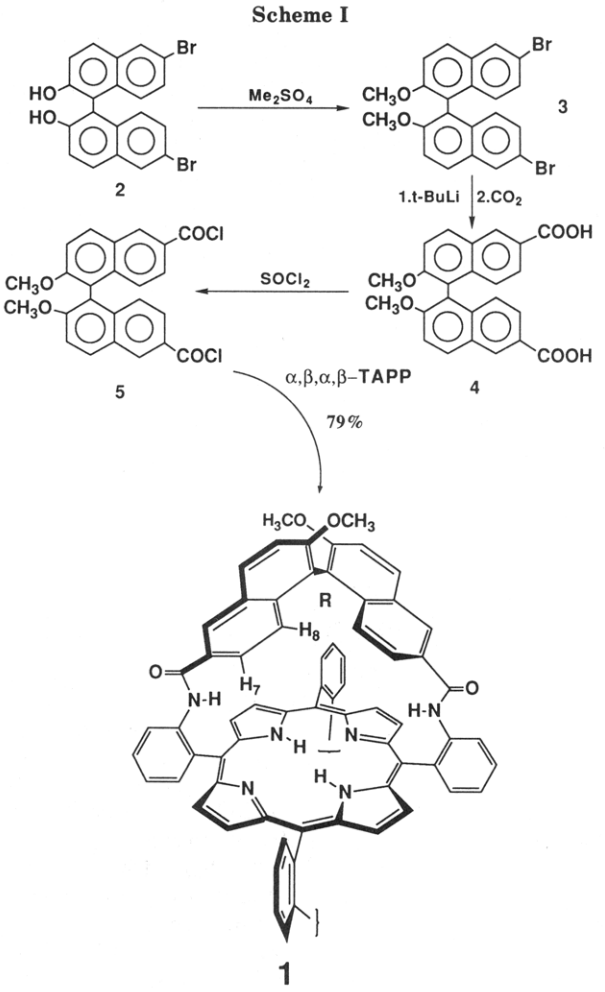


Figure 2. Idealized molecular geometry of **1** (above) and atomic coordinate structure for **1** (below) as calculated with MacroModel 1.1 and minimized with the MM-2 85 force field by the block-diagonal Newton–Raphson method.

Scheme I



annular *o*-amino groups of a 5α,10β,15α,20β-tetra(*o*-aminophenyl)porphyrin [α,β,α,β-TAPP]. Thus, the bis-binaphthyl vaulted porphyrin **1** was selected for synthesis

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Table I. Olefin Epoxidation Catalyzed by 1-$Fe^{III}Cl$ and 1-$Mn^{III}Cl$

substrate	epoxide confign	% major enantiomer	ee (%)	yield[a] (%)	epoxide CO compds
		1-$Fe^{III}Cl$ Catalyst			
styrene	*R*-(+)	65	30	23	2.1
p-chlorostyrene	*R*-(+)	69	38	39	
tert-butylethylene[b]	*S*-(+)	70	40	14	11
trans-β-methylstyrene[c]	1*S*,2*S*-(−)	51	~1	43	5.9
cis-β-methylstyrene	1*S*,2*R*-(+)	79	58/20 °C	64	18.8
	1*S*,2*R*-(+)	81	62/0 °C	35	
	1*S*,2*R*-(+)	85	70/−5 °C	12	
	1*S*,2*R*-(+)	86	72/−15 °C	9	
trans-2-pentene	1*S*,2*S*-(+)	66	32	42	3
indene[d]	1*S*,2*R*-(−)	60	20	73	3.3
1,2-dihydronaphthalene	1*S*,2*R*-(−)	71	42	61	1.8
		1-$Mn^{III}Cl$ Catalyst			
styrene	*R*-(+)	68	36	21	2.0
cis-β-methylstyrene	1*S*,2*R*-(+)	53 (cis)	6	27	
	1*S*,2*S*-(−)	53 (trans)	6		

[a] Yields are based on iodosylbenzene. [b] Solvent, iodobenzene; all the others, toluene. [c] The enantiomer in excess was identified by comparing the gas chromatograms with that of the authentic sample. [d] ee was determined by means of NMR, all the others by GC.

and evaluation as an asymmetric catalyst.

Synthesis. The requisite binaphthyl derivative was synthesized as shown in Scheme I. (*R*)-(+)-6,6′-Dibromo-1,1′-bi-2-naphthol (**2**) was prepared according to a known method.[30] Methylation of **2** with dimethyl sulfate in the presence of sodium methylate was effected in very dilute THF solution since the solubility of the monomethylated compound was so low in suitable solvents that it precipitated from the reaction mixture and prevented the second methylation.

(*R*)-(+)-6,6′-Dibromo-2,2′-dimethoxy-1,1′-binaphthalene (**3**) was first converted to the corresponding 6,6′-dilithium derivative and, without isolation, was reacted with dry carbon dioxide to afford [(*R*)-(+)-2,2′-dimethoxy-1,1′-binaphthalene]-6,6′-dicarboxylc acid (**4**). This diacid, **4**, was converted to the corresponding diacid chloride (**5**) with thionyl chloride and, without isolation, was reacted with α,β,α,β-TAPP. This reaction was slow, but provided a remarkably high yield (79%) due to the complementary span of the 6,6′-1,1′-binaphthyl and the 5,15-(*o*-aminophenyl) groups of the porphyrin and the limited degrees of freedom between the reactive termini of each molecule. The optical purity of the product was determined by examination of the ^1H NMR spectrum in the presence of tris[3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato]europium(III) as a chiral shift reagent. That a single enantiomer of the porphyrin **1** had been obtained was confirmed by the lack of any of the meso diastereomer of **1**. An authentic sample of the meso diastereomer prepared from racemic **4** was shown to separate readily from racemic **1** upon TLC analysis.

The structure of the porphyrin **1** was confirmed by its spectral data. The ^1H NMR spectrum was particularly diagnostic (Figure 3). Two singlets for the pyrrole protons at δ 8.67 and 8.93 are in accord with the D_2 symmetry of this molecule. Thus, adjacent pyrrole rings are expected to be nonequivalent while those protons of the meso diastereomer, with S_4 symmetry, showed, only one singlet at δ 8.89. Space-filling models and MM-2 calculations indicated a rigid conformation of the bridging binaphthyl group in **1** such that H_7 and H_8 are suspended above the plane of the porphyrin ring. The high-field AB quartet centered at δ 5.5 was assigned to these protons. The remaining resonances were readily assigned on the basis of intensity and multiplicity. Pure **1** gave a satisfactory elemental analysis and the FAB mass spectrum showed a cluster centered at the expected mass, m/z = 1407.

The iron(III) and manganese(III) complexes of **1**, 1-$Fe^{III}Cl$ and 1-$Mn^{III}Cl$, were prepared by standard methods.

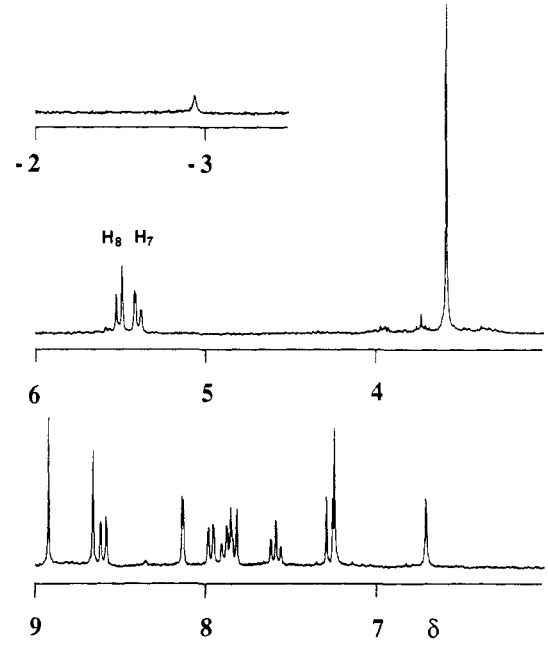

Figure 3. ^1H NMR spectrum of **1** determined at 250 MHz at room temperature in $CDCl_3$.

Epoxidations. In a typical oxidation reaction, 1 equiv of the metalloporphyrin catalyst, 1-$Fe^{III}Cl$ or 1-$Mn^{III}Cl$, 100 equiv of iodosylbenzene, and 1000 equiv of substrate were used under anaerobic conditions. The product enantiomer in excess was identified by polarimetric measurements. A similar protocol was followed for the hydroxylation and sulfoxidation reactions.

Results for the catalytic epoxidation of a number of olefins are shown in Table I. Toluene provided higher enantiomeric excesses than dichloromethane or benzene for the same reactions. For low-boiling substrates (<100 °C) iodobenzene was used in place of toluene. Pentafluoroiodosylbenzene was found to be an ineffective oxidant. For reasons that are not clear this oxidant gave very low yields even if large excesses were used. The metalloporphyrin catalyst was recovered unchanged, however.

Optical yields were measured by gas chromatography using a chiral column based on bis[3-(perfluorobutyryl)-(1*R*)-camphorato]manganese(II).[10] In cases in which GC analysis failed, the ee was determined by ^1H NMR spectroscopy with tris[3-[(heptafluoroproyl)hydroxymethylene]-(+)-camphorato]europium(III) as a chiral shift reagent.[23]

Table II. Hydroxylations Catalyzed by 1-$Fe^{III}Cl$ and 1-$Mn^{III}Cl$[a]

substrate	alcohol confign	major enantiomer (%)	ee (%)	yield (%)	alcohol/ketone
ethylbenzene	*R*-(+)	70 (63)	40 (26)	40 (77)	2.3 (1.3)
4-methoxyethylbenzene	*R*-(+)	83	66	20	1.8
1-phenylpropane	*R*-(+)	72 (58)	44 (16)	32 (98)	5.0 (1.4)
indan	*R*-(+)	77 (59)	54 (18)	72 (82)	7.2 (4.5)
tetrahydronaphthalene	*R*-(-)	86 (56)	72 (12)	47 (46)	20.2 (1.3)
2-ethylnaphthalene	*R*-(+)	84	68	28	10.1
1-ethylnaphthalene	*R*-(+)	84	68	19	0.2

[a] Reactions carried out in CH_2Cl_2 at 0 °C in the absence of oxygen. The relative ratio of catalyst, iodosylbenzene, and substrate was 1:100:1000 in every case. Numbers in parentheses were obtained with [1]-Mn(III)Cl as the catalyst, all others were obtained with 1-Fe(III)Cl.

The catalyst survived the reaaction without detectable decomposition in all cases. After isolation, a second oxidation with recycled catalyst produced the same results for up to five iterations. Similarly, the addition of five successive aliquots of iodosylbenzene to a reaction mixture caused only a slight decomposition of the catalyst as evidenced by the visible spectrum and TLC.

Variable amounts of ketones and aldehydes were also detected as products. As we have shown elsewhere,[23] these compounds are primary products and did not arise from subsequent rearrangement of the epoxide.

As shown in Table I, epoxide yields between 20% and 73% were obtained with enantiomeric excesses as high as 72% at -75 °C for *cis*-β-methylstyrene (S/R = 6.1). The absolute stereochemistry obtained in excess with this substrate and all of the others except the two styrenes were in accord with expectations based on a side-on approach of the olefin to the iron–oxo moiety. Nearly racemic epoxide was obtained with *trans*-β-methylstyrene for which this side-on approach is sterically precluded. Styrene and *p*-chlorostyrene appear to be anomalous, while *tert*-butylethylene gave the anticipated *S*-(-) epoxide as the major enantiomer.

The appearance of trans epoxides in the case of *cis*-β-methylstyrene epoxidation catalyzed by 1-$Mn^{III}Cl$ is indicative of an intermediate oxo-Mn(IV)porphyrin.[31] Sterically unhindered manganese porphyrins afford rather little isomerization with iodosylbenzene, however. While the reason for this change is not clear, it is conceivable that the 2,2′-dimethoxybinaphthyl group is electron-rich enough to reduce an initially formed oxomanganese(V) porphyrin to manganese(IV). When *m*-chloroperoxybenzoic acid (*m*-CPBA) was used as the oxidant without a metalloporphyrin catalyst, there was no reaction between -75 °C and -35 °C. Above this temperature the uncatalyzed reaction of *m*-CPBA with olefins interfered with the catalytic process.

Catalytic Asymmetric Hydroxylations. The two catalysts, 1-$Fe^{III}Cl$ and [1]-$Mn^{III}Cl$, were found to hydroxylate benzylic methylene groups with good efficiency. The results are presented in Table II. Rotations of the product alcohols were determined in porphyrin-free solutions. The product alcohols were esterified with (*R*)-(-)-2-phenylpropionyl chloride and the ratios between the diastereomeric ester pairs were determined by gas chromatography. The reliability of this method was checked by examining the esters prepared from racemic alcohols. This derivatization provided complete, base-line separation of the diastereomeric esters, and, furthermore, the esters had an uncomplicated parent region in their mass spectra.

The catalysts were about as durable during these hydroxylation reactions as had been observed for the epoxidations and, also similarly, the iron complex 1-$Fe^{III}Cl$ provided higher enantiomeric excesses than the manganese complex 1-$Mn^{III}Cl$.

The data in Table II show that the hydroxylation of these benzylic compounds proceeded with yields of 20–72% for 1-$Fe^{III}Cl$. More interesting was the high degree of enantioselectivity observed, 41–72% ee. In every case the expected *R* enantiomers of the product alcohols were produced in excess.

Every hydroxylation reaction also produced some of the corresponding ketone. The oxidation of racemic 1-phenylethanol under similar reaction conditions produced negligible amounts of acetophenone, however, indicating that the ketones did not arise from further oxidation of the initially formed alcohols. As we have described elsewhere,[26] the first step of metalloporphyrin-catalyzed hydroxylations with iodosylbenzene is hydrogen atom removal from the substrate to form a carbon radical. We associate the ketone product with subsequent reactions of these radicals with oxygen or iodosylbenzene.

The data clearly indicate that the shape and size of substrate have a very strong influence on the enantiomeric excess. The larger substrates that would be expected to have greater nonbonded interactions with the chiral pocket of the catalyst had the higher enantiomeric excesses. It is also interesting that in this group the highest enantiomeric excesses were found in those cases with the lowest amount of ketone.

The manganese complex 1-$Mn^{III}Cl$ provided higher alcohol yields and also provided the expected *R* enantiomers in excess but with much lower selectivity (Table II). This trend is also consistent with longer lived radical intermediates expected[32] for the manganese case.

We have described elsewhere the stereochemical course of the hydroxylation of (*R*)- and (*S*)-1*d*-ethylbenzene.[33] From the enantiomeric and isotopic composition of the product alcohols, removal of the *pro-R* hydrogen was found to be favored by a factor of 2:1 over that of the *pro-S* hydrogen. Surprisingly, the radical produced by *pro-R* hydrogen removal was found to be captured with >90% *retention* of configuration at carbon. By contrast, hydroxylation via removal of the *pro-S* hydrogen proceeded with up to 40% racemization. This difference in behavior has been interpreted to result from differential rates or efficiencies of radical cage collapse due to nonbonded interactions between the incipient radical and the catalyst superstructure. It is clear also from this analysis that the stereoselectivity of carbon radical captured by 1-Fe^{III}-Cl is intrinsically higher than that of hydrogen atom removal.

Sulfoxidations. Results for the oxygenation of sulfides with 1-$Fe^{III}Cl$ are listed in Table III. Yields were determined by gas chromatography and the enantiomeric excesses were established by ^1H NMR spectroscopy using a chiral shift reagent. Rotations were determined by polarimetry. Small amounts of sulfones were detected in

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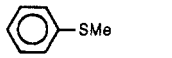
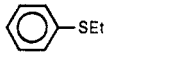
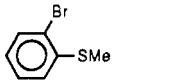
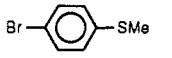
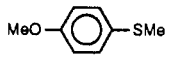
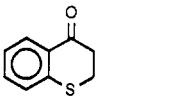
Table III. Oxidation of Prochiral Sulfides by 1-Fe^{III}Cl

substrate	config	major enantiomer (%)	ee	yield (%)	sulfoxide/ sulfone
	R-(+)	62	24	84	8.2
	R-(+)	71	42	73	7.9
	(+)	74	48	74	8.4
	R-(+)	60	20	88	7.5
	(+)	57	14	70	6.2
	(+)	64	28	67	8.9

addition to sulfoxides. The catalyst was recovered unchanged at the end of the reaction. In cases where the absolute configuration was possible to determine based on rotation, the *R* enantiomers formed in excess. High yields were observed (67–88%), but the enantiomeric excesses were less than 50%.

Conclusions

An efficient synthesis of the vaulted binaphthyl porphyrin 1 has been described. The metal complexes 1-Fe^{III}Cl and 1-Mn^{III}Cl have been shown to be efficient and robust catalysts for oxygenation reactions. The disposition of the binaphthyl bridge in 1 enforces the approach of substrates from the side of the reactive oxometal group in the manner we have suggested[21b] to explain the pronounced difference in reactivity of *cis*- and *trans*-olefins in metalloporphyrin-catalyzed epoxidation reactions.

For most oelfins examined the epoxide enantiomer produced in excess could be predicted by accomodating the larger olefin substituent in the open cleft of the spanning binaphthyl strap as in Figure 1. The anomalous behavior of styrene and *p*-chlorostyrene in this regard argue that such simple lock and key interpretations must be applied with caution. The striking difference in behavior between styrene and either *tert*-butylethylene or *cis*-β-methylstyrene deserves additional comment, however. We suggest that the lack of a second substituent on the double bond of the styrenes allows a close approach to the catalyst and conjugation of the double bond with the pendant phenyl group in the transition state for oxygen transfer. Accordingly, a specific π–π interaction between the styrene and the binaphthyl group of the catalyst appears to be possible for these two anomalous substrates but is precluded by nonbonded interactions with the other, larger substrates.

Both 1-Fe^{III}Cl and 1-Mn^{III}Cl catalyzed benzylic hydroxylation with remarkable efficiency. Interestingly, only the iron catalyst afforded a significant asymmetric induction, up to 72% ee, in what is apparently the first reported catalytic, asymmetric hydroxylation of simple hydrocarbons. We suggest that hydrogen abstraction from the substrate by the ferryl intermediate and radical cage recombination to afford the product alcohols is fast enough to compete with diffusion of the benzylic radical from the cage or rotation of this radical within the cage. This result is reminiscent of the result we have reported for the allylic hydroxylation of cyclohexene catalyzed by simple iron porphyrins and by cytochrome P-450 for which *incomplete* allylic scrambling was observed.[34]

The sulfoxidation of alkyl sulfides gave the lowest enantioselectivities. Taken in light of the results for hydroxylation and epoxidation, it is apparent that the more easily oxidized functional group gave the lower enantiomeric excess (alkyl sulfide < olefin < benzylic methylene). All of these reactions are considerably exothermic. Accordingly, the transition states are expected to be early and the activation energies will be low. Under these circumstances differential energies of diasteriomeric transition states are expected to be smaller for the more reactive substrates and the large relative stereoselectivities for aliphatic hydroxylation can be understood in these terms.

Experimental Section

Optical yield determinations were made by gas chromatography with a flame ionization detector. For GC-MS the HP5980 was equipped with a HP5970 mass selective detector. SPB-35, or chiral fused silica capillary columns prepared according to Schurig et al.,[35] were used. ^{1}H NMR spectra were obtained ~300- or 250-MHz spectrometers. Optical rotations were determined on a Perkin-Elmer 141 polarimeter.

(*R*)-(+)-6,6′-Dibromo-1,1′-bi-2-naphthol (2) was prepared by the published method.[30b] (+)-1,1-Binaphthol (99%) was obtained from the Aldrich Chemical Co. Its optical purity was confirmed by ^{1}H NMR in the presence of Eu(hfc)$_3$. α,β,α,β-Tetra(*o*-aminophenyl)porphyrin (TAPP) was prepared by a slight modification of previously described methods.[23,24] The separation of rotational isomers was performed on basic alumina (ICN Biomedicals, 02069), with benzene/ethyl acetate (4:1) as the eluent. In this way the α,β,α,β isomer could be separated quantitatively in one step. All hydrocarbon substrates were purified by chromatography on basic alumina.

(*R*)-(−)-6,6′-Dibromo-2,2′-dimethoxy-1,1′-binaphthalene (3). To a sodium ethoxide solution made of 1.15 g (0.05 mol) and 20 mL of ethanol, was added 10 g (0.025 mol) of **2**. After stirring the mixture for 10 min at room temperature, it was diluted with 1500 mL of dry THF and 11.35 g (8.4 mL; 0.09 mol) of dimethyl sulfate was added. The reaction mixture was stirred overnight; then the precipitate was filtered off, the supernatant solution was reduced in volume to 250 mL, and the new precipitate was filtered off again. Both fractions were recrystallized from THF to afford **3**, 10.1 g (95%): mp 239–41 °C; $[\alpha]^{20}_D$ = −21.3°; IR (KBr) 3060–2884 m, 2837 m, 1583 s, 1492 s, 1316 m, 896 s, 803 m, 668 cm^{-1} m; ^{1}H NMR ($CDCl_3$) δ 8.04 (Ar H, 2 H, s), 7.91 (Ar H, 2 H, d, *J* = 9 Hz), 7.49 (Ar H, 2 H, d, *J* = 9 Hz), 7.29 (Ar H, 2 H, d, *J* = 9 Hz), 7.26 (Ar H, 2 H, d, *J* = 9 Hz), 3.78 (Me H, 6 H, s).

[(*R*)-(−)-2,2′-Dimethoxy-1,1′-binaphthalene]-6,6′-dicarboxylic Acid (4). A 10-g (0.021 mol) sample of **3** was dissolved in 500 mL of dry THF, and the solution was cooled to −75 °C. *tert*-Butyllithium (30 mL of a 1.7 mol solution) was added over a period of 30 min, and the reaction mixture was allowed to warm to −20 °C; a large excess of dry CO_2 was introduced for 1 h and then the cooling bath was removed. The suspension was stirred for 2 h at room temperature; then it was diluted with water and acidified with a 10% HCl solution. The voluminous precipitate was filtered off and recrystallized from 2-propanol to afford 6.65 g (78%) of **4**: mp 318–320 °C; $[\alpha]^{20}_D$ = −32.3° (2-propanol); IR (KBr) 3854 m, 3300–2600 w, 1692 s, 1477 s, 1274 s, 808 cm^{-1} s; ^{1}H NMR (DMSO-d_6) δ 12.8 (COOH, 2 H, s), 8.62 (Ar H, 2 H, s), 8.27 (Ar H, 2 H, d, *J* = 9 Hz), 7.70 (Ar H, 2 H, d, *J* = 9 Hz), 7.69 (Ar H, 2 H, d, *J* = 9 Hz), 7.68 (Ar H, 2 H, d, *J* = 9 Hz), 6.94 (Ar H, 2 H, d, *J* = 9 Hz), 3.73 (Me H, 6 H, s). Anal. Calcd for $C_{24}H_{18}O_6$: C, 71.63; H, 4.5. Found: C, 71.44; H, 4.3.

Porphyrin Free Base 1. A 0.13-g (3.2×10^{-4} mol) sample of **4** and 2 mL of thionyl chloride in 10 mL of benzene were gently refluxed overnight and then concentrated; 3 × 10 mL of benzene was added and distilled off. The acid chloride **5** was dried under reduced pressure [^{1}H NMR ($CDCl_3$): δ 8.82 (Ar H, 2 H, s), 8.20 (Ar H, 2 H, d, *J* = 9 Hz), 7.80 (Ar H, 2 H, d, *J* = 9 Hz), 7.59 (Ar

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H, 2 H, d, J = 9 Hz), 7.12 (Ar H, 2 H, d, J = 9 Hz), 3.82 (MeO, 6 H, s)] and without isolation was taken up in 50 mL of dichloromethane. A 0.1-g (1.5×10^{-4} mol) sample of $\alpha,\beta,\alpha,\beta$-TAPP was dissolved in 50 mL of dichloromethane and both solutions were added simultaneously over a period of 6 h to a solution of 300 mL of dichloromethane containing 1 mL of triethylamine and ca. 3 mg of powdered KI. The reaction mixture was stirred for 72 h at room temperature, then extracted with water, dried (Na_2SO_4), and concentrated. The crude product was column chromatographed on silica (benzene/ethyl acetate = 1:1) to afford 0.165 g (79%) of 1: $[\alpha]^{20}_D = -22.1°$; UV–vis (THF) λ_{max} 428 nm (ϵ = 210 900 cm^{-1} M^{-1}), 520 (ϵ = 25 000), 556 (ϵ = 17 600), 549 (ϵ = 16 900), 650 (η = 147 788; IR (KBr) 3416 m, 2952–2841 m, 1732 m, 1684 s, 1621 s, 1580 s, 1516 s, 1445 s, 1238 cm^{-1} s; ^1H NMR ($CDCl_3$) δ 8.95 (Pyr-H, 4 H, s), 8.69 (Pyr-H, 4 H, s), 8.64 (Nap-H, 4 H, d, J = 9 Hz), 8.17 (Nap-H, 4 H, s), 7.98 (Ph-H, 4 H, d, J = 6 Hz), 7.89 (Ph-H, 4 H, t, J = 9 Hz), 7.85 (Ph-H, 4 H, D, J = 9 Hz), 7.62 (Ph-H, 4 H, t, J = 6 Hz), 7.31 (Nap-H, 4 H, d, J = 9 Hz), 6.73 (CONH, 4 H, s), 5.54 (Nap-H, 4 H, d, J = 9 Hz), 5.43 (Nap-H, 4 H, d, J = 9 Hz), 3.61 (OMe, 12 H, s), −2.90 (Pyr-NH, 2 H, s); FAB MS [m/z (obsd rel intensity; calcd rel intensity)] 1405 (17; 0), 1406 (58; 96), 1407 (100; 100), 1408 (80; 51), 1409 (49; 17), 1410 (21: 4.3). Anal. Calcd for $C_{92}H_{62}H_8O_8$; C, 78.5; H, 4.4; N, 7.96. Found: C, 78.37; H, 4.61; N, 7.68. When this condensation was carried out with racemic 4, two diastereomeric porphyrins, *meso*- and DL-1, were obtained. These compounds separated readily on silica TLC plates. Thus, the absence of a TLC spot corresponding to the meso diastereomer in 1 confirmed its optical purity.

Iron Complex 1-$Fe^{III}Cl$. To a solution of 0.1 g (7×10^{-5} M) of 1 and 0.5 g (2×10^{-3} mol) of iodine in 40 mL of toluene was added 0.138 g (7×10^{-3} mol) of iron pentacarbonyl under nitrogen. The reaction mixture was stirred at 100 °C for 4 h and then at room temperature for 3 h exposed to the air. The solids were filtered off and washed with benzene and then taken up in ethyl acetate. This solution was shaken with 10% HCl until the visible spectrum stabilized and then was dried over $CaCl_2$ and concentrated. The crude product was chromatographed on silica gel (ethyl acetate) to afford 0.97 mg (91%) of 1-$Fe^{III}Cl$: UV–vis (THF) λ_{max} 428.4 nm (ϵ = 87 700 cm^{-1} M^{-1}), 518.8 (ϵ = 16 200), 627.6 (ϵ = 11 800), 650.4 (ϵ = 11 800); $[\alpha]^{20}_D$ −64.18°; IR (KBr) 3411 m, 2956–2933 m, 1676 m, 1619 m, 1579 s, 1515 s, 1444 s, 1333 s, 1301 s, 1240 s, 999 cm^{-1} w; FAB MS [m/z (observed rel intensity; calcd rel. intensity)] 1458 (12; 6.1), 1459 (21; 6.3), 1460 (81; 96), 1461 (100; 100), 1462 (72; 51), 1463 (40; 17), 1464 (18; 4.3). Anal. Calcd for $C_{92}H_{60}ClN_8O_8Fe$: C, 73.66; H, 4.03; N, 7.47; Cl, 2.37. Found: C, 73.72; H, 4.11; N, 7.51; Cl, 2.44.

Manganese Complex 1-$Mn^{III}Cl$. Under an inert atmosphere to a solution of 0.1 g (7×10^{-5} mol) of 1 and 0.5 g (2×10^{-3} mol) of iodine in 40 mL of toluene was added 0.7 g (1.7×10^{-3} mol) of dimanganese decarbonyl. The reaction mixture was stirred at 100 °C for 5 h and then at room temperature, exposed to air overnight. The solids were filtered off, washed with benzene, and taken up in ethyl acetate. This solution was shaken with 10% HCl, dried over $CaCl_2$, and concentrated. The crude product was chromatographed on silica (eluent/ethyl acetate) to afford 1-$Mn^{III}Cl$: 76 mg (71.7%); UV–vis λ_{max} 481.2 nm (ϵ = 98 500 cm^{-1} M^{-1}), 590 (ϵ = 15 500), 627 (ϵ = 15 500), 681 (ϵ =13 200); $[\alpha]^{20}_D$ = −943.82°; IR (KBr) 3492 m, 2995–2857 m, 1733 m, 1683 m, 1620 m, 1583 m, 1515 s, 1484 m, 1443 s, 1300 m, 1279 w, 1269 m, 1236 m, 804 m, 757 cm^{-1} m; FAB MS [m/z (obsd rel intensity; calcd rel intensity)] 1456 (5; 0), 1457 (8; 0), 1458 (12; 0), 1459 (89; 96), 1460 (100; 100), 1461 (65; 51), 1462 (29; 17), 1463 (15; 4.3). Anal. Cald for $C_{92}H_{60}ClN_8O_8Mn$: C, 73.86; H, 4.04; N, 7.49; Cl, 2.37. Found: C, 73.66; H, 4.40; N, 7.64; Cl, 2.30.

Epoxidations. In a standard experiment, 0.022 g (10^{-4} mol) of iodosylbenzene was added under an inert atmosphere to a solution of 10^{-6} mol of metalloporphyrin and 10^{-3} mol of substrate in 2 mL of toluene at 0 °C. The reaction mixture was stirred for 2 h. The yields and enantiomeric excesses were determined by GLPC, using the Schurig column described above.[10,23]

To establish the absolute configuration of the major product, the reaction mixture was filtered, concentrated, and then chromatographed on basic alumina, first eluted with cyclohexane and then benzene. In cases when the retention times of the products were too low, iodobenzene was used as solvent. The direction of polarimetric rotation was compared to literature values.[36]

Hydroxylations. To a solution of 1.5 mg (10^{-6} mol) of porphyrin catalyst in 2 mL of degassed dichloromethane was added 106 mg (10^{-3} mol) of ethylbenzene under a nitrogen atmosphere, and the mixture was cooled to 0 °C. Iodosylbenzene, 22 mg (10^{-4} mol), was added and the reaction mixture was stirred at 0 °C for 1 h.

Derivatization. After filtering off the insoluble products, the above solution was chromatographed on silica (dichloromethane). The alcohol-containing fractions were concentrated and taken up in 1 mL of dry pyridine, and 100 mg (7.1×10^{-4} mol) of (*R*)-2-phenylpropionyl chloride was added and stirred at 70 °C for 1 h. The reaction mixture was poured into ice–water and the product mixture of diastereomeric esters was extracted with ether. The combined organic phases were dried over sodium sulfate and concentrated. This purification procedure was shown not to change the enantiomeric composition of the original reaction mixture. More importantly, this derivatization afforded a complete separation of the diastereomeric esters upon GLPC analysis and the electron impact mass spectrum displayed a significant molecular ion peak. Thus, ee's could be determined directly by integration of the diasteromeric ester peaks. Absolute configurations were determined by comparison of literature polarimetric rotations.[36] The hydroxylation of other hydrocarbons was carried out analogously.

Sulfoxidations. To a solution of 10^{-6} mol catalyst (6) in 2 mL of dichloromethane were added 10^{-3} mol of substrate and then 0.22 g of (10^{-4} M) iodosylbenzene at 0 °C under an inert atmosphere. The reaction mixture was stirred for 1 h, and the insoluble products were filtered off. The yields and the sulfoxide/sulfone ratios were determined by GLPC. The solution was chromatographed on silica (dichloromethane eluent) and the sulfoxide-containing fractions were based on the integral values of the resolved, peaks, which in most cases were the aromatic ortho protons.

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Registry No. 1, 126218-72-2; *meso*-1, 126218-75-5; *dl*-1, 126218-76-6; 1-$Fe^{III}Cl$, 126218-85-7; 1-$Mn^{III}Cl$, 126218-86-8; 2, 65283-60-5; 3, 117745-45-6; 4, 126218-73-3; (±)-4, 126371-64-0; 5, 126218-74-4; $\alpha,\beta,\alpha,\beta$-TAPP, 68070-28-0; PhSMe, 100-68-5; PhSEt, 622-38-8; *o*-BrC_6H_4SMe, 19614-16-5; *p*-BrC_6H_4SMe, 104-95-0; *p*-$MeOC_6H_4SMe$, 1879-16-9; (*R*)-(+)-PhS(O)Me, 4850-71-9; (*R*)-(+)-PhS(O)Et, 51207-25-1; (+)-*o*-$BrC_6H_4S(O)Me$, 126218-83-5; (*R*)-(+)-*p*-$BrC_6H_4S(O)Me$, 28227-62-5; (*R*)-(+)-*p*-$MeOC_6H_4S$-(O)Me, 93381-75-0; styrene, 100-42-5; *p*-chlorosytrene, 1073-67-2; *tert*-butylethylene, 558-37-2; *trans*-β-methylstyrene, 873-66-5; *cis*-β-methylstyrene, 766-90-5; *trans*-2-pentene, 646-04-8; indene, 95-13-6; 1,2-dihydronaphthalene, 447-53-0; (*R*)-(+)-styrene epoxide, 20780-53-4; (*R*)-(+)-*p*-chlorostyrene epoxide, 21019-51-2; (*S*)-(+)-*tert*-butylethylene epoxide, 40102-55-4; (1*S*,2*S*)-(−)-β-methylstyrene epoxide, 4518-66-5; (1*S*,2*R*)-(+)-β-methylstyrene epoxide, 14212-53-4; (1*S*,2*S*)-(+)-2-pentene epoxide, 93132-82-2;

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(1S,2R)-(-)-indene epoxide, 85354-35-4; (1S,2R)-(-)-3,4-dihydronaphthalene epoxide, 24825-01-2; indan, 496-11-7; 2-ethylnaphthalene, 939-27-5; 1-ethylnaphthalene, 1127-76-0; (R)-(+)-(1-hydroxyethyl)benzene, 1517-69-7; (R)-(+)-4-methoxy-1-(1-hydroxyethyl)benzene, 1517-70-0; (R)-(+)-1-phenylpropanol, 1565-74-8; (R)-(+)-1-indanol, 697-64-3; (R)-(-)-1,2-dihydro-1-naphthalenol, 123849-23-0; (R)-(+)-2-(1-hydroxyethyl)-naphthalene, 52193-85-8; (R)-(+)-1-(1-hydroxyethyl)naphthalene, 42177-25-3; 1-(1-naphthalenyl)ethanone, 941-98-0; [1(R)-[(2-(R)-phenylpropionyl)oxy]ethyl]benzene, 79121-13-4; 4-methoxy-1-[1(R)-[(2(R)-phenylpropionyl)oxy]ethyl]benzene, 126218-77-7; 1(R)-phenyl-1-[(2(R)-phenylpropionyl)oxy]propane, 126218-78-8; 1(R)-[(2(R)-phenylpropionyl)oxy]indan, 126218-79-9; 1(R)-[(2-(R)-phenylpropionyl)oxy]-1,2-dihydronaphthalene, 126218-80-2; 2-[1-[(2(R)-phenylpropionyl)oxy]ethyl]naphthalene, 126218-81-3; 1-[1-[(2(R)-phenylpropionyl)oxy]ethyl]naphthalene, 126218-82-4; ethylbenzene, 100-41-4; 4-methoxyethylbenzene, 1515-95-3; 1-phenylpropane, 103-65-1; 2,3-dihydro-4H-1-benzothiopyran-4-one, 3528-17-4; (+)-2,3-dihydro-4H-1-benzothiopyran-4-one 1-oxide, 126218-84-6.

Nucleophilic Additions to Ketenes by (Trimethylsilyl)lithium and by Enolates[1]

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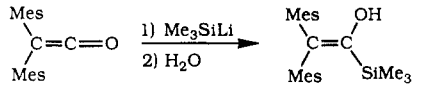
Reaction of t-$Bu_2C{=}C{=}O$ (**5**) with Me_3SiLi at -78 °C followed by trapping of the intermediate enolate with Ac_2O gave t-$Bu_2C{=}C(OAc)SiMe_3$ (**9**). Other ketenes gave similar products. Reaction of ketenes $PhCR{=}C{=}O$ (R = Me, **13**; R = Et, **3**) with enolates $CH_2{=}C(OLi)R^1$ (R^1 = H, Me, t-Bu, Ph) at -78 °C followed by warming to 25 °C and hydrolysis gave vinyl esters $PhCHRCO_2C(R^1){=}CH_2$, along with 10% $PhCHMeCOCH_2COPh$ for R = Me, R^1 = Ph. Under the same conditions the ketenes $PhCR{=}C{=}O$ with enolates $CH_2{=}C(OK)R^1$ (R^1 = Me, t-Bu, Ph) gave only 1,3-diketones $PhCHRCOCH_2COR^1$, but vinyl esters were the major products if the reactions were quenched at -78 °C. It is proposed that enolates undergo preferential O-acylation by ketenes in a kinetically favored process, but that these intermediates can revert to thermodynamically more stable C-acylated products.

Nucleophilic additions to ketenes[2] have been the subject of synthetic,[1,3] mechanistic,[4] and theoretical[5] studies in our laboratory. We now report results on the addition of (trimethylsilyl)lithium (Me_3SiLi) and enolates to ketenes.

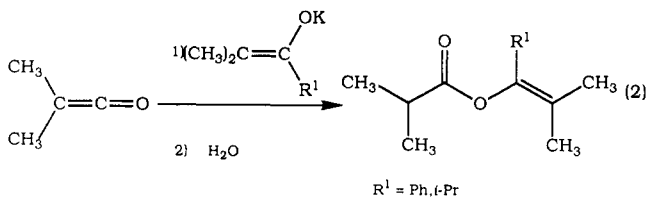
One previous example of the addition of Me_3SiLi to a ketene has been reported, namely to dimesitylketene (**1**, eq 1).[6] The product of addition to the carbonyl carbon was obtained in 49% yield and exists as the enol tautomer **2**. Such reactions appear promising for the preparation of silyl derivatives, and we have accordingly examined several other examples.



(1)

1 (Mes = 2,4,6-$(CH_3)_3C_6H_2$) **2**

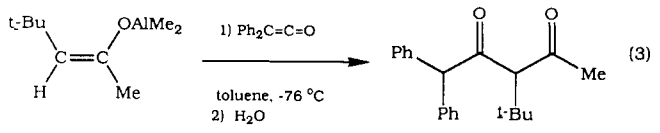
There have been a few previous studies of the reactions of enolates with ketenes.[7] Interestingly, these have shown that enolates reacted with ketenes mainly by O-acylation in relatively polar solvents. Thus, Yoshida et al. have reported[7a] that the reaction of dimethylketene with the potassium enolates of isobutyrophenone and diisopropyl ketone in dimethyl ether resulted in the formation of the O-acylation products exclusively, at -30 °C (eq 2). Similarly, the reaction of ketene itself with the sodium enolate of propiophenone afforded the alkenyl ester in 23-28% yield.[7b]



(2)

R^1 = Ph, t-Pr

However, the Z isomer of dimethylaluminum 4,4-dimethylpent-2-en-2-olate underwent C-acylation on reaction with diphenylketene in toluene. It has been suggested that this was due to the covalent nature of the Al-O bond (eq 3).[7c]



(3)

(57%)

Because of the synthetic potential and theoretical interest of the addition of Me_3SiLi and of enolates to ketenes, we have undertaken further study of both reactions.

Results and Discussion

Silylations. The reactions of Me_3SiLi with ketenes **3-5** gave the enol acetates **6-9** as shown in eqs 4-6 on trapping

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