Pergamon

Tetrahedron, Vol. 53, No. 23, pp. 7753-7776, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00470-5

Synthesis and Catalytic Epoxidation Activity of Terpene-Derived D_4-Symmetric Metalloporphyrins

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Abstract: We report here a flexible synthesis of chiral, D_4-symmetric porphyrins from cyclic ketone starting materials. Two porphyrins have been synthesized from the terpene 1-R-(+)-nopinone, obviating the need to perform a resolution. The chloromanganese derivative of one of these porphyrins is a good catalyst for the epoxidation of terminal alkenes, providing epoxides with e.e.'s of 70% with high turnover numbers. A predictive model for oxygen atom transfer in the chiral pocket is discussed.

The growing demand for enantiomerically pure compounds has stimulated great interest in the development of new asymmetric catalysts. The most common type consists of a catalytically active metal atom bound by a chiral ligand. Metalloporphyrin complexes are a potentially attractive arena in which to explore the rational design of such catalysts. Manganese, iron and rhodium porphyrins are known to catalyze alkane hydroxylation, alkene epoxidation,[1,2] cyclopropanation[3,4] and aziridination,[5] and aluminum porphyrins have been shown to mediate Diels-Alder reactions[6] and initiate the living polymerization of a variety of monomers.[7,8] Furthermore, the relatively rigid structure of tetraaryl porphyrins provides a general template to which a variety of chiral directing groups can be appended. This should make the rational design of highly enantioselective catalysts somewhat more straightforward than is the case with conformationally mobile ligands. For these reasons, a number of groups have embarked upon such studies.[9-15] However, despite many innovative approaches, synthetically useful systems have remained elusive. One problem is that the syntheses of many chiral porphyrins are tedious, inefficient and often inflexible. This a major drawback, since the development of highly selective catalysts inevitably involves some empirical experimentation.[16,17]

Another concern, particularly in the design of asymmetric epoxidation catalysts, is the stability of the porphyrin and the chiral appendages attached to it. Tetraaryl porphyrins bearing electron-donating substituents usually suffer rapid decomposition of the aromatic macrocycle under the strongly oxidizing conditions employed for these reactions.[18]

An apparently general solution to the oxidative stability problem is to employ tetraryl porphyrins that lack destabilizing π-donating aromatic substituents and have rigid pockets that cannot contact the metal-oxo center. For example, the chloromanganese (III) derivative of the "chiral wall" porphyrin **1**[14] (Figure 1) proved to be an extremely efficient epoxidation catalysts (over 3000 turnovers using styrene as the substrate and bleach as the terminal oxidant). Unfortunately, the enantiomeric excesses observed ranged from only 10-50%. Even more problematic, the synthesis of aldehyde **2** was relatively tedious and did not lend itself to the straightforward construction of derivatives with different pocket geometries.[4] Finally, the condensation of aldehyde **2** and pyrrole led to three other atropisomers in addition to **1**, which necessitated a difficult chromatographic purification of the desired $\alpha,\beta,\alpha,\beta$ species.

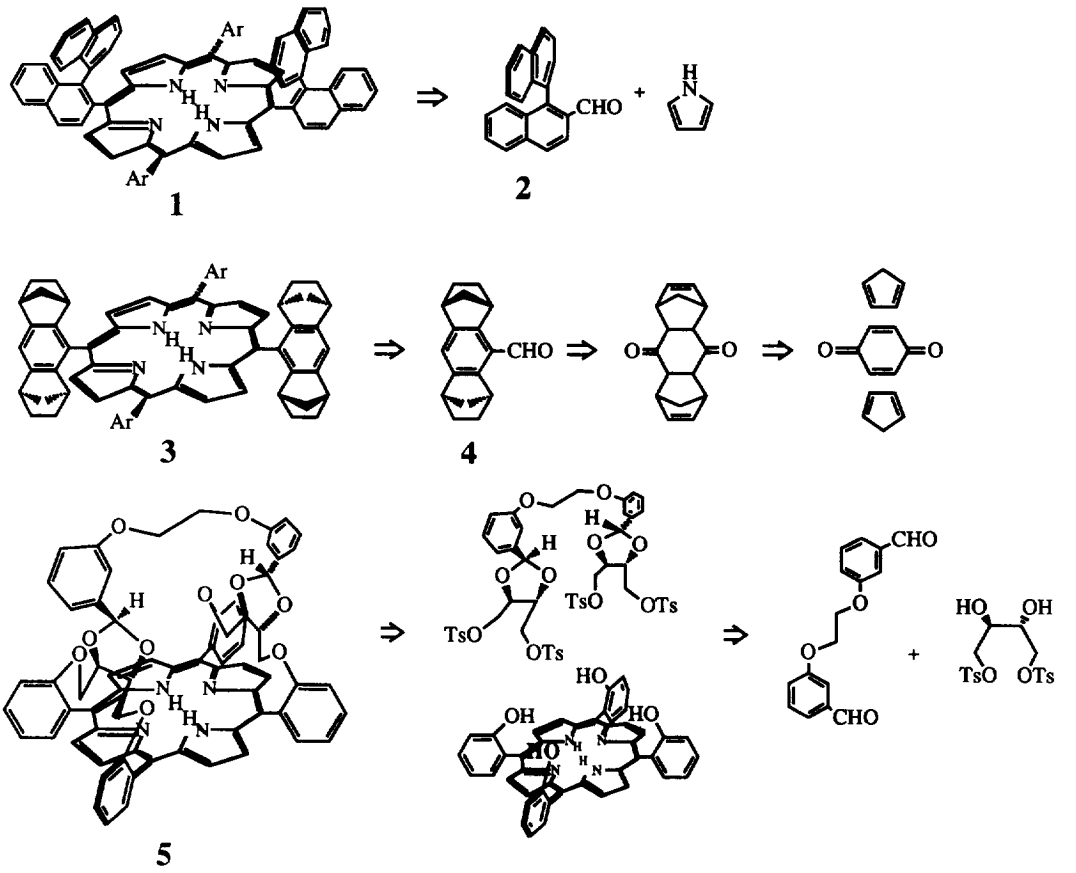


Fig 1. Some earlier chiral porphyrin ligands. The "Ar" groups in porphyrins **1** and **3** are identical to those shown at the other meso positions. In porphyrin **1**, the naphthyl groups not shown are on the bottom face of the porphyrin (**1** is C_2-symmetric).

Halterman and coworkers made an important advance with the synthesis of the first D_4-symmetric chiral porphyrin **3** (Figure 1).[11] These workers also employed a route involving the condensation of pyrrole and a chiral aldehyde to build the porphyrin macrocycle. The symmetry of the product obviated the possibility of obtaining atropisomers, thus greatly simplifying the task of obtaining large quantities of this novel ligand. The chloromanganese derivative of **3** was found to catalyze the epoxidation of styrene and *cis*-1-phenylpropene with respectable enantiomeric excesses. Like the chiral wall porphyrin, ligand **3** proved to be extremely stable

under the reaction conditions and high turnover numbers were obtained. The synthesis of aldehyde **4** was accomplished via a route that employed as its key step a double Diels-Alder reaction between benzoquinone and cyclopentadiene.

A completely different approach was employed by Collman and coworkers in the construction of the "threitol-strapped" porphyrins **5** (Figure 1).[10] In this case, a preformed porphyrin template was coupled to a mixture of isomers of a tetratosylate derived from the condensation of two molecules of 1,4-ditosylthreitol and a bis-aldehyde. This procedure produces three isomers that must be separated. The chloromanganese (III) derivative of the "Out/Out" isomer shown in Figure 1 catalyzed the epoxidation of aromatic alkenes with e.e.'s ranging from 21% to 88% using iodosylbenzene as the oxidant. Unfortunately, the e.e.'s declined over time due to oxidation of the chiral strap. This work is significant in that the synthetic route employed can readily produce a family of structurally related porphyrins by simply varying the bis-aldehyde linker and because it employs a cheap, optically active starting material (threitol), thereby avoiding the need to carry out a resolution.

In order to stimulate the development of porphyrin-based asymmetric catalysts, it would be desirable to devise a synthetic scheme that could rapidly and easily produce families of oxidatively robust chiral porphyrin ligands, preferably starting from cheap, optically active materials. In this way, the best features of existing systems could be combined. Given the many attractive features of the all-hydrocarbon D_4-symmetric porphyrins, it seemed reasonable to focus on this class of macrocycles. Two new syntheses of such porphyrins, starting from a readily available cyclic ketone starting material, are reported here.[19] It is also shown that the chloromanganese derivative of one of these ligands is a good catalyst for the asymmetric epoxidation of terminal alkenes, providing e.e.'s of 70-85% and thousands of turnovers. These results compare favorably with those obtained with the best catalysts of any type presently available for this substrate class. The high symmetry of the D_4 pocket, which limits the number of different geometries available for the substrate-catalyst interaction, has allowed the formulation of a model for oxygen atom transfer that accomodates the currently available data and should facilitate the rational design of more selective porphyrin catalysts.

Results

Synthetic Strategy. The central focus of the synthetic work was to develop a flexible synthetic route to chiral D_4-symmetric porphyrins in which carbocyclic rings bearing one or more asymmetric centers are fused above and below each of the arene rings attached to the *meso* carbons of the macrocycle. This class of compounds, of which the Halterman porphyrin **3** is representative, was chosen because the carbocyclic rings ensure a rigid chiral environment. It was envisioned that these compounds could be made from a condensation reaction between pyrrole and the appropriate chiral aldehyde, as was the case for porphyrins **1** and **3**. The poor to mediocre yields generally associated with this reaction demand that the syntheses of the C_2-symmetric aldehydes must be short, efficient and employ inexpensive starting materials if the catalysts are to be of practical value.

Porphyrins **6** and **7** were chosen as the initial targets (Figure 2). These macrocycles could be derived from pyrrole and compounds **8** and **9**, respectively. These closely related aldehydes contain a central aromatic ring flanked by cycles derived from the commercially available terpenic ketone 1R-(+)-nopinone. The approach envisioned was to link the nopinone-derived rings by a methylene bridge and then to employ some type of "5+1" condensation to form the central aromatic ring. By employing single carbon units with the appropriate

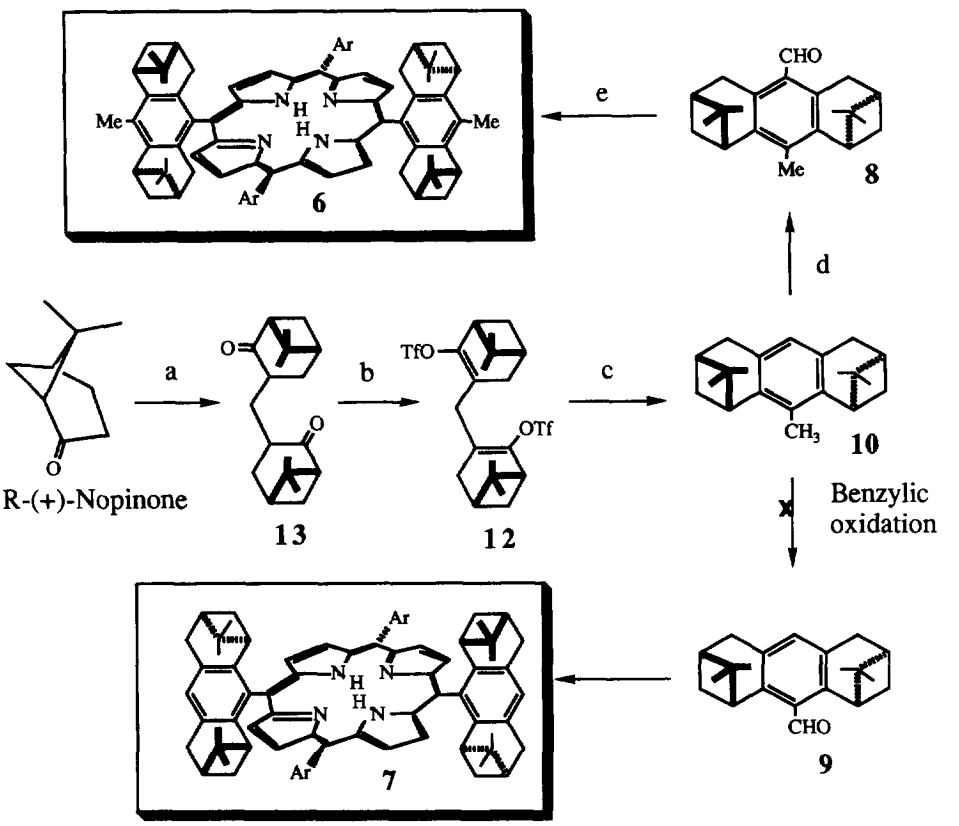


Fig 2. Synthesis of porpyrin **6**.[19] (a) KH/DMF, 50°C (60 % yield), or KH/THF, then Eschenmoser's salt , 65°C (54 %). (b) KHMDS, THF, -78°C , Commin's reagent (65 %). (c) LiCl, $Pd(PPh_3)_4$, TEA, N-methyl pyrrolidinone (NMP), 75°C, then vinyl tributyltin (55 %). (d) α,α-Dichloromethyl methyl ether,Ti Cl_4, CH_2Cl_2,-15°C (78 %). (e) i) pyrrole, ethanol (cat.), CH_2Cl_2, BF_3-OEt_2 ii) *p*-chloranil (15 %).

functionality, it was hoped that both aldehydes could be accessed from a common precursor.

Synthesis of highly substituted chiral arenes through a Pd-catalyzed "5+1" condensation as the key step in the construction of D_4 -symmetric porphyrins. The first step was accomplished by the method of Kiyooka.[20] Addition of nopinone in THF to a suspension of potassium hydride in DMF at 40-50 °C gave the desired 1,5-

diketone **13** in 60% yield when conducted on a scale of 15 grams or less. However, this reaction was somewhat capricious when carried out on a larger scale. In these cases, poor yields of the diketone (typically 10-20%) were often obtained and the α-methylene derivative of nopinone was the major product. Therefore, an alternative preparation of **13** was developed which involved addition of Eschenmoser's salt[21] to a two-fold molar excess of the potassium enolate of nopinone in THF. This procedure was found to be reproducible (58% yield) even on a large scale.

Perusal of the literature did not reveal a simple and straightforward protocol to transform the 1,5-diketone into an aromatic ring. Therefore, new chemistry was explored. Double deprotonation of **13** with potassium hexamethyl disilylamide (KHMDS), cooling of the bis-enolate to -78 °C, and addition of Comin's reagent (5-chloro-2-bistriflylamino-pyridine) [32] gave bis-enoltriflate **12** (Figure 2). **12** was then treated with a vinylstannane in the presence of a palladium catalyst to provide arene **10** in 55% yield.

It is reasonable to speculate that conversion of **12** to arene **10** proceeds by initial Stille displacement of one of the triflates by the vinylstannane followed by an intramolecular Heck reaction and isomerization to the aromatic product (Figure 3, top pathway). This methodology represents a new "5+1" route to aromatic rings.

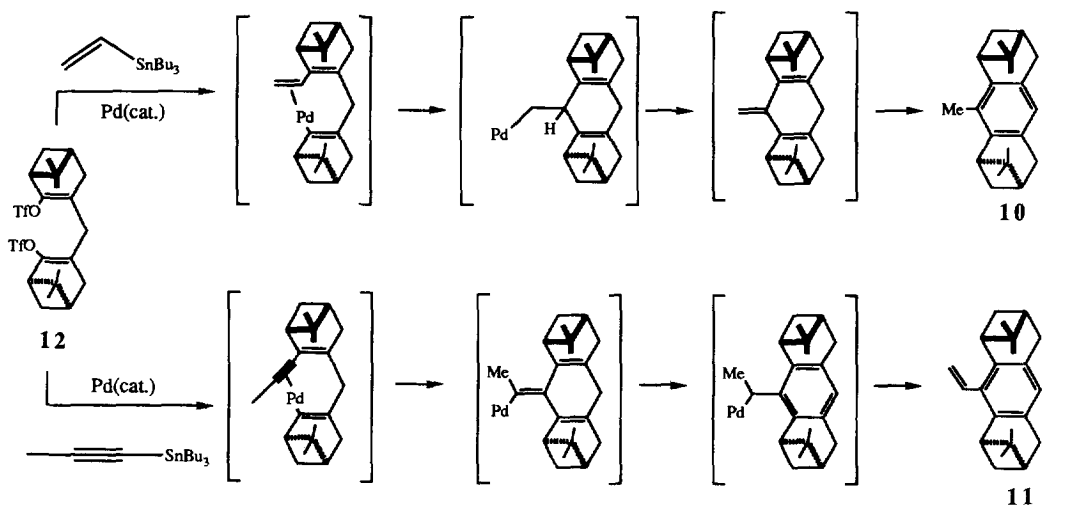


Fig. 3. Proposed mechanisms for the "5+1" Pd-mediated benzannelation reactions between bistriflate **12** and alkenyl and alkynyl stannanes.

Arene **10** was then formylated (α,α-dichloromethyl ether, $TiCl_4$, 78%)[22] to provide the penultimate aldehyde **8**. Contrary to the claim made by the manufacturer, commercial nopinone is not of high optical purity, so **8** was recrystallized and its enantiomeric purity was checked by a ^{1}H-NMR chiral shift experiment using tri(3-(heptafluoropropylhydroxymethylene)-(+)-camphorato) europium (III). No splitting of the aldehyde peak

was observed for the pure crystalline material, although splitting could be observed in the product prior to recrystallization. The structure of **8** was confirmed by X-ray crystallography. The synthesis of porphyrin **6** was completed by condensation of aldehyde **8** with pyrrole under Lindsey conditions (15%).[23]

To access aldehyde **9**, the precursor to porphyrin **7**, several unsuccessful attempts were made to oxidize the benzylic methyl group of **10** directly to an aldehyde. Subsequently it was found that **9** could be accessed from an earlier intermediate, the bis-enoltriflate **12**. This was accomplished by treatment of **12** with 1-(tributylstannyl)propyne in the presence of palladium tetrakis(triphenylphosphine) in DMF, from which a 25% yield of **11** was obtained (Figure 4).

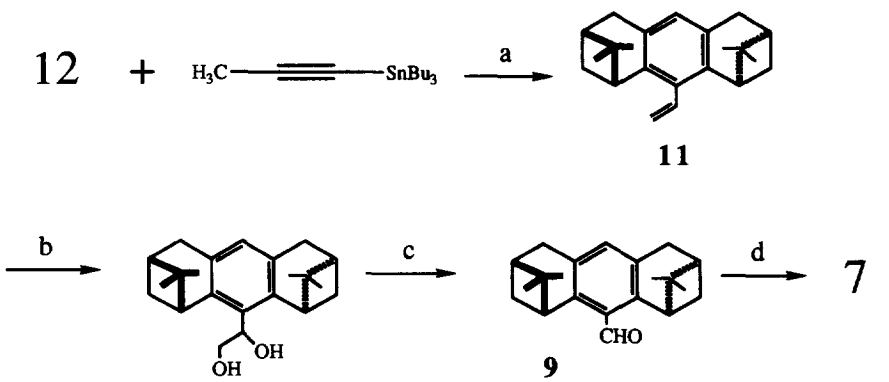


Fig. 4. Synthesis of porphyrin **7** from bis-triflate **12**. (a) LiCl, Pd $(PPh_3)_4$, TEA, DMF, 75°C; then tributyltin-1-propyne (25 % yield). (b) OsO_4, N-methyl morpholine-N-Oxide, acetone (63 %). (c) $NaIO_4$, EtOH/ H_2O (87 %). (e) i) pyrrole, ethanol (cat.), CH_2Cl_2, BF_3-OEt_2 ii) *p*-chloranil (10 %).

As was the case for the palladium-catalyzed addition of a vinylstannane to the bis-enoltriflate, the conversion of **12** to **11** probably proceeds through subsequent Stille and Heck reactions (Figure 3, lower pathway). In this case however, a vinylpalladium intermediate is produced, which cannot β-hydride eliminate in the fashion that led to the formation of **10**. Instead, it appears to isomerize to a benzylic alkylpalladium complex which then undergoes β-hydride elimination to provide the vinyl group in **11**. While speculative, this mechanism is precedented by the work of Nuss, *et al.*,[24] who have employed related chemistry in the synthesis of enediynes.

The vinyl group was then cleaved oxidatively in two steps (catalytic OsO_4, N-morpholine oxide, followed by $NaIO_4$, 60% overall) to give the desired aldehyde **9** (Figure 4). Condensation of **9** with pyrrole under Lindsey conditions yielded porphyrin **7** in 10% yield.

Because of the modest yield obtained in the palladium-catalyzed transformation of **12** to **11**, an alternative route was explored (Figure 5). Tributyltin-2-ethyl acrylate[25] was substituted for the propynylstannane in the Stille/Heck sequence, providing ester **14**, which was reduced using $LiAlH_4$ (THF, -78 °C) to give alcohol **15**.

15 was then treated with *p*-toluene sulfonyl chloride and the resulting mixture was added directly to potassium *tert*-butoxide in DMSO[26] to provide styrene **11**. The overall yield of these three operations was about the same as the one-step protocol employing the alkynyl stannane. For small scale applications, the more direct route using the propynyl stannane is preferred, but because of the large mole fraction of palladium catalyst required for this reaction the route shown in Figure 5 is more practical for large scale preparations.

Porphyrins **6** and **7** were converted to their chloromanganese(III) derivatives in 80% and 70% yield, respectively.

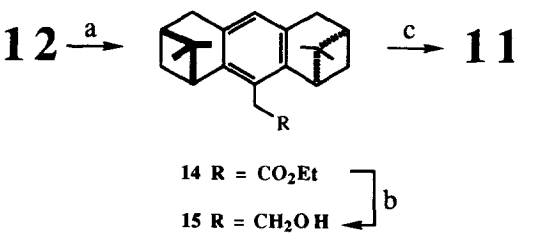


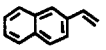
Fig. 5. An alternative route to styrene **11**. (a) $Pd(AsPh_3)_4$, LiCl, NMP, TEA, 75°C, then 2-tributyltin ethyl acrylate/NMP (67 % yield). (b) $LiAlH_4$, THF, -78°C (96 %). (c) i) Pyridine, DMAP, THF, and PTSCl. ii) Added to ^{t}-BuOK, DMSO, 40°C (59 %).

Catalytic Asymmetric Epoxidation Reactions. The chloromanganese derivative of **7** was evaluated as a catalyst for the epoxidation of several aromatic alkenes using LiOCl as the terminal oxidant and dicyclohexylimidazole as the axial ligand in a phase transfer system.[27,28] Mn-7-Cl was a very efficient catalyst, providing thousands of turnovers (Table 1). These experiments were conducted under conditions of limiting substrate so as to maximize the conversion of substrate to product, as would be the case in a synthetic procedure. Most catalytic epoxidation reactions are run with a large excess of substrate present, which better protects the porphyrin against oxidative degradation. Under these more forgiving conditions, extremely high turnover numbers were observed. For example, after mediating the formation of almost 19,000 equivalents of epoxide from α-methylstyrene, close to 70% of Mn-**7** remained intact as deduced by UV-Visible spectroscopy. This is by far the largest turnover number ever reported for an asymmetric epoxidation catalyst.

Terminal aromatic alkenes are the best substrates for this catalyst. Styrene, 1-vinylnaphthalene and α-methylstyrene were all epoxidized in 65-70% e.e.. Mn-7-Cl was quite stable under the reaction conditions. Using recycled catalyst that had already turned over more than 1000 times, the e.e. obtained in the epoxidation of α-methylstyrene was identical, within experimental error, to that observed in the original reaction.

Indene and *cis*-β-methylstyrene were epoxidized with e.e.'s of 40% and 24%, respectively. Thus, within a series of comparable substrates (styrene, indene and *cis*-β-methylstyrene) it appears that the e.e. obtained is

Table 1. Results of Aromatic Alkene Epoxidation Reactions Catalyzed By Mn-7-Cl.

Alkene	% Yield	Turnovers	% e.e.	Enantiomer
	70	2520	**70**	1R
	46	2918	**69**	1R
	68	2516	**66**	1R
	67	18,720[a]	**65**	1R
	91	2110	**40**	1R,2S
	33	957	**24**	1R,2S

[a] Large excess of substrate present. n.d. = not determined. The e.e.'s shown are accurate to within ± 5%.

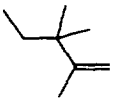
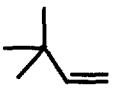
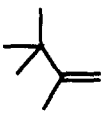
inversely related to the size of the cis-β-substituent. However, placing a methyl group on the α carbon had little effect; α-methylstyrene and styrene were epoxidized with similar e.e.'s and with the same absolute stereochemistry. These results are quite different than those obtained with many other chiral porphyrins, which have lower symmetry pockets. In most cases, *cis*-disubstituted aromatic alkenes are epoxidized in higher e.e. than terminal alkenes.

The epoxidation of aliphatic alkenes by Mn-7-Cl was also examined, although they are generally poorer substrates for porphyrin-mediated epoxidations than aromatic or other conjugated alkenes. The results are shown in Table 2. Most of the substrates were converted to epoxides with reasonable efficiencies, with the exception of monosubstituted and *trans*-disubstituted species. In most cases, the e.e.'s of the epoxides were relatively low.

A major exception to these mediocre results proved to be the epoxidation of 1,1-disubstituted aliphatic alkenes. These proved to be excellent substrates, providing e.e.'s in excess of 80% with good chemical efficiency as well (for example, 83% e.e. and 5300 catalyst turnovers in the epoxidation of 2-neopentylpropene). These are the best results with this class of alkenes yet reported in the literature using any type of epoxidation catalyst.

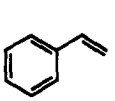
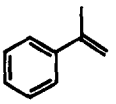
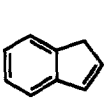
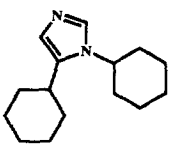
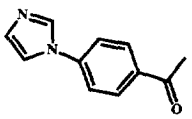
Axial ligand effects. The epoxidation reactions carried out in this study employ as an axial ligand 1,5-

Table 2. Epoxidation of Aliphatic Alkenes Catalyzed By Mn-7-Cl·

Alkene	% e.e.	Total turnovers
	85	15,000
	47	13,000
	74	5,000

The e.e.'s shown are accurate to within ± 5%. The absolute configurations of the epoxides were not determined.

Table 3. Axial Ligand Effects on the Mn-7-Cl-Catalyzed Epoxidations.

Axial Ligand \ Substrate			
	68%	66%	33%
	33%	37%	15%

dicyclohexylimidazole (DCI).[10] As shown in Table 3, this ligand provides superior results when Mn-7-Cl is employed as the catalyst compared to N-acetophenone imidazole (NAcPhIm). The mechanistic basis

of this axial ligand effect is unknown. It could be that the bulkier DCI orients the cyclic appendages of Mn-7-Cl in a particular orientation when coordinated to the metal, or that the more electron-donating DCI exerts some kind of electronic effect. These possibilities are not mutually exclusive.

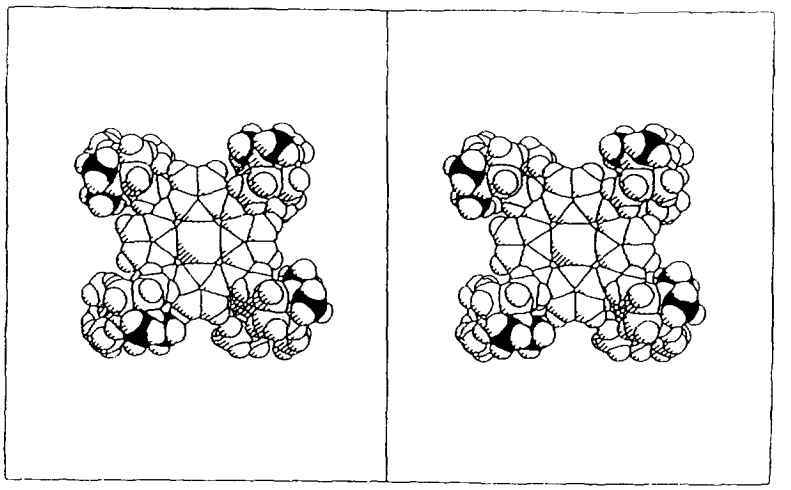
Discussion

A new synthesis of D_4 -symmetric porphyrins. A central goal of this study was to develop a relatively efficient flexible synthetic route that would provide access to a family of oxidatively robust, D_4-symmetric chiral porphyrins, preferably employing optically active starting materials. The chemistry reported here represents a significant step towards this goal. The key reaction is a novel palladium-catalyzed "5+1" condensation of a bis-enoltriflate and an organostannane to provide an arene product. It should be possible to apply this methodology to many cyclic ketones that can be linked via a methylene group. A bonus of this chemistry is that two porphyrins can be made from any starting material depending on the type of organostannane that is employed in the arene-forming step. The pairs differ mainly on which "side" of the arene ring the porphyrin is assembled (compare **6** and **7**).

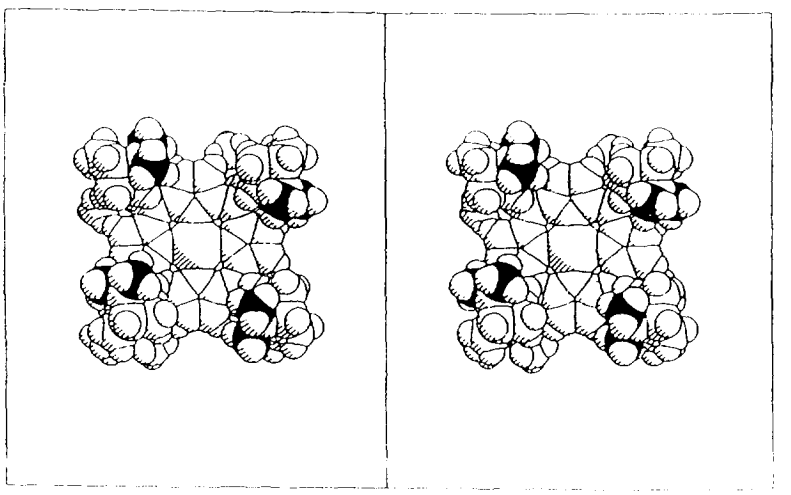
The overall yield of porphyrins **6** and **7** were 2.6% and 0.6%, respectively. These will have to be raised significantly if metalloporphyrins constructed by this route are to find practical application. This may be feasible with extensive empiricial experimentation, since the lowest yielding step is the cyclization of pyrrole and the chiral aldehyde, which is notoriously sensitive to the reaction conditions. However, even assuming that the present yields prove to be typical for other porphyrins that will be made via this route, the fact that only 5-6 steps are required makes it relatively straightforward to obtain tens or hundreds of milligrams of the target porphyrin. Given the very high turnover numbers exhibited by these catalysts, this is more than enough to conduct a preliminary evaluation of the catalytic epoxidation activity. If good e.e.'s are observed using a particular catalyst, it would then be worthwhile to invest more time in optimizing the yield of each step.

This chemistry is complementary to the D_4-symmetric porphyrin synthesis reported by Halterman and coworkers (see Fig. 1), which features a double-Diels-Alder reaction as the key ring-forming step.[11] The Halterman chemistry is best suited for using reactive diene precursors to form what will eventually become the chiral rings flanking each aromatic ring, while the route described here most conveniently employs cyclic ketones as starting materials.

Catalytic asymmetric epoxidation reactions. The chloromanganese derivative of porphyrin **7** has been shown to be a good catalyst for the epoxidation of certain terminal alkenes. In particular, conjugated mono- and 1,1-disubstituted alkenes and aliphatic 1,1-disubstituted olefins are epoxidized with excellent turnover numbers and moderate to good enantioselectivities. This is interesting since terminal alkenes are usually poorer substrates than more highly substituted species in asymmetric epoxidation reactions. Mn-**6**-Cl is a rather unselective catalyst, as shown previously.[19] The large difference is the enantioselectivities exhibited by these two species was expected on the basis of their structures (see Fig. 6).[29,30] While both chiral superstructures are derived from nopinone molecules, the chiral centers are packed much more proximal to the reactive metal center in porphyrin **7**.



Porpyhrin 6 derived from 8.



Porpyhrin 7 derived from 9.

Fig. 6. Stereoviews of structural models representing metal derivatives of porphyrins **6** and **7**. These models were constructed by combining the experimentally-determined X-ray crystal structures of ruthenium tetramesityl porphyrin[30] and aldehydes **8** and **9**. The darkened carbon atoms are the nopinone-derived gem-methyl groups.

A model for oxygen atom transfer in the cavity of D_4 -symmetric chiral porphyrins. We have attempted to rationalize these results and construct a model for oxo transfer in a D_4-symmetric pocket that will help guide future catalyst design. While there is general agreement that the alkene approaches the oxo complex in a twisted "side-on" geometry (Fig. 7A), two crucial issues remain. One involves from which "point on the compass" the alkene approaches the metal-oxo intermediate (with respect to a top view of the cavity with the metal-nitrogen bond axes representing "north", "east", "south" and "west", as in Fig. 7B). The second issue is which enantioface of the alkene would be directed towards the oxygen atom.

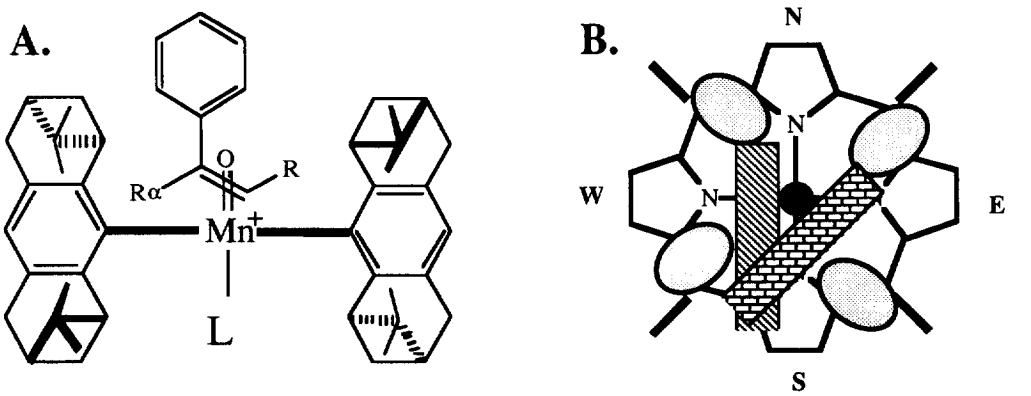


Fig. 7. **A.** Depiction of the side-on approach thought to occur prior to oxygen atom transfer in reactions catalyzed by Mn-7-DCI (L=DCI). For clarity, only two of the four pendant tricyclic rings are shown. The porphyrin macrocycle is represented as the bold horizontal lines on both sides of the metal. **B.** Top view of a D_4-symmetric chiral porphyrin, showing the "slots" available for docking of the alkene into the pocket. Epoxidations catalyzed by Mn-7-DCI are thought to occur through alkene approach in the "bricked" slot as this predicts the absolute epoxide sterochemistry observed experimentally (see text).

In porphyrin cavities with C_2 or lower symmetry, many geometries seem feasible, which has made the development of predictive models difficult. However, examination of space-filling models suggests that the pocket of Mn-7 creates only two "slots" into which the alkene can fit given a side-on approach (the striped and bricked slots in Fig. 7B). Consider the two transition state models shown in Figure 8 in which the aromatic alkene occupies the bricked slot. (The same conclusions discussed below would be reached for a series of alkenes that occupied the "striped" slot in Fig. 7B, except that the absolute stereochemistry would be opposite. The aromatic alkenes employed in this study provide (R)-epoxides, arguing that they approach the metal-oxo intermediate via the bricked slot.) These differ in the olefin enantioface directed at the oxo moiety. The upper transition state, which leads to the 1-(R)-epoxide, will be most favorable when the cis-β substituent (represented by the stipled ball in Fig. 8) is very small, since this group is pointed directly at the chiral superstructure. As the

size of this group increases, this transition state is predicted to be destabilized relative to the one that leads to the 1-(S)-epoxide. While the catalyst-substrate phenyl ring interaction is more pronounced in this transition state than the one leading to the 1-(R)-epoxide, the arene group is pointed up and away from the porphyrin and so this can be tolerated to some extent (Fig. 7A). However, for α-methylstyrene, both substituents avoid serious interactions with the catalyst in the upper transition state in Fig. 8. The model predicts that mono and 1,1-disubstituted alkenes should be epoxidized with the highest e.e.'s. A *cis*-β substituent will decrease the e.e. since the interactions of the catalyst with the phenyl and *cis*-β substituent oppose one another. This decrease should parallel the size of the R group. These predictions are in accord with the observed results using aromatic substrates and also rationalize why relatively high e.e.'s are obtained with 1,1-disubstituted aliphatic substrates.

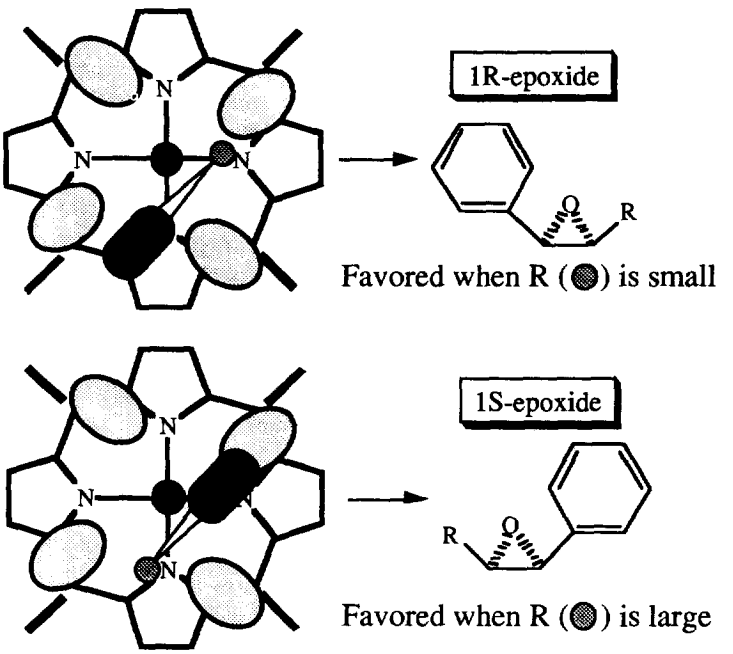


Fig. 8. Model for oxygen atom transfer in a four-fold symmetric porphyrin pocket. The dark oval represents the large substituent on an alkene substrate. The smaller stipled ball represents the *cis*-β-substituent. The large, lightly stipled ovals represent bulky groups protruding from a chiral center into the porphyrin pocket. The black circle represents the metal-oxo species The approach leading to the (R)-epoxide is favored when the cis-β-substituent is small since there is a severe steric clash in this geometry between this substituent and the chiral moiety on the porphyrin (see also Fig. 7A).

It is possible in this scheme to obtain a higher e.e. for a *cis*-disubstituted alkene than the corresponding monosubstituted substrate if the lower transition state in Fig. 8 predominates. The model makes the strong prediction that in these cases the epoxides should have different absolute stereochemistries at the benzylic carbon. This nicely rationalizes Halterman's results using Mn-**2**-Cl in which *cis*-β-methylstyrene was epoxidized in higher e.e. than styrene, but with the opposite absolute stereochemistry.[11] The Fig. 8 model, although crude, provides considerable predictive power and should be useful in designing new and more selective D_4-symmetric porphyrin catalysts.

Synthetic utility of porphyrin catalysts. The practical utility of this, or any other, porphyrin-based asymmetric epoxidation catalyst lags far behind the widely used salen-based systems developed by Jacobsen and coworkers[31] (also see ref. 32). Though the D_4-symmetric porphyrins are chemically more efficient catalysts with regard to turnover numbers, they remain far more difficult to synthesize than salens, and for most substrates do not provide e.e.'s approaching the often excellent numbers provided by the salen catalysts. However, it is interesting that Mn-**7** epoxidizes 1,1-disubstituted aliphatic alkenes with e.e.'s that are close to being synthetically useful. These are not good substrates for the salen catalysts, which work best on conjugated alkenes, so there may exist a niche for future D_4 porphyrin-based catalysts in the epoxidation of this particular substrate class.

Acknowledgements

This work was supported by grants from the Exxon Education Foundation, the National Science Foundation (CHE-9202931), and the Hoechst-Celanese Corporation (Corpus Christi, TX). We thank Dr. Vincent Lynch of this department for solving the crystal structures of aldehydes **8** and **9** and helping to construct the structural models shown in Fig. 6. We also thank Mr. Scott Lokey (Univ. of Texas at Austin) for help with the preparation of Fig. 6. We thank Dr. Shu-hai Zhao of Hoechst-Celanese Corporation (Corpus Christi, TX) for help with product analysis and Dr. Jennifer Robbins Wolf for helpful discussions.

Experimental Procedures

General. All ^1H & ^{13}C NMR spectra were obtained from chloroform-d_1 solutions and recorded at 300 MHz and 75 MHz, respectively, on a GEC 300 nuclear magnetic resonance spectrometer. Chemical shifts are reported in δ units, parts per million (ppm) upfield from the singlet at 7.24 for chloroform-d_1. ^{13}C NMR spectra are reported in ppm relative to the center line triplet at 77 ppm for chloroform-d_1. Infrared spectra were obtained from thin films of chloroform solutions, and recorded on a Perkin-Elmer 1600 FT instrument. Mass spectra were obtained using the chemical ionization technique, unless stated otherwise. Gas chromatographic analysis was performed using a Hewlett and Packard 5890 model fitted with a flame ionization detector. THF was distilled from sodium / benzophenone. All other materials used were obtained from commercial sources unless stated otherwise. Preparative column (flash) chromatography was carried out using Whatman 60Å 230-

400 mesh silica gel. Compositions of solvent mixtures are quoted as ratios of volume.

Epoxidations of Styrene by Chloromanganese porphyrin **7.** Epoxidations of olefins was carried out according to the method of Collman *et al.*[33] The porphyrin (2 mg, 1.3 μmole), 4'-(imidazol-1-yl)acetophenone (6.5 mg, 34 μmole), and benzyldimethyltetradecylammonium chloride (11 mg, 27 μmole) were dissolved in CH_2Cl_2 containing tridecane as an internal standard(5 mL (4.1 mM)). To this solution styrene ((22.7 mg, 219 μmole, 25 μl) filtered through an alumina plug) was added. This solution was then cooled to 0°C. An aliquot (10 μl) of this mixture was added to a solution of triphenyl phosphine in CH_2Cl_2 (1 mL, (76 mM)) and the intensity of the Soret band ($\lambda_{482\ nm}$) was measured. An aqueous solution of lithium hypochlorite ((0.45 M) standardized by thiosulfate titration) was prepared as specified by Collman, *et al.*[31] and 1.6 mL of this solution was added to the reaction mixture. Vigorous stirring was initiated and the reaction temperature was maintained between 0 °C and 5 °C. Gas chromatography was used to monitor the progress of the reaction. The epoxide yield was determined by comparing the area of the product and tridecane peaks using a correction factor determined with standardized solutions of tridecane (4.1mM) and styrene oxide (0.0135 mM) in CH_2Cl_2. The final absorbance ($\lambda_{482\ nm}$) of the solution was measured (as above) to determine the amount of active porphyrin remaining. The olefin was consumed after 265 minutes and the product was isolated as described by Collman,[31] giving a red oil (0.018g, yield 49 % (adjusted by determination of the ratio of product to tridecane in the ^{1}H NMR spectrum)). The product was analysed using chiral gas chromatography (Chiraldex G-TA capillary column (0.25mm x 20 m) (Advanced separation technologies inc., N.J.)). The major enantiomer had the same retention time as a commercially available sample of R-(+) styrene oxide. The enantiomeric excess was determined both by gas chromatography and by ^{1}H-NMR, using the chiral shift reagent Eu(hfc)$_3$. The same procedure was employed for all other alkenes with the following exceptions. Only 94 equivalents of olefin was used for the epoxidation of *cis* phenyl propene and 1,2-dihydronaphthalene when using chloromanganese porphyrin **7**. The *cis* phenyl propene oxide isolated from reaction with **7** had a number of unidentifiable impurities. Decane (4.1 mM) was used as the internal standard for the epoxidation of 1,2-dihydronaphthalene and 2-vinylnaphthalene oxide. For the epoxidation of aliphatic alkenes undecane was employed as the standard.

Reagent Preparations. Commin's reagent (5-chloro-2-bistrifylamino-pyridine) was prepared according to the literature procedure.[34] Tributyltin-1-propyne was prepared according to the method of Lipshutz.[35] 1R-(+)-Nopinone is commercially available or can be prepared conveniently on a large scale from pinane-2α,10-diol[36] by oxidative cleavage with sodium metaperiodate. Pinane-2α,10-diol was prepared by osmylation of β-pinene, according to the method of van Rheenan.[37]

Methylene bis(3,3'-(6,6-dimethylbicyclo(3.1.1)heptan-2-one) (**13**). Potassium hydride (35% wt. mineral oil dispersion (12.6 g, 0.11 moles)) was washed with anhydrous hexane (3 aliquots (50 mL)), under an argon atmosphere. The flask was then charged with anhydrous DMF (100 mL). A solution of 1R-(+)-nopinone (13.8 g, 0.1 moles, 12.84 mL) in freshly distilled THF (60 mL) was added slowly to the hydride suspension. The

reaction mixture was then heated at 50 °C for 3 h. The reaction mixture was then quenched by slow addition of 5 % HCl (300 mL) at 0 °C. The product **3** was extracted into ethyl acetate (300 mL) and washed with a saturated NaCl solution (300 mL). The organic layer was separated and dried over magnesium sulfate. After removal of the solvent a waxy white solid remained. This material was dissolved in hot ethyl acetate (40 mL) and diluted with hexane (200 mL). Upon cooling of this solution the product **13** was obtained as white crystals (8.64 g,60 % yield); mp 155 °C. ; ν_{max} 1702 cm^{-1}; ^{1}H NMR 2.6 (2H, dt), 2.49 (2H, t), 2.32 (2H, q,), 2.2 (2H, m), 2.15 (2H, q), 1.85 (2H, t), 1.59 (2H, d), 1.39 (2H, dd), 1.19 (3H, s), and 0.6 (2H, s); ^{13}C NMR 216 (CO), 58, 43, 41, 39, 29.9, 28.5, 26.5, 25.5, and 21; m / z 289 (M^+ + 1(100%)), 271 (15), 154 (10), and139 (15). HRMS calculated for $C_{19}H_{28}O_2$ (M^+) 288.2089, found 288.2095.

Methylene bis(3,3'-(6,6-dimethylbicyclo(3.1.1)heptan-2-one) (**13**) via Eschenmoser's salt. Potassium hydride (35% wt. mineral oil dispersion (64 g, 0.56 moles)) was washed with anhydrous hexane (2 aliquots (100 mL)). Anhydrous THF (150 mL) was added and the resultant suspension was cooled in an ice bath. 1R -(+)-Nopinone (74.6 g, 0.54 moles) was then introduced slowly under an argon atmosphere. This mixture was allowed to stir for 180 minutes, giving a cream colored suspension. N,N-Dimethylmethyleneammonium iodide (50 g, 0.27 moles) was then added in 2 gram aliquots over one hour. This suspension was then allowed to stir for 60 minutes and the solution was left to reflux gently for a further 12 h. Extra Eschenmoser's salt. (20 g, 0.11 moles) was added after 24 h, the remaining nopinone was then consumed within 4 h. The reaction mixture was then quenched and isolated as described above, giving crystals of **13** (42 g, 54% yield), mp 155 °C.

Methylene bis (3,3'-(6,6-dimethylbicyclo(3.1.1) heptenyl-2-triflate) (**12**). The diketone **13** (6 g, 0.021 moles) was dissolved in THF (60 mL) under an argon atmosphere. To this solution was added KHMDS (0.5 M solution in toluene (88 mL, 0.042 moles)) at room temperature. After 30 minutes this solution was cooled to -78°C and a solution of freshly prepared 5-chloro-2-bistrifylamino-pyridine (16.49 g, 0.042 moles) in THF (40 mL) was added over ten minutes. The reaction mixture was then allowed to warm to room temperature, and left to stir for a further 10 hours. A saturated NaCl solution (200 mL) was then added to the flask. The product was extracted into ethyl acetate (200 mL), washed with cold NaOH (10 % aqueous), and the organic layer dried over anhydrous potassium carbonate, filtered, and the solvent was removed *in vacuo* to give a yellow oil. The product was then purified by chromatography (silica / hexane: ethyl acetate 4:1) to give a colorless oil (7.56 g, 65 % yield); ν_{max} 2939, 1421, 1209, 1055, and 999 cm^{-1}; ^{1}H NMR 3.15 (2H, s,), 2.6 (2H, dt), 2.49 (2H, t), 2.29 (4H, t), 2.19 (2H, m), 1.39 (6H,s), 1.35 (2H, d), and 0.9 (6H, s); ^{13}C NMR 151.5 (2C), 121.5 (2C), 119.5 (2C, q, J 319 Hz, CF_3), 47 (2C),42 (1C), 41.5 (2C), 31.9 (2C) 31.5 (2C),28 (2C), 26.3 (2C), and 21 (2C); m/z 553 (M^+ +1, 7.3%), 552 (M^+, 6.5), 422 (61), 404 (49), 404 (100), 359 (58), 283 (70), 270 (71), 270 (80), and 253 (100). HRMS calculated for $C_{21}H_{26}O_6F_2S_2$ (M^+) 552.1075, found 552.1077.

C_2-symmetric arene (**10**). The bistriflate **12** (7 g, 0.013 moles) was dissolved in N-methyl pyrrolidinone

(NMP) (100 mL) with LiCl (3.3 g, 0.078 moles, 6 mol. eq.) and tetrakis(triphenylphosphine) -palladium(0) (0.6 g, 0.52 mmoles, 0.04 mol. eq.). Triethylamine (1.44 g,1.98 mL , 0.014 moles, 1.1 mol. eq.) was added and the solution warmed to 75 ^{o}C. Vinyl tributyltin (4.95 g, 4.56 mL, 0.0156 moles, 1.2 mol. eq.) dissolved in NMP (5 mL) was added dropwise to this solution over 30 minutes. The resultant mixture was then allowed to stir for 22 h. After cooling, the reaction mixture was poured into a saturated NaCl solution and the product was extracted into ethyl acetate. The organic layer was then separated, stirred with activated charcoal, dried over $MgSO_4$ and filtered. Removal of the solvent under reduced pressure gave a yellow oil. The desired product was isolated by column chromatography (silica / hexane) to give a white waxy solid (2 g, 55% yield).; ^{1}H NMR 6.65 (1H, s), 3.07 (2H, t), 2.95 (4H, t), 2.55 (2H, m), 2.2 (2H, m), 1.99 (3H, s, Ar-CH_3), 1.19 (6H, s), 1.09 (2H, d), and 0.6 (6H, s); ^{13} C NMR 141 (1C), 131.2 (1C), 128.2 (1C), 125 (1C), 43 (2C), 41 (2C), 38.9 (1C), 33.5 (2C), 31.9 (2C), 26.9 (2C), and 21.5 (1C); m/z 281 (M^+ + 1 (80 %), 280 (M^+ 100%), 265 (30), 253 (29), 237 (45.4), 225 (28),.181 (29), and 69 (32). HRMS calculated for C_{21} H_{28} (M^+) 280.2191, found 280.2202.

C_2-symmetric aldehyde (**8**). Arene **10** (1.68 g, 0.006 moles) was dissolved in CH_2Cl_2 (50 mL (freshly distilled over CaH_2) under an argon atmosphere and cooled to -15^{o}C using an salt / ice bath. To this solution titanium tetrachloride (1.88 g, 1.09 mL, 0.01 moles) in CH_2Cl_2 (10 mL) was added dropwise (10 mins.). α,α-Dichloromethyl methyl ether (0.756 g, 0.6 mL, 0.066 moles, 1.1 mol. eq.) was then added, and the solution was left to warm to ambient temperature. After 18 h, the reaction mixture was quenched with cold $NaHCO_3$ (aq) and filtered through a Celite plug. The organic layer was separated dried over sodium sulfate and filtered. The solvent was removed to give **8** as a yellow powder. Subsequent slow recrystallization from hexane gave yellow needle-like crystals (1.45 g,78 % yield) m.p. 199°C ; ν_{max} 1676 cm^{-1}; ^{1}H NMR 10.6 (1H, s), 3.29 (4H, dq, *J* 1.5, 9 Hz), 3.1 (2H, t, *J* 5.6Hz), 2.55 (2H, m,), 2.3 (2H, m), 2.05 (3H, s, Ar-CH_3), 1.35 (6H, s), 1.15 (2H, d), and 0.59 (6H, s); ^{13}C NMR194 , 143.8, 135.9, 135, 129, 44, 40.05, 38, 33, 31.9, 26, and 21.9; m/z 309 (M^++1, 83 %), 265 (100), 253 (16.5), and 209 (19.9). HRMS calculated for C_{22} H_{29} O (M^+) 309.2218, found 280.2219.

Preparation of n-tributyltin-2-ethylacrylate (mixture of *cis* and *trans* isomers). These organotin reagents were prepared in a manner similar to that described by Marsman, *et. al.*[25] A mixture of ethyl propiolate (10 mL, 9.68 g, 99 mmol), tri-n-butyltin hydride (31.3 mL, 33.94 g, 0.116 mol) and AIBN (0.05 g, 0.3 mmol) was heated at 50°C for 12 h. The *cis* and *trans* ^{n}-tributyltin-2-ethylacrylate a mixture was isolated as a colorless oil by vacuum distillation (28.4 g, 74 %) b.p. 0.2 mm Hg 120 - 160^{o}C. The ^{1}H NMR showed two pairs of doublets, one set at 6.25 (*J* 19.65 Hz) and 7.7 ppm (*J* 19.65 Hz) that corresponded to the *trans* isomer. The other set was at 7.15 (*J* 13 Hz) and 6.75 (*J* 13 Hz) *cis* isomer. These values are in agreement with those published by Seitz.[38] The ratio of *cis* to *trans* isomers was 1.4 : 1 by ^{1}H-NMR.

C_2 Symmetric ester **14**. Tetrakis(triphenylarsine)-palladium(0) was prepared in situ under an argon atmosphere by dissolving tris(dibenzylideneacetone)-dipalladium(0) (1.14 g, 1.25 mmole, 3 mol. %) in NMP (150 mL), giving a purple solution. Triphenylarsine (3.1 g, 10.05 mmole) was then added and the color of the solution became yellow. LiCl (10.57 g, 0.245 moles, 3.1 mol. eq.), bistriflate **12** (44.6 g, 80.5 mmoles), and triethylamine ((freshly distilled from NaOH) 25.2 g, 35 mL , 0.245 moles) were then added. The reaction mixture was then placed in an oil bath at *ca* 70 ^{o}C,.and stirred mechanically. To this mixture a solution of *cis* and *trans* n-tributyltin-2-ethylacrylate (35.62 g, 91.7 mmole) in NMP (75 mL) was added over 6 h. Stirring was then continued for a further 5 h at 70 ^{o}C. The reaction mixture was poured into saturated NaCl solution (500 mL) and the product was extracted into ethyl acetate. The organic layer was then separated, stirred with activated charcoal, dried over $MgSO_4$ and then filtered through a silica plug. Removal of the solvent under reduced pressure gave the product as a yellow oil. The product was further purified by column chromatography (silica / hexane / ethyl acetate (9:1)) to give a yellow waxy solid (24.2 g). ^{1}H-NMR analysis showed this material to contain organotin impurities (~ 22%) that were difficult to separate from the desired product (calculated yield 18.9 g, 66.7 %). Melting point: 95^{o}C; ^{1}H NMR : 6.8 (1H, s), 4.05 (2H, q), 3.5 (2H, s), 3.05 (2H, t), 2.9 (4H, m), 2.5 (2H, dt), 2.2 (2H, m), 1.39 (6H, s), 1.3 (2H, d), 1.1 (3H, t), and 0.6 (6H, s); ^{13}C NMR172, 142, 131.9, 127, 126, 60, 43.5, 40.5, 33.5, 31.9, 26.5, 21.5, 17.5, 14.3, and 13.5 ; m/z 353 (M^+ + 1 (100 %), 352 (M^+ 60%), 339 (28), 309 (25), 307 (16), 281 (15),.280 (19), 279 (77), 273 (100), 235 (25) and 223 (19). HRMS calculated for $C_{24}H_{32}O_2$ (M^++1) 353.2481, found 353.2465.

C_2-Symmetric alcohol **15**. The ester **14** (18.9 g, 54 mmol) in THF (100 mL) was added cautiously to a 1 M solution of lithium aluminium hydride in THF (340 mL, 0.34 moles) at -78^{o}C and then allowed to stir for 4 h while warming to room temperature. The solution was then cooled in an ice / water bath and saturated Na_2SO_4 $_{(aq)}$ (500 mL) was added slowly over 30 minutes The resultant white precipitate was removed by filtration and washed with ethyl acetate (250 mL). The filtrate was combined and the organic layer separated, dried over $MgSO_4$ and refiltered. Removal of the solvent under reduced pressure gave the product as a colorless oil. The product was further purified by column chromatography (silica / hexane / ethyl acetate (9:1)) to give a white semicrystalline material (16 g, 96 %).; m.p. 103 ^{o}C ; ν_{max} 3523, 2980, and 2917 cm^{-1}; ^{1}H NMR: 6.75 (1H, s), 3.4 (2H, m), 3.1 (2H, t), 2.9 (4H, m), 2.8 (2H, t), 2.6 (2H, dt), 2.2 (2H, m), 1.6 (1H, s), 1.39 (6H, s), 1.2 (2H, d), and 0.6 (6H, s); δ_C 142 (1C), 134 (1C), 132 (2C), 126.5 (2C), 64 (1C), 43 (2C), 40.5 (2C), 39 (1C), 33 (2C), 31 (2C), 30.5 (2C), 26.5 (2C), and 21.5 (2C) ; m/z 311 (M^+ + 1 (39 %), 310 (M^+ 55 %), 309 (45), 295 (25), 294 (49),.293 (100), and 267 (13). HRMS calculated for $C_{22}H_{30}O$ (M^+) 310.2296, found 310.2281.

C_2-symmetric styrene **11** from alcohol **15.** Anhydrous pyridine (100 mL) was added to a solution of the alcohol **15** (16.0 g, 51.6 mmol) and 4-dimethylaminopyridine (0.05 g, 0.4 mmol) in THF (100 mL) stirring under an argon atmosphere. This solution was cooled in an ice bath and *p*-toluene sulfonyl chloride (43 g,

0.227 moles, 4.4 mol. equivalents.) was added cautiously. The resultant solution was then allowed warm to room temperature. The reaction was stirred for 12 h and then added to a solution of potassium *tert*-butoxide (100 g, 0.89 moles) in anhydrous DMSO (300 mL) at 40°C over 30 minutes This mixture was then delivered to an ice / water bath (200 mL), and acidified with 10% HCl (300 mL). The product **11** was then extracted into ethyl acetate (300 mL), dried over $MgSO_4$ and filtered. Removal of the solvent under reduced pressure gave a dark brown tar. This product was purified by column chromatography (silica / pentane / ethyl acetate (100:1)) to give a yellow waxy material (10 g, 66 %). This material was dissolved in pentane and gave white, plate-like crystals of **11** (8.84, 58.6 %) ; m.p. 107 °C; $(\alpha)_D$ = - 0.459 (C 2.0,CH_2Cl_2); ν_{max} 2908, 1682, and 1681 cm^{-1}; ^1H NMR 6.75 (1H, s), 6.5 (1H, dd, *J* 17.3, 11.3 Hz), 5.25 (1H, dd, *J* 11.3, 2.3 Hz), 4.75 (1H, dd, *J* 17.3, 2.3 Hz), 2.9 (2H, t), 2.8 (4H, m), 2.4 (2H, dt), 2.1 (2H, m), 1.21 (6H, s), 1.05 (2H, d), and 0.55 (6H, s); ^{13}C NMR 141 (1C), 134.5 (2C), 133 (1C), 131.5 (2C), 126 (1C), 119.5 (1C), 43 (2C), 40 (2C), 38.5 (2C), 33 (2C), 31.7 (2C), 26.5 (2C), and 21.5 (2C) ; m/z 293 (M^+ + 1 (100 %), 292 (M^+ 65 %), 291 (32), 277 (22), 249 (33), and 211 (13.5). HRMS calculated for $C_{22}H_{28}$ (M^+) 292.2199, found 292.2191.

C_2-symmetric styrene **11** from bistriflate **12.** The bistriflate **12** (0.15 g, 0.27 mmol), LiCl (0.060 g, 1.4 mmol.), tetrakis(triphenylphosphine)palladium(0) (0.16 g, 0.14 mmol, 0.5 equiv), and triethylamine (0.1 mL,0.072 g, 0.7 mmol) was dissolved in DMF (5 mL, anhydrous) at 75 °C. Tributyltin-1-propyne (0.43 g, 1.3 mmol, 4.5 equiv) in DMF (5 mL), was then added dropwise to **12** over 2 h at 75°C. The reaction mixture was poured into a saturated NaCl solution (20 ml) and then added to ethyl acetate (50 ml). The organic layer was separated, stirred with activated charcoal, dried over $MgSO_4$ and filtered. Removal of the solvent under reduced pressure gave the product as a yellow oil. The product was further purified by column chromatography (pentane) to give a white solid (0.02 g, 25 % yield) This material was recrystallized from pentane giving white, crystals of **11** (0.015 g, 22 % yield) ; m.p. 107°C.

C_2-symmetric aldehyde **9**. N-methyl morpholine-N-Oxide (60% wt. aqueous solution (9 g,76 mmole, 15 mL)) was added to a solution of alkene **11** (2.5 g, 8.6 mmol) dissolved in acetone (50 mL). Osmium tetraoxide (1.5 mL of 2.5 wt. % in *t*-butanol, 0.98 mmole) was then added at 0°C. The reaction was stirred for 22 h and then sodium metabisulfite (60 g, 0.32 moles) was added cautiously, and stirred for another 5 h. The suspension was then filtered and the product extracted from the filtrate with ethyl acetate (150 mL), dried over Na_2SO_4 and refiltered. Removal of the solvent under reduced pressure gave an oily residue. The product was then purified by column chromatography (silica / hexane / ethyl acetate (4:1)) to give a white powder (2.2 g). Recrystallization from hexane gave white opaque crystals of the C_2-symmetric diol (1.77 g, 63.3 %) ; m.p. 94 °C); ν_{max} 3393, 2910, and 1731 cm^{-1}; ^1H NMR 6.8 (1H, s), 5.5 (1H, dt), 4.0 (2H, m,), 3.8 (2 H, m,), 3.2 (4H,m), 3.1 (2H,br s), 2.95 (2H, m), 2.5 (2H, m), 1.79 (6H, s), 1.5 (2H, d), and 0.95 (6H, s); ^{13}C NMR 141.5 (1C), 141 (1C), 132.5 (1C), 132. (1C), 131.2 (1C), 130.9 (1C), 127.9 (2 C), 71.5 (1C), 71 (1C), 66.1 (1C), 66 (1C),43.5 (1C),43 (1C), 40 (2C), 38.5 (1C), 38 (1C) 34.9 (2C), 31.75 (1C), 31.7 (1C), 26.2 (2C),

and 21.5 (2C) ; m/z 327 (M^+ + 1 (2 %), 326 (M^+ 5), 309 (65), 295 (87), 291 (100), 265 (88), and 265 (88). HRMS calculated for $C_{22}H_{30}O_2$ (M^+) 326.2246, found 326.2243. The C_2-symmetric diol (1.12 g, 3.4 mmol) was dissolved in absolute ethanol (25 mL), and distilled water (16 mL). A solution of $NaIO_4$ (0.77 g, 3.6 mmoles) in water (6 mL) was then added slowly. After 30 minutes the reaction was complete, as judged by TLC, and the product was extracted into ethyl acetate (20 mL). The organic layer was then separated, dried over $MgSO_4$ and filtered. Removal of the solvent under reduced pressure gave a white powder (0.98 g). The product was purified by column chromatography (silica / hexane), and recrystallized from pentane, giving transparent needles (0.88 g, 87 %); m.p. 113 ^oC; $(\alpha)_D$ = - 11.4, (C 2.0,CH_2Cl_2);ν_{max} 1681 cm^{-1}; ^1H NMR10.4 (1H, s), 7.0 (1H, s), 3.55 (2H, t), 2.9 (4H, m,), 2.6 (2 H,dt,), 2.25 (2H,m), 1.4 (6H, s), 1.2 (2H, d), and 0.65 (6H, s); ^{13}C NMR194.5 (1C), 145.5 (1C), 133 (2C), 132.7. (2C), 130.5 (1C), 42 (2C), 39.9 (2 C), 38.5 (2C), 33.5 (2C), 31.5 (2C), 26.3 (2C), and 21.5 (2C) ; m/z 295 (M^+ + 1 (100 %), 294 (M^+ 20), 293 (16), 279 (9), and 267 (11); HRMS calculated for $C_{21}H_{26}O$ (M^++) 295.2061, found 295.2056.

Enantiomeric purity of aldehydes 8 and 9 The enantiopurity of **8** was determined by the addition of small aliquots of tris[3–(heptafluoropropylhydroxy-methylene)-(+)-camphorato], europium (III) derivative (5 mg) to the $CDCl_3$ ^1H NMR solution. The ^1H NMR of this solution was then recorded and addition of the chiral shift reagent was continued until the singlet at δ10.6 had split into two well-resolved peaks (ratio 7:1) for the crude material. A similar experiment was performed with the crystals of **8**, and no splitting of the aldehyde peak was observed. Furthermore, X-ray diffraction analysis of a crystal of **8** was consistent with a C_2-symmetric aromatic aldehyde. Therefore, we are confident that the crystalline form of aldehyde **8** is of high enantiomeric purity. 1R-(+)-Nopinone ($[\alpha]^{25}_D$ = + 16 (neat)) obtained from the Aldrich chemical company was used to prepare **8;** the 1 R-(+)-nopinone ($[\alpha]^{25}_D$ = + 17 (neat)) used to prepare aldehyde **9** was obtained from β-pinene ($[\alpha]^{20}_D$ = -21 (neat, 92.1 % ee))[39] and should therefore be of higher enantiomeric purity than **8**. Indeed, chiral shift experiments on this aldehyde failed to split the carbonyl proton. X-ray diffraction analysis of the crystalline styrene **11** and aldehyde **9** showed these materials to be C_2-symmetric.

D_4-symmetric porphyrin **6**. Under an inert atmosphere the aldehyde **8** (0.3 g, 9.7 mmole) was dissolved in CH_2Cl_2 (50 mL (distilled from CaH_2)). The reaction vessel was wrapped with aluminium foil and freshly distilled pyrrole (0.063 g , 0.0631 mL, 0.1 mmoles) was added. Anhydrous ethanol ((freshly distilled from Mg / I_2) 0.375 mL) was then added (0.75 % vol / vol). Boron triflouride etherate (0.047 g, 0.04 mL, 0.33 mmole) in CH_2Cl_2 (2 mL) was then added to the above mixture over 10 minutes It is important to use BF_3-OEt_2 from a fresh, unopened bottle. Formation of the porphyrinogen was followed by visible spectroscopy. An aliquot (0.05 mL) was added to *p*-chloranil (3 mL of a 0.04 M solution in toluene) and heated gently for 1 minutes 0.05 mL of this solution was added to 3 mL of ethanol / CH_2Cl_2 (1:1) and the intensity of the Soret band measured. The intensity of the Soret band peaked at 3 h. At this point *p*- chloranil (0.177 g, 0.72 mmole) was added and the resultant mixture was allowed to reflux for 1 h, then a further aliquot of oxidant (0.067 g, 0.27

mmole) was added. Triethylamine (0.051 g, 0.071 mL, 0.5 mmoles) was added followed by Florosil ® 100-200 mesh (1 g) . The solvent was then removed under reduced pressure, resulting in adsorption of the product onto Florosil ®. This powder was packed into a column and eluted with hexane. The leading fractions yielded the porphyrin as a purple glass-like material (0.05 g, 14.7 % yield). ν_{max} 3167 and 2944 cm^{-1} ; ^1H NMR 8.6 (8H, s, pyrrole H), 3.39 (8H, m), 3.0 (8H, t), 2.85 (8H, m), 2.49 (16H, m,), 2.39 (12H, s, Ar-CH_3), 1.2 (8H,d), 0.9 (24H, s), 0.6 (24H,s) and -2.59 (2H, br. s, N-H)); (FAB / CI) m/z 1424 (M^+ + 1 (1%)), 1423 (M^+ 0.75)), 1160 (3), 1133 (4), 359 (45), 269 (50), 239 (100), and 183 (40); Visible spectrum 402.1 (sh.), λ_{max} 417.6, 514, 545, 591.5, and 649.1 nm. HRMS calculated. for $C_{104}H_{188}N_4$ (FAB M^+) 1422.9357, found 1422.9332

D_4-symmetric Porphyrin **7**. This porphyrin was prepared in an almost identical procedure to **6**. The weights and volumes of materials used were; aldehyde **9** (0.54 g, 1.85 mmole), CH_2Cl_2 (123 mL), pyrrole (0.149 g , 0.155 mL, 2.22 mmoles, 1.2 mol. eq.), anhydrous ethanol (0.5 mL), boron triflouride etherate (0.088 g, 0.076 mL, 0.62 mmole) which was dissolved in CH_2Cl_2 (2 mL). This reaction was allowed to proceed for 4 h. At this point *p*-chloranil (0.454 g, 1.85 mmole) was added and the resultant mixture was allowed to stir in an oil bath at 60°C for 1 h. A further aliquot of oxidant (0.114 g, 0.46 mmole). The heat source was turned off after 2 h and the solution was left to stir for 12 h. The reaction was worked up as described above, except that pentane was employed to elute the porphyrin from the column. The foremost fractions yielded the porphyrin as a purple glass-like powder (0.06 g, 9.7 % yield) ν_{max} 3314, and 2907 cm^{-1} ; ^1H NMR 8.5 (8H, s, Pyrrole H), 7.35 (4H, s, Ar-H) 3.3 (16H, m), 2.2 (16H, t), 1.9 (8H, t), 1.5 (8H, t), 0.95 (24H, s), 0.65 (24H,s) and -2.59 (2H, br. s, N-H)); (FAB / CI) m/z 1368 (M^+ + 1 , 17%), 1367 (M^+ , 28), 1366 (33), and 1365 (17); Visible spectrum 402.1 (sh.), λ_{max} 424, 520, 554, 614, and 666 nm. HRMS calculated for $C_{100}H_{110}N_4$ (FAB M^+) 1366.8731, found 1366.8742..

Metallation of the D_4-symmetric porphyrin **6**. Under an inert atmosphere the porphyrin **6** (0.05 g, 0.037 mmole) was dissolved in benzene (5 mL (distilled over CaH_2)) / THF (5 mL) and to this mixture 2,6-lutidine (0.138 g, 0.15 mL, 1.29 mmole) was added. Anhydrous $MnBr_2$ (0.117 g, 0.19 mmole) was subsequently added, and the solution was heated to reflux for 90 minutes The solvent was then removed under reduced pressure and the residue washed with 4% HCl (25 mL) for 10 minutes The resultant chloromanganese (III) porphyrin was then extracted into CH_2Cl_2 (50 mL), the organic layer dried over Na_2SO_4, filtered and the solvent removed by rotary evaporation to give a green solid. The desired material was then purified by column chromatography (silica / CH_2Cl_2 / MeOH (50/50)) to give a dark green material (0.044 g, 80%) ν_{max} 3420, and 2925 cm^{-1} ; λ_{max} 479 nm (log ε 4.56).; (FAB / CI) m/z 1478 (m^+ - Cl +1 (46%)), 1477 (m^+ - Cl (100)), 1476 (95%),.and 1475 (57%).HRMS calculated for $C_{104}H_{116}N_4Mn$ (FAB M^+) 1475.8580, found 1475.8560.

Metallation of the D_4-symmetric porphyrin **7**. The same procedure as that described for metallation of **6** was employed. (22.9 mg, 69%); (M^++1 found 1419.804. $C_{100}H_{108}N_4Mn$ requires 1419.808); ν_{max} 3354, and 2907 cm^{-1} ; λ_{max} 482 nm (log ε 4.75); (FAB / CI) m/z 1419 (m^+ - Cl (100%)); HRMS calculated for $C_{100}H_{108}N_4Mn$ (FAB M^+) 1419.8080, found 1419.8037.

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(*Received in USA* 2 *April* 1997; *accepted* 22 *April* 1997)