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Catalytic Asymmetric Epoxidation of Unfunctionalized Alkenes Using the First D_4-Symmetric Metallotetraphenylporphyrin

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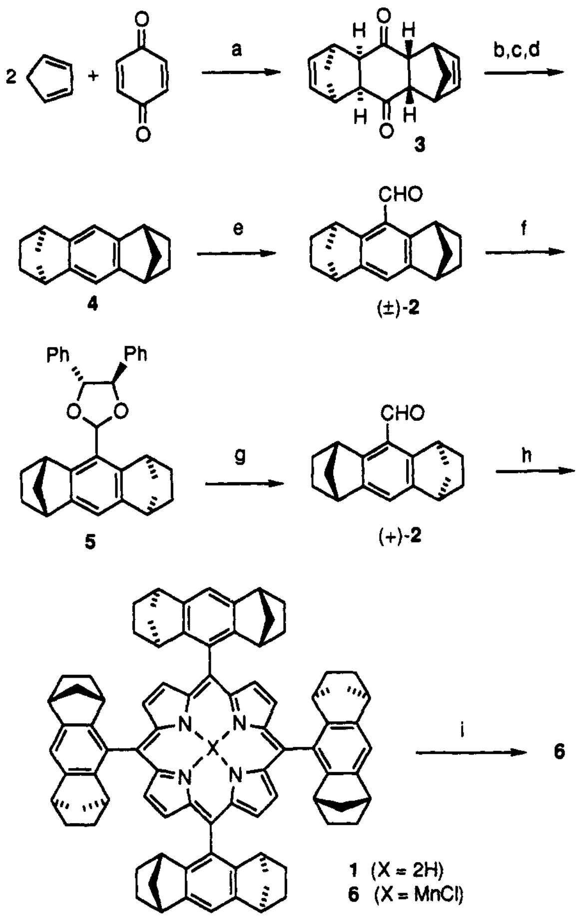
Summary: The condensation of the resolved C_2-symmetric benzaldehyde, 1,2,3,4,5,6,7,8-octahydro-1:4,5:8-dimethanoanthracene-9-carboxaldehyde, with pyrrole produced a new chiral tetraphenylporphyrin exhibiting D_4 symmetry. A manganese chloride complex of this porphyrin was used as a catalyst (0.5 mol %) for the asymmetric epoxidation of aromatic-substituted alkenes in the presence of excess sodium hypochlorite, providing for terminal or *Z* alkene yields above 90% and enantioselectivities ranging from 41 to 76% ee.

Catalytic asymmetric derivatization of alkenes bearing coordinating functional groups using transition metals bearing chiral ligands has developed remarkably over the past few years and includes highly stereoselective hydrogenation and epoxidation reactions.[1] The ability of chiral catalysts to achieve similar high stereoselectivity in the derivatization of alkenes not bearing coordinating functional groups is being actively developed.[2] We believe a key to achieving high stereoselectivity in additions to the more general class of unfunctionalized alkenes requires an efficient transfer of asymmetry from the catalyst to the substrate via nonbonded interactions and that this transfer of asymmetry is best achieved by holding sterically different portions of a rigid ligand above the reactive site of the metal. Due to their known ability to catalyze epoxidations of alkenes, asymmetrically modified tetraphenylporphyrin–metal complexes are being developed as catalysts for asymmetric epoxidations.[2d–f] We report here the efficient preparation of tetraphenylporphyrin **1** bearing chiral elements annulated onto the phenyl rings and exhibiting D_4 symmetry, and we describe the use of a manganese complex of **1** to catalyze the asymmetric epoxidation of aromatic alkenes in the presence of sodium hypochlorite.

The key feature in our preparation of chiral tetraphenylporphyrin **1** was the development of an efficient synthesis of the C_2-symmetric benzaldehyde **2**, which contains two norbornane groups fused to the central benzene ring (Scheme I). The requisite stereochemical relationship between the two norbornane moieties was established in an initial, well-established Diels–Alder reaction between benzoquinone and cyclopentadiene, producing isomerically pure diketone **3**.[3] Catalytic hydrogenation of **3** followed by reduction formed a diol that was dehydrated and oxidized to produce arene **4**.[4] No purification of the nearly quantitatively formed intermediates leading up to **4** was needed; arene **4** was readily purified by recrystallization (40% overall yield from benzoquinone). Friedel–Crafts formylation[5] of **4** produced the desired racemic C_2-symmetric benzaldehyde **2**, which was converted to a mixture of diastereomeric ketals[6] using readily available (*R*,*R*)-hydrobenzoin.[7] The less polar of the two diastereomers, compound **5**, was crystalline and could be readily obtained by recrystallization. The second diastereomeric ketal could be isolated from the mother liquor by column chromatography. On the basis of known configuration of the (*R*,*R*)-hydrobenzoin, the absolute stereochemistry of crystalline diastereomer **5** was established

Scheme I[a]



[a] Reagents and conditions: (a) benzene, 40 °C, 20 h, 100%; (b) 42 psi H_2, 5% Pd/C, EtOAc, 23 °C, 15 h, 99%; (c) $NaBH_4$, MeOH, 0–23 °C, 2 h, 95%; (d) 85% H_3PO_4 open to air, 110 °C, 14 h, 45% (recryst from 95% EtOH); (e) Cl_2CHOCH_3 (1.5 equiv), $TiCl_4$ (2.0 equiv), CH_2Cl_2, −15 °C, 2 h, 87%; (f) (*R*,*R*)-hydrobenzoin (1.2 equiv), PPTS (cat.), benzene, 80 °C, 12 h, 89% mixture of diastereomers; pure **5** 45%; (g) 1:4 3% H_2SO_4/THF, 65 °C, 2 h, 100%; (h) pyrrole (1.0 equiv), $BF_3{\cdot}Et_2O$ (0.3 equiv), $CHCl_3$ 23 °C, 1.5 h; *p*-Chloranil (0.75 equiv), 60 °C, 1 h, 29% **1** (alumina, 1:9 CH_2Cl_2/hexane); (i) $MnCl_2{\cdot}4H_2O$ (10 equiv), DMF, 152 °C, 6 h; 1 N HCl extraction, 82% **6** (alumina, 1:19 $MeOH/CH_2Cl_2$).

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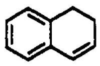
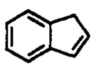
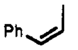
Table I. Asymmetric Epoxidation of Aromatic Alkenes[a]

entry	alkene	time,[b] h	yield,[c] %	ee,[d] %	abs[e] config
1		1	90	52	*S* (–)
2		1	97	56	1*R*,2*S* (+)
3		1	98	41	1*R*,2*S* (–)
4		4	91 (7, *E*)	76 (34, *E*)	1*R*,2*S* (–) (1*S*,2*S*)
5		8	40[f]	4	1*R*,2*R* (+)

[a] Reactions were run at 20 °C typically with 0.5 mmol of alkene, 2.5 mL of Clorox bleach, 2mL of CH_2Cl_2, 0.0025 mmol of **6**, 0.075 mmol of 4-*tert*-butylpyridine, 0.075 mmol of n-$C_{14}H_{29}(CH_3)_2(PhCH_2)NCl - 2H_2O$. [b] Time for complete consumption of alkene, except entry 5. [c] Isolated yield of epoxide after filtration through silica gel. [d] Determined by Chrompak cyclodextrin chiral capillary GC column and by ^1H NMR spectroscopy in the presence of Eu(hfc)$_3$. [e] Assigned by comparison of polarimetry measurements with literature (ref 2e, 12). [f] Percent conversion after 8 h.

by X-ray crystallography and is as shown in Scheme I. Removal of the ketal protecting group provided resolved aldehyde **2** in quantitative yield[8] and an 85% recovery of unisomerized (*R*,*R*)-hydrobenzoin. Condensation of benzaldehyde **2** with pyrrole according to Lindsey's procedure for the synthesis of hindered tetraphenylporphyrins[9] followed by oxidation afforded a 29% yield of the chiral tetraphenylporphyrin **1**, which exhibited D_4 symmetry in the ^1H NMR spectrum. Manganese was introduced by heating **1** with $MnCl_2{\cdot}4H_2O$ in DMF for 6 h, followed by treatment with HCl to provide a manganese–porphyrin complex **6**.[10]

Epoxidation reactions of several aromatic alkenes in the presence of commercial bleach, methylene chloride, a phase-transfer catalyst, and an axial amine ligand in the presence of 0.5 mol % of **6** were studied and the results are shown in Table I.[11] The enantioselectivities were determined either by resolution on a chiral gas chromatography column or by obtaining the ^1H NMR spectra in the presence of a chiral lanthanide shift reagent. The absolute configurations were assigned by polarimetry. In the cases where the alkene was terminal or cis-disubstituted the epoxidation was complete within 4 h, and following filtration of the crude reaction mixture through a plug of silica gel gave very high chemical yields of isolated epoxide with good enantioselectivity. Epoxidation of a trans alkene was markedly slower, not going to completion even after 8 h and gave much lower enantioselectivity. The epoxidation of styrene in the presence of 0.05 mol % of **6** was complete within 3 h with the identical chemical yield and enantioselectivity as the reaction using 0.5 mol % catalyst. The metalloporphyrin complex recovered from the reactions exhibited idential spectral characteristics as the original complex **6** and gave identical results when used in subsequent asymmetric epoxidation reactions.

The catalytic epoxidation results obtained with a manganese complex of the D_4-symmetrical porphyrin **1** are encouraging in that inexpensive commercial bleach can be used as the stoichiometric oxidant, very high (200–2000) rapid turnovers are possible, complete conversion of alkenes to epoxides are seen with most substrates, and the catalyst can be recycled.

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Supplementary Material Available: Experimental procedures, spectral data, and selected ^1H NMR and ^{13}C NMR spectra for compounds **4**, **5**, (+)-**2**, **1**, and **6** (13 pages). Ordering information is given on any current masthead page.

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Resonance Stabilization of Heteroallylic Radicals

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Summary: Estimates of the H–A BDEs in H—A—C═X, where A may be C, N, or O and X may be C, N, O, or S, support theoretical calculations suggesting that resonance energies in heteroallylic radicals decrease as the electronegativities of the terminal atoms increase.

In earlier papers we have found some remarkable differences in the homolytic bond dissociation energies (BDEs) of the H–A bonds in allylic heteroatom systems of the type H—A—C═X.[1-3] Thus, in the ketones, acetone and acetophenone, where C═X is a carbonyl group (H—C—C═O system), the H-C BDEs are lowered by 11-12 kcal/mol, relative to the H–CH_3 bond, presumably because of delocalization of the odd electron in the radical into the

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