

Catalytic asymmetric epoxidation with a chiral ruthenium porphyrin and *N*-oxides

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The enantiomerically pure ruthenium porphyrin **3** was synthesized in very high yield by refluxing the porphyrin **2** with $\text{Ru}_3(\text{CO})_{12}$ in phenol; its subsequent use in the catalytic asymmetric epoxidation of olefins with 2,6-dichloropyridine *N*-oxide as terminal oxidant, to afford epoxides in good yields and with enantioselectivities up to 77%, is reported.

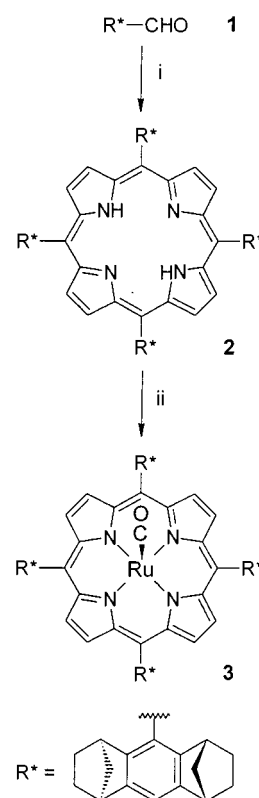
The development of an efficient catalytic process for the asymmetric oxygenation of hydrocarbons is still a challenging goal in organic chemistry.¹ Great progress has been made in the field of enantioselective epoxidation by the development of the Jacobsen catalyst.² Nevertheless, metalloporphyrins present the most promising class of catalysts due to their stability against oxidative degradation.³ A notable catalyst is the ruthenium porphyrin–2,6-dichloropyridine *N*-oxide system introduced by Hirobe *et al.* which shows very high turnover numbers for the catalytic oxygenation of alkanes and alkenes.⁴ As part of our work on transition metal catalyzed asymmetric epoxidations,⁵ we were interested in developing an efficient catalytic system for the enantioselective epoxidation of unfunctionalized olefins based on pyridine *N*-oxides as terminal oxidants. We chose the D_4 -symmetric porphyrin **2** as a chiral ligand. It can easily be prepared in high yields from the readily available enantiopure aldehyde precursor **1**.⁶ Here we describe the synthesis of the corresponding ruthenium carbonyl porphyrin **3**, using a modification of the acetylacetonate method⁷ with $\text{Ru}_3(\text{CO})_{12}$ as the metal source. Furthermore, we present the first results for the asymmetric epoxidation of unfunctionalized olefins using the complex **3** as catalyst.

The porphyrin ligand **2** was synthesized as described.⁶ The separation of the starting enantiomeric aldehydes **1** and *ent*-**1** was achieved by preparative HPLC of their respective diastereomeric acetals.⁶ The enantiomeric purity of the aldehyde **1** was >98% ee (HPLC). Unfortunately, our first attempts to prepare the ruthenium carbonyl complex **3** from porphyrin **2** using standard methods, *i.e.* refluxing the porphyrin **2** with $\text{Ru}_3(\text{CO})_{12}$ in an inert solvent (benzene, toluene, decalin or diethylene glycol dimethyl ether) failed, or gave only poor yields (<15%), of the desired metalloporphyrin. Finally, phenol turned out to be the solvent of choice: refluxing the porphyrin **2** with excess $\text{Ru}_3(\text{CO})_{12}$ gave the metallated porphyrin **3** (Scheme 1) within 30 min in high yields (up to 90% for *ent*-**2**).[†]

The catalytic epoxidations were run using the enantiomerically pure ruthenium carbonyl complex **3** in benzene at room temperature under argon. 2,6-Dichloropyridine *N*-oxide served

as the terminal oxidant. The ratio of substrate:oxidant:catalyst was 1000:1100:1.[‡] The reaction proceeded smoothly and almost complete conversion of the substrates was achieved within *ca.* 48 h (see Table 1). The chemical yields of the epoxides were quite high (up to 88%, Table 1, entry 3), and the enantiomeric excesses obtained for (1*R*,2*S*)-1,2-epoxy-1,2,3,4-tetrahydronaphthalene (Table 1, entry 2) and (*S*)-styrene oxide (Table 1, entry 10) were 77 and 70%, respectively. The latter value is the highest one obtained in the asymmetric epoxidation of styrene using a chiral porphyrin system.⁸ Interestingly, the enantioselectivities obtained by us with the ruthenium complex **3** were higher than those found by Halterman *et al.* for the corresponding manganese complex using hypochlorite as terminal oxidant.⁶ As expected, terminal olefins like oct-1-ene (Table 1, entry 12) showed only moderate reactivity and poor enantiomeric excesses. No stereoselectivity was observed for *trans*-disubstituted alkenes like (*E*)-stilbene (Table 1, entry 13) which reacted only sluggishly.

Running the reaction at higher temperatures (125 °C, Table 1, entry 3) resulted in a dramatic increase in the turnover frequency. Nearly full conversion was achieved within 2 h, albeit at somewhat lower enantioselectivities (55%). Variation of the solvent revealed that aromatic solvents gave the best results, a fact also observed by Gross *et al.*⁹ The use of other *N*-oxides like 2,6-dibromopyridine *N*-oxide or *N*-methylmorpholine *N*-

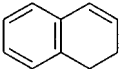
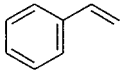
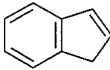

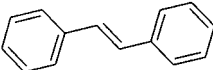


Scheme 1 Reagents and conditions: i, pyrrole, $\text{BF}_3 \cdot \text{Et}_2\text{O}$, CHCl_3 ; 29%; ii, $\text{Ru}_3(\text{CO})_{12}$, PhOH, 200 °C; 84%

[†] FAB-HRMS (NBA): found M^+ , 1270.5104. $\text{C}_{85}\text{H}_{76}\text{ON}_4$ ^{102}Ru requires M^+ , 1270.5063.

[‡] Typical epoxidation experiment: a Schlenk flask was charged under argon with a solution of **3** (0.4 mg, 315 nmol) in 1 ml benzene, and 1,2-dihydronaphthalene (40.0 μl , 315 μmol), 2,6-dichloropyridine *N*-oxide (55.4 mg, 347 μmol) and 1,2-dibromobenzene (internal standard) (37 μl , 315 μmol) were added. The reaction mixture was stirred at room temperature. Conversions, yields and ees were determined by capillary GC. The product epoxides can be isolated by removal of the solvent and subsequent silica gel chromatography, eluting with pentane–diethyl ether [40:1 (v/v)].

Table 1 Asymmetric epoxidation of prochiral olefins using **3** and 2,6-dichloropyridine *N*-oxide in benzene

Entry	Alkene	<i>t</i>	Conversion (%)	Yield (%) ^a	ee ^a
1		2 d	90	85	71
2		2 d ^b	90	85	77
3		2 h ^c	94	88	55
4		2 d ^d	80	65	72
5		2 d ^e	35	25	71
6		2 d ^f	9	4	71
7		2 d ^g	10	7	69
8		2 d ^h	80	65	64
9		2 d ⁱ	80	52	62
10		2 d	100	79	70
11		2 d	65	55	54
12		2 d	6 ^j	5	28
13		2 d	6	5	0

^a Determined by GC using a 2,6-di-*O*-methyl-3-*O*-pentyl- β -cyclodextrin column. ^b A substrate: catalyst ratio of 100:1 was used. ^c Reaction run at 125 °C in a sealed Schlenk tube. ^d Toluene was used as solvent. ^e 2,6-Dibromopyridine *N*-oxide was used as terminal oxidant. ^f *N*-Methylmorpholine *N*-oxide was used as terminal oxidant. ^g Methanol-ethyl acetate [2:1 (v/v)] was used as solvent. ^h Methylene chloride was used as solvent. ⁱ Ethyl acetate was used as solvent. ^j No further reaction was observed.

oxide resulted in slower conversion, but the high enantioselectivities remained unaffected (Table 1, entries 5 and 6). When iodosobenzene was used as terminal oxidant, the epoxide of 1,2-dihydronaphthalene was obtained in only moderate yields and with enantioselectivities up to 52%. Other oxidants, like

hydrogen peroxide, aqueous sodium hypochlorite or aqueous potassium caroate ('oxone') showed no reaction at all under our reaction conditions.

In conclusion, we report the first highly efficient catalytic system for the asymmetric epoxidation of unfunctionalized olefins using an enantiomerically pure ruthenium porphyrin and 2,6-dichloropyridine *N*-oxide. The mechanistic aspects of the oxygen transfer by the ruthenium porphyrin-2,6-dichloropyridine *N*-oxide system are currently under investigation

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