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HIGHLY EFFICIENT EPOXIDATION OF OLEFINS WITH PYRIDINE N-OXIDES CATALYZED BY RUTHENIUM PORPHYRINS

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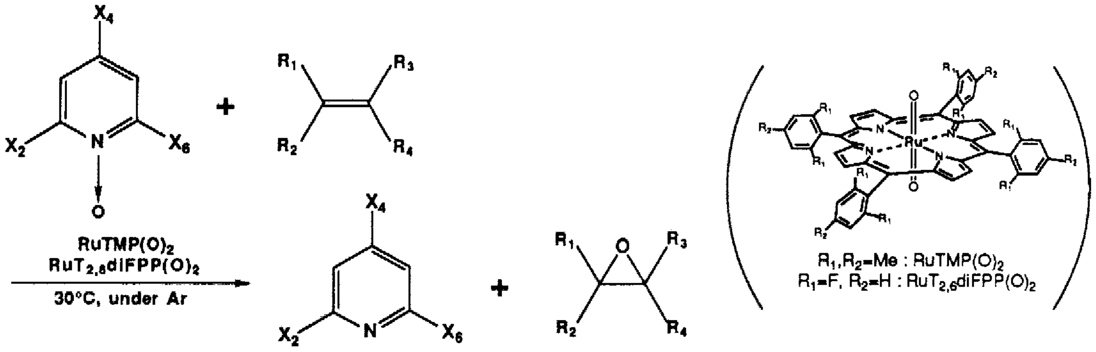
SUMMARY Oxygen transfer reactions from 2,6-disubstituted pyridine N-oxides to olefins were efficiently catalyzed by ruthenium porphyrins under mild conditions, and various olefins were converted into their epoxides in high yield.

The reaction of cytochrome P-450 has aroused wide interest because of its unique reactivity for the oxidation of various compounds. The shunt-pass reaction, in particular, has been studied using model compounds to try to elucidate the reaction mechanism of the enzyme and to explore synthetic applications. In this type of reaction, oxidants such as peroxides, iodosylbenzene, OCl^- or aliphatic amine oxides are used to directly produce metal-oxo porphyrin complexes1). However these oxidants themselves have moderate reactivity toward various substrates or are instabile and may cause side reactions or lowering of the selectivity in catalytic oxidations. In contrast, heteroaromatic N-oxides, represented by pyridine N-oxide, while highly stable, have not been reported yet as oxidants which can convert metalloporphyrins to high valent metalloxenoids followed



Table

Entry	Catalyst	Olefin	Substituents on Pyridine Ring	Yield[d] Epoxide[e]	Pyridine[f]
1	$RuTMP(O)_2$	styrene	none	trace	n.d.[g]
2			2-monoMe	26%	n.d.
3			2-monoCl	94%	100%
4			2,6-diMe	95%	n.d.
5			2,4,6-triMe	93%	95%
6			2,6-diBr	98%	100%
7			2,6-diCl	100%	95%
8		*p*-chlorostyrene	2,6-diMe	99%[i]	88%[i]
9[a]			2,4,6-triMe	99%[i]	n.d.
10		*p*-phenylstyrene	2,4,6-triMe	87%[i]	n.d.
11[a]		*cis*-stilbene	2,4,6-triMe	98%[i,j]	n.d.
12		*trans*-stilbene	2,6-diCl	7%[k]	n.d.
13[b]		*l*-carvone	2,6-diCl	70%[i,l]	n.d.
14[c]	$RuT_{2,6}diFPP(O)_2$	styrene	none	trace	n.d.
15[c]			2-monoCl	84%	100%
16[c]			2,4,6-triMe	14%	27%
17[c]			2,6-diBr	100%	100%
18[c]			2,6-diCl	94%	97%
19	RuTMP(CO)	styrene	2,6-diCl	99%	93%
20[c]	$RuT_{2,6}diFPP(CO)$			72%	80%
21	RuTPP(CO)			26%	55%
22	$Ru(PPh_3)_3Cl_2$			0%	0%
23	$Ru(PPh_3)_4Cl_2$			0%	0%
24	FeTMPCl			0%	0%
25	MnTPPCl			0%	0%
26[c]	$MnT_{2,6}diFPPCl$			0%	0%
27	CoTPP			0%	0%
28	MoTMP(O)(OH)			0%	0%

These reactions were carried out in benzene at 30°C under Ar ([olefin]=170mM, [pyridine N-oxide]=180mM, [catalyst]=1mM). a) [catalyst]=0.5mM b) [catalyst]=2mM c) Carried out in dichloromethane. d) Detected by G.L.C. e) Based on olefins. f) Based on pyridine N-oxides. g) Not determined. h) Overnight i) Isolated yield. j) *cis*-Epoxide. k) *trans*-Epoxide l) Only the terminal olefin was epoxidized.

by oxygenation of substrates such as olefins[2),3)]. Here we report that pyridine N-oxide derivatives epoxidize olefins in the presense of catalytic amounts of ruthenium porphyrins with high efficiency and selectivity under mild conditions.

2,6-Disubstituted pyridine N-oxide together with dioxo(tetramesitylporphyrinato)-ruthenium(VI) [RuTMP(O)$_2$][4)] are the reagents of choice for epoxidation. In this system, Ru porphyrins work very efficiently as catalysts for a turnover reaching 9000.

p-Chlorostyrene oxide can be prepared by a typical procedure. A solution of *p*-chlorostyrene (0.14 g, 1.0 mmol), 2,6-lutidine N-oxide[5)] (0.14 g, 1.1 mmol) and RuTMP(O)$_2$ (5 mg, 6 μmol) in benzene (6 ml) is stirred at 30°C under Ar for 6 hr. The reaction mixture is chromatographed on silica gel to afford *p*-chlorostyrene oxide (0.15 g, 99%) (entry 8).

This epoxidation reaction was conducted under a wide variety of conditions, as summarized in the Table. The difference of oxygen transfer reactivity among various pyridine N-oxide derivatives indicated that substituents at the 2 and 6 positions on the pyridine rings were necessary for the high activity. 2-Mono-substituted pyridine N-oxides had lower efficiency than that of the 2,6-disubstituted types on comparison of the rate of epoxidation, and simple pyridine N-oxide had almost no activity (entries 1~7,14~18). This difference in reactivity may arise because in the case of simple pyridine N-oxide, pyridine formed by the oxygen transfer reaction coordinates strongly with ruthenium atom, causing pyridine to inhibit the catalytic activity of Ru porphyrin, but not 2,6-disubstituted pyridines. 2,6-Disubstituted pyridine N-oxides had to be purified by passing them through an alumina column before use in this reaction[5)].

Chloro-substituted pyridine N-oxides proved to be more effective than the methyl-substituted ones. For example, when collidine N-oxide was used as the oxidant, it took 6 hours to complete the reaction, while in the case of 2,6-dichloropyridine N-oxide, it took only 2 hour.

To investigate the reactivity of other metal complexes in this system, the abilities of various metal complexes to catalyze the oxidation of styrene by 2,6-dichloropyridine N-oxide were examined. Only Ru porphyrin complexes showed catalytic activity (entries 19~28). No oxidation products were detected using Ru(PPh$_3$)$_n$ or porphyrin complexes containing other metals. As shown in the Table, a good yield was obtained using the Ru(II)TMP complex coordinated with CO (entry 19). However the rate of oxidation was slower than when RuTMP(O)$_2$ was used (entry 7).

Epoxidation of *p*-phenylstyrene was accompanied by the formation of *p*-phenylphenylacetaldehyde (y.< 5%) (entry 10). However, no aldehyde was detected in the oxidation of olefins tested other than *p*-phenylstyrene.

cis-Stilbene was epoxidized with this system to quantitatively afford the cis-epoxide, while epoxidation of *trans*-stilbene did not proceed efficiently (y. 7%) (entry 11,12). This difference in reactivity and the stereoselectivity of the epoxidation resemble those of the iron(IV) porphyrin oxenoid π cation radical[6]. Therefore these results suggest that the reactive intermediate of "Ru porphyrin - 2,6-disubstituted pyridine N-oxides system" is a metal-oxo complex.

Only a terminal olefin of *l*-carvone was epoxidized and the *α,β*-unsaturated ketone group was unaffected under the conditions of entry 13.

2,6-Disubstituted pyridine N-oxides[7] are readily available, and safe to handle, and the pyridines formed can be easily removed. Ruthenium porphyrins can be prepared easily, can be stored for months with almost no decomposition, and are only needed in small amounts. The present reagent system offers the advantages of high chemo-selectivity, mild conditions and simple handling procedures. Our system is thought to be the most efficient one among the epoxidation systems reported using Ru porphyrins[8],[9].

A plausible explanation for the mechanism of our system is as follows : $Ru(VI)TMP(O)_2$ epoxidizes olefin to afford Ru(IV)TMP(O), and the Ru(II)TMP, which is formed by disproportionation of Ru(IV)TMP(O) as postulated by Groves et al. in their aerobic epoxidation[9], is oxygenated by pyridine N-oxides to be converted to Ru(IV)TMP(O), followed by reformation of $Ru(VI)TMP(O)_2$. Further investigation on the mechanistic details is in progress in our laboratory.

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References and Notes

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5) 2,6-Lutidine N-oxide, which was purchased from Wako Co., Ltd., almost did not work in the system when it was used without purification or after simple distillation. In contrast, epoxidation proceeded smoothly using the N-oxide which had been passed through alumina column. Perhaps a small amount of acid in the N-oxide inhibits the catalytic reaction.
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