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High conversion of olefins to *cis*-diols by non-heme iron catalysts and H_2O_2

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Efficient and highly stereoselective oxidation of olefins to *cis*-diols as the major product is obtained by using biomimetic non-heme Fe^{II} catalysts in combination with H_2O_2.

Current methodologies for catalytic *cis*-dihydroxylation of olefins in organic synthesis center on osmium compounds.[1–9] However the cost and toxicity of the Os catalyst provide a good rationale for the development of more economical and environmentally benign alternatives. Enantioselective *cis*-dihydroxylation of arene and alkene double bonds is catalyzed by Rieske dioxygenases,[10–15] bacterial enzymes which utilize a mononuclear non-heme iron active site.[16] We have thus initiated an effort to identify iron complexes capable of catalysing such transformations and have in fact reported the first iron catalysts for olefin *cis*-dihydroxylation.[17–20] These catalysts are complexes of tetradentate N4 ligands such as TPA [tris(2-pyridylmethyl)amine] and BPMEN [*N,N'*-bis(2-pyridylmethyl)-1,2-diaminoethane](Fig. 1). The conditions used for these reactions afforded a high conversion of H_2O_2 oxidant into oxidation products (up to 85%) but required the use of excess substrate (catalyst : substrate : H_2O_2 = 1 : 1000 : 10), making this method impractical for synthetic applications. In this report, we have extended the chemistry developed for *cis*-dihydroxylation in a more practical direction and demonstrate high conversion of olefins to *cis*-diols under conditions of limiting substrate.

White *et al.* recently reported that $[Fe^{II}(BPMEN)(CH_3CN)_2](SbF_6)_2$ is a catalyst capable of high conversion of olefins to epoxides under conditions of excess H_2O_2 (catalyst : substrate : H_2O_2 = 1:33:66), affording epoxide in ~ 70% yield.[21] Applying similar conditions, we have found that $[Fe^{II}(5\text{-}Me_3\text{-}TPA)(CH_3CN)_2](ClO_4)_2$ (**1**) is also an effective catalyst for olefin oxidation. Table 1 shows that treatment of olefins with a threefold excess of H_2O_2 in the presence of 3 mol% catalyst at 4 °C afforded oxidation products in yields of 73–87%. In contrast to $[Fe^{II}(BPMEN)(CH_3CN)_2](SbF_6)_2$, where the oxidation product was essentially the epoxide, both epoxidation and *cis*-dihydroxylation products were observed for the reaction catalysed by **1**. In fact, the *cis*-diol product was the predominant product in all cases with a diol : epoxide ratio of 3–4, a value up to twofold larger than that observed for corresponding reactions under conditions of limiting H_2O_2 (Table 1). Terminal olefins and disubstituted olefins were all converted in good yield, while cyclohexene was oxidised with only trace amounts of allylic oxidation. Furthermore catalytic oxidation by **1** under the conditions used in this study was also highly stereoselective. For example, the oxidation of *trans*-hept-2-ene to the diol and epoxide products occurred essentially with retention of configuration, while the oxidation of *cis*-hept-2-ene exhibited very high %RC values (RC = (*cis* − *trans*)/(*cis* + *trans*) × 100, see Table 1). These results emphasize the notion that **1**–H_2O_2 generates quite a stereoselective oxidant under these conditions.

We then surveyed our family of TPA catalysts to determine if they are also effective catalysts for oct-1-ene oxidation under these conditions of limiting substrate (Table 2). One group of catalysts consisting of complexes of TPA, 3-Me_3-TPA, and 5-Me_3-TPA were effective catalysts for the oxidation of olefin to epoxide and *cis*-diol products with yields of 69–87%, conversion efficiencies comparable to those obtained under conditions of limiting H_2O_2. All three catalysts also afforded diol : epoxide ratios of 3.3, much higher than those observed under conditions of limiting H_2O_2. The complexes in this subclass all lack 6-methyl substituents and give rise to low-spin Fe^{III}-OOH intermediates.[22–24]

On the other hand, complexes with two or three 6-methyl substituents, *i.e.* 6-Me_2-BPMEN, 6-Me_2-TPA and 6-Me_3-TPA,

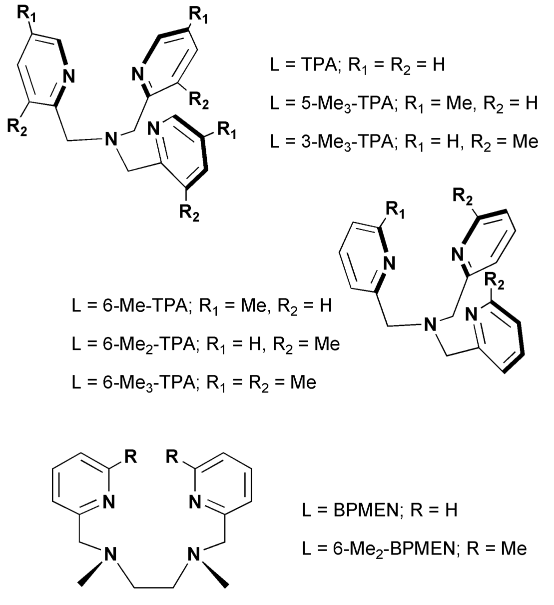

Fig. 1 Structures of the ligands used in this work.

Table 1 Oxidation of various olefins with **1**[a]

Substrate	% Diol[b]	% Epoxide[b]	Diol/ epoxide[c]
Oct-1-ene	67%	20%	3.3 (2.4)
Dec-1-ene	62%	18%	3.4
Vinylcyclohexane	57%	16%	3.5 (2)
Cyclohexene	45%	30%	1.5
cis-Hept-2-ene	60% (RC = 97%)	20% (RC = 92%)	3.0 (1.4)
trans-Hept-2-ene	61% (RC > 99%)	14% (RC > 99%)	4.3 (2.2)

[a] H_2O_2 (0.48 mmol) diluted in CH_3CN (1.2 mL) was added *via* syringe pump over 30 min to a CH_3CN solution (0.45 mL) containing the iron catalyst (3.5 μmol) and the olefin (0.12 mmol) at 4 °C. Final catalyst : substrate : H_2O_2 ratio = 1 : 34 : 137. [b] % Conversion of substrate into product determined by GC analysis. [c] Values in parentheses reflect diol : epoxide ratios obtained under conditions of limiting H_2O_2 as reported in ref. 19.

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Table 2 Oxidation of oct-1-ene with different iron catalysts[a]

Catalyst	Diol yield (%)	Epoxide yield (%)
$[Fe(L)(CH_3CN)_2]^{2+}$		
L = 5-Me_3-TPA	67	20
L = 3-Me_3-TPA	62	19
L = TPA	53	16
L = 6-Me-TPA	32	6
L = 6-Me_2-TPA	3	1
L = 6-Me_3-TPA	5	1
L = BPMEN[b]	3	73
L = 6-Me_2-BPMEN[b]	1	1
$[Fe_2(\mu\text{-}O)(TPA)_2(H_2O)_2]^{4+}$	59	21
$[Fe_2(\mu\text{-}O)(L)_2(OAc)]^{3+}$		
L = 5-Me_3-TPA	0	1
L = TPA	0	2
L = BPMEN[b]	0	2

[a] Unless otherwise indicated, reaction conditions are the same as listed in footnote *a* of Table 1. [b] H_2O_2 (0.18 mmol) diluted in CH_3CN (0.3 mL) was added *via* syringe pump over 10 min to a CH_3CN solution (0.45 mL) containing the iron catalyst (3.5 μmol) and the olefin (0.12 mmol) at 4 °C. Final catalyst : substrate : H_2O_2 ratio = 1 : 34 : 51.

were essentially ineffective catalysts under conditions of limiting substrate. These observations are in contrast to those obtained under excess substrate, where conversion efficiencies were comparable to the complexes with no 6-methyl substituents.[19] Due to the steric effect of the 6-methyl group, these complexes are expected to give rise to high-spin Fe^{III}-OOH intermediates.[24] The 6-Me-TPA complex was found to exhibit a catalytic efficiency intermediate between those of the TPA and the 6-Me_2-TPA or 6-Me_3-TPA complexes. This behaviour can be rationalised by the expectation that the 6-Me-TPA complex would give rise to both low-spin and high-spin Fe^{III}-OOH species.[24]

We also tested whether the (μ-oxo)diiron(III) complexes were effective catalysts under these conditions (Table 2). The only effective dinuclear catalyst found in our survey was $[Fe_2(\mu\text{-}O)(TPA)_2(H_2O)_2]^{4+}$; this complex with readily displaceable aqua ligands showed a catalytic activity comparable to that of its mononuclear counterpart under conditions of limiting substrate as well as under conditions of excess substrate as reported earlier.[19,25] On the other hand, isolated (μ-oxo)diiron(III) complexes supported by an additional carboxylate bridge, such as $[Fe_2(\mu\text{-}O)(L)_2(\mu\text{-}OAc)]X_3$ (L = TPA, 5-Me_3-TPA, BPMEN), were essentially ineffective at olefin oxidation, affording at best 1–2% yield of epoxide from olefin and no *cis*-diol. This lack of catalytic activity of the (μ-oxo)(μ-carboxylato)diiron(III) complexes is in disagreement with the observations of White *et al.*,[21] but is precedented in our previously reported studies of hydrocarbon oxidation,[19,25,26] where we demonstrated a requirement for two *cis* labile sites. The two labile sites are needed for peroxide binding and its subsequent activation. We thus attribute the lack of catalytic activity of the (μ-oxo)(μ-carboxylato)diiron(III) complexes to the presence of the carboxylate bridge, which hinders the facile coordination of the added H_2O_2 to the metal centers and instead promotes H_2O_2 disproportionation.

In summary, we have demonstrated that Fe(TPA) complexes can catalyse the oxidation of olefins to *cis*-diols under conditions of limiting substrate with high conversion efficiency. Although some epoxide is also generated, these complexes represent the first examples of iron catalysts capable of olefin *cis*-dihydroxylation. These results open the possibility of developing more environmentally benign metal catalysts to replace the traditional toxic and more expensive osmium reagents. Further efforts are in progress to tune the iron ligand environment to afford *cis*-diol products even more selectively and with a high conversion.

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