Alkene Hydroxylation

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Highly Enantioselective Iron-Catalyzed *cis*-Dihydroxylation of Alkenes with Hydrogen Peroxide Oxidant via an Fe^{III}-OOH Reactive Intermediate

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Abstract: *The development of environmentally benign catalysts for highly enantioselective asymmetric cis-dihydroxylation (AD) of alkenes with broad substrate scope remains a challenge. By employing* $[Fe^{II}(L)(OTf)_2]$ *(L = N,N′-dimethyl-N,N′-bis(2-methyl-8-quinolyl)-cyclohexane-1,2-diamine) as a catalyst, cis-diols in up to 99.8 % ee with 85 % isolated yield have been achieved in AD of alkenes with* H_2O_2 *as an oxidant and alkenes in a limiting amount. This "*$[Fe^{II}(L)(OTf)_2] + H_2O_2$*" method is applicable to both (E)-alkenes and terminal alkenes (24 examples > 80 % ee, up to 1 g scale). Mechanistic studies, including* ^{18}O*-labeling, UV/Vis, EPR, ESI-MS analyses, and DFT calculations lend evidence for the involvement of chiral* Fe^{III}*-OOH active species in enantioselective formation of the two C−O bonds.*

Asymmetric *cis*-dihydroxylation (AD) of alkenes, usually using osmium reagents, is an important reaction in organic synthesis.[1] To date, metal-free reagents for alkene *cis*-dihydroxylation remain underdeveloped;[2] examples include cyclic peroxide anhydrides,[3a] or chiral hypervalent iodine(III).[3b] On the other hand, notable progress has been achieved for alkene *cis*-dihydroxylation with non-osmium metal compounds,[1d,4] including that of ruthenium,[4b,5] manganese,[4d,6,7] and iron.[4a,c,d,8] However, there are only a few examples of AD reactions catalyzed by complexes of the earth-abundant metals iron[9] and manganese.[10,11] An enantioselectivity of > 90 % *ee* was reported for α-$[Fe^{II}$(*R*,*R*-6-Me_2-BPBP)$(OTf)_2]$-catalyzed AD of electron-rich alkenes (*E*)-2-octene and (*E*)-2-heptene (96–97 % *ee*); the method, which was developed by Que and co-workers, employed H_2O_2 as a terminal oxidant and alkenes in a 50-fold excess.[9b] $[Mn^{II}$(*S*,*S*-BQCN)$Cl_2]$-catalyzed AD of electron-deficient (*E*)-alkenes with Oxone (five examples, 93–96 % *ee*) have been reported in our previous work.[11] It has been proposed that non-heme iron-catalyzed alkene *cis*-dihydroxylation reactions proceed via intermediate $Fe^{III}(OOH)$,[12] $Fe^{V}(O)(OH)$,[12,13] $Fe^{IV}(OH)_2$,[14] or $Fe^{II}(OOH)$[15] as active oxidant, depending on the ligand systems employed. Herein, we describe the realization of iron-catalyzed AD reactions with a reasonably broad substrate scope and with alkene substrates used in a limiting amount,[8b,c] yielding *cis*-diols in up to 99.8 % *ee* (85 % isolated yield) when H_2O_2 is used as a terminal oxidant. An enantioselectivity of > 95 % *ee* was achieved for 14 examples spanning both electron-deficient and electron-rich (*E*)-alkenes. A chiral $Fe^{III}(OOH)$ reactive intermediate is suggested to be responsible for the highly enantioselective AD reactions.

The tetradentate N_4 ligands L2, L4, and L6 (featuring different chiral diamine backbones compared to that of *R*,*R*-BQCN (L1)),[16] along with L1 derivatives L3, L5, L7, and L8, were synthesized according to a reported method (see Figure 1 and the Supporting Information). Treatment of these ligands with $[Fe(OTf)_2{\cdot}(MeCN)_2]$ in THF afforded $[Fe^{II}(L)(OTf)_2]$ (L = L1–L8) in 37–87 % yields. Layering of hexane on top of CH_2Cl_2 solutions of the complexes gave X-ray diffraction quality crystals of $[Fe^{II}(L2)(OTf)_2]$, $[Fe^{II}(L3)(H_2O)_2](OTf)_2$ (coordinated H_2O is presumably derived from trace moisture in the solvent), and $[Fe^{II}$(L8)-$(OTf)_2]$; the complexes in the crystals (Figure 2) all adopt a *cis*-α configuration. ^{1}H NMR analysis revealed *cis*-α configuration of $[Fe^{II}(L3)(OTf)_2]$ in MeCN solution (no conversion to *cis*-β isomer was observed after 24 hours at 27 °C), in

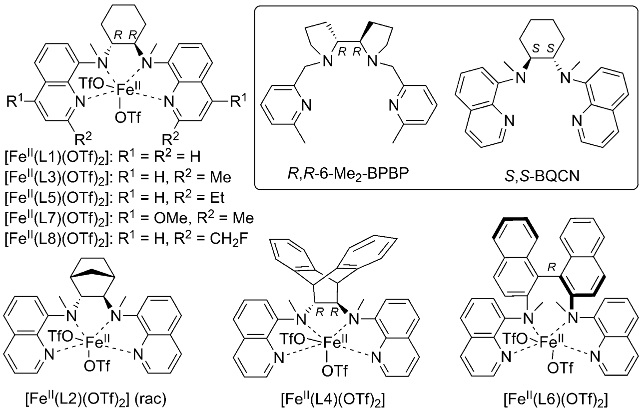

Figure 1. Chiral iron(II) catalysts described herein. Inset: examples of reported chiral ligands.

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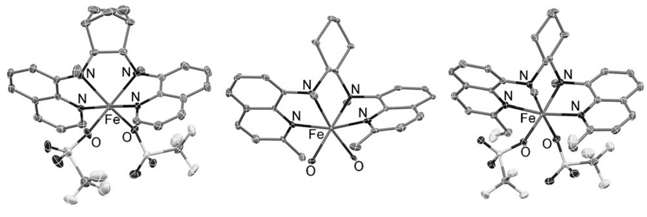
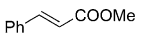
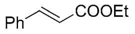
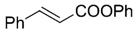
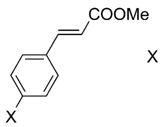
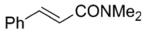
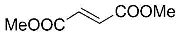
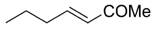
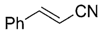
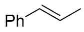
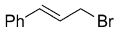
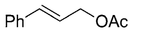
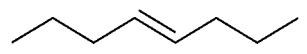
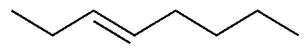
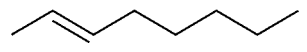


Figure 2. X-ray crystal structures of $[Fe^{II}(L2)(OTf)_2]$, $[Fe^{II}(L3)(H_2O)_2](OTf)_2$ (triflate counteranions not shown), and $[Fe^{II}(L8)(OTf)_2]$. Hydrogen atoms are omitted; thermal ellipsoids are set at a 30% probability level.

Table 1: $[Fe^{II}(L3)(OTf)_2]$-catalyzed AD of (*E*)-alkenes with H_2O_2 as an oxidant.

Entry[a]	Alkene	Conv. [%][b]	*cis*-Diol [%][c,d]	*ee* [%]
1		94	100(85)	99.8
2[e]		92	99	98.1
3[f]		82	99	97.7
4[g]		40	95	99.0
5		97	98(74)	99.0
6		95	96(82)	96.7
7	 X = Me	91	98(89)	93.0
8	F	98	97	99.6
9	Cl	100	93(85)	96.1
10	Br	100	99	99.2
11	CF_3	100	98	98.5
12		77	99	98.4
13[h]		89	93	97.8
14		97	95	98.1
15		74	99	99.2
16		70	93	94.7
17		78	88	87.4
18		89	68	89.3
19		68	96	89.0
20		50	86	99.0
21		45	87	98.3
22		48	89	98.4

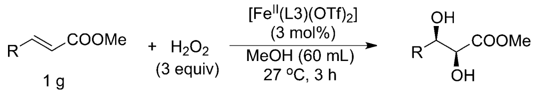
[a] Reaction conditions: alkenes (0.2 mmol), $[Fe^{II}(L3)(OTf)_2]$ (0.006 mmol, 3 mol%), H_2O_2 (0.6 mmol, 3.0 equiv), MeOH (2 mL), 27 °C, 1.5 h. [b] Determined by ^1H NMR or by GC. [c] Yields determined by ^1H NMR and based on conversions. [d] Isolated yields based on starting substrates were shown in brackets. [e] Open to air. [f] NaOTf (0.2 mmol) was added. [g] $[Fe^{II}(L8)(OTf)_2]$ was used. [h] $[Fe^{II}(L3)(OTf)_2]$ (5 mol%) was used.

contrast to the *cis*-β configuration of $[Fe^{II}(BQCN)(OTf)_2]$.[16a] In MeCN, $[Fe^{II}(L1)(OTf)_2]$ and $[Fe^{II}(L3)(OTf)_2]$ display reversible/quasi reversible couples at +0.82 and +0.85 V (vs. $Ag/AgNO_3$), respectively (Supporting Information, Figure S1), assignable to a Fe^{III}/Fe^{II} redox process.

Initially, $[Fe^{II}(L)(OTf)_2]$ (L = L1–L6) complexes were screened for *cis*-dihydroxylation of (*E*)-4-octene in MeCN with H_2O_2 as a terminal oxidant. The highest diol/epoxide ratios and *ee* values were achieved with $[Fe^{II}(L3)(OTf)_2]$ (72% *ee*) and $[Fe^{II}(L5)(OTf)_2]$ (98% *ee*; Supporting Information, Table S1). For AD of methyl (*E*)-cinnamate with H_2O_2 (3 equiv) in MeOH, $[Fe^{II}(L3)(OTf)_2]$ gave a better result than $[Fe^{II}(L1)(OTf)_2]$ and $[Fe^{II}(L5)(OTf)_2]$ (Supporting Information, Table S2). Changing the solvent to EtOH, MeCN, *tert*-butanol, and *tert*-amyl alcohol led to poor substrate conversions. The alkene substrate remained intact when urea–H_2O_2 was used as the oxidant, and a $<1\%$ *cis*-diol yield was obtained (though with 47% substrate conversion) using Oxone as the oxidant. Replacement of the methyl groups of $[Fe^{II}(L3)(OTf)_2]$ with CH_2F groups, to give $[Fe^{II}(L8)(OTf)_2]$, markedly lowered the catalytic activity but the enantioselectivity remained high (99.8 vs. 99.0% *ee*; compare entries 1 and 4, Table 1).

Using the “$[Fe^{II}(L3)(OTf)_2] + H_2O_2$” method with MeOH as a solvent, the AD of various (*E*)-alkenes with H_2O_2 (3 equiv) at 27 °C gave the *cis*-diols in up to 99.8% *ee* with 85% isolated yield (Table 1). Entry 3 in Table 1 shows that OTf^-, in an ca. 33 times excess relative to $[Fe^{II}(L3)(OTf)_2]$, has an insignificant effect on the enantioselectivity. Electron-deficient (*E*)-cinnamates bearing different ester groups or *para*-substituents resulted in 93.0–99.8% *ee* (entries 1–11, Table 1). Upon changing of the ester groups to amide, carbonyl, and cyano groups, the enantioselectivity was still high (94.7–99.2% *ee*; entries 12, 13, 15, 16; Table 1). For electron-rich (*E*)-alkenes, substituted 1-phenyl propenes led to 87.4–89.3% *ee* (entries 17–19, Table 1) whereas internal aliphatic alkenes gave 98.3–99.0% *ee* (entries 20–22, Table 1). Under similar conditions, with $[Fe^{II}(L3)(OTf)_2]$ (3.0 mg) at a catalyst/alkene/H_2O_2 ratio of 1:800:500 (H_2O_2 added with a syringe pump over 5 h), the AD of methyl (*E*)-cinnamate and (*E*)-methyl 3-(4-chlorophenyl)acrylate gave the *cis-diols* in 98.1 and 99.6% *ee* with turnover numbers (TON) of 150 and 200, respectively. These values are the highest TON for iron-catalyzed *cis*-dihydroxylation reported in the literature. Compared with $[Mn^{II}(S,S\text{-BQCN})Cl_2]$-catalyzed AD of similar substrates with Oxone,[11] better enantioselectivity, improved product yields, and broader substrate scope have been observed in this work, and the selectivity of *cis*-diols increased significantly (epoxide and C=C bond cleavage side products formed in $<1\%$ yield).

A gram-scale AD reaction using the “$[Fe^{II}(L3)(OTf)_2] + H_2O_2$” method has been achieved with methyl (*E*)-cinnamates and dimethyl fumarate as substrates. As depicted in Scheme 1, a one-pot AD reaction with 1 g of methyl (*E*)-cinnamate, (*E*)-methyl 3-(4-chlorophenyl)acrylate, or dimethyl fumarate, furnished the *cis*-diol product in up to 99.0% *ee* (87% isolated yield). The enantioselectivity was better than that reported for the $[Mn^{II}(S,S\text{-BQCN})Cl_2]$-catalyzed AD of methyl (*E*)-cinnamate with Oxone (92% *ee*).[11] Sharpless and co-workers reported similar AD reaction



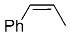
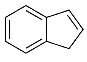
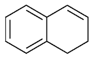
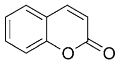
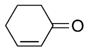
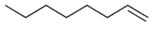
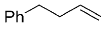
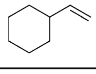
	conv. [%]	yield [%]	*ee* [%]
R = Ph:	68	65 (96[a])	95.9
R = *p*-ClC_6H_4:	92	87 (95[a])	99.0
R = COOMe:	100	95 (95[a])	97.2

Scheme 1. Gram-scale AD of methyl (*E*)-cinnamates and dimethyl fumarate with H_2O_2 (3 equiv) catalyzed by $[Fe^{II}(L3)(OTf)_2]$. [a] Yield based on conversion (%).

on a 1 mol scale affording the *cis*-diol, after recrystallization, in 99% *ee* and 72% yield.[17]

$[Fe^{II}(L3)(OTf)_2]$-catalyzed AD of (*Z*)-alkenes, (*Z*)-β-methyl styrene, indene, dihydronaphthalene, coumarin, and 2-cyclohexene-1-one, gave the corresponding *cis*-diols in 22.6–83.1% *ee* (entries 1–5, Table 2). For 1,2-dihydronaphthalene, the *cis*-diol was obtained in 83.1% *ee* with 53% yield. For terminal alkenes, *tert*-butyl acrylate gave the *cis*-diol in nearly quantitative yield with 92.3% *ee* (entry 6, Table 2); 1-octene, homoallyl benzene, and cyclohexyl ethylene afforded the *cis*-diols in 81.6–84.9% *ee* and with high selectivity (94–96%, entries 7–9, Table 2).

Table 2: $[Fe^{II}(L3)(OTf)_2]$-catalyzed AD of (*Z*)-alkenes and terminal alkenes with H_2O_2 as an oxidant.

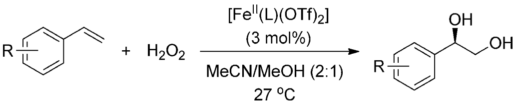
Entry[a]	Alkene	Conv. [%][b]	*cis*-Diol [%][c]	*ee* [%]
1[d,e]		62	50	22.6
2[d,e]		87	54	40.6
3[d]		89	53	83.1
4[f]		31	81	75.1
5		52	21[g]	46.4
6		99	99	92.3
7		31	94	81.6
8		40	95	84.9
9		24	96	83.8

[a] Reaction conditions: alkenes (0.2 mmol), $[Fe^{II}(L3)(OTf)_2]$ (0.006 mmol, 3 mol%), H_2O_2 (0.6 mmol, 3.0 equiv), MeOH (2 mL), 27 °C, 1.5 h. [b] Determined by ^1H NMR or GC. [c] Yields determined by ^1H NMR and based on conversions. [d] MeCN/MeOH (2:1, 3 mL). [e] $[Fe^{II}(L3)(OTf)_2]$ (0.01 mmol, 5 mol%) was used. [f] MeCN/MeOH (2:1, 3 mL). [g] Isolated yield based on conversion.

The AD of styrene with H_2O_2 (3 equiv) in MeOH catalyzed by $[Fe^{II}(L1)(OTf)_2]$, $[Fe^{II}(L3)(OTf)_2]$, or $[Fe^{II}(L7)(OTf)_2]$ gave the *cis*-diol in 7, 4, and 12% *ee*, respectively (Supporting Information, Table S3). With MeCN/MeOH (2:1, v/v) as solvent, the AD of styrene and *p*-Br, *m*-Cl, and *o*-F substituted styrenes afforded the *cis*-diols in 15.0–36.9% *ee* for $[Fe^{II}(L3)(OTf)_2]$, and in 15.6–32.0% *ee* for $[Fe^{II}(L7)(OTf)_2]$; $[Fe^{II}(L6)(OTf)_2]$ catalyzed the AD of these styrenes to give the *cis*-diols in significantly higher *ee* values of 40.3–59.8% (Table 3).

The L6 ligand, with a binaphthyl backbone, could be a promising chiral ligand scaffold. The (*Z*)-alkenes, coumarin, indene, and (*Z*)-β-methyl styrene, also underwent AD by the "$[Fe^{II}(L6)(OTf)_2] + H_2O_2$" method, giving the *cis*-diols in higher *ee* values (83, 67, and 56% *ee*, respectively; Supporting Information, Scheme S1), than that obtained with $[Fe^{II}(L3)(OTf)_2]$. The increased enantioselectivity achieved using $[Fe^{II}(L6)(OTf)_2]$ indicates that the AD of styrenes and (*Z*)-alkenes may be feasibly improved by modification of the N_4 ligand system.

Table 3: $[Fe^{II}(L3)(OTf)_2]$, $[Fe^{II}(L6)(OTf)_2]$, and $[Fe^{II}(L7)(OTf)_2]$-catalyzed AD of styrene and its *p*-Br, *m*-Cl, or *o*-F derivatives with H_2O_2.[a]

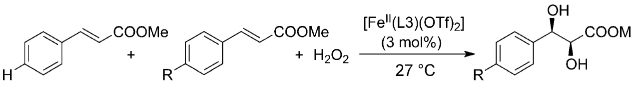


% *ee* (conversion [%],[b] yield [%][c])

R	$[Fe^{II}(L3)(OTf)_2]$	$[Fe^{II}(L6)(OTf)_2]$[d]	$[Fe^{II}(L7)(OTf)_2]$
H	17.5 (83, 90)	59.8 (33, 94)	19.8 (60, 65)
p-Br	32.3 (83, 98)	58.5 (54, 65)	25.7 (60, 63)
m-Cl	36.9 (81, 95)	49.7 (34, 79)	32.0 (54, 69)
o-F	15.0 (77, 84)	40.3 (21, 86)	15.6 (38, 63)

[a] Reaction conditions: alkenes (0.2 mmol), catalyst (0.006 mmol, 3 mol%), H_2O_2 (0.6 mmol, 3.0 equiv), MeCN/MeOH (2:1, 3 mL), 27 °C, 1.5 h. [b] Determined by ^1H NMR or GC. [c] Determined by ^1H NMR based on conversions. [d] Catalyst (5 mol%) with MeOH (2 mL) as solvent. Change of catalyst loading from 3 to 5 mol% increased the conversion and *cis*-diol yield but did not affect the enantioselectivity.

A number of mechanistic studies have been performed for the $[Fe^{II}(L3)(OTf)_2]$-catalyzed AD reactions with H_2O_2. 1) Time-course experiments revealed that the AD of methyl (*E*)-cinnamate at 27 °C is >90% complete within 0.5 h (Supporting Information, Figure S3). Competitive AD reactions (Scheme 2) revealed that electron-withdrawing *para*-substituents (Cl, CF_3, Br, and NO_2) of methyl (*E*)-cinnamate significantly accelerate the reaction by up to 6.1-fold, while electron-donating groups (*p*-MeO and *p*-Me) showed little effect on the reaction, and for *para*-substituted styrenes the *p*-Cl group accelerated the reaction more than a *p*-Me group (Supporting Information, Scheme S2). This coincides with a coordinated "nucleophilic" hydroperoxide oxidant but disfavors a highly oxidizing Fe^V-oxo reaction intermediate for the reaction (DFT calculated $E = 1.58$ V vs. SCE for $[Fe^{V}(L3)(O)(OH)]^{2+}/[Fe^{III}(L3)(OH)(OH_2)]^{2+}$ at pH 1; Supporting Information). 2) The *ee*, *cis*-diol yield, and substrate conversion for the AD of methyl (*E*)-cinnamate were almost unaffected by the presence of air (compare entries 1 and 2, Table 1), disfavoring a radical autoxidation pathway. 3) Treatment of styrene epoxide with H_2O_2 or H_2O in the presence of catalyst $[Fe^{II}(L3)(OTf)_2]$ mainly gave 2-methoxy-2-phenylethanol (45% or 97%) with the diol obtained in a minor amount (9% or 2%; Supporting Information, Scheme S3). Thus, a pathway featuring alkene epoxidation and ring-opening of epoxides could be ignored. 4) GC-MS measurements revealed very low ^{18}O-incorporation into the *cis*-diol product ($^{16}O^{16}O/^{16}O^{18}O/^{18}O^{18}O$ ratio $= 98.6{:}1.2{:}0.2$) for the AD of styrene in the presence of $H_2{}^{18}O$ ($H_2{}^{16}O_2/H_2{}^{18}O = 1{:}10$; Supporting Information, Scheme S4),



R =	OMe	Me	H	F	Cl	CF_3	Br	NO_2
conv./R = H	1.3	1.0	1.0	1.6	3.1	3.2	4.0	6.1

Scheme 2. Competitive AD of methyl (*E*)-cinnamates with H_2O_2 catalyzed by $[Fe^{II}(L3)(OTf)_2]$.

indicating that the two oxygen atoms in the *cis*-diol did not come from water.[8b,12b,13d,14b] 5) Using $H_2{}^{18}O_2$ as an oxidant, the AD of methyl (*E*)-cinnamate gave the *cis*-diol in 91 % yield (based on oxidant); GC-MS analysis showed that both the *cis*-diol oxygen atoms were labeled by ^{18}O and should come from $H_2{}^{18}O_2$. 6) High-resolution ESI-MS analysis of a reaction mixture of $[Fe^{II}(L3)(OTf)_2]$ in MeOH (1 mm) with dimethyl fumarate (20 equiv) and H_2O_2 (2 equiv) at 27 °C revealed a new cluster peak at *m*/*z* 328.62 attributable to intermediate **I** (Figure 3 a, mass accuracy = 2 ppm). Incorporation of ^{18}O into **I** was not observed in the presence of $H_2{}^{18}O$ (Figure 3 b), but both the oxygen atoms of **I** were ^{18}O-labeled if $H_2{}^{18}O_2$ was used (Figure 3 c). This demonstrates that these oxygen atoms are both derived from hydrogen peroxide rather than from water. 7) Reaction of $[Fe^{II}(L3)(OTf)_2]$ with H_2O_2 at −50 °C in acetone/CF_3CH_2OH generated a transient species exhibiting a UV/Vis absorption band at approximately 580 nm, which decayed via an isosbestic point at 500 nm after reaching maximum intensity at about 32 s (Figure 4 a; Supporting Information, Figure S4). The 580 nm absorption of this transient species is similar to that reported for $Fe^{III}(OOH)$ species.[18] X-band EPR measurements revealed that reaction of $[Fe^{II}(L3)(OTf)_2]$ (1.5 mm) with H_2O_2 (10 equiv) in acetone/CF_3CH_2OH at −50 °C for 90 s generated new signals with $g = 6.7$, 5.3, and 4.5 (Figure 4 b; Supporting Information, Figure S5), which can be attributed to high-spin $Fe^{III}(OOH)$ species with $S = 5/2$.[18] Considering also the aforementioned ^{18}O-labeling studies, which indicate a non-water assisted mechanism,[12] we propose that this transient species is $[Fe^{III}(L3)(OOH)]^{2+}$ (**A**).[12] The very fast formation of this transient $Fe^{III}(OOH)$ species apparently coincides with the lack of induction period observed in the time-course experiment (Supporting Information, Figure S3).

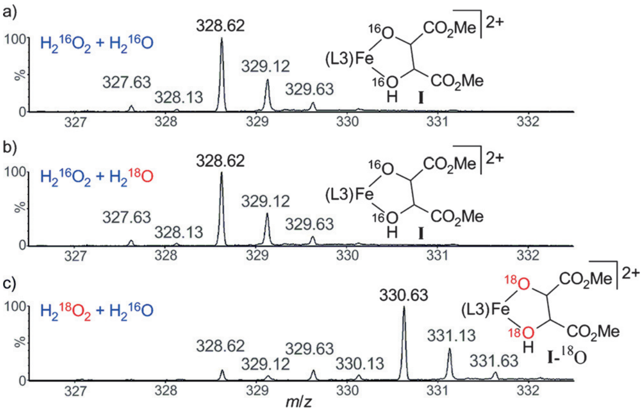


Figure 3. ESI-MS signals attributed to **I**, generated under the conditions: $[Fe(L3)(OTf)_2]/H_2O_2/alkene/H_2O = 1:2:20:200$ (reaction time: 10 min) using a) unlabeled H_2O_2 and H_2O, b) ^{18}O-labeled H_2O, and c) ^{18}O-labeled H_2O_2.

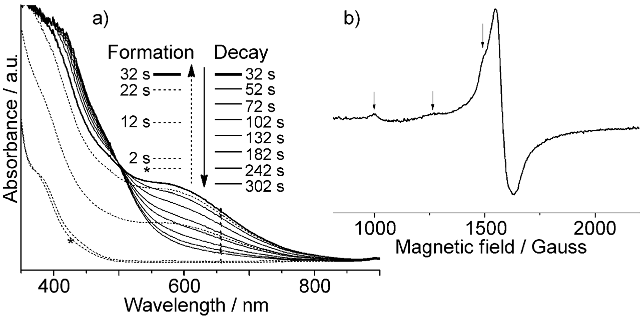


Figure 4. a) UV/Vis spectral changes upon reaction of $[Fe^{II}(L3)(OTf)_2]$ (1.5 mm) with H_2O_2 (10 equiv) at −50 °C in acetone/CF_3CH_2OH (3:1) at various reaction times (* = spectrum of $[Fe^{II}(L3)(OTf)_2]$). b) X-band EPR spectrum (at 10 K) of a reaction mixture of $[Fe^{II}(L3)(OTf)_2]$ (1.5 mm) and H_2O_2 (10 equiv) in acetone/CF_3CH_2OH (3:1) at −50 °C for a mixture quenched/frozen at a reaction time of 90 s.

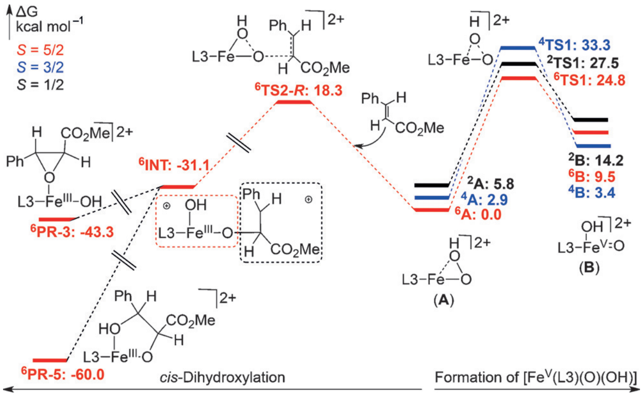


Figure 5. Computed potential energy surface in *cis*-dihydroxylation by $[Fe^{III}(L3)(OOH)]^{2+}$ (**A**) and formation of *cis*-$[Fe^{V}(L3)(O)(OH)]^{2+}$ (**B**).

DFT calculations revealed that a direct attack of $[Fe^{III}(L3)(OOH)]^{2+}$ (**A**, sextet ($S = 5/2$) ground state) on methyl (*E*)-cinnamate, giving intermediate **^{6}INT**, is both kinetically and thermodynamically more favorable than the O–O bond heterolysis of **A** to form $Fe^{V}(O)(OH)$ intermediate **B** ($\Delta G^{\neq} = 18.3$ vs. 24.8–33.3 kcal mol^{-1}, $\Delta G = -31.1$ vs. 3.4–14.2 kcal mol^{-1}; Figure 5). In the ring-closure reactions of **^{6}INT**, the dihydroxylation product **^{6}PR-5** should be overwhelming (compared with epoxidation product **^{6}PR-3**) due to the large diol/epoxide free energy difference ($\Delta G_{5\text{-}3}$) of −16.7 kcal mol^{-1}. The $\Delta G_{5\text{-}3}$ value increases to −22.4 kcal mol^{-1} upon changing the alkene substrate to 4-octene, but decreases to −6.8 kcal mol^{-1} with styrene as the substrate; the latter can account for the epoxidation related products (2-methoxy-2-phenylethanol and styrene epoxide, ≤ 10 % total yield) in the AD of styrene. The enantioselectivity can be accounted for by the difference in free energy ($\Delta\Delta G^{\neq}$) for the transition states **TS2-*R*** and **TS2-*S*** (Supporting Information, Figure S6) in the rate-determining step. The computed $\Delta\Delta G^{\neq}$ for the AD of methyl (*E*)-cinnamate is −2.6 kcal mol^{-1} which corresponds to 97.7 % *ee*, in good agreement with the experimental *ee* value of 99.8 % (entry 1, Table 1). For AD of (*E*)- and (*Z*)-β-methyl styrene via **A**, the *ee* values predicted from computed $\Delta\Delta G^{\neq}$ (−1.83 and −0.94 kcal mol^{-1}; Supporting Information, Figure S7) are 91.3 % and 66.1 %, respectively, which is consistent with the lower *ee* value found experimentally for the (*Z*)-alkene compared to that for the (*E*)-alkene.

Based on the experimental mechanistic studies and DFT calculations, the $[Fe^{II}(L3)(OTf)_2]$-catalyzed AD of alkenes involves chiral intermediate $[Fe^{III}(L3)(OOH)]^{2+}$ (**A**) as an active oxidant. The highly oxidizing electrophilic Fe^{V}-oxo oxidants, such as *cis*-$[Fe^{V}(L3)(O)(OH)]^{2+}$ (**B**) with a high E value of 1.58 V (calculated, vs. SCE), is deemed to play a minor role, if any, in the catalysis particularly in view of the findings depicted in Scheme 2 and the insignificant $C{=}C$ bond oxidative cleavage products observed in the AD reactions.

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