DOI: 10.1002/adsc.201100267

Chiral Bioinspired Non-Heme Iron Complexes for Enantioselective Epoxidation of α,β-Unsaturated Ketones

Mei Wu,[a,b,d] Cheng-Xia Miao,[a,d] Shoufeng Wang,[a] Xiaoxue Hu,[a] Chungu Xia,[a] Fritz E. Kühn,[c] and Wei Sun[a,*]

[a] State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences Lanzhou 730000, People's Republic of China
Fax: (+86)-931-827-7088; phone: (+86)-931-496-8278; e-mail: wsun@licp.cas.cn
[b] Graduate School of the Chinese Academy of Sciences, Beijing 100039, People's Republic of China
[c] Molecular Catalysis, Catalysis Research Center, Technische Universität München, 85747 Garching, Germany
[d] Both authors contributed equally to this work

Received: April 10, 2011; Revised: June 6, 2011; Published online: October 20, 2011

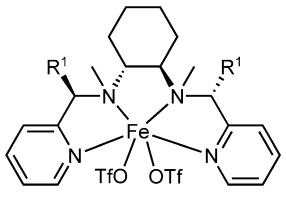
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adcs.201100267.

Abstract: Chiral bioinspired iron complexes of N_4 ligands based on the ethylenediamine backbone display remarkable levels of enantioselectivity for the first time in the asymmetric epoxidation of α,β-unsaturated ketones using hydrogen peroxide (up to 87% *ee*) or peracetic acid as oxidant, respectively. Notablely, isotopic labeling with $H_2{}^{18}O$ strongly demonstrated that there is a reversible water binding step prior to generation of the significant intermediate. Besides, the complex $[L_2Fe(III)_2(\mu\text{-}O)(\mu\text{-}CH_3CO_2)]^{3+}$ usually derived from the decay of the LFe(IV)=O species or thermodynamic sinks for a number of iron complexes was identified by HR-MS. In addition, the possible mechanisms were proposed and LFe(V)=O species may be the main active intermediate in the catalytic system.

Keywords: chiral N_4 ligand; enantioselectivity; epoxidation; iron; α,β-unsaturated carbonyl compounds

Introduction

Iron complexes have been extensively studied as models for non-heme iron oxygenases, demonstrating catalytic potential for the oxidation of organic substrates. Depending on the coordination sphere around the iron atom, these complexes can promote hydroxylation, epoxidation, *cis*-dihydroxylation, and a number of other organic transformations.[1–3] Among the developed ligands, tetradentate nitrogen ligands (N_4) based on an ethylenediamine backbone such as *N*,*N*′-dimethyl-*N*,*N*′-bis(2-pyridylmethyl)ethane-1,2-diamine (**mep** or **BPMEN**), (*R*,*R*)-*N*,*N*′-dimethyl-*N*,*N*′-bis(2-pyridylmethyl)-cyclohexane-1,2-diamine (**mcp** or **BPMCN**) have been established as promising ligand frameworks (Figure 1). In 2001, Que et al. reported [Fe(**6-Me$_2$-bpmcn**)$(CF_3SO_3)_2$] (CF_3SO_3 = OTf) as catalyst for *cis*-dihydroxylation of *trans*-2-octene with hydrogen peroxide providing up to 82% *ee*.[4] Meanwhile, Jacobsen and co-workers discovered an excellent catalyst based on an Fe(**mep**) complex that can efficiently promote epoxidation of a variety of aliphatic olefins with aqueous H_2O_2.[5] The asymmetric version of this highly active Fe catalyst is currently a challenge, although several analogous catalyst systems have been developed.[6] A breakthrough in the biomimetic oxidation has been achieved by Que and coworkers who reported highly enantioselective *cis*-dihydroxylation of alkenes with Fe complexes of N_4 ligands.[7] Notably, the rational design of proper ligands could lead to a significant success. We also developed a novel family of N_4 ligands, through the introduction



Complex **1**: R^1 = Ph
Complex **2**: R^1 = 4-*t*-Bu-C_6H_4
R,*R*-**mcp**-Fe: R^1 = H

Figure 1. Chiral Fe complexes used in this study.

of aryl groups at the 2-pyridinylmethyl positions of the **mcp** ligand. Their manganese complexes exhibited a clear enhancement in the asymmetric induction for the epoxidation reaction.[8]

As a part of our continuing interest in bioinspired oxidation, we describe herein the development of chiral Fe(II) complexes of N_4 ligands for the asymmetric epoxidation of α,β-enones employing H_2O_2 or peracetic acid as oxidant, respectively (Figure 1). In addition, the strategy of isotopic labeling with $H_2{}^{18}O$ was adopted to have a rough insight into the mechanism. Besides, $[L_2Fe(III)_2(\mu\text{-}O)(\mu\text{-}CH_3CO_2)]^{3+}$ usually derived from the decay of the LFe(IV)=O species or thermodynamic sinks for a number of iron complexes was identified by HR-MS.

Results and Discussion

Iron complexes **1** and **2** are readily prepared by the reaction of N_4 ligands *R,R,R,R*-**pmcp** (L_1) or *R,R,R,R*-**bpmcp** (L_2) and $FeCl_2$ in CH_3CN, then the anion can be changed to OTf^- by the addition of AgOTf.[8a,9] Complexes **1** and **2** are isolated as pale yellow solids and were characterized by elemental analysis and ESI-TOF-MS. The crystal structure of **1** is shown in Figure 2, indicating that the ligand coordinates the iron centre in a *cis*-α topology.[10,11]

Since the initial report of Jacobsen about the effect of acetic acid on non-heme iron-catalyzed epoxidation,[5] Que and co-workers demonstrated that the use of acetic acid as an additive in iron catalysis could lead to a shift of the oxidation reaction away from *cis*-dihydroxylation towards epoxidation.[12] During the process, peracetic acid may be formed *in situ* from H_2O_2 and acetic acid in the presence of non-heme iron catalysts.[12a] Based on these previous studies, we firstly evaluated the catalytic property of these new iron catalysts in the asymmetric epoxidation of chalcone with H_2O_2 as oxidant, in the presence of acetic acid (Table 1). Obviously, the reaction did not occur when the anion of the catalyst was chlorine (see Supporting Information, Table S1, entries 1 and 2). When 1 mol% of complex **1** was employed, epoxidation of chalcone occurred with 33% yield and 66% *ee* (Table 1, entry 1). Encouraged by these preliminary results, further optimization of the reaction conditions was performed. Using 2 mol% of complex **1** or **2** as catalyst led to nearly same yield and asymmetric induction (>70%) with 2 equivalents of H_2O_2 at room temperature (Table 1, entries 4 and 6). However, employing $[Fe(\mathbf{mcp})(CF_3SO_3)_2]$ as catalyst, a 54% *ee* was observed under the identical conditions. Remarkably, the asymmetric induction of epoxidation reached 77% *ee* using 2 mol% complex **2** as catalyst at −15 °C (Table 1, entry 8). And further decreases in temperature did not lead to an evident increase in enantioselectivity. In addition, some other acids were also

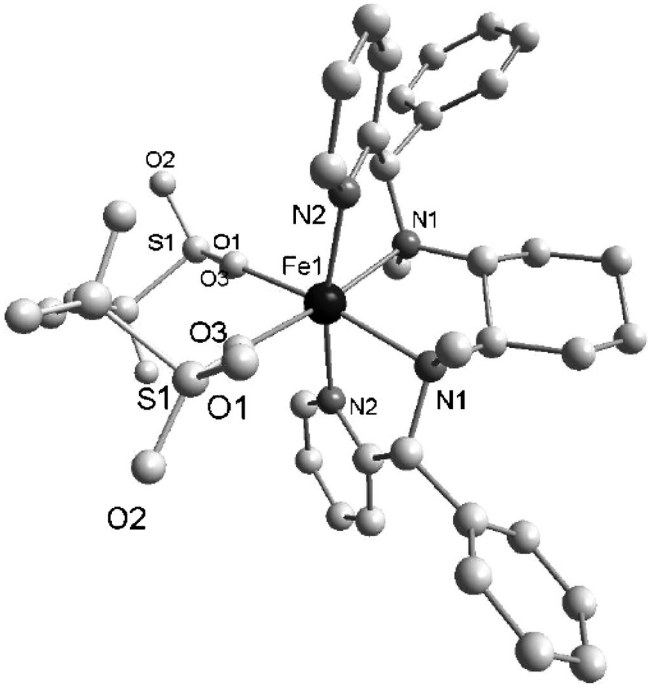
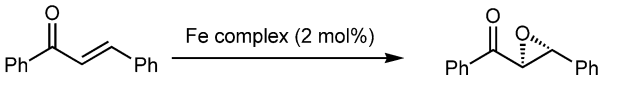


Figure 2. X-ray structure of Fe complex **1** (hydrogen atoms are omitted for clarity).

Table 1. Screening of the catalysts and reaction conditions for catalytic asymmetric epoxidation of chalcone using H_2O_2 as the oxidant.[a]



Entry	Cat. (mol%)	*T* [°C]	H_2O_2 (equiv.)	Yield [%][b]	*ee* [%][c]
1	**1** (1)	r.t.	6.0	33	66
2	**1** (2)	r.t.	6.0	42	68
3	**1** (2)	r.t.	1.5	36	69
4	**1** (2)	r.t.	2.0	45	71
5	*R,R*-(**mcp**)Fe (2)	r.t.	2.0	47	54
6	**2** (2)	r.t.	2.0	47	72
7	**2** (2)	0	2.0	50	73
8	**2** (2)	−15	2.0	53	77
9	**2** (2)	−30	2.0	52	78
10[d]	**2** (2)	r.t.	2.0	33	67

[a] *Reaction conditions:* 0.25 mmol chalcone, 1.0 mL CH_3CN, 5 equiv. of AcOH, 50% H_2O_2 in 0.5 mL CH_3CN was slowly added over a period of 60 min with a syringe pump, and 60 extra minutes of stirring were allowed.
[b] Isolated yield.
[c] Determined by HPLC with a Daicel OD-H column.
[d] 0.125 mmol chalcone, 0.5 mL CH_3CN, 20 equiv. of $H_2{}^{18}O$, 50% H_2O_2 in 0.25 mL CH_3CN was slowly added over a period of 60 min with a syringe pump, and 60 extra minutes of stirring were allowed.

Table 2. Screening of the catalysts and reaction conditions for catalytic asymmetric epoxidation of chalcone using AcOOH as the oxidant.[a]

Entry	Cat. (mol%)	Amount of peracid (%)	T [°C]	t [h]	Yield [%][b]	*ee* [%][c]
1	**1** (2)	1.2	r.t.	2	57	55
2	**2** (2)	1.2	r.t.	2	56	55
3	**1** (2)	1.2	−15	3	20	60
4	**2** (2)	1.2	−15	3	53	45
5[d]	**2** (2)	1.2	r.t.	2	60	56
6	**2** (2)	1.5	r.t.	2	54	55
7	**2** (2)	1.0	r.t.	2	46	56
8	**2** (1)	1.2	r.t.	4	42	54
9	**2** (0.5)	1.2	r.t.	4	24	56
10[e]	**2** (2)	1.2	r.t.	2	22	56

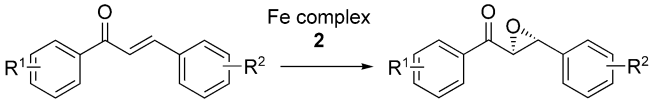
[a] *Reaction conditions:* 0.25 mmol chalcone, 1.0 mL CH_3CN, 1.2 equiv. of 8% AcOOH in 0.5 mL CH_3CN was added quickly with a syringe pump.
[b] Isolated yield.
[c] Determined by HPLC with a Daicel OD-H column.
[d] 1.2 equiv. of 8% AcOOH in 0.5 mL CH_3CN was added over a period of 60 min with a syringe pump.
[e] 0.125 mmol chalcone, 0.5 mL CH_3CN, 20 equiv. of $H_2{}^{18}O$, 1.2 equiv of 8% AcOOH in 0.25 mL CH_3CN was added quickly with a syringe pump.

tested, such as benzoic acid, formic acid, substituted acetic acid and so on. Unfortunately, the yield and the *ee* were poorer than those with acetic acid (see the Supporting Information, Table S1). Thus, the optimum conditions for epoxidation appear to be 2 mol% of complex **2**, 2 equivalents of H_2O_2, and 5 equivalents of AcOH in CH_3CN at −15 °C.

Subsequently, pre-prepared peracetic acid as the oxidant was examined for the reaction and the results are summarized in Table 2. Notably, all chiral Fe complexes used in the study showed a certain activity for the epoxidation of chalcone (Table 2, entries 1 and 2 and Supporting Information, Table S2, entries 1 and 2). Similar results were also obtained using complex **1** or **2** as the catalyst. After rough optimization of the reaction conditions, moderate yield and *ee* were obtained at mild conditions (2 mol% catalayst **2**, room temperature, 1.2 equiv. of peracetic acid, 2 h). As a whole, H_2O_2 as the oxidant led to a slightly higher *ee* and lower yield compared with peracetic acid. Besides, the catalysts used in the study were inert to the chalcone epoxidation using PhIO as the terminal oxidant.[13]

To explore the substrate scope and the potential for the asymmetric bioinspired epoxidation, the enantioselective epoxidation of a variety of α,β-unsaturated ketones[14,15] with H_2O_2 or peracetic acid as the oxidant was then evaluated, respectively, using complex **2** under the optimized conditions. The results are listed in Table 3. In general, the data presented the

Table 3. Asymmetric epoxidation of α,β-enones catalyzed by iron complex **2**.



Entry	Substrate	Yield [%][c]	*ee* [%][d]
1[a]	$R^1=H$; $R^2=H$	53	77
2[b]		57	55
3[a]	$R^1=H$; $R^2=p$-Cl	90	84
4[b]		83	68
5[a]	$R^1=H$; $R^2=o$-Cl	80	83
6[b]	$R^1=H$; $R^2=o$-Br	63	82
7[a]	$R^1=H$; $R^2=p$-F	73	87
8[b]		62	70
9[a]	$R^1=H$; $R^2=p$-CH_3	52	78
10[a]	$R^1=p$-Cl; $R^2=H$	40	69
11[b]		53	50
12[a]	$R^1=p$-F; $R^2=H$	56	74
13[b]		67	53
14[a]	$R^1=p$-CH_3; $R^2=H$	61	82
15[b]		48	62
16[a]	$R^1=p$-CH_3; $R^2=p$-F	84	84
17[b]		51	73

[a] *Reaction conditions:* 0.25 mmol substrates, 1 mL CH_3CN, 2 mol% complex **2**, 5 equiv. of AcOH, 2 equiv. of 50% H_2O_2 in 0.5 mL CH_3CN was slowly added over a period of 60 min with a syringe pump, and 60 extra minutes of stirring were allowed at −15 °C.
[b] *Reaction conditions:* 0.25 mmol substrate, 1.0 mL CH_3CN, 2 mol% complex **2**, 1.2 equiv of 8% AcOOH in 0.5 mL CH_3CN was added quickly with a syringe pump and then the mixture was stirred for 2 h at room tempreture.
[c] Isolated yield.
[d] Determined by HPLC with Daicel chiral column.

similar trend as with the epoxidation of chalcone: a slight higher *ee* and similar yield were obtained with H_2O_2 as the oxidant compared with peracetic acid as the oxidant. Meanwhile, based on our previous bioinspired Mn complex-catalyzed epoxidation, the outcome of the asymmetric induction definitively depended on the groups of the α,β-unsaturated ketones.[8,16] The same phenomena were also observed in the Fe-catalyzed epoxidation system. Clearly, the substituent groups of different electronic characters on the phenyl ring of the olefin side gave rise to considerable improvement in epoxide yield and enantioselectivity either with H_2O_2 or with AcOOH as oxidant (Table 2, entries 3–9). For example, *p*-F substituted substrate led to 87% *ee* with H_2O_2 as oxidant (entry 7). Additionally, the effect of the groups on the phenyl ring connected to the carbonyl was subsequently investigated. Epoxides were isolated in slight lower or similar yields for both electron-withdrawing and electon-donating groups on the phenyl ring of the

carbonyl side compared with that of chalcone (entries 10–15). Interestingly, substrates substituted either on the carbonyl side or on the olefin side could be both transformed to the desired epoxide in 84% *ee* with an 84% yield using H_2O_2 as the oxidant (entry 16). Hence, the bioinspired Fe-complexes of N_4 ligands show nearly equal asymmetric inductions as the corresponding Mn(II) complexes in the epoxidation of α,β-unsaturated ketones.[8] Importantly, the amount of H_2O_2 could be reduced from 6.0 equiv. to 2.0 equiv. with respect to the substrate by virtue of a slow addition protocol.[17] Unfortunately, the catalytic system was unsuitable for traditional olefins such as styrene, which was almost recovered and just transformed to a spot of benzyl aldehyde.

Up to now, iron-oxo species were speculated as the active species during the epoxidation in many reports.[18] Also, the exchange of their oxygen atom between the non-heme iron-oxo species and water through an oxo-hydroxo tautomerism before attack to a substrate was widely accepted.[19] Although much progress has been made in mechanistic research, the exact pathway for the epoxidation catalyzed by non-heme iron complexes, especially our designed catalyst, remains obscure. Therefore, a rough insight into the epoxidation mechanism of α,β-enones catalyzed by our catalytic system was first obtained by means of isotopic labeling with $H_2{}^{18}O$. Studies of the epoxidation of chalcone using H_2O_2 as the oxidant in the presence of $H_2{}^{18}O$ (20 equiv.) indicated that only 10% of the oxygen atoms in the epoxide derived from $H_2{}^{18}O$ (Figure 3 *vs.* Figure 4). On the other hand, experiments with peracetic acid as the oxidant by adding 20 equivalents of $H_2{}^{18}O$ showed a 17% incorporation of oxygen atoms from water into epoxide (Figure 3 *vs.* Figure 5). The different extents of label incorporation from labeled water may be ascribed to the different mole ratios of $H_2{}^{16}O$:$H_2{}^{18}O$ in the two catalytic systems. The above results and the previous reports strongly demonstrated that there is a reversible water binding step prior to the generation of the significant intermediate [LFe(V)=O **a** or LFe(IV)=O **b**] in our catalytic systems.[20] Besides, HR-MS was also used to trap the intermediate of the reaction. As shown in Figure 6, Figure 7, and Supporting Information, Figure S1 and Figure S2, **d** $[L_2Fe(III)_2(\mu\text{-}O)(\mu\text{-}CH_3CO_2)]^{3+}$ and its isotopic labeling with ^{18}O were obviously identified: $[L_2Fe(III)_2(\mu\text{-}O)(\mu\text{-}CH_3CO_2)]^{3+}$ ($m/z = 454.5727$) and $[L_2Fe(III)_2(\mu\text{-}{}^{18}O)(\mu\text{-}CH_3CO_2)]^{3+}$ ($m/z = 455.2399$). Also, labeled **d** with ^{18}O may derive from both the previous water binding and simple exchange between non-labeled **d** and $H_2{}^{18}O$ (Scheme 1, **d**→**d′**). Unfortunately, neither LFe(V)=O nor LFe(IV)=O has been detected during the reaction, probably because of their too short half-life times under the test conditions. Although it was reported that the decay of the LFe(IV)=O species or thermodynamic sinks for a number of iron complexes usually lead to its conversion to $[L_2Fe(III)_2(\mu\text{-}O)(\mu\text{-}CH_3CO_2)]^{3\pm}$,[12b,19a,21] LFe(IV)=O species could not be

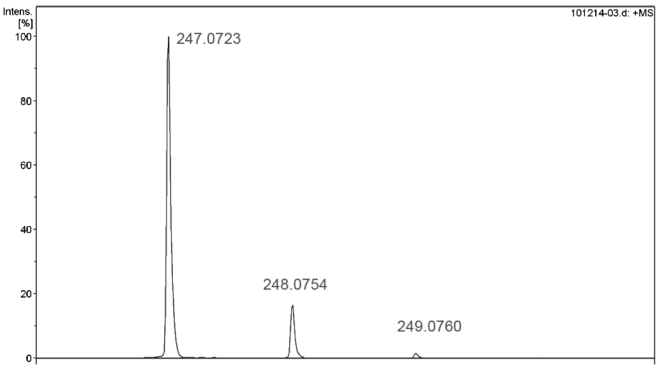


Figure 3. The HR-MS of the product obtained under standard conditions.

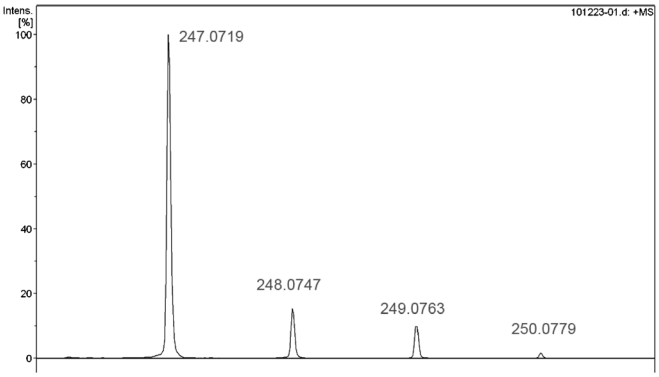


Figure 4. The HR-MS of the product obtained under the following conditions: 0.125 mmol chalcone, 0.5 mL CH_3CN, 20 equiv. of $H_2{}^{18}O$, 50% H_2O_2 in 0.25 mL CH_3CN was slowly added over a period of 60 min with a syringe pump, and 60 extra minutes of stirring were allowed.

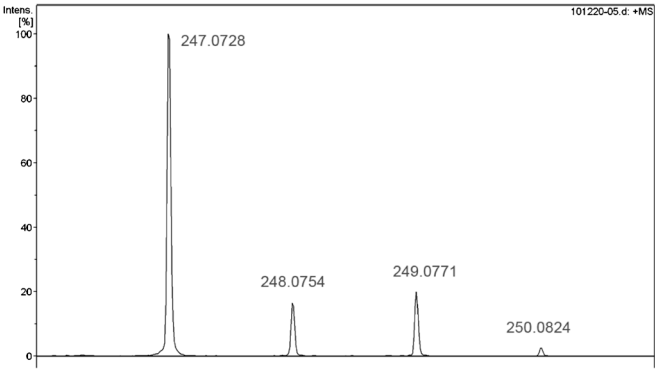


Figure 5. The HR-MS of the product obtained under the following conditions: 0.125 mmol chalcone, 0.5 mL CH_3CN, 20 equiv. of $H_2{}^{18}O$, 1.2 equiv. of 8% AcOOH in 0.25 mL CH_3CN was added quickly with a syringe pump and then the mixture was stirred for 2 h.

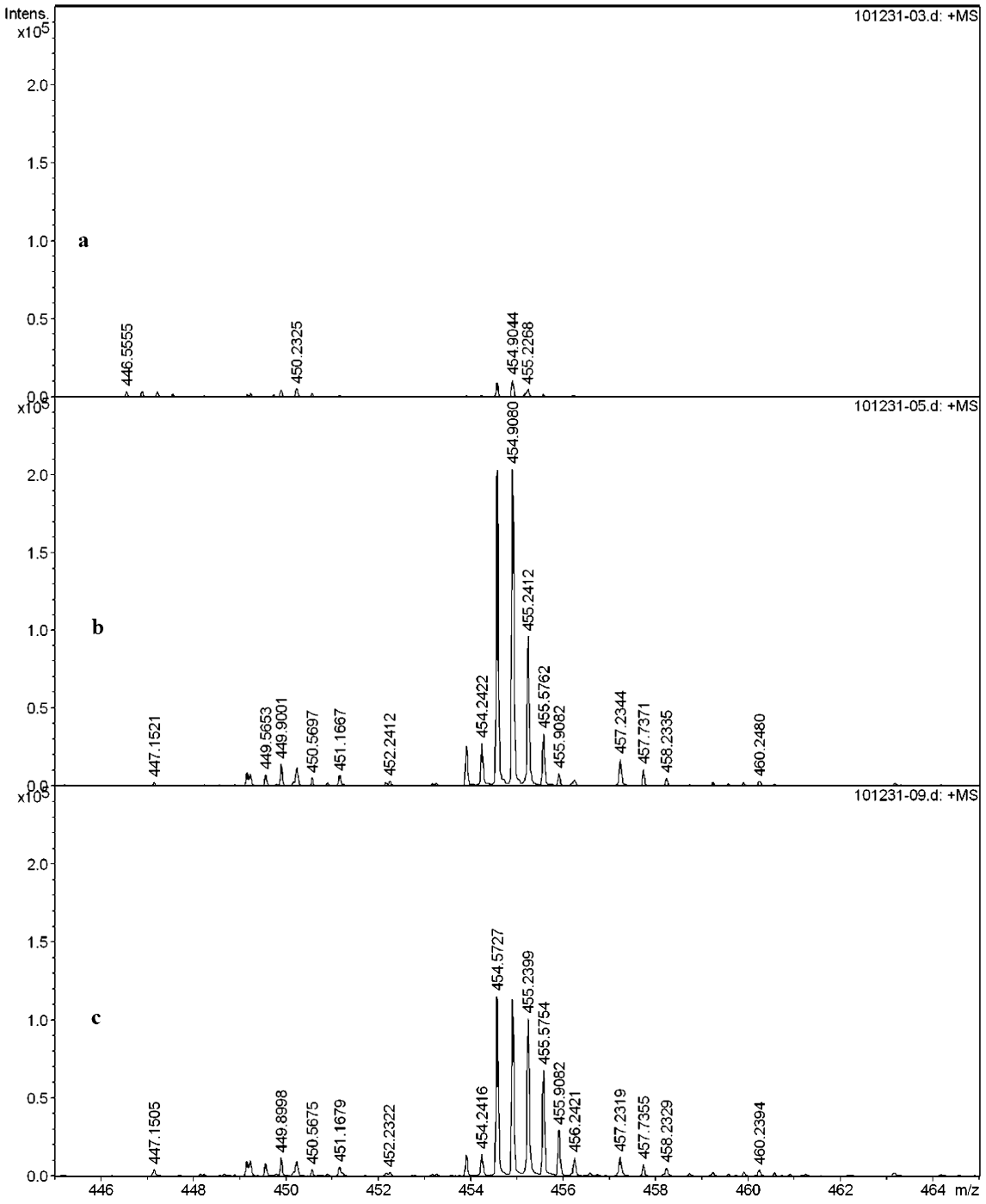


Figure 6. a: The chiral complex **2** (0.25 μmol) in 0.5 mL CH_3CN; **b**: 0.625 mmol AcOH and 0.25 mmol of 50% H_2O_2 was added sequentially into the above system; **c**: based on **b**, 2.5 mmol $H_2{}^{18}O$ was added.

deduced to be the active intermediate. Moreover, most researchers supported LFe(V)=O as the active intermediate in similar catalytic systems with comparabel structures related to our designed catalyst.[12b,22] Therefore, up to now, both path **A** and path **B** may be involved in the system (Scheme 1) and path **A** may be the main route to achieve the epoxidation. In addition, the detailed mechanism still needs evidence to confirm LFe(V)=O or LFe(IV)=O as the active intermediate.

Conclusions

In summary, this report describs the first example of Fe complexes of N_4 ligands based on the ethylenedi-

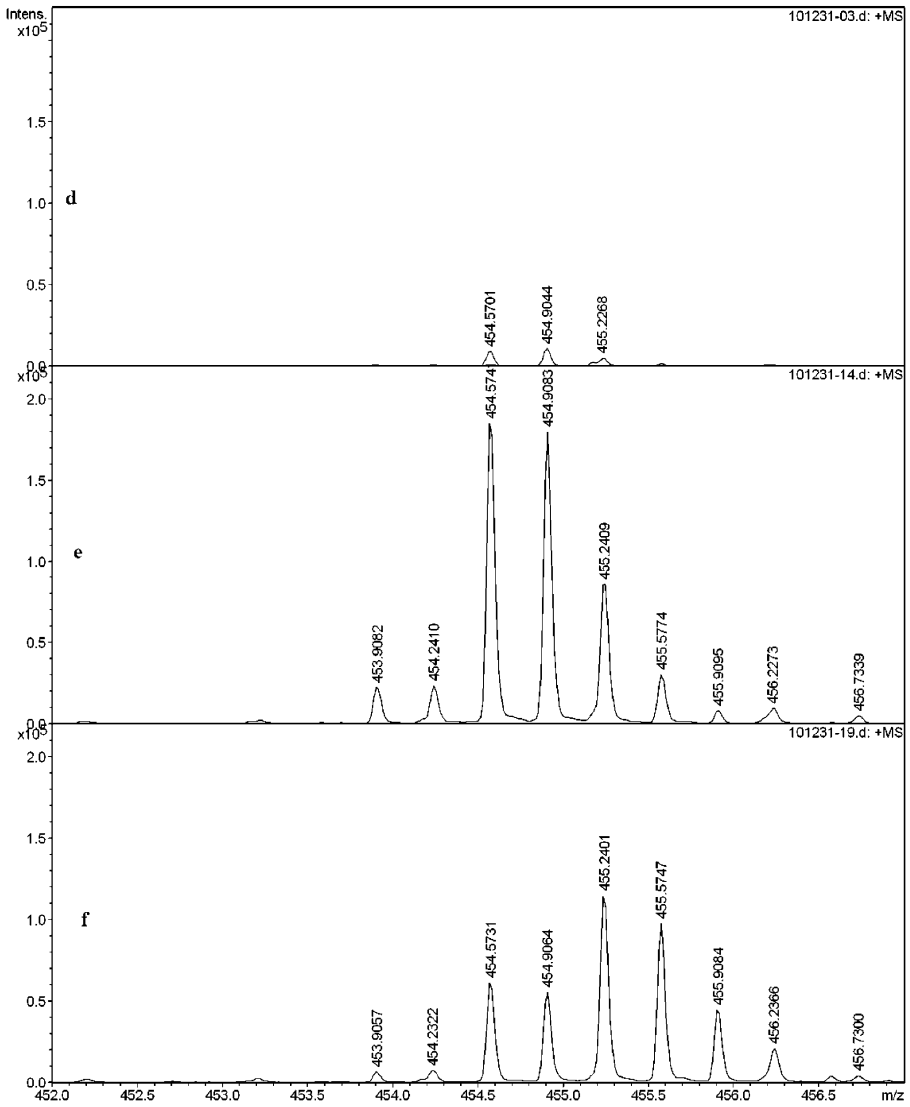


Figure 7. d: The chiral complex **2** (0.25 μmol) in 0.5 mL CH_3CN; **e**: 0.15 mmol AcOOH was added into the above system; **f**: based on **e**, 2.5 mmol $H_2{}^{18}O$ was added.

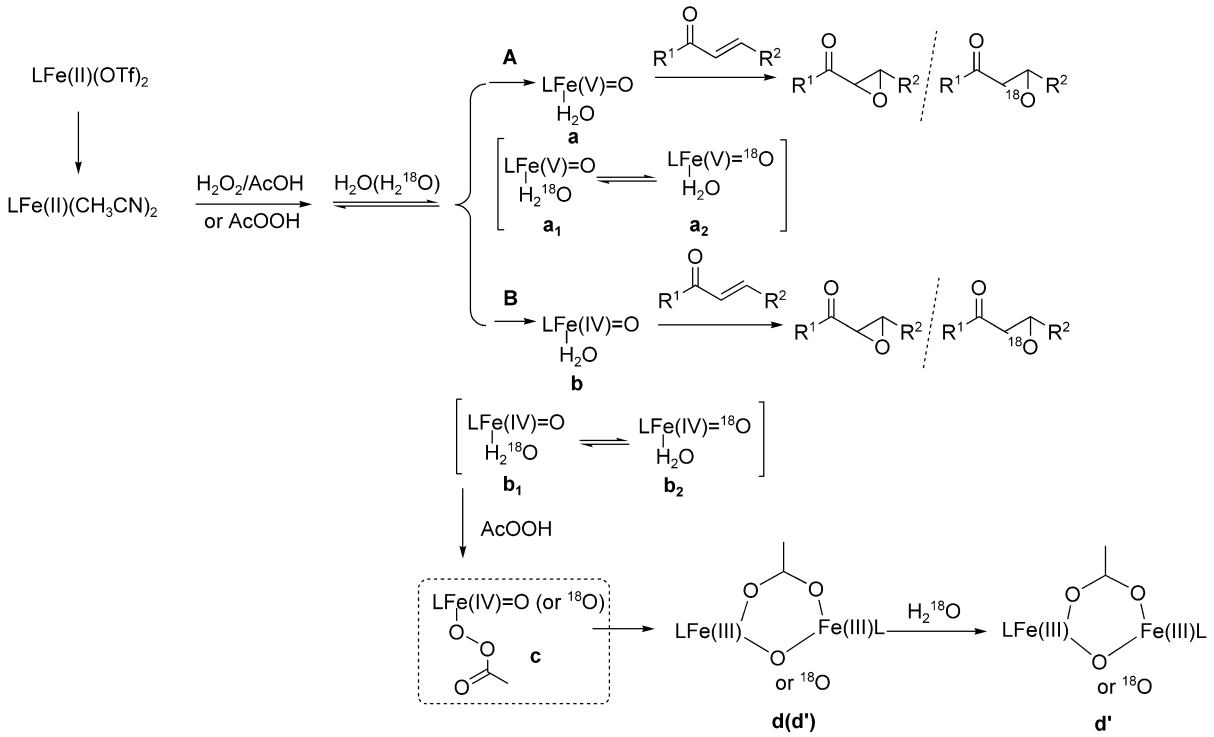
amine backbone as catalysts for asymmetric epoxidation. These complexes display remarkably high enantioselectivities (up to 87% *ee*), using H_2O_2 or peracetic acid as oxidant, respectively. Notably, we indirectly demonstrated that there is a reversible water binding step prior to the generation of the most significant intermediate. Besides, $[L_2Fe(III)_2(\mu\text{-}O)(\mu\text{-}CH_3CO_2)]^{3+}$ usually derived from the decay of the LFe(IV)=O species or thermodynamic sinks for a number of iron complexes was identified by HR-MS. In addition, both path **A** and path **B** may be involved in the system and path **A** may be the main route to achieve the epoxidation. Further studies on expanding the scope of this catalytic asymmetric epoxidation of olefins, the detailed mechanism as well as the development of even more efficient catalysts are in progress.

Experimental Section

General information

The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance III 400 MHz spectrometer. The chemical shifts (δ) are reported in ppm and coupling constants (*J*) in Hz. High resolution mass spectra (HR-MS) were obtained on a Bruker Daltonics micrOTOF-Q^{II} mass spectrometer. HPLC analysis was performed on Waters-Breeze (2487 Dual λ Absorbance Detector and 1525 Binary HPLC Pump). Chiralpak OD-H, AD-H, OB-H, OJ, AS columns were purchased from Daicel Chemical Industries, LTD. Column chromatography was generally performed on silica gel (200–300 mesh) and TLC inspections were on silica gel GF254 plates.

All reactions were carried out under argon in dried glassware. All chemicals and solvents were used as received unless otherwise stated. THF, diethyl ether (Na, benzophe-



Scheme 1. The proposed mechanism catalyzed by the designed catalytic system.

none), acetonitrile (CaH_2) were distilled under argon prior to use. α,β-Enones were prepared according to the reported procedures.[23] Ligand **1** (*R,R,R,R*-**pmcp**) and ligand **2** (*R,R,R,R*-**bpmcp**) were prepared according to our reported procedures.[8a]

Synthesis and Characterization of Complexes 1 and 2

Under an argon atmosphere, $FeCl_2$ (37.5 mg, 0.3 mmol) was added to a stirred solution of chiral ligands **1** or **2** (0.3 mmol) in CH_3CN (3 mL). The reaction mixture was refluxed for 12 h to allow the complete precipitation of a pale yellow solid which corresponds to [$LFeCl_2$]. The solution was filtered and the solid was washed with CH_3CN and dried under vacuum to afford a light orange solid. Under an argon atmosphere, to a stirred mixture of [$LFeCl_2$] (0.15 mmol) in CH_3CN (2 mL) was added $AgCF_3SO_3$ (0.3 mmol). The mixture was stirred for 2 h and filtered through Celite to remove precipitated AgCl. Then the solvent was removed under vacuum to give the desired Fe complexes. If necessary, several drops of CH_2Cl_2 were added to remove the CH_3CN under vacuum. Then complex **1** or **2** was washed with ether three times and dried under vacuum.

Complex 1 Fe(II)(**pmcp**)$(CF_3SO_3)_2$: ^{19}F NMR (CD_3CN, 298 K): $\delta = -78.2$; ESI-TOF-MS: $m/z = 681.1786$, calcd. for $C_{33}H_{36}F_3FeN_4O_3S$ $[M-OTf]^+$: 681.1805; anal. calcd. for $C_{34}H_{36}F_6FeN_4O_6S_2 \cdot H_2O$: N 6.60, C 48.12, H 4.51; found: N 6.62, C 48.10, H 4.46.

Complex 2 Fe(II)(**bpmcp**)$(CF_3SO_3)_2$: ^{19}F NMR (CD_3CN, 298 K): $\delta = -77.8$; ESI-TOF-MS: $m/z = 793.3050$, calcd. for $C_{33}H_{36}F_3FeN_4O_3S$ $[M-OTf]^+$: 793.3057; anal. calcd. for $C_{42}H_{52}F_6FeN_4O_6S_2 \cdot CH_2Cl_2$: N 5.45, C 50.25, H 5.30; found: N 5.86, C 49.94, H 5.26.

General Procedure for the Fe-Catalyzed Epoxidation of α,β-Enones using H_2O_2 as the Oxidant

The chiral complex **1** or **2** (0.5 μmol), substrate (0.25 mmol) and 5 equiv. of AcOH were added to CH_3CN (1.0 mL) under an argon atmosphere and the solution was stirred for 5 min. Then 2 equiv. of 50% H_2O_2 (0.5 mmol, diluted with 0.5 mL MeCN) were delivered by a syringe pump over 60 min and the mixture was stirred at −15 °C for 60 min. The crude product was purified by chromatography on silica gel (EtOAc/PET = 50:1) to afford the epoxide product.

General Procedure for the Fe-Catalyzed Epoxidation of α,β-Enones using AcOOH as the Oxidant

The chiral complex **1** or **2** (0.5 μmol) and substrate (0.25 mmol) were added to CH_3CN (1.0 mL) under an argon atmosphere and the solution was stirred for 5 min. Then 1.2 equiv. of 8% AcOOH (diluted with 0.5 mL MeCN) was added quickly with a syringe pump. And the mixture was subsequently stirred for 2 h at room temperature. The crude product was also purified by chromatography on silica gel (EtOAc/PET = 50:1) to afford the epoxide product.

***trans*-(2*S*,3*R*)-Epoxy-1,3-diphenylpropan-1-one:** Yield: 53%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.01$ (d, $J = 8.4$ Hz, 2H, ArH), 7.62 (t, $J = 8.4$ Hz, 1H, ArH), 7.49 (t, $J = 8.0$ Hz, 2H, ArH), 7.43–7.36 (m, 5H, ArH), 4.29 (d, $J = 2.0$ Hz, 1H, CH), 4.08 (d, $J = 2.0$ Hz, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 193.1$, 135.5, 135.4, 134.0, 129.1, 128.9, 128.8, 128.4, 125.8, 61.0, 59.4; HPLC (Chiralcel OD-H, 20 °C, 254 nm, 98/2 hexane/EtOH, 1.0 mL min^{-1}): $t_{major} = 16.56$ min, $t_{minor} = 18.94$ min.

***trans*-(2*S*,3*R*)-Epoxy-3-(4-chlorophenyl)-1-phenylpropan-1-one**: Yield: 90%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.00$ (d,

J=7.6 Hz, 2H, ArH), 7.64 (t, J=7.6 Hz, 1H, ArH), 7.50 (t, J=7.6 Hz, 2H, ArH), 7.39 (d, J=8.4 Hz, 2H, ArH), 7.31 (d, J=8.4 Hz, 2H, ArH), 4.26 (d, J=1.6 Hz, 1H, CH), 4.07 (d, J=1.6 Hz, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.7, 135.4, 135.0, 134.1, 134.0, 129.0, 128.9, 128.4, 127.1, 60.9, 58.7; HPLC (Chiralcel OJ, 20 °C, 254 nm, 90/10 hexane/*i*-PrOH, 1.0 mL min^{-1}): t_{major}=20.59 min, t_{minor}=30.00 min.

***trans*-(2*S*,3*R*)-Epoxy-3-(2-chlorophenyl)-1-phenylpropan-1-one:** Yield: 80%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.06 (dd, J_1=1.2 Hz, J_2=8.4 Hz, 2H, ArH), 7.64 (t, J=10.0 Hz, 1H, ArH), 7.51 (t, J=7.2 Hz, 2H, ArH), 7.42–7.40 (m, 2H, ArH), 7.34–7.32 (m, 2H, ArH), 4.41 (d, J=2.0 Hz, 1H, CH), 4.18 (d, J=2.0 Hz, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=192.8, 135.3, 134.1, 133.8, 133.3, 129.8, 129.3, 128.9, 128.4, 127.3, 126.1, 60.1, 57.2; HPLC (Chiralcel AD-H, 20 °C, 254 nm, 99/1 hexane/*i*PrOH, 1.0 mL min^{-1}): t_{major}= 22.22 min, t_{minor}=19.59 min.

***trans*-(2*S*,3*R*)-Epoxy-3-(2-bromophenyl)-1-phenylpropan-1-one:** Yield: 63%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.06 (d, J=3.2 Hz, 2H, ArH), 7.64–7.58 (m, 2H, ArH), 7.51 (t, J= 7.6 Hz, 2H, ArH), 7.40–7.38 (m, 2H, ArH), 7.28–7.26 (m, 1H, ArH), 4.36 (d, J=1.6 Hz, 1H, CH), 4.17 (d, J=1.6 Hz, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=192.8, 135.4, 135.3, 134.1, 132.5, 130.1, 128.9, 128.5, 127.8, 126.5, 122.5, 60.0, 59.4; HPLC (Chiralcel AD-H, 20 °C, 254 nm, 99/1 hexane/*i*-PrOH, 1.0 mL min^{-1}): t_{major}=28.27 min, t_{minor}= 24.86 min.

***trans*-(2*S*,3*R*)-Epoxy-3-(4-fluorophenyl)-1-phenylpropan-1-one:** Yield: 73%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.00 (d, J=8.4 Hz, 2H, ArH), 7.63 (t, J=7.6 Hz, 1H, ArH), 7.49 (t, J=8.0 Hz, 2H, ArH), 7.37–7.33 (m, 2H, ArH), 7.09 (t, J= 8.4 Hz, 2H, ArH), 4.25 (d, J=2.0 Hz, 1H, CH), 4.07 (d, J= 2.0 Hz, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=192.9, 164.4, 161.9, 135.4, 134.1, 131.3, 131.2, 128.9, 128.4, 127.6, 127.5, 116.0, 115.8, 60.9, 58.8; HPLC (Chiralcel OJ, 20 °C, 254 nm, 90/10 hexane/*i*-PrOH, 1.0 mL min^{-1}): t_{major}= 17.46 min, t_{minor}=20.65 min.

***trans*-(2*S*,3*R*)-Epoxy-3-(4-methylphenyl)-1-phenylpropan-1-one:** Yield: 52%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.00 (d, J=6.8 Hz, 2H, ArH), 7.61 (t, J=7.6 Hz, 1H, ArH), 7.49 (t, J=7.6 Hz, 2H, ArH), 7.28–7.21(m, 4H, ArH), 4.30 (d, J= 1.6 Hz, 1H, CH), 4.04 (d, J=1.6 Hz, 1H, CH), 2.38 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=193.2, 139.1, 136.0, 134.0, 132.4, 129.5, 128.9, 128.3, 125.8, 61.1, 59.5, 21.3; HPLC (Chiralcel OD-H, 20 °C, 254 nm, 98/2 hexane/*i*-PrOH, 1.0 mL min^{-1}): t_{major}=17.58 min, t_{minor}=18.78 min.

***trans*-(2*S*,3*R*)-Epoxy-3-phenyl-1-(4-chlorophenyl)-propan-1-one:** Yield: 40%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.97 (d, J=8.8 Hz, 2H, ArH), 7.47 (d, J=8.8 Hz, 2H, ArH), 7.44–7.35 (m, 5H, ArH), 4.25 (d, J=2.0 Hz, 1H, CH), 4.08 (d, J= 2.0 Hz, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=192.1, 140.6, 135.2, 133.7, 129.8, 129.3, 129.2, 128.8, 125.8, 61.1, 59.4. HPLC (Chiralcel OJ, 20 °C, 254 nm, 90/10 hexane/*i*-PrOH, 1.0 mL min^{-1}): t_{major}=23.02 min, t_{minor}=18.70 min.

***trans*-Epoxy-3-phenyl-1-(4-fluorophenyl)-propan-1-one:** Yield: 56%; ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.09–8.04 (m, 2H, ArH), 7.44–7.36 (m, 5H, ArH), 7.17 (t, J=8.4 Hz, 2H, ArH), 4.25 (d, J=1.6 Hz, 1H, CH), 4.08 (d, J=1.6 Hz, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=191.6, 167.5, 165.0, 135.3, 131.9, 131.8, 131.2, 131.1, 129.2, 128.8, 125.8, 116.3, 116.0, 61.1, 59.3; HPLC (Chiralcel AD-H, 20 °C, 254 nm, 90/10 hexane/*i*-PrOH, 1.0 mL min^{-1}): t_{major}=14.63 min, t_{minor}= 12.10 min.

***trans*-(2*S*,3*R*)-Epoxy-3-phenyl-1-(4-methylphenyl)-propan-1-one:** Yield: 61%; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.92 (d, J=8.0 Hz, 2H, ArH), 7.43–7.35 (m, 5H, ArH), 7.28 (d, J=8.4 Hz, 2H, ArH), 4.27 (d, J=2.0 Hz, 1H, CH), 4.07 (d, J=1.6 Hz, 1H, CH), 2.42 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=192.6, 145.1, 135.6, 133.0, 129.6, 129.0, 128.8, 128.8, 125.8, 60.9, 59.3, 21.8; HPLC (Chiralcel OB-H, 20 °C, 254 nm, 90/10 hexane/*i*-PrOH, 1.0 mL min^{-1}): t_{major}=20.90 min, t_{minor}=27.43 min.

***trans*-Epoxy-3-(4-fluorophenyl)-1-(4-methylphenyl)-propan-1-one:** Yield: 84%; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.91 (d, J=8.0 Hz, 2H, ArH), 7.36–7.28 (m, 4H, ArH), 7.11–7.07 (m, 2H, ArH), 4.23 (d, J=2.0 Hz, 1H, CH), 4.06 (d, J=1.6 Hz, 1H, CH), 2.43 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=192.4, 164.4, 162.0, 145.2, 133.0, 131.5, 131.4, 129.6, 128.5, 127.6, 127.5, 116.0, 115.7, 60.9, 58.7, 21.8; HPLC (Chiralcel OJ, 20 °C, 254 nm, 90/10 hexane/*i*-PrOH, 1.0 mL min^{-1}): t_{major}=17.46 min, t_{minor}= 20.65 min.

Acknowledgements

We are grateful for financial support from the Chinese Academy of Sciences and National Natural Science Foundation of China (20873166 and 21073210).

References

[1] a) M. Costas, M. P. Mehn, M. P. Jensen, L. Que Jr, *Chem. Rev.* **2004**, *104*, 939–986; b) E. Y. Tshuva, S. J. Lippard, *Chem. Rev.* **2004**, *104*, 987–1012; c) P. D. Oldenburg, L. Que Jr, *Catal. Today* **2006**, *117*, 15–21; d) L. Que Jr, W. B. Tolman, *Nature* **2008**, *455*, 333–340.

[2] a) C. Krebs, D. G. Fujimori, C. T. Walsh Jr, J. M. Bollinger, *Acc. Chem. Res.* **2007**, *40*, 484–492; b) C. Bolm, J. Legros, J. Le Paih, L. Zani, *Chem. Rev.* **2004**, *104*, 6217–6254.

[3] a) M. S. Chen, M. C. White, *Science* **2007**, *318*, 783–787; b) M. S. Chen, M. C. White, *Science* **2010**, *327*, 566–571; c) A. Company, L. Gómez, M. Güell, X. Ribas, J. M. Luis, L. Que Jr, M. Costas, *J. Am. Chem. Soc.* **2007**, *129*, 15766–15767; d) L. Gómez, I. Garcia-Bosch, A. Company, J. Benet-Buchholz, A. Polo, X. Sala, X. Ribas, M. Costas, *Angew. Chem.* **2009**, *121*, 5830–5833; *Angew. Chem. Int. Ed.* **2009**, *48*, 5720–5723.

[4] M. Costas, A. K. Tipton, K. Chen, D.-H. Jo, L. Que Jr, *J. Am. Chem. Soc.* **2001**, *123*, 6722–6723.

[5] M. C. White, A. G. Doyle, E. N. Jacobsen, *J. Am. Chem. Soc.* **2001**, *123*, 7194–7195.

[6] a) M. B. Francis, E. N. Jacobsen, *Angew. Chem.* **1999**, *111*, 987–991; *Angew. Chem. Int. Ed.* **1999**, *38*, 937–941; b) F. G. Gelalcha, B. Bitterlich, G. Anilkumar, M.-K. Tse, M. Beller, *Angew. Chem.* **2007**, *119*, 7431–7435; *Angew. Chem. Int. Ed.* **2007**, *46*, 7293–7296; c) F. G. Gelalcha, G. Anilkumar, M.-K. Tse, A. Brückner, M. Beller, *Chem. Eur. J.* **2008**, *14*, 7687–7698; d) C. Marchi-Delapierre, A. Jorge-Robin, A. Thibon, S.

Ménage, *Chem. Commun.* **2007**, 1166–1168; e) H.-L. Yeung, K.-C. Sham, C.-S. Tsang, T.-C. Lau, H.-L. Kwong, *Chem. Commun.* **2008**, 3801–3803.

[7] K. Suzuki, P. D. Oldenburg, L. Que Jr, *Angew. Chem.* **2008**, *120*, 1913–1915; *Angew. Chem. Int. Ed.* **2008**, *47*, 1887–1889.

[8] a) M. Wu, B. Wang, S. F. Wang, C. G. Xia, W. Sun, *Org. Lett.* **2009**, *11*, 3622–3625; b) W. Sun, H. W. Wang, C. G. Xia, J. W. Li, P. Q. Zhao, *Angew. Chem.* **2003**, *115*, 1072–1074; *Angew. Chem. Int. Ed.* **2003**, *42*, 1042–1044; c) Z. Li, Z. H. Tang, X. X. Hu, C. G. Xia, *Chem. Eur. J.* **2005**, *11*, 1210–1216; d) W. Sun, X. M. Wu, C. G. Xia, *Helv. Chim. Acta* **2007**, *90*, 623–626; e) Q. G. Cheng, F. G. Deng, C. G. Xia, W. Sun, *Tetrahedron: Asymmetry* **2008**, *19*, 2359–2362; f) M. Wu, B. Wang, S. F. Wang, W. Sun, *Chin. J. Mol. Catal.* **2010**, *24*, 235–239.

[9] L_1, **pmcp**, is *N*,*N*′-dimethyl-*N*,*N*′-bis[(*R*)-phenyl(2-pyridinylmethyl)]cyclohexane-1*R*,2*R*-diamine; L_2, **bpmcp**, is *N*,*N*′-dimethyl-*N*,*N*′-bis[(*R*)-4-*tert*-butylphenyl(2-pyridinylmethyl)]cyclohexane-1*R*,2*R*-diamine.

[10] a) J. R. Aldrich-Wright, R. S. Vagg, P. A. Williams, *Coord. Chem. Rev.* **1997**, *166*, 361–389; b) U. Knof, A. von Zelewsky, *Angew. Chem.* **1999**, *111*, 312–332; *Angew. Chem. Int. Ed.* **1999**, *38*, 302–322.

[11] Crystal data for complex **1**: $C_{34}H_{36}F_6FeN_4O_6S_2$, MW = 830.64, tetragonal, space group *P*4(3)2(1)2, a = 15.037(4), b = 15.037(4), c = 15.916(4) Å, β = 90°, V = 3598.8(15) Å^3, Z = 4, ρ_{calcd} = 1.533 Mg m^{-3}, T = 296(2) K, wavelength: 0.71073. Final R indices [I > 2σ(I)], *R1* = 0.0497, *wR2* = 0.0955; Reflections collected/unique: 27517/3536 [R_{int} = 0.1162]; GOF = 1.020. CCDC 778933 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

[12] a) A. Fujita, L. Que Jr, *Adv. Synth. Catal.* **2004**, *346*, 190–194; b) R. Mas-Ballesté, L. Que Jr, *J. Am. Chem. Soc.* **2007**, *129*, 15964–15972; c) I. Garcia-Bosch, X. Ribas, M. Costas, *Adv. Synth. Catal.* **2009**, *351*, 348–352.

[13] *Reaction conditions:* 0.25 mmol chalcone, 1.0 mL CH_3CN, 2 mol% of complex **2**, 1.1 equiv. of PhIO in 0.5 mL CH_3CN, T = room temperature, t = 8 h.

[14] For reviews, see: a) M. J. Porter, J. Skidmore, *Chem. Commun.* **2000**, 1215–1225; b) D. Díez, M. G. Núñez, A. B. Antón, P. García, R. F. Moro, N. M. Garrido, I. S. Marcos, P. Basabe, J. G. Urones, *Curr. Org. Synth.* **2008**, *5*, 186–216.

[15] Recent examples in asymmetric epoxidation of α,β-enones: a) T. Nemoto, T. Ohshima, K. Yamaguchi, M. Shibasaki, *J. Am. Chem. Soc.* **2001**, *123*, 2725–2732; b) J. X. Ye, Y. C. Wang, R. H. Liu, G. F. Zhang, Q. Zhang, J. P. Chen, X. M. Liang, *Chem. Commun.* **2003**, 2714–2715; c) X. J. Lu, Y. Liu, B. F. Sun, B. Cindric, L. Deng, *J. Am. Chem. Soc.* **2008**, *130*, 8134–8135; d) T. Ooi, D. Ohara, M. Tamura, K. Maruoka, *J. Am. Chem. Soc.* **2004**, *126*, 6844–6845; e) X. W. Wang, L. Shi, M. X. Li, K. L. Ding, *Angew. Chem.* **2005**, *117*, 6520–6524; *Angew. Chem. Int. Ed.* **2005**, *44*, 6362–6366; f) X. W. Wang, C. M. Reisinger, B. List, *J. Am. Chem. Soc.* **2008**, *130*, 6070–6071; g) C. M. Reisinger, X. W. Wang, B. List, *Angew. Chem.* **2008**, *120*, 8232–8235; *Angew. Chem. Int. Ed.* **2008**, *47*, 8112–8115; h) J. Lu, Y. H. Xu, F. Liu, T.-P. Loh, *Tetrahedron Lett.* **2008**, *49*, 6007–6008; i) Y. W. Li, X. Y. Liu, Y. Q. Yang, G. Zhao, *J. Org. Chem.* **2007**, *72*, 288–291; j) L. He, W. J. Liu, L. Ren, T. Lei, L. Z Gong, *Adv. Synth. Catal.* **2010**, *352*, 1123–1127.

[16] For recent biomimetic Mn-catalyzed asymmetric epoxidation examples, see: a) A. Murphy, G. Dubois, T. D. P. Stack, *J. Am. Chem. Soc.* **2003**, *125*, 5250–5251; b) A. Murphy, A. Pace, T. P. D. Stack, *Org. Lett.* **2004**, *6*, 3119–3122; c) A. Murphy, T. D. P. Stack, *J. Mol. Catal. A: Chem.* **2006**, *251*, 78–88; d) L. Gómez, I. Garcia-Bosch, A. Company, X. Sala, X. Fontrodona, X. Ribas, M. Costas, *Dalton Trans.* **2007**, 5539–5545; e) G. Guillemot, M. Neuburger, A. Pfaltz, *Chem. Eur. J.* **2007**, *13*, 8960–8970; f) R. V. Ottenbacher, K. P. Bryliakov, E. P. Talsi, *Inorg. Chem.* **2010**, *49*, 8620–8628; g) R. V. Ottenbacher, K. P. Bryliakov, E. P. Talsi, *Adv. Synth. Catal.* **2011**, *353*, 885–889.

[17] a) C. Kim, K. Chen, J. Kim, L. Que Jr, *J. Am. Chem. Soc.* **1997**, *119*, 5964–5965; b) N. A. Vermeulen, M. S. Chen, M. C. White, *Tetrahedron* **2009**, *65*, 3078–3084.

[18] a) L. Que Jr, *Acc. Chem. Res.* **2007**, *40*, 493–500; b) W. Nam, *Acc. Chem. Res.* **2007**, *40*, 522–531.

[19] a) A. Company, I. Prat, J. R. Frisch, D. R. Mas-Ballesté, M. Güell, G. Juhász, X. Ribas, D. E. Münck, J. M. Luis, L. Que Jr, M. Costas, *Chem. Eur. J.* **2011**, *17*, 1622–1634; b) M. S. Seo, J.-H. In, S. O. Kim, N. Y. Oh, J. Hong, J. Kim, L. Que Jr, W. Nam, *Angew. Chem.* **2004**, *116*, 2471–2474; *Angew. Chem. Int. Ed.* **2004**, *43*, 2417–2420; c) J. Yoon, S. A. Wilson, Y. K. Jang, M. S. Seo, K. Nehru, B. Hedman, K. O. Hodgson, E. Bill, E. I. Solomon, W. Nam, *Angew. Chem.* **2009**, *121*, 1283–1286; *Angew. Chem. Int. Ed.* **2009**, *48*, 1257–1260.

[20] a) K. Chen, L. Que Jr, *J. Am. Chem. Soc.* **2001**, *123*, 6327–6337; b) K. Chen, M. Costas, J. Kim, A. K. Tipton, L. Que Jr, *J. Am. Chem. Soc.* **2002**, *124*, 3026–3035; c) K. Chen, M. Costas, L. Que Jr, *J. Chem. Soc. Dalton Trans.* **2002**, 672–679.

[21] X. P. Shan, L. Que Jr, *Chem. Commun.* **2008**, 2209–2211.

[22] a) A. Company, Y. Feng, M. Güell, X. Ribas, J. M. Luis, L. Que Jr, M. Costas, *Chem. Eur. J.* **2009**, *15*, 3359–3362; b) O. V. Makhlynets, E. V. Rybak-Akimova, *Chem. Eur. J.* **2010**, *16*, 13995–14006.

[23] J. V. Sinisterra, A. Garcia-Raso, J. A. Cabello, J. M. Marinas, *Synthesis* **1984**, 502–504.

