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Highly enantioselective epoxidation of olefins by H_2O_2 catalyzed by a non-heme Fe(II) catalyst of a chiral tetradentate ligand

A new chiral tetradentate nitrogen-donor ligand and Fe(II) complexes of this ligand have been synthesised. The resultant chiral iron complexes function as enantioselective catalysts for the epoxidation of alkenes by hydrogen peroxide.

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[View Journal](#) | [View Issue](#) Cite this: *Dalton Trans.*, 2019, **48**, 6123Highly enantioselective epoxidation of olefins by H₂O₂ catalyzed by a non-heme Fe(II) catalyst of a chiral tetradentate ligand†Mainak Mitra, ^{‡a} Olaf Cusso,^b Satish S. Bhat, ^a Mingzhe Sun,^a Marco Cianfanelli,^b Miquel Costas ^{*b} and Ebbe Nordlander ^{*a}

The chiral tetradentate N4-donor ligand, 1-methyl-2-(((S)-2-((S)-1-(1-methylbenzimidazol-2-yl methyl) pyrrolidin-2-yl)pyrrolidin-1-yl)methyl) benzimidazole (*S,S*-PDB^zL), based on a chiral dipyrrolidine backbone, has been synthesized and its corresponding Fe(II) complex has been prepared and characterized. The X-ray structure of the complex reveals that the Fe(II) ion is in a distorted octahedral coordination environment with two *cis*-oriented coordination sites occupied by (labile) triflate anions. The ability of the iron complex to catalyze asymmetric epoxidation reactions of olefins with H₂O₂ was investigated, using 2-cyclohexen-1-one, 2-cyclopenten-1-one, *cis*- β -methylstyrene, isophorone, chalcones and tetralones as substrates. Different carboxylic acids were used as additives to enhance yields and enantioselectivities, and 2-ethylhexanoic acid was found to give the best results. The catalysis results indicate that the Fe(II) complex is capable of effecting comparatively high enantioselectivities (>80%) in the epoxidation reactions.

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Introduction

Optically active (chiral) epoxides are widely used in organic synthesis and industry as intermediates and building blocks for the synthesis of drugs and agrochemicals.¹ Amongst various methods developed over the years to synthesize chiral epoxides,¹ catalytic asymmetric epoxidation of olefins has proven to be a very useful technique that is employed both in fine chemical and industrial syntheses. Since the pioneering work by Sharpless and coworkers in the 1980s,² there have been numerous efforts to develop efficient catalytic systems,^{1a-c,3,4} including chiral metal complexes^{5,6} and organocatalysts,^{7,8} for such transformations. The development of environmentally benign and cheap catalysts and oxidants with wide ranges of applications remains a great challenge to synthetic chemists.⁹ With the growing demand for green and sustainable chemistry, the use of iron-based catalysts employing H₂O₂ as an oxidant has been an attractive research area

because of the low cost, low toxicity and high abundance of iron in nature.¹⁰ Collman *et al.*¹¹ reported in 1999 the first enantioselective epoxidation of styrene derivatives catalysed by iron-porphyrin complexes with iodosobenzene as an oxidant. Beller and co-workers¹² have reported a methodology for the asymmetric epoxidation of stilbene derivatives using an *in situ* iron-based catalyst, giving up to 97% ee. Several non-heme iron-catalysed asymmetric epoxidation reactions are reported with various olefin substrates giving moderate to good yields and enantioselectivities.^{13–18}

The factors that indirectly control the yield and enantioselectivity in iron-catalysed asymmetric epoxidation need to be thoroughly investigated. The presence of catalytic amounts of a carboxylic acid has been found to enhance both the yield and enantioselectivity in epoxide formation.^{14b,16,18} A mechanistic scenario that has been proposed by Que and co-workers for the iron-catalysed epoxidation of alkenes with H₂O₂/acetic acid involves the formation of a carboxylate-Fe(V) species as the active oxidant *via* acetic acid-assisted heterolytic O–O bond cleavage of the hydro-peroxide ligand in an Fe(III)(OOH) (HOOCCH₃) precursor (Scheme 1).¹⁹ Spectroscopic evidence for the formation of a formal Fe(V)-oxo-carboxylato species (A in Scheme 1) has been gained^{20,21a} but its exact electronic structure is a matter of debate.^{21,22}

A recent computational study suggests that the carboxylic acid, owing to its non-innocent redox nature, can be oxidized by one electron and reduce the Fe ion to form a Fe(IV)-carboxyl radical intermediate²³ similar to the cytochrome P450 compound I

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Scheme 1 A proposed mechanism for the enhancement of olefin epoxidation catalyzed by a non-heme Fe(II) complex via the addition of a carboxylic acid, RCO_2H .¹⁹

intermediate. In addition, the possible implication of a ferric peroxycarboxylate intermediate has been proposed²⁴ and debated.²⁵

Electronic factors imposed by the ligand on the iron ion play an important role in the activation of H_2O_2 and O-atom transfer, as observed in the epoxidation of different olefin substrates catalysed by a series of $[\text{Fe}^{\text{II}}(\text{PDP})(\text{CF}_3\text{SO}_3)_2]$ complexes ($\text{PDP} = 2-\{[(S)-2-[(S)-1-(\text{pyridyl}-2\text{-ylmethyl})\text{pyrrolidin-2-yl}] \text{pyrrolidin-1-yl}]\text{methyl}\}\text{pyridine}$),²⁶ where the pyridine rings are substituted with electron withdrawing or donating moieties (Me_2N , MeO , Me , H , Cl , CO_2Et) at the *meta* and *para*-positions, Fig. 1, giving up to 99% yield and 99% enantioselectivity.¹⁶ It was proposed that electron-rich ligands decrease the electrophilicity of the Fe-oxo entity, favouring the transition state to be shifted towards a more product-like complex, while elec-

tron-deficient ligands increase the electrophilicity of the Fe-oxo unit, making it more indiscriminate and less stereoselective.¹⁶

In a recent study, the effects of different side arms attached to the chiral (*S,S*)-2,2'-bispyrrolidine backbone on the Fe(II)-catalyzed asymmetric epoxidation of olefins were investigated, and the study concluded that complexes containing (*N*-methyl) benzimidazole and electron rich pyridine or bulky pyridine resulted in excellent yields and enantioselectivities (Fig. 1).¹⁸ We have previously observed that an (*N*-methyl)benzimidazolyl-containing ligand can enhance the catalytic reactivity of an Fe(II) complex in stereospecific C-H hydroxylation reactions,²⁷ and were therefore interested in investigating the influence of a chiral ligand containing (*N*-methyl)benzimidazolyl donor moieties on Fe(II)-catalyzed asymmetric epoxidation. For this purpose we have employed the tetradentate chiral ligand, S,S -^{PDBz}L (1-methyl-2-((*S*)-2-[(*S*)-1-(1-methylbenzimidazol-2-ylmethyl)pyrrolidin-2-yl]pyrrolidin-1-yl)methyl)benzimidazole) (Fig. 1), where the two (*N*-methyl)benzimidazolylmethyl arms are attached to the two nitrogen atoms of the chiral (*S,S*)-2,2'-bispyrrolidine backbone. Notably, Sun and co-workers reported high enantioselectivity (up to 96% ee) by the use of a Mn(II)-catalyst incorporating (*R,R*)-2,2'-bispyrrolidine and (*N*-methyl)benzimidazole into the ligand framework.²⁸ Herein we report the synthesis and characterization of a non-heme Fe(II)-complex based on the ligand S,S -^{PDBz}L and the results obtained on alkene epoxidation catalysed by this complex.

Results and discussion

Synthesis and characterization of the ligand and metal complex

The chiral ligand S,S -^{PDBz}L was synthesized by the reaction of one eq. of (*S,S*)-2,2'-bispyrrolidine tartrate with two eq. of 2-(chloromethyl)-1-methylbenzimidazole²⁹ in the presence of a base (NaOH), and was characterized by ¹H NMR and ¹³C NMR spectroscopy as well as high resolution mass spectrometry (cf. Experimental section).

The reaction of equimolar amounts of S,S -^{PDBz}L and $[\text{Fe}^{\text{II}}(\text{CH}_3\text{CN})_2(\text{CF}_3\text{SO}_3)_2]$ in THF under an inert atmosphere gave the metal complex $[\text{Fe}^{\text{II}}(S,S\text{-}^{\text{PDBz}}\text{L})(\text{CF}_3\text{SO}_3)_2]$ (**1**^{OTf}) as a light yellow solid (Scheme 2, cf. Experimental section). The analogous acetonitrile derivative $[\text{Fe}^{\text{II}}(S,S\text{-}^{\text{PDBz}}\text{L})(\text{CH}_3\text{CN})_2]$ (**1**^{SbF6}) was prepared in two steps: the initial reaction of

Fig. 1 Structures of different Fe(II)-complexes based on the chiral (*S,S*)-2,2'-bispyrrolidine backbone employed for asymmetric epoxidation.¹⁶

Scheme 2 Synthesis of the metal complex $[\text{Fe}^{\text{II}}(S,S\text{-}^{\text{PDBz}}\text{L})(\text{CF}_3\text{SO}_3)_2]$ (**1**^{OTf}).

one eq. S,S - $PDBz$ L with one equivalent of $FeCl_2$ in MeCN to afford $[Fe^{II}(S,S\text{-}PDBzL)Cl_2]$, followed by the reaction of two eq. $AgSbF_6$ with one eq. of $[Fe^{II}(S,S\text{-}PDBzL)Cl_2]$ in CH_3CN to form the desired complex, 1^{SbF_6} as a red microcrystalline solid.

Complexes 1^{OTf} and 1^{SbF_6} were characterized by high resolution mass spectrometry (HRMS). The HRMS of 1^{OTf} in CH_3CN showed a prominent mass peak at m/z 242.1042 corresponding to the formulation $[Fe^{II}(S,S\text{-}PDBzL)]^{2+}$ (*i.e.* $z = 2$, calc. 242.1014) and at m/z 633.1517 corresponding to the formulation of $[Fe^{II}(S,S\text{-}PDBzL)(CF_3SO_3)]^+$ (calc. 633.1558) (Fig. S1–S3, ESI†). The HRMS of complex 1^{SbF_6} in MeCN also showed prominent mass peaks at m/z 242.1022 and 719.0956 corresponding to the formulations of $[Fe^{II}(S,S\text{-}PDBzL)]^{2+}$ (calc. 242.1014) and $[Fe^{II}(S,S\text{-}PDBzL)(SbF_6)]^+$ (calc. 719.0980), respectively (Fig. S4 and S5, ESI†).

The 1H -NMR spectra of 1^{OTf} and 1^{SbF_6} were recorded in CD_3CN . The spectral window exhibited by both complexes ranges from -20 to 140 ppm, which is indicative of a high spin $Fe(II)$ complex (Fig. S6 and S7, ESI†). The number of resonances and relative integration are consistent with a C_2 -symmetric complex,¹⁸ as shown by its crystal structure (*vide infra*).

Crystal and molecular structure of complex 1^{OTf}

The solid state structure of complex 1^{OTf} was confirmed by X-ray crystallography. The details of the structure determination are found in the Experimental Section and selected bond distances and bond angles are listed in Table 1. The molecular structure (Fig. 2) shows that the iron ion adopts a distorted octahedral coordination geometry. Four coordination sites are occupied by the nitrogen atoms of the tetradentate S,S - $PDBz$ L ligand while the remaining two *cis*-sites are occupied by the oxygen atoms of the triflate anions. The two (*N*-methyl)benzimidazole rings remain above and below the plane containing the iron, the two nitrogens of the S,S -bis-pyrrolidine backbone and the two oxygen atoms of the triflate anions, and are almost perpendicular with respect to each other. The Fe–N bond distances range from 2.15 to 2.25 Å and the Fe–O bond

Fig. 2 A Mercury plot of the molecular structure of 1^{OTf} , showing the atom numbering scheme. The thermal ellipsoids are drawn with 30% probability and the hydrogen atoms are omitted for clarity.

distances range from 2.12 to 2.17 Å, which are in agreement with a high spin $Fe(II)$ ion.³⁰ The bulky (*N*-methyl)benzimidazolyl moieties introduce steric strain making the O–Fe–O angle smaller ($96.7(2)^\circ$) relative to the corresponding angle in $[Fe^{II}(MeOPDP)(CF_3SO_3)_2]$ ($108.47(5)^\circ$).¹⁶

Catalytic asymmetric epoxidation studies

Relatively simple cyclic enones have been generally less explored as substrates for asymmetric epoxidation than α,β -unsaturated aromatic ketones. Therefore, this study focuses on using the challenging substrate 2-cyclohexene-1-one for asymmetric epoxidation. In a typical catalytic experiment, H_2O_2 was delivered using a syringe pump to a stirred solution of CH_3CN containing the Fe catalyst, 1^{OTf} , and the substrate (Scheme 3, *cf.* Experimental section for detailed catalytic conditions). The catalytic reactions were carried out in air and at a low temperature ($-30^\circ C$). As mentioned above, previous studies have shown that the presence of a carboxylic acid enhances the efficiency of the catalyst, and the choice of carboxylic acid plays an important role in tuning the efficiency and selectivity of the asymmetric epoxidation reactions. In recent studies, Bryliakov, Talsi and co-workers showed that racemic 2-ethylhexanoic acid (2-eha) resulted in high enantiomeric excess (ee) and relative good yields in iron-catalyzed asymmetric epoxidation reactions.^{13b} Therefore, the study of epoxidation of 2-cyclohexene-1-one was performed using 2-eha.

Scheme 3 Schematic depiction of the epoxidation reaction of 2-cyclohexene-1-one by 1^{OTf} using H_2O_2 , with 2-ethylhexanoic acid as an additive.

Table 1 Selected bond distances (Å) and bond angles ($^\circ$) in complex 1^{OTf}

Fe(1)–N(1)	2.148(4)
Fe(1)–O(1)	2.115(6)
Fe(1)–N(3)	2.249(6)
Fe(1)–N(4)	2.237(6)
Fe(1)–O(4)	2.168(6)
Fe(1)–N(5)	2.149(5)
N(1)–Fe(1)–O(1)	96.8(2)
N(1)–Fe(1)–N(3)	76.5(2)
N(1)–Fe(1)–N(4)	98.1(2)
N(1)–Fe(1)–O(4)	90.0(2)
N(1)–Fe(1)–N(5)	170.8(2)
O(1)–Fe(1)–N(3)	91.1(2)
O(1)–Fe(1)–N(4)	160.6(2)
O(1)–Fe(1)–O(4)	96.7(2)
O(1)–Fe(1)–N(5)	87.5(2)
N(3)–Fe(1)–N(4)	80.3(2)
N(3)–Fe(1)–O(4)	165.1(2)
N(3)–Fe(1)–N(5)	95.4(2)
N(4)–Fe(1)–N(5)	76.1(2)
O(4)–Fe(1)–N(5)	97.6(2)

Table 2 Catalytic epoxidation of 2-cyclohexen-1-one by complex **1**^{OTf}^a

Entry	Catalyst (mol%)	CA ^b (eq.)	Eq. of H ₂ O ₂	Conversion of substrate (%)	Yield of epoxides (%)	ee ^c (%)
1	1 ^{OTf} (4)	2-eha (3)	2	43	16	89
2	1 ^{OTf} (4)	2-eha (5)	2	52	10	86
3	1 ^{OTf} (4)	2-eha (10)	2	64	13	87
4	1 ^{OTf} (2)	2-eha (10)	2	30	10	87
5	1 ^{OTf} (8)	2-eha (10)	2	66	11	84
6	1 ^{OTf} (4)	2-eha (10)	1.3	55	11	87
7	1 ^{OTf} (4)	2-eha (10)	1.6	59	12	87
8	1 ^{OTf} (4)	2-eha (10)	3	68	7	74
9	1 ^{SbF₆} (4)	2-eha (10)	2	64	13	86
10	1 ^{SbF₆} (4)	(CH ₃) ₃ CO ₂ H (10)	2	72	2	60
11	1 ^{SbF₆} (4)	S-Ibuprofen (10)	2	2	1	58

^a Reaction conditions: *cf.* Experimental section. ^b CA = carboxylic acid. ^c Enantiomeric excess.

The complex **1**^{OTf} (4 mol%) oxidized 2-cyclohexen-1-one to form the epoxide with a low yield (16%) in the presence of H₂O₂ (2 eq. w.r.t. substrate) and 2-eha (3 eq. w.r.t. substrate; Scheme 3), although the conversion of the substrate into oxidized products was 43% (based on the oxidant). The ee value obtained was 89%. An increase of the carboxylic acid loading did not lead to any significant change in the epoxide yield or the ee value (with 5 eq. of acid the yield of epoxides was 10% and ee was 86% and with 10 eq. of acid the yield of epoxides was 13% and ee was 87%; entries 1–3, Table 2). The effect of different amount of catalyst loading on the substrate conversion, yield of epoxides and ee value was examined. In all cases, the amounts of H₂O₂ (2 eq. w.r.t. substrate) and carboxylic acid (10 eq. w.r.t. substrate) were kept fixed. Changing the catalyst loading from 4 mol% to 2 mol% resulted in a decrease in the conversion of the substrate into oxidized products (30%) and the yield of epoxides (10%), while maintaining a high ee value (87%; entry 4, Table 2). Increasing the catalyst loading from 4 mol% to 8 mol% (or 10 mol%) increased the conversion of the substrate into products (66 and 67% for 8 and 10 mol% catalyst loading, respectively), but the epoxide yield was more or less similar (entry 5, Table 2). Finally, the amount of H₂O₂ was varied while the amounts of the catalyst (4 mol%) and carboxylic acid (10 eq. w.r.t. substrate) were kept fixed. The addition of 1.3 eq. of H₂O₂ resulted in a conversion of 55% with a yield of epoxides of 11% and an ee value of 84%, while the addition of 3 eq. of H₂O₂ resulted in a conversion of 68% but poor yield of epoxides (7%) and lowering of the ee value (74%; entries 6–8, Table 2).

Product analysis by GC and GC-MS spectrometry of the reaction of **1**^{OTf} with cyclohexenone in the presence of H₂O₂ (2 eq. w.r.t. substrate) and 2-eha or acetic acid (10 eq. w.r.t. substrate in each case) revealed that in addition to the desired (chiral) epoxide, small amounts of a number of oxidized products were formed, *viz.* 3-hydroxycyclohexanone, cyclohexene-1,4-dione, and 4-hydroxycyclohexenone when eha was used (in addition to small amounts of lactones from the oxidation of eha). When acetic acid was used, the minor side products were cyclohexene-1,4-dione, 4-hydroxycyclohexenone and 2,3-hydroxycyclohexanone (*cf.* ESI, Fig. S10–S13†). The relatively low yields of these side products cannot explain the overall low

yield in the reactions (Table 2). No ring-opened products were detected, but it is possible that ring-opening occurs and that further substrate degradation leads to (oxidized) products of low molecular weight that could not be identified.

As expected, complex **1**^{SbF₆} exhibited the same behaviour as **1**^{OTf} (entries 3 and 9, Table 2). On changing the carboxylic acid, both the yields and enantioselectivities were diminished (2% yield and 60% ee for pivalic acid and 1% yield and 58% ee for S-Ibuprofen; entries 9–11, Table 2).

Complex **1**^{OTf} was further investigated in the oxidation of 2-cyclopenten-1-one where it provided a low conversion of the substrate (52%) with a very low yield of the epoxide (4%) and moderate enantioselectivity (ee 76%).

cis-β-Methylstyrene was also employed as a substrate and the conditions for catalysis were used as reported earlier,¹⁶ in order to enable direct comparison of **1**^{OTf} with related Fe(II) complexes. Under catalytic conditions (*cf.* Experimental section for details), complex **1**^{OTf} oxidized *cis*-β-methylstyrene to form the epoxide with 60% yield and an ee of 43% (Table 3). Under the same conditions, the catalyst [Fe^{II}(^HPDP)(CF₃SO₃)₂] (**1**) (^HPDP = 2-((S)-2-[(S)-1-(pyridyl-2-ylmethyl)pyrrolidin-2-yl]pyrrolidin-1-yl)methylpyridine) and [Fe^{II}(^{Me2N}PDP)(CF₃SO₃)₂] (**Me2N1**) (^{Me2N}PDP is the modified PDP ligand where the *para*-positions of the two pyridyl rings are occupied by Me₂N groups, *cf.* Fig. 1) provided an epoxide yield of 26% with an ee of 19% and 87% with an ee of 62%, respectively.¹⁶

Very poor epoxidation yield and enantioselectivity were obtained for other substrates such as *trans*-β-methylstyrene and 4-chloro-α-methylstyrene (Table S1†). For isophorone a very good enantioselectivity of 91% was obtained but the epoxide yield was unfortunately poor (12%); attempts to optimise the epoxide yield proved futile (Table S2†).

In organic synthesis, the trisubstituted cyclic α,β-epoxyketones are resourceful intermediates because of the presence of a chiral quaternary carbon center.³¹ The development of an iron catalyst for the enantioselective construction of such quaternary carbon centers coordinated to an oxygen atom is still highly attractive.³² Using tetralone derivatives as substrates for this type of reaction, we obtained good yields of trisubstituted α,β-epoxyketones with quaternary carbon centers with excellent enantioselectivities (up to 97%, Table 4).

Table 3 Catalytic epoxidation of *cis*- β -methylstyrene by complex **1**^a

Entry	Catalyst (mol%)	CA ^b (mol%)	Temp. (°C)	Eq. of H ₂ O ₂	Conversion of substrate (%)	Yield of epoxides (%)	ee ^c (%)
1	1 ^{OTf} (1)	AcOH (3)	−30	1.6	41	27	43
2	1 ^{OTf} (1)	AcOH(1.4)	−30	1.6	84	60	43
3	1 ^{OTf} (2)	AcOH(1.4)	−30	1.6	99	52	46
4	1 ^{OTf} (2)	AcOH(1.4)	0	1.6	99	49	40
5	1 ^{OTf} (2)	2-eha (1.4)	−30	1.6	100	61	61
6	1 ^{OTf} (2)	2-eha (1.4)	0	1.6	100	60	55

^a Reaction conditions: Experimental section. ^b Carboxylic acids. ^c Enantiomeric excess determined by GC.

Table 4 Enantioselective epoxidation of trisubstituted enones^a

Entry	R-group	CA ^b (mol%)	Yield ^c (%)	ee ^d (%)
1	Ph	2-eha (1.4)	71	93
2	<i>p</i> -Me-C ₆ H ₄	2-eha (1.4)	76	97
3	<i>p</i> -Cl-C ₆ H ₄	2-eha (1.4)	54	93
4	<i>p</i> -t-Bu	2-eha (1.4)	98	97

^a Reaction conditions: Experimental section. ^b Carboxylic acids. ^c Isolated product yield. ^d Enantiomeric excess determined by HPLC analysis.

Table 5 Enantioselective epoxidation of chalcone derivatives^a

Entry	R ¹	R ²	CA ^b (mol%)	Yield ^c (%)	ee ^d (%)
1	Ph	Ph	2-eha (1.4)	76	97
2	Ph	Ph	AcOH (1.4)	71	91
3	<i>p</i> -Me-C ₆ H ₄	Ph	2-eha (1.4)	56	97
4	<i>p</i> -Cl-C ₆ H ₄	Ph	2-eha (1.4)	84	97
5	Ph	<i>p</i> -CF ₃ -C ₆ H ₄	2-eha (1.4)	66	94

^a Reaction conditions: Experimental section. ^b Carboxylic acids. ^c Isolated product yield. ^d Enantiomeric excess determined by HPLC analysis.

Furthermore, the epoxidation of α,β -unsaturated ketones was evaluated. For chalcone and its derivatives, a higher epoxide yield and ee (up to 97%) were obtained with 2-eha than AcOH as the auxiliary carboxylic acid (Table 5, entries 1–5). Having electron withdrawing or donating groups at the *para* position of the substrate phenyl ring did not affect the

enantioselectivity. As expected, the complex with the corresponding *R,R*-^{PDBz}L ligand (with an (*R,R*)-2,2'-bispyrrolidine backbone) gave 84% chalcone epoxide formation with an ee value of 96% under catalytic conditions similar to those of complex **1**^{OTf} (entry 1, Table 2) but with the opposite absolute configuration.

Conclusions

A tetradentate N4 ligand *S,S*-^{PDBz}L, with an *S,S*-dipyrrolidine chiral backbone, has been synthesized. The corresponding Fe(II) complexes, [Fe^{II}(*S,S*-^{PDBz}L)(CF₃SO₃)₂] (**1**^{OTf}) and [Fe^{II}(*S,S*-^{PDBz}L)(CH₃CN)₂](SbF₆)₂ (**1**^{SbF6}), were synthesized and characterized. The complex **1**^{OTf} exhibited high enantioselectivity (ee > 80%) in the epoxidation of the cyclic olefin 2-cyclohexen-1-one, albeit with low yields of the chiral epoxides (10–15%). It has previously been shown that while the complex [Fe^{II}(^{Me2N}PDP)(CF₃SO₃)₂] provided a poor yield (12%) and moderate enantioselectivity (ee 76%) in the epoxidation of 2-cyclohexen-1-one, the related complex [Fe^{II}(^{MeO}PDP)(CF₃SO₃)₂] (Fig. 1) showed excellent yield (99%) and high enantioselectivity (ee 84%) under similar conditions. This difference was attributed to the rapid deactivation of the former catalyst during the course of oxidation of the substrate, a phenomenon that takes place when the substrate oxidizes slowly under the reaction conditions. The similar reactivities of **1**^{OTf} and [Fe^{II}(^{Me2N}PDP)(CF₃SO₃)₂] towards the substrate 2-cyclohexen-1-one might therefore be due to similar rapid deactivation of the Fe-catalyst. With *cis*- β -methylstyrene, **1**^{OTf} provided moderate yield (60%) and lower enantioselectivity (ee 41%). In the case of tetralone and chalcones excellent epoxide yield and enantioselectivity (up to 97%) were obtained. The relative orientation of the bulky (*N*-methyl)benzimidazole groups may also provide excessive steric constraints against the approach of the incoming substrate to the reactive metal oxo species (*cf.* Scheme 1), causing a poor yield of the epoxides and unwanted side products. Further studies on the catalytic properties of **1**^{OTf} and **1**^{SbF6} to explore a wider range of substrates are warranted.

Experimental section

Reagents and materials

Reagents and solvents were of at least 99% purity and used as received without any further purification. All reagents and solvents were purchased from Sigma Aldrich or Fisher Scientific. Dichloromethane and acetonitrile were dried by distillation from CaH_2 ; diethyl ether was dried by distillation from Na/benzophenone. The starting material 2-(chloromethyl)-1-methylbenzimidazole was synthesized according to a literature procedure.²⁹

Instrumentation

Infrared spectra were recorded on a Nicolet Avatar 360 FTIR spectrometer. UV-Visible spectroscopy was performed in a 1 cm quartz cell using an Agilent Technology 8453 UV-Vis spectrophotometer equipped with a diode-array detector. NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer in CDCl_3 or CD_3CN solvent under standard conditions and were referenced to the residual proton signal of the solvent. Elemental analysis was performed on a 4.1 Vario EL 3 elemental analyzer from Elementar. The ESI-MS experiments were performed with a Bruker Esquire 6000 LC/MS chromatograph, using acetonitrile as a mobile phase. The product analyses after catalysis experiments were carried out on an Agilent Technology 7820A gas chromatograph equipped with a 16-sample automatic liquid sampler, flame ionization detector and EzChrom Elite Compact software.

Syntheses

Synthesis of 1-methyl-2-((S)-2-[(S)-1-(1-methylbenzimidazol-2-ylmethyl)pyrrolidin-2-yl]pyrrolidin-1-yl)methylbenzimidazole (S,S - PDBzL). A 100 ml round bottom flask was charged with (S,S)-2,2'-bispyrrolidine tartrate (0.4 g, 1.38 mmol, 1 equiv.) in CH_2Cl_2 (15 ml). To this stirring solution, 2-(chloromethyl)-1-methylbenzimidazole (0.573 g, 3.174 mmol, 2.3 equiv.) was added. Then, 5.0 ml of a 1 M NaOH solution was added. After 72 h of stirring at room temperature, the reaction mixture was diluted with 30 ml 1 M NaOH solution. The aqueous layer was extracted with 3×15 ml CH_2Cl_2 and the organic part was collected, dried over Na_2SO_4 and concentrated under vacuum to obtain the crude product. The crude ligand was then passed through a column packed with silica gel and eluted with 5% CH_3OH :2% 1 M NaOH:82% CH_2Cl_2 :11% petroleum ether. The collected fractions were combined, washed with 1 M NaOH solution, dried over Na_2SO_4 and the solvent was evaporated to obtain the ligand as a pale orange solid. Yield: 0.366 g (63.2%). HRMS: 429.2760 $[\text{M} + \text{H}]^+$, calc. 429.2761. ^1H -NMR (400 MHz, CDCl_3) δ (ppm): 7.72 (m, 2H), 7.33–7.21 (m, 6H), 4.23 (d, 2H), 3.80 (s, 6H), 3.66 (d, 2H), 2.80 (dt, 4H), 2.32 (m, 2H), 1.79 (m, 4H), 1.68 (m, 4H). ^{13}C -NMR (100 MHz, CDCl_3) δ (ppm): 152.4, 142.2, 136.1, 122.4, 121.8, 119.6, 109.0, 65.2, 55.6, 52.5, 29.9, 26.2, 24.0.

Synthesis of $[\text{Fe}^{\text{II}}(\text{S},S\text{-PDBzL})(\text{CF}_3\text{SO}_3)_2]$ (1^{OFF}). This reaction was performed inside a dry atmosphere box.

$[\text{Fe}^{\text{II}}(\text{CH}_3\text{CN})_2(\text{CF}_3\text{SO}_3)_2]$ (166.8 mg, 0.38 mmol) was dissolved in 1 ml THF and added drop-wise to a stirring solution of $S,S\text{-PDBzL}$ (163.2 mg, 0.38 mmol) in THF (1 ml). A yellow precipitate appeared upon the addition of the Fe salt to the ligand solution. After stirring for about 1 h, the yellow precipitate was filtered off and dried under vacuum. The resultant solid was dissolved in 3 ml CH_2Cl_2 and filtered through a Celite pad. The resulting filtrate was removed under vacuum to afford a light yellow microcrystalline product. Yield: 225.8 mg (76%). HRMS: (m/z) 242.1042 $[\text{Fe}^{\text{II}}(\text{S},S\text{-PDBzL})]^{2+}$ ($z = 2$), calc. 242.1014; 633.1517 $[\text{Fe}^{\text{II}}(\text{S},S\text{-PDBzL})(\text{CF}_3\text{SO}_3)]^+$ ($z = 1$), calc. 633.1558; elemental analysis $\text{C}_{28}\text{H}_{32}\text{N}_6\text{O}_6\text{F}_6\text{S}_2\text{Fe}$ (MW = 782.554 g mol^{-1}) calc. (%) C 42.97, H 4.12, N 10.74; found (%) C 43.16, H 4.01, N 10.29; FT-IR (ATR) ν (cm^{-1}) 3011, 2956, 1456, 1304, 1214, 1157, 1034, 752, 634, 513, 429.

Synthesis of $[\text{Fe}^{\text{II}}(\text{S},S\text{-PDBzL})(\text{CH}_3\text{CN})_2](\text{SbF}_6)_2$ (1^{SbF_6}). The ligand $S,S\text{-PDBzL}$ (108.9 mg, 0.254 mmol) was dissolved in 1.5 ml CH_3CN . A total of 32 mg FeCl_2 (32.3 mg, 0.254 mmol) was added into the stirring solution. A yellow precipitate appeared within a few seconds of stirring. After 4 h of stirring, the solvent of the reaction mixture was removed under vacuum and the resultant solid was washed with CH_3CN and ether, and dried under an N_2 flow to afford $[\text{Fe}^{\text{II}}(\text{S},S\text{-PDBzL})\text{Cl}_2]$ (88.6 mg, yield 63%). This complex (88.6 mg, 0.16 mmol) was suspended in 5 ml CH_3CN . A total of 110 mg of AgSbF_6 (109.7 mg, 0.32 mmol) was added into the stirred suspension, whereupon a white precipitate immediately appeared. The colour of the solution gradually changed from light yellow to orange. After 4 h of stirring, the mixture was filtered through a Celite column in the dark. The solvent was removed under vacuum to provide $[\text{Fe}^{\text{II}}(\text{S},S\text{-PDBzL})(\text{CH}_3\text{CN})_2](\text{SbF}_6)_2$ as a red solid. Yield: 157.7 mg (95%). HRMS: (m/z) 242.1022 $[\text{Fe}^{\text{II}}(\text{S},S\text{-PDBzL})]^{2+}$ ($z = 2$), calc. 242.1014; 719.0956 $[\text{Fe}^{\text{II}}(\text{S},S\text{-PDBzL})(\text{SbF}_6)]^+$ ($z = 1$), calc. 719.0980; elemental analysis $\text{C}_{30}\text{H}_{38}\text{N}_8\text{F}_{12}\text{Sb}_2\text{Fe}$ (MW = 1038.021 g mol^{-1}) calc. (%) C 34.71, H 3.69, N 10.79; found (%) C 35.97, H 4.33, N 10.44.

Crystal structure determination

Orange crystals of 1^{OFF} were grown by slow diffusion of diethyl ether into a CH_2Cl_2 solution of the compound. Collection of diffraction data was carried out at (100(2) K) on a BRUKER SMART APEX CCD diffractometer using graphite-monochromated Mo $\text{K}\alpha$ radiation ($\lambda = 0.71073$ Å). The measurements were made in the θ range 2.172 to 27.744°. A full-sphere data collection was carried out with ω and ϕ scans. A total of 82 922 reflections were collected of which 8370 were unique (Table 6). Programs used: data collection, Smart;³³ data reduction, Saint+;³⁴ absorption correction, SADABS.³⁵ Structure solution and refinement were done using SHELXTL.³⁶

The structure was solved by direct methods and refined by full-matrix least-squares methods on F^2 . The non-hydrogen atoms were refined anisotropically. The H-atoms were placed at geometrically optimized positions and forced to ride on the atom to which they are attached. The structure crystallized in the chiral space group $P6_5$.

Table 6 Crystal data for complex **1**^{OTf}

Empirical formula	C ₂₈ H ₃₂ F ₆ FeN ₆ O ₆ S ₂ ·CH ₂ Cl ₂ (1 ^{OTf})
Formula weight	867.49
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Hexagonal
Space group	<i>P</i> 6 ₅
Unit cell dimensions	<i>a</i> = 10.8264(3) Å <i>b</i> = 10.8264(3) Å <i>c</i> = 52.532(2) Å α = 90° β = 90° γ = 120°
Volume	5332.4(4) Å ³
<i>Z</i>	6
Density (calculated)	1.621 Mg m ^{−3}
Absorption coefficient	0.775 mm ^{−1}
<i>F</i> (000)	2664
Crystal size	0.3 × 0.3 × 0.25 mm ³
Theta range for data collection	2.172 to 27.744°
Index ranges	−14 ≤ <i>h</i> ≤ 14, −14 ≤ <i>k</i> ≤ 14, −68 ≤ <i>l</i> ≤ 68
Reflections collected	82 922
Independent reflections	8370
Completeness	100% (to theta = 25.242)
Absorption correction	Empirical
Max. and min. transmission	1.0 and 0.900775
Refinement method	Full-matrix least-squares on <i>F</i> ²
Data/restraints/parameters	8370/3/471
Goodness-of-fit on <i>F</i> ²	1.053
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> ₁ = 0.0592, <i>wR</i> ₂ = 0.1622
<i>R</i> indices (all data)	<i>R</i> ₁ = 0.0632, <i>wR</i> ₂ = 0.1668
Largest diff. peak and hole	2.223 and −1.601 e Å ^{−3}

Reaction conditions for catalysis

Conditions for the epoxidation of 2-cyclohexen-1-one and 2-cyclopenten-1-one. An acetonitrile solution (750 μL) of the alkene substrate (0.0825 mmol, final concentration 0.11 M) and **1**^{OTf} or **1**^{SbF₆} (3.32 μmol, 4 mol%, final concentration 4.4 mM) was prepared in a 10 ml vial equipped with a stir bar and cooled in an acetonitrile freeze bath (temp. −30 °C). A total of 12 μL of the carboxylic acid in CH₃CN was directly added to the reaction solution. Then 37.7 μL of 1:1 (v:v) H₂O₂ (30% wt/wt in H₂O): CH₃CN was delivered to the reaction solution over a period of 30 min, using a syringe pump. After the addition of H₂O₂, the reaction solution was further stirred at 30 °C for 30 min. At this point, a known amount of biphenyl solution was added as the internal standard. The solution was passed through a small alumina column and the column was rinsed with 2 × 1 ml ethyl acetate and the resultant elute was subjected to GC analysis. The racemic products were identified by their GC retention times and the yields were determined from the integration area of the GC spectrum.

Conditions for the epoxidation of *cis*-β-methylstyrene. An acetonitrile solution (750 μL) of *cis*-β-methyl styrene (0.0825 mmol, final concentration 0.11 M) and **1**^{OTf} (final concentration 1.1 mM) was prepared in a 10 ml vial equipped with a stir bar and cooled in an acetonitrile freeze bath (temp. −30 °C). A total of 12.5 μL of the acetic acid (0.2 M solution, 3 mol%) in CH₃CN was directly added to the reaction solution. Then 26.7 μL of 1:1 (v:v) H₂O₂ in water (30% wt/wt): CH₃CN

was delivered to the reaction solution over a period of 30 min using a syringe pump. After this addition, the reaction solution was further stirred at 30 °C for 30 min. At this point, a known amount of biphenyl solution was added as the internal standard. The solution was passed through a small alumina column and the column was rinsed with 2 × 1 ml ethyl acetate, and the resultant elute was subjected to GC analysis. The racemic products were identified by their GC retention times and the yields were determined from the integration area of the GC spectrum.

Conflicts of interest

The authors declare no conflicts of interest.

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Notes and references

- (a) M. J. Porter and J. Skidmore, *Chem. Commun.*, 2000, 1215–1225; (b) B. S. Lane and K. Burgess, *Chem. Rev.*, 2003, **103**, 2457–2473; (c) Q. H. Xia, H. Q. Ge, C. P. Ye, Z. M. Liu and K. X. Su, *Chem. Rev.*, 2005, **105**, 1603–1662; (d) O. A. Wong and Y. Shi, *Chem. Rev.*, 2008, **108**, 3958–3987; (e) D. Diez, M. G. Nunez, A. B. Anton, P. Garcia, R. F. Moro, N. M. Garrido, I. S. Marcos, P. Basabe and J. G. Urones, *Curr. Org. Synth.*, 2008, **5**, 186–216; (f) K. Matsumoto and T. Katsuki, in *Catalytic Asymmetric Synthesis*, ed. I. Ojima, Wiley-VCH, New York, 3rd edn, 2010, pp. 839–890; (g) G. De Faveri, G. Ilyashenko and M. Watkinson, *Chem. Soc. Rev.*, 2011, **40**, 1722–1760.
- K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2002, **41**, 2024–2032.
- Representative examples: (a) H. Wynberg and B. J. Greijdanus, *J. Chem. Soc., Chem. Commun.*, 1978, 427–428; (b) S. Julia, J. Guixer, J. Masana, J. Rocas, S. Colonna, R. Annuziata and H. J. Molinari, *J. Chem. Soc., Perkin Trans. 1*, 1982, 1317–1324; (c) D. Enders, J. Zhu and G. Raabe, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1725–1728; (d) D. Yang, Y.-C. Yip,

- M.-W. Tang, M.-K. Wong, J.-H. Zheng and K.-K. Cheung, *J. Am. Chem. Soc.*, 1996, **118**, 491–492; (e) M. Bougauchi, S. Watanabe, T. Arai, H. Sasai and M. Shibakasi, *J. Org. Chem.*, 1998, **63**, 8090–8091; (f) E. J. Corey and F.-Y. Zhang, *Org. Lett.*, 1999, **1**, 1287–1290; (g) O. Jacques, S. J. Richards and R. F. W. Jackson, *Chem. Commun.*, 2001, 1712–1713; (h) C. Li, E. A. Pace, M. C. Liang, E. Lobkovsky, T. D. Galimore and J. A. Porco Jr., *J. Am. Chem. Soc.*, 2001, **123**, 11308–11309; (i) A. Berkessel, M. Guixa, F. Schimdt, J. M. Neudorfl and J. Lex, *Chem. – Eur. J.*, 2007, **13**, 4482–4498; (j) A. Erkkila, P. M. Pihko and M.-R. Clarke, *Adv. Synth. Catal.*, 2007, **349**, 802–806; (k) G. Peris, C. E. Jakobsche and S. J. Miller, *J. Am. Chem. Soc.*, 2007, **129**, 8710–8711; (l) W. Zhang and H. Yamamoto, *J. Am. Chem. Soc.*, 2007, **129**, 286–287.
- 4 (a) W. Adam, C. R. Saha-Moller and P. A. Ganeshpure, *Chem. Rev.*, 2001, **101**, 3499–3548; (b) A. Lattanzi, *Curr. Org. Synth.*, 2008, **5**, 117–133.
 - 5 (a) T. Katsuki and K. B. Sharpless, *J. Am. Chem. Soc.*, 1980, **102**, 5974–5976; (b) W. Zhang, J. L. Loebach, S. R. Wilson and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1990, **112**, 2801–2803; (c) R. Irie, K. Noda, Y. Ito, N. Matsumoto and T. Katsuki, *Tetrahedron Lett.*, 1990, **31**, 7345–7348; (d) K. Matsumoto, Y. Sawada, B. Saito, K. Sakai and T. Katsuki, *Angew. Chem.*, 2005, **117**, 5015–5019; (e) Y. Sawada, K. Matsumoto, S. Kondo, H. Watanabe, T. Ozawa, K. Suzuki, B. Saito and T. Katsuki, *Angew. Chem., Int. Ed.*, 2006, **45**, 3478–3480; (f) A. U. Barlan, A. Basak and H. Yamamoto, *Angew. Chem., Int. Ed.*, 2006, **45**, 5849–5852.
 - 6 E. M. McGarrigle and D. G. Gilheany, *Chem. Soc. Rev.*, 2005, **105**, 1563–1602.
 - 7 (a) Y. Shi, *Acc. Chem. Res.*, 2004, **37**, 488–496; (b) D. Yang, *Acc. Chem. Res.*, 2004, **37**, 497–505; (c) Y. Zhu, Q. Wang, R. G. Cornwall and Y. Shi, *Chem. Rev.*, 2014, **114**, 8199–8256.
 - 8 (a) T. Ooi, D. Ohara, M. Tamura and K. Maruoka, *J. Am. Chem. Soc.*, 2004, **126**, 6884–6845; (b) M. Marigo, J. Franzen, T. B. Poulsen and K. A. Jorgensen, *J. Am. Chem. Soc.*, 2005, **127**, 6964–6965; (c) X. W. Wang, C. M. Reisinger and B. List, *J. Am. Chem. Soc.*, 2008, **130**, 6070–6071; (d) X. J. Lu, Y. Liu, B. F. Sun, B. Cindric and L. Deng, *J. Am. Chem. Soc.*, 2008, **130**, 8134–8135; (e) C. M. Reisinger, X. W. Wang and B. List, *Angew. Chem., Int. Ed.*, 2008, **47**, 8112–8115.
 - 9 F. G. Gelalcha, *Adv. Synth. Catal.*, 2014, **356**, 261–299.
 - 10 (a) L. Que Jr. and W. B. Tolman, *Nature*, 2008, **455**, 333–340; (b) E. B. Bauer, *Curr. Org. Chem.*, 2008, **12**, 1341–1369; (c) S. Enthaler, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2008, **47**, 3317–3321; (d) A. Correa, O. G. Mancheno and C. Bolm, *Chem. Soc. Rev.*, 2008, **8**, 1108–1117; (e) L.-X. Liu, *Curr. Org. Chem.*, 2010, **14**, 1099–1126; (f) C.-L. Sun Chang-Liang, B.-J. Li and Z.-J. Shi, *Chem. Rev.*, 2011, **111**, 1293–1314; (g) M. Darwish and M. Wills, *Catal. Sci. Technol.*, 2012, **2**, 243–255; (h) K. Gopalaiah, *Chem. Rev.*, 2013, **113**, 3248–3296.
 - 11 J. P. Collman, Z. Wang, A. Straumanis, M. Quelquejeu and E. Bose, *J. Am. Chem. Soc.*, 1999, **121**, 460–461.
 - 12 F. G. Gelalcha, B. Bitterlich, G. Anilkumar, M. K. Tse and M. Beller, *Angew. Chem., Int. Ed.*, 2007, **46**, 7293–7296.
 - 13 (a) F. G. Gelalcha, G. Anilkumar, M. K. Tse, A. Bruckner and M. Beller, *Chem. – Eur. J.*, 2008, **14**, 7687–7698; (b) O. Lyakin, R. V. Ottenbacher, K. P. Bryliakov and E. P. Talsi, *ACS Catal.*, 2012, **2**, 1196–1202; (c) T. Niwa and M. Nakada, *J. Am. Chem. Soc.*, 2012, **134**, 13538–13541; (d) V. A. Yazerski, A. Orue, T. Evers, H. Kleijn and R. J. M. Klein Gebbink, *Catal. Sci. Technol.*, 2013, **3**, 2810–2818.
 - 14 (a) M. Wu, C.-X. Miao, S. Wang, X. Hu, C. Xia, F. E. Kühn and W. Sun, *Adv. Synth. Catal.*, 2011, **353**, 3014–3022; (b) X. Wang, C. Miao, S. Wang, C. Xia and W. Sun, *ChemCatChem*, 2013, **5**, 2489–2494; (c) W. Wang, Q. Sun, D. Xu, C. Xia and W. Sun, *ChemCatChem*, 2017, **9**, 420–424.
 - 15 Y. Nishikawa and H. Yamamoto, *J. Am. Chem. Soc.*, 2011, **133**, 8432–8435.
 - 16 O. Cusso, I. Garcia-Bosch, X. Ribas, J. Lloret-Fillol and M. Costas, *J. Am. Chem. Soc.*, 2013, **135**, 14871–14878.
 - 17 O. Cusso, X. Ribas and M. Costas, *Chem. Commun.*, 2015, **51**, 14285–14298.
 - 18 (a) O. Cusso, M. Cianfanelli, X. Ribas, R. J. M. Klein Gebbink and M. Costas, *J. Am. Chem. Soc.*, 2016, **138**, 2732–2738; (b) O. Cussó, X. Ribas, J. Lloret-Fillol and M. Costas, *Angew. Chem., Int. Ed.*, 2015, **54**, 2729–2733; (c) O. Cussó, M. W. Giuliano, X. Ribas, S. J. Miller and M. Costas, *Chem. Sci.*, 2017, **8**, 3660–3667.
 - 19 R. Mas-Balleste and L. Que Jr., *J. Am. Chem. Soc.*, 2007, **129**, 15964–15972.
 - 20 (a) A. M. Zima, O. Y. Lyakin, R. V. Ottenbacher, K. P. Bryliakov and E. P. Talsi, *ACS Catal.*, 2016, **6**, 5399–5404; (b) O. Y. Lyakin, A. M. Zima, D. G. Samsonenko, K. P. Bryliakov and E. P. Talsi, *ACS Catal.*, 2015, **5**, 2702–2707; (c) W. N. Oloo, R. Banerjee, J. D. Lipscomb and L. Que Jr., *J. Am. Chem. Soc.*, 2017, **139**, 17313–17326.
 - 21 (a) J. Serrano-Plana, W. N. Oloo, L. Acosta-Rueda, K. K. Meier, B. Verdejo, E. Garcia-Espana, M. G. Basallote, E. Munck, L. Que Jr., A. Company and M. Costas, *J. Am. Chem. Soc.*, 2015, **137**, 15833–15342; (b) R. Fan, J. Serrano-Plana, W. N. Oloo, A. Draksharapu, E. Delgado-Pinar, A. Company, V. Martin-Diaconescu, M. Borrell, J. Lloret-Fillol, E. Garcia-Espana, Y. Guo, E. L. Bominaar, L. Que Jr., M. Costas and E. Munck, *J. Am. Chem. Soc.*, 2018, **140**, 3916–3928.
 - 22 B. Mondal, F. Neese, E. Bill and S. Ye, *J. Am. Chem. Soc.*, 2018, **140**, 9531–9544.
 - 23 Y. Wang, D. Janardanan, D. Usharani, K. Han, L. Que Jr. and S. Shaik, *ACS Catal.*, 2013, **3**, 1334–1341.
 - 24 A. M. Zima, O. Y. Lyakin, R. V. Ottenbacher, K. P. Bryliakov and E. P. Talsi, *ACS Catal.*, 2017, **7**, 60–69.
 - 25 O. Cusso, J. Serrano-Plana and M. Costas, *ACS Catal.*, 2017, **7**, 5046–5053.
 - 26 (a) E. N. Jacobsen, W. Zhang, A. R. Muci, J. R. Ecker and L. Deng, *J. Am. Chem. Soc.*, 1991, **113**, 7063–7064;

- (b) M. S. Chen and M. C. White, *Science*, 2007, **318**, 783–787.
- 27 M. Mitra, J. Lloret-Fillol, M. Haukka, M. Costas and E. Nordlander, *Chem. Commun.*, 2014, **50**, 1408–1410.
- 28 D. Shen, C. Miao, S. Wang, C. Xia and W. Sun, *Eur. J. Inorg. Chem.*, 2014, 5777–5782.
- 29 S. V. Amrutkar, U. D. Bhagat, P. Pargharmol, S. S. Kotgire and M. S. Ranawat, *Int. J. Pharm. Pharm. Sci.*, 2010, **2**, 84–92.
- 30 (a) A. Diebold and K. S. Hagen, *Inorg. Chem.*, 1998, **37**, 215–223; (b) D. W. Blakesley, S. C. Payne and K. S. Hagen, *Inorg. Chem.*, 2000, **39**, 1979–1989; (c) K. Chen and L. Que Jr., *J. Am. Chem. Soc.*, 2001, **123**, 6327–6337; (d) G. J. P. Britovsek, J. England and A. P. J. White, *Inorg. Chem.*, 2005, **44**, 8125–8134; (e) A. J. Simaan, S. Dopner, F. Banse, S. Bourcier, G. Bouchoux, A. Boussac, P. Hildebrandt and J. J. Girerd, *Eur. J. Inorg. Chem.*, 2000, 1627–1633; (f) I. Prat, A. Company, T. Corona, T. Parella, X. Ribas and M. Costas, *Inorg. Chem.*, 2013, **52**, 9229–9244.
- 31 (a) K. Fuji, *Chem. Rev.*, 1993, **93**, 2037–2066; (b) E. J. Corey and A. Guzman-Perez, *Angew. Chem., Int. Ed.*, 1998, **37**, 388–401; (c) B. M. Wang and Y. Q. Tu, *Acc. Chem. Res.*, 2011, **44**, 1207–1222.
- 32 (a) B. Wang, S. Wang, C. Xia and W. Sun, *Chem. – Eur. J.*, 2012, **18**, 7332–7335; (b) E. J. Corey and F.-Y. Zhang, *Org. Lett.*, 1999, **1**, 1287–1290; (c) Y. Liu, B. A. Provencher, K. J. Bartelsoand and L. Deng, *Chem. Sci.*, 2011, **2**, 1301–1304.
- 33 Bruker Advanced X-ray Solutions. SMART: Version 5.631, 1997–2002.
- 34 Bruker Advanced X-ray Solutions. SAINT+, Version 6.36A, 2001.
- 35 G. M. Sheldrick, *Empirical Absorption Correction Program*, Universität Göttingen, 1996; Bruker Advanced X-ray Solutions. SADABS Version 2.10, 2001.
- 36 G. M. Sheldrick, *Program for Crystal Structure Refinement*, Universität Göttingen, 1997; Bruker Advanced X-ray Solutions, SHELXTL Version 6.14, 2000–2003. SHELXL-2013 (Sheldrick, 2013).