Supporting Information

Dramatic Effect of Carboxylic Acid on the Electronic Structure of the Active Species in Fe(PDP)-Catalyzed Asymmetric Epoxidation

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1. Materials

All chemicals and solvents were purchased from Aldrich, Acros Organics, or Alfa Aesar and were used without additional purification unless noted otherwise. For the EPR experiments, $\approx 95\%$ H_2O_2 was obtained by distillation of commercial 30% H_2O_2 from the phosphate buffer, followed by concentration of the distillate under reduced pressure at room temperature. *Caution: Concentrated hydrogen peroxide is potentially explosive and should be handled with care!* The exact H_2O_2 concentrations in the prepared solutions were determined by iodometric titration under argon. Cyclohexene was purified by distillation over sodium metal in Ar. Iron complexes [((S,S)-PDP)Fe^{II}(OTf)$_2$] (**1**),[S1] [((R,R)-PDP)Fe^{II}(OTf)$_2$] (**1^{R,R}**)[S1] and [((S,S)-PDP*)Fe^{III}(μ-OH)$_2$Fe^{III}((S,S)-PDP*)](OTf)$_4$ (**5**)[8a] were prepared as described.

2. Instrumentation

EPR spectra (−196 °C) were measured in 3 mm quartz tubes on a Bruker ER-200D spectrometer at 9.3–9.4 GHz, modulation frequency 100 kHz, modulation amplitude 5 G. The dual EPR cavity furnished with the spectrometer was used. Periclase crystal (MgO) with impurities of Mn^{2+} and Cr^{3+}, which served as a side reference, was placed into the second compartment of the dual cavity. Measurements were conducted in a quartz finger Dewar filled with liquid nitrogen. EPR signals were quantified by double integration with a frozen solution of copper(II) acetylacetonate as a standard at −196 °C. Enantioselective chromatographic resolutions of epoxide enantiomers were performed on a Shimadzu LC-20 chromatograph equipped with a set of chiral columns as reported previously.[8a,S2]

3. Sample preparation for EPR measurements

Using a gastight microsyringe connected with polyethylene capillary, an appropriate amount of H_2O_2 in 0.05 mL of a CH$_2$Cl$_2$/CH$_3$CN mixture was added to 0.25 mL of a solution of iron complex and carboxylic acid in CH$_2$Cl$_2$/CH$_3$CN mixture at −75…−65 °C directly in a quartz EPR tube (d = 3 mm). After stirring for 1–3 min with polyethylene capillary at −80…−75 °C, the sample was frozen by immersion in liquid nitrogen, and the EPR spectrum was measured at −196 °C. For kinetic EPR studies, this sample was placed in a thermostat at required temperature directly in the EPR tube. To stop the reaction, the tube was again immersed in liquid nitrogen, followed by registration of the EPR spectrum at −196 °C.

To measure the reactivity of intermediates of the type **1a^{EHA}** (**1a^{EHA}**, **1a^{EBA}** and **1a^{PVA}**) towards cyclohexene oxidation, the appropriate amount of cyclohexene solution in 1.8:1 CH$_2$Cl$_2$/CH$_3$CN mixture was placed to the tip of glass capillary using connected microsyringe, and frozen by immersion of capillary in liquid nitrogen. Then this capillary was rapidly (during 2–3 s) placed into the EPR tube containing frozen solution of preliminary generated intermediate of the type **1a^{EHA}**, and the tube with the

capillary inside was placed in thermostat at −90 °C. In 10–15 sec, solvent in the tube melted that allow injection of alkene solution and careful mixing the reagents by glass capillary during <1 min. After that, the glass capillary was removed and the decay rate of the intermediate at −75 °C was monitored. It was found that in the presence of cyclohexene the half-life times of intermediates of the type $\mathbf{1a}^{\mathbf{EHA}}$ decreased at least by an order of magnitude. The blank experiments with capillary containing a 1.8:1 CH_2Cl_2/CH_3CN mixture without cyclohexene display no changes in the decay rates of the intermediates.

4. Procedure for catalytic olefin epoxidations with H_2O_2

Substrate (100 μmol) and carboxylic acid (55 μmol) were added to the solution of **1** (1 μmol, 0.7 mg) or complex **5** (0.5 μmol, 0.8 mg) in CH_3CN (400 μL), and the mixture was thermostated at 0 °C. Then, 100 μL of the H_2O_2 solution in CH_3CN (200 μmol of H_2O_2) was injected by a syringe pump over 30 min upon stirring. The resulting mixture was stirred for 2.5 h at 0 °C. The reaction was quenched with saturated aqueous solution of Na_2CO_3 and the products were extracted with pentane (3 × 2 mL). The solvent was carefully removed in a stream of air, the residue was dissolved in 1 mL of CCl_4 and dried over anhydrous Na_2SO_4. The mixture was filtered and the filtrate was analyzed by ^{1}H NMR spectroscopy as previously described.[3a,S2] To measure the enantiomeric excess values of epoxides, 20 μL of the CCl_4 solution were collected, and the solvent was carefully removed in a stream of air. Then, the residue was dissolved in isopropanol and subjected to LC analysis as previously described.[3a,8a] Experimental uncertainty of enantiomer amount measurements did not exceed ±1%.

**Table S1.** EPR Spectroscopic Data for All Oxoferryl Intermediates Discussed Herein

intermediate	g_1	g_2	g_3
type $\mathbf{1a^{AA}}$:			
$\mathbf{1a^{AA}}$ [a]	2.66	2.42	1.71
$\mathbf{1a^{BA}}$	2.70	2.42	1.67
$\mathbf{1a^{CA}}$	2.70	2.42	1.66
$\mathbf{1a^{IBA}}$	2.72	2.42	1.66
$\mathbf{1a^{CHA}}$	2.69	2.42	1.67
$[((S,S)\text{-PDP})Fe^V\text{=}O(OC(O)R)]^{2+}$, type $\mathbf{1a^{EHA}}$:			
$\mathbf{1a^{EHA}}$	2.069	2.007	1.963
$\mathbf{1a^{EBA}}$	2.069	2.007	1.961
$\mathbf{1a^{PVA}}$	2.069	2.007	1.962
$[((S,S)\text{-PDP*})Fe^V\text{=}O(OC(O)R)]^{2+}$, type $\mathbf{5a}$:			
$\mathbf{5a^{AA}}$ [b]	2.071	2.008	1.960
$\mathbf{5a^{BA}}$	2.070	2.008	1.958
$\mathbf{5a^{CA}}$	2.069	2.008	1.957
$\mathbf{5a^{IBA}}$	2.069	2.007	1.957
$\mathbf{5a^{CHA}}$	2.070	2.008	1.957
$\mathbf{5a^{EHA}}$	2.070	2.008	1.958
$\mathbf{5a^{EBA}}$	2.069	2.008	1.957
$\mathbf{5a^{PVA}}$	2.069	2.007	1.958

[a] From ref. 3a. [b] From ref. 8a.

Table S2. Asymmetric Epoxidation of Chalcone with H_2O_2 in the Presence of Enantiopure Additives [a]

catalyst (0.5-1 mol.%)
H_2O_2 (2 equiv)
RCOOH (55 mol.%)
————————————→
CH_3CN, 0 °C, 3 h

entry	catalyst [b]	additive	conversion (%) / epoxide yield (%)	e.r. [c]
1	**1**	D-(−)-tartaric acid	10 / 10	80 : 20
2	**1**	L-(+)-tartaric acid	9 / 9	79 : 21
3	**5**	D-(−)-tartaric acid	17 / 17	81 : 19
4	**5**	L-(+)-tartaric acid	18 / 18	81 : 19
5	**1**	N-Boc-L-Pro	39 / 39	78 : 22
6	**1**[R,R]	N-Boc-L-Pro	43 / 43	79 : 21

[a] At 0 °C, [substrate]:[H_2O_2]:[additive] = 100 μmol : 200 μmol : 55 μmol, catalyst load 1 mol.% of Fe, oxidant was added by a syringe pump over 30 min, and the mixture was stirred for an additional 2.5 h followed by LC analysis. To dissolve tartaric acid, H_2O (18 μL, 1 mmol) was added prior to the reaction onset [b] Complex [((S,S)-PDP)Fe^{II}(OTf)$_2$] is designated as **1**, and complex [((R,R)-PDP)Fe^{II}(OTf)$_2$] is designated as **1**[R,R]. [c] Absolute configuration of chalcone epoxide was (2R,3S) for entries 1-5, and (2S,3R) for entry 6.

L-(+)-tartaric acid   D-(-)-tartaric acid   N-Boc-L-Pro   N-NPha-L-Ileu
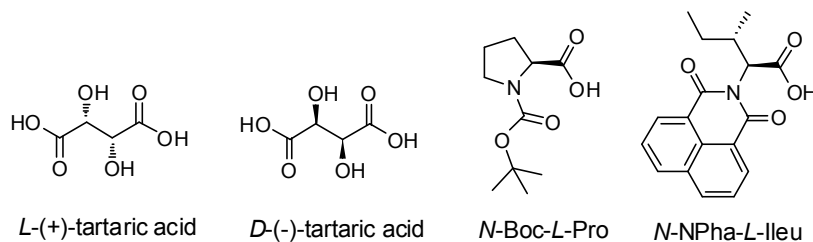
Previously, highly enantioselective epoxidation of substituted styrenes with aqueous H_2O_2 was described using complex **3** as the catalyst, and twelve N-protected amino acids as the co-ligands.[3c] Since both the iron catalyst and the amino acid co-ligand were chiral, the matching-mismatching effects, resulting from the combination of the respective chiralities, were evaluated by using two enantiomeric (R,R)- and (S,S)-forms of the catalyst. Pronounced effect (14.4 vs. 2.9 e.r.) was observed only for N-NPha-L-Ileu.[3c]

In this work, we have compared the e.r. values for chalcone epoxidation, using catalysts **1**, **5** and D-, and L-tartaric acids as the catalytic additives. Virtually identical e.r. values were obtained for D- and L-forms of the co-ligand (3.8-4 e.r. with **1**, 4.3 with **5**, see Table S2).

Using equivalent approach, we have evaluated the matching-mismatching effect for the epoxidation of chalcone with H_2O_2 in the presence of complexes [((S,S)-PDP)Fe^{II}(OTf)$_2$] (**1**) and [((R,R)-PDP)Fe^{II}(OTf)$_2$] (**1**[R,R]) as the catalysts, and with N-Boc-L-Pro as the catalytic additive. Again very similar e.r. values were obtained in both cases (3.5 e.r. for **1**, and 3.7 e.r. for **1**[R,R], Table S2). These results witness negligible matching-mismatching effect for chalcone epoxidation in the presence of enantiopure catalysts **1** and **5**, and enantiomerically pure catalytic additives.
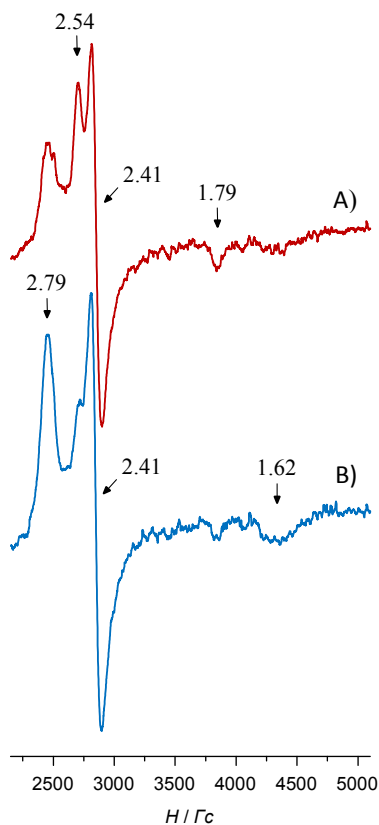
Figure S1. EPR spectra ($-196\ °C$) of the samples **5**/EHA ($[Fe] = 0.04$ M) frozen 10 min after mixing the reagents at room temperature in a 1.8:1 CH_2Cl_2/CH_3CN mixture. (A) [Fe]:[EHA] = 10, (B) [Fe]:[EHA] = 50.

To assign **1b** more definitely, we have studied the interaction of the second complex $Fe^{III}(PDP*)(\mu\text{-}OH)_2Fe^{III}(PDP*)$ (**5**) considered herein with an excess of 2-ethylhexanoic acid at room temperature. In contrast to ferrous complex **1**, ferric nature of the initial complex **5**, together with its EPR-silence proved to be fruitful for the EPR study of stable mononuclear ferric species formed after the addition of the carboxylic acid. It was found that two types of $S = 1/2$ ferric species form upon interaction of **5** with 2-ethylhexanoic acid. At low excess of RCOOH ([RCOOH]/[Fe] = 10, Figure S1A), mononuclear ferric complex with $g_1 = 2.54$, $g_2 = 2.41$, $g_3 = 1.79$ predominated in the solution. At high excess of RCOOH ([RCOOH]/[Fe] = 50, Figure S1B), mononuclear ferric complex with $g_1 = 2.79$, $g_2 = 2.41$, $g_3 = 1.62$ became the predominant species. Both complexes are relatively stable at room temperature (half-life time > 1 h). The EPR spectrum of the latter complex is virtually identical to that of **1b**^{EHA}. In our previous paper, species with $g_1 = 2.54$, $g_2 = 2.41$, $g_3 = 1.79$ was proposed to be ferric complex $[((S,S)\text{-}PDP*)Fe^{III}(\kappa^2\text{-}OC(O)R)]^{2+}$.[8a] Apparently, the increase of the carboxylic acid concentration may favor the formation of a ferric complex with two carboxylic ligands, e.g. $[((S,S)\text{-}PDP*)Fe^{III}(OC(O)R)(RCOOH)]^{2+}$. Thus, **1b**^{EHA} can be tentatively assigned to the complex $[((S,S)\text{-}PDP)Fe^{III}(OC(O)R)(RCOOH)]^{2+}$.
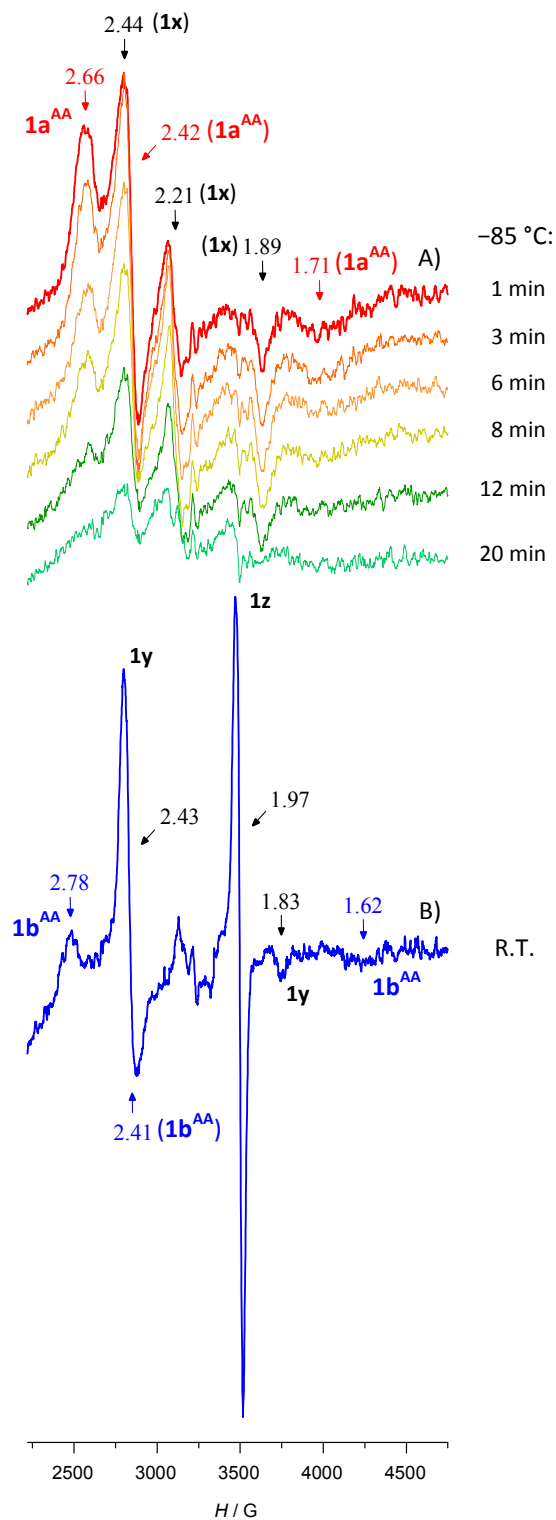
Figure S2. (A) EPR spectra ($-196\,°C$) of the sample $\mathbf{1}/H_2O_2/CH_3COOH$ ($[\mathbf{1}]:[H_2O_2]:[CH_3COOH] = 1:3:10$, $[\mathbf{1}] = 0.04\,M$) frozen 1 min after mixing the reagents at $-75\,°C$ in a 1.8:1 CH_2Cl_2/CH_3CN mixture and storing the sample at $-85\,°C$ for various times. (B) EPR spectrum ($-196\,°C$) of the sample in "A" after storing at room temperature for 2 min. Unstable species $\mathbf{1x}$ was previously assigned to ferric hydroxo complex $[((S,S)\text{-}PDP)Fe^{III}\text{-}OH(CH_3CN)]^{2+}$ (ref. 3a). Signals marked with $\mathbf{1y}$ and $\mathbf{1z}$ belong to unidentified complexes stable at room temperature. The signal of $\mathbf{1a^{AA}}$ at $g_2 = 2.42$ overlaps with the signal of $\mathbf{1x}$ at $g_1 = 2.44$. The signal of $\mathbf{1b^{AA}}$ at $g_2 \approx 2.41$ overlaps with the signal of $\mathbf{1y}$ at $g_1 = 2.43$.
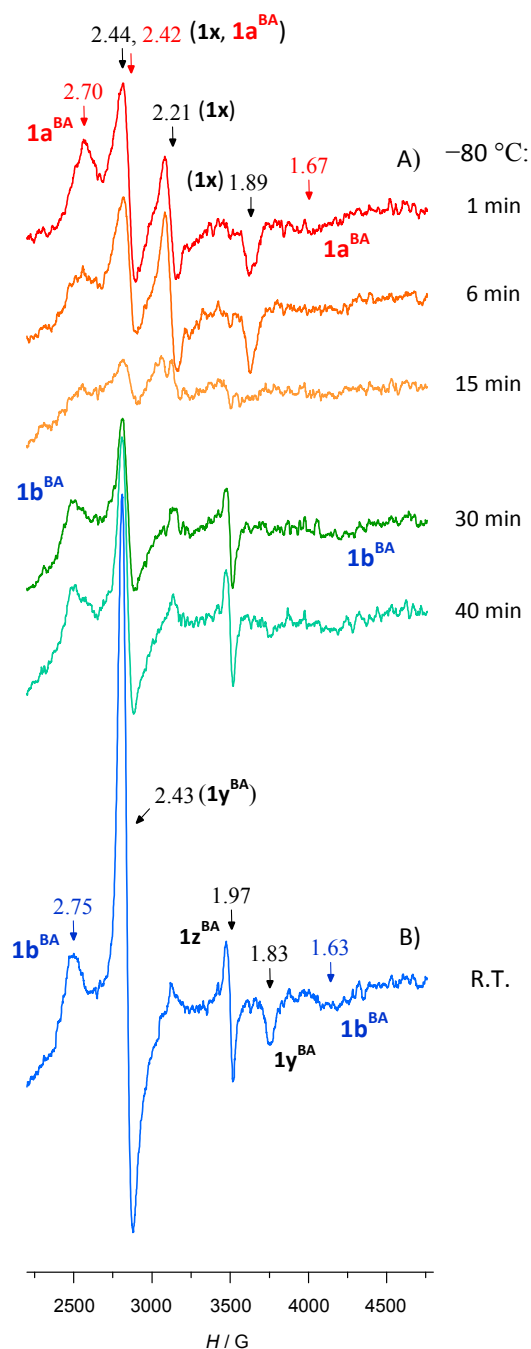
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Figure S3. (A) EPR spectra (−196 °C) of the sample $1/H_2O_2/BA$ ([**1**]:[H_2O_2]:[BA] = 1:3:10, [**1**] = 0.04 M) frozen 1.5 min after mixing the reagents at −70 °C in a 1.8:1 CH_2Cl_2/CH_3CN mixture and storing the sample at −80 °C for various times. (B) EPR spectrum (−196 °C) of the sample in "A" after storing at room temperature for 2 min. Complex **1x** is described in the caption for Figure S2. Unidentified complexes **1y**[BA] and **1z**[BA] are stable at room temperature and exhibit EPR parameters identical to those of complexes **1y** and **1z** in Figure S2. The signal of **1a**[BA] at $g_2 \approx 2.42$ overlaps with the signal of **1x** at $g_1 = 2.44$. The signal of **1b**[BA] at $g_2 \approx 2.42$ overlaps with the signal of **1y**[BA] at $g_1 = 2.43$.
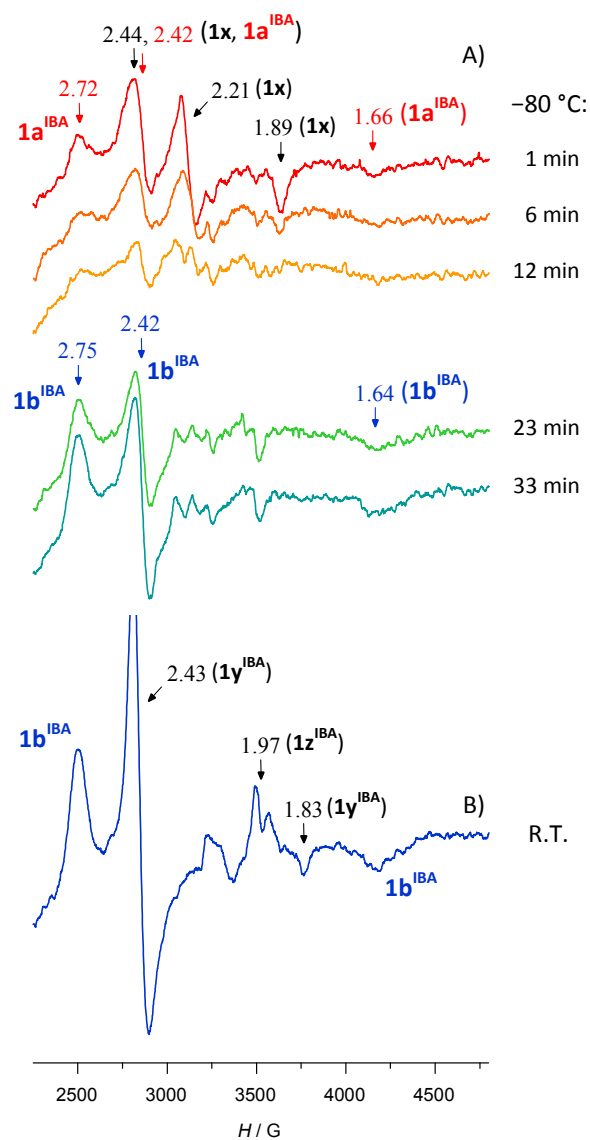
Figure S4. (A) EPR spectra ($-196\ °C$) of the sample 1/H_2O_2/IBA ($[1]$:$[H_2O_2]$:$[IBA]$ = 1:3:10, $[1]$ = 0.04 M) frozen 1.5 min after mixing the reagents at $-70\ °C$ in a 1.8:1 CH_2Cl_2/CH_3CN mixture and storing the sample at $-80\ °C$ for various times. (B) EPR spectrum ($-196\ °C$) of the sample in "A" after storing at room temperature for 2 min. Complex **1x** is described in the caption for Figure S2. Unidentified complexes **1y^{IBA}** and **1z^{IBA}** are stable at room temperature and exhibit EPR parameters identical to those of complexes **1y** and **1z** in Figure S2. The signal of **1a^{IBA}** at $g_2 \approx 2.42$ overlaps with the signal of **1x** at $g_1 = 2.44$.

Additional References

(S1)   Suzuki, K.; Oldenburg, P. D.; Que, L., Jr. *Angew. Chem. Int. Ed.* **2008**, *47*, 1887–1889.

(S2)   Ottenbacher, R. V.; Bryliakov, K. P.; Talsi, E. P. *Adv. Synth. Catal.* **2011**, *353*, 885–889.