

Asymmetric Fe^{II}-Catalyzed Thia-Michael Addition Reaction to α,β -Unsaturated Oxazolidin-2-one Derivatives

Samuel Lauzon,[†] Hoda Keipour,[†] Vincent Gandon,^{*,‡,§} and Thierry Ollevier^{*,†}

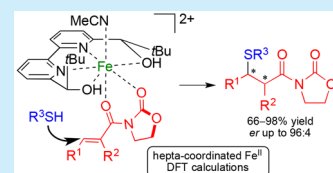
[†]Département de chimie, Université Laval, 1045 avenue de la Médecine, Québec, QC G1V 0A6, Canada

[‡]Institut de Chimie Moléculaire et des Matériaux d'Orsay, CNRS UMR 8182, Univ. Paris-Sud, Université Paris-Saclay, Orsay 91405 Cedex, France

[§]Institut de Chimie des Substances Naturelles, CNRS UPR 2301, Univ. Paris-Sud, Université Paris-Saclay, 1 av. de la Terrasse, 91198 Gif-sur-Yvette, France

Supporting Information

ABSTRACT: A highly enantioselective Fe^{II}-catalyzed thia-Michael addition to α,β -unsaturated carbonyl derivatives was developed. The scope of the reaction was demonstrated with a selection of aromatic, heterocyclic and aliphatic thiols, and various Michael acceptors. The corresponding β -thioethers were obtained in good to excellent yields (up to 98%) and moderate to excellent enantioselectivities (up to 96:4 er). Unusual hepta-coordination of the metal and chelation to α,β -unsaturated oxazolidin-2-one derivatives allowed the construction of a coherent model rationalizing the enantioselective event. DFT calculations support the proposed model for observed stereoselectivities.



The use of iron complexes as catalysts has arisen from traditional transition-metal catalysis in various synthetic transformations of modern organic chemistry.¹ Many catalysts are originally derived from rare metals such as palladium, ruthenium, platinum, and iridium. Their low availability, toxicity, and high market prices encourage their replacement by alternative metals.² From a sustainable chemistry perspective, developing new synthetic methods using iron, which is abundant, inexpensive, environmentally benign, and relatively nontoxic in comparison with other metals, is a major advantage.^{2b,3} The ability to use iron in homogeneous asymmetric catalysis is promising for the development of greener synthetic methods,⁴ contributing to major improvements for both academia and pharmaceutical industries.⁵ The 1,4-addition to α,β -unsaturated carbonyl derivatives is one of the most powerful and efficient ways to create new C–C bonds and various heteroatom–carbon bonds, such as N–C, O–C, and S–C bonds.⁶ Sulfur-containing compounds, which are essential building blocks for biologically active pharmaceutical agents, are important targets.⁷ Chiral Brønsted acids and bases,⁸ such as thiourea and squaramide cinchona alkaloid derivatives,⁹ and a noncovalent NHC¹⁰ have been reported to be efficient catalysts for the thia-Michael addition reaction. Previous work has been disclosed using chiral Lewis acid catalysts derived from Ni^{II},¹¹ Hf^{IV},¹² Sc^{III},¹³ and Co^{II} salts¹⁴ for the asymmetric 1,4-addition of thiols to α,β -unsaturated oxazolidin-2-ones. Chiral Fe^{II} and Fe^{III} complexes afforded β -thioethers with excellent yields and enantioselectivities.¹⁵ However, most of the methods use costly transition metals, high catalytic loadings, or chlorinated solvents.

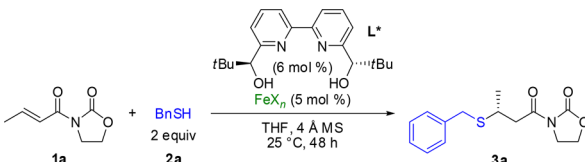
In our continuing studies in asymmetric catalysis using iron salts, i.e., Mukaiyama aldol, *meso*-epoxide opening, and aromatic sulfide oxidation reactions, Fe^{II}/chiral bipyridine complexes have proven to be efficient enantioselective catalysts.¹⁶ A simple and

highly asymmetric thia-Michael addition on acyclic α,β -unsaturated derivatives using iron salts as environmentally benign chiral catalysts is disclosed herein. Experimental insights into the influence of the nucleophile on the stereoselectivity control, together with DFT calculations, are also presented.

Asymmetric Michael addition of benzylthiol **2a** to (*E*)-3-crotonoyloxazolidin-2-one **1a**, run in THF, was initially selected as the model reaction for the screening of various iron salts with (*S,S*)-Bolm's ligand¹⁸ **L*** (Table 1). FeCl₂ showed a moderate chiral induction in a low conversion (entry 1). Fe(BF₄)₂·6H₂O, Fe(OTf)₂, and Fe(ClO₄)₂·6H₂O afforded (3*R*)-**3a** with good enantioselectivities and moderate to good conversions (entries 2–4). Fe^{III} salts, such as FeCl₃ and Fe(acac)₃, allowed the formation of thioether (3*R*)-**3a** with low chiral inductions (entries 5 and 6). Fe(OTf)₃ and Fe(ClO₄)₃·6H₂O led to good er's with low conversions (entries 7 and 8). Overall, both conversions and enantioselectivities were higher when Fe^{II} vs Fe^{III} salts were used. An optimum 95:5 er was obtained, together with high conversion, when Fe(ClO₄)₂·6H₂O was used, and thus, this system was used as a chiral catalyst in our study (entry 4). It is noteworthy to mention that the addition of 4 Å molecular sieves, known as attractive additives in asymmetric reactions,¹⁹ enhanced the enantioselectivity but extended the reaction time.²⁰ Since 4 Å MS were advantageous in terms of er, they were used as an additive in the thia-Michael addition reaction.

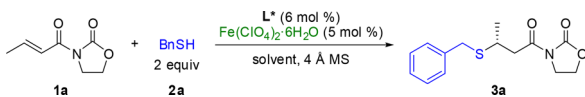
The optimization study was first performed using various solvents (Table 2). An increase of the substrate concentration from 0.5 to 1 M in THF led to a higher conversion and shorter reaction time but unchanged er (entry 1 vs Table 1, entry 4). Et₂O and CH₂Cl₂ led to good yields with lower enantioselectiv-

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Table 1. Iron-Catalyzed Thia-Michael Addition to (*E*)-3-Crotonoyloxazolidin-2-one—Catalyst Optimization^a


entry	FeX _n	yield ^b (%)	er ^c
1	FeCl ₂	14	63:37
2	Fe(BF ₄) ₂ ·6H ₂ O	50	91:9
3 ^d	Fe(OTf) ₂	42	93:7
4	Fe(ClO ₄) ₂ ·6H ₂ O	77	95:5
5	FeCl ₃	20	62:38
6	Fe(acac) ₃	64	55:45
7	Fe(OTf) ₃	19	88:12
8	Fe(ClO ₄) ₃ ·6H ₂ O	28	89:11

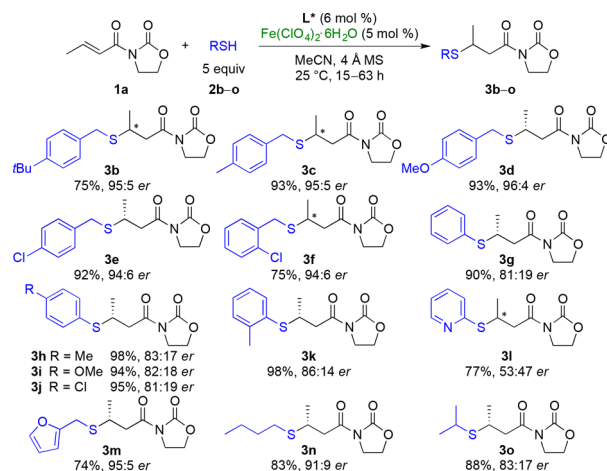
^aConditions: FeX_n (5 mol %), L* (6 mol %), 4 Å MS, 1a (0.5 mmol), and 2a (1 mmol), THF. ^bConversion by ¹H NMR. ^cDetermined by chiral HPLC (OD–H column). ^dReaction stopped after 72 h.

Table 2. Fe^{II}-Catalyzed Thia-Michael Addition to (*E*)-3-Crotonoyloxazolidin-2-one—Solvent Optimization^a


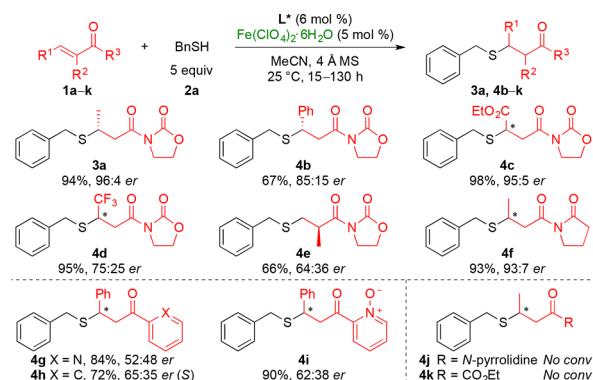
entry	solvent	T (°C)	time (h)	yield ^b (%)	er ^d
1	THF	25	24	88	95:5
2	Et ₂ O	25	24	82	84:16
3	CH ₂ Cl ₂	25	24	77	82:18
4	PhMe	25	72	89	89:11
5	MeCN	25	24	94	96:4
6	MeCN	−10	48	67 ^c	98:2
7 ^c	MeCN	−20	144	36 ^c	97:3
8 ^f	MeCN	25	144	51 ^c	94:6
9 ^g	MeCN	25	24	94	51:49

^aConditions: Fe(ClO₄)₂·6H₂O (5 mol %), L* (6 mol %), 4 Å MS, 1a (0.5 mmol), 2a (1 mmol), solvent. ^bYield of isolated product. ^cConversion by ¹H NMR. ^dDetermined by chiral HPLC (OD–H column). ^eWith 7.5 mol % of Fe(ClO₄)₂·6H₂O and 9 mol % of L*. ^fWith 1 equiv of 2a. ^g6 mol % of L* used in the absence of Fe(ClO₄)₂·6H₂O.

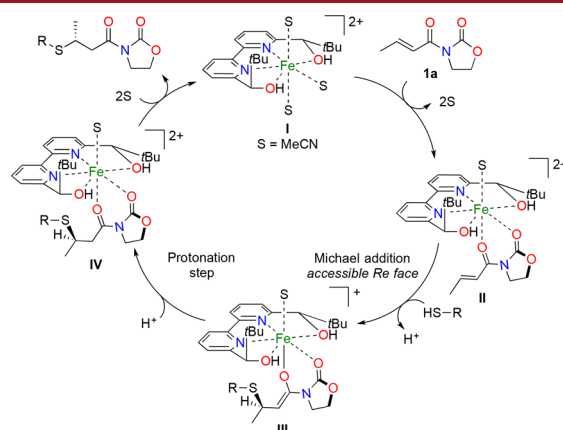
ities (entries 2 and 3). Using PhMe as a solvent afforded a good er, albeit in an extended reaction time (entry 4). A coordinating and polar solvent, such as MeCN, afforded (3*R*)-3a in high yield and excellent enantioselectivity (entry 5). Considering the azaphilicity of iron,^{21a,b} the binding of MeCN in the coordination sphere of Fe^{II} increased the transition-state stability, which affected both the rate and selectivity.^{21c} These optimized catalytic conditions involving Fe(ClO₄)₂·6H₂O/L* in MeCN were chosen for further studies.²² The temperature was then decreased from +25 to −10 °C, and then −20 °C, and up to 98:2 er's were obtained, whereas conversions were low (entries 6 and 7). However, pursuing this study at 25 °C appeared to be the most practical alternative inducing minor er variations. When a stoichiometric quantity of thiol 2a was used, a similar er was obtained in a prolonged reaction time (entry 8). Virtually no enantioselectivity was obtained when (S,S)-Bolm's ligand was used in the absence of an Fe^{II} salt (entry 9).

Scheme 1. Fe^{II}-Catalyzed Conjugate Addition of Different Thiols to (*E*)-3-Crotonoyloxazolidin-2-one^{a–c}


^aConditions: Fe(ClO₄)₂·6H₂O (5 mol %), L* (6 mol %), 4 Å MS, 1a (0.5 mmol), 2b–o (2.5 mmol), MeCN. ^bDetermined by chiral HPLC. ^cAbsolute configurations assigned from the literature, except for optically active 3b, 3c, 3f, and 3l (unknown absolute configurations).

Scheme 2. Fe^{II}-Catalyzed Conjugate Addition of Benzylthiol to α,β -Unsaturated Carbonyl Compounds^{a–c}


^aConditions: Fe(ClO₄)₂·6H₂O (5 mol %), L* (6 mol %), 4 Å MS, 1a–k (0.5 mmol), 2a (2.5 mmol), MeCN. ^bDetermined by chiral HPLC. ^cAbsolute configurations assigned from the literature, except for optically active 4c, 4d, 4f, 4g, and 4i (unknown absolute configurations).


Figure 1. Postulated mechanism.

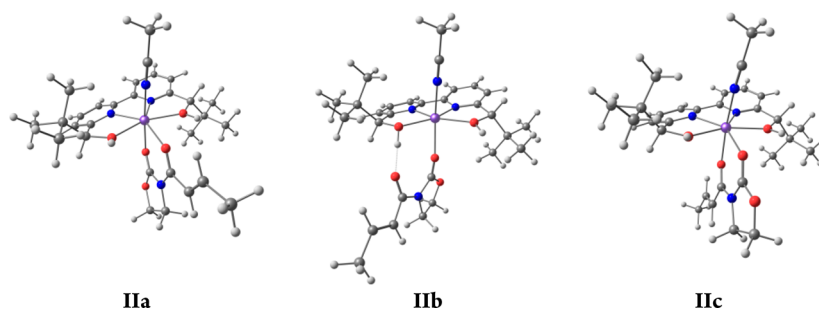


Figure 2. Geometries of the computed complexes IIa.

To demonstrate the scope of the $\text{Fe}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ -catalyzed asymmetric Michael addition, a range of thiols was studied. Substituted aromatic, heterocyclic, and aliphatic thiols were used. As previously shown, the stereoselectivity does not depend on thiol concentration. Consequently, 5 equiv of thiol was used to promote the conversion.²³ Michael addition reactions of various substituted thiols (**2b–o**) on (*E*)-3-crotonoyloxazolidin-2-one **1a** were run under the optimal reaction conditions (Scheme 1).

The Fe^{II} -catalyzed Michael addition of various thiols to (*E*)-3-crotonoyloxazolidin-2-one **1a** surprisingly led to a wide range of enantioselectivities. Up to 96:4 er's were obtained when *para*- and *ortho*-substituted benzylthiols were used (**3b–f**). In comparison, lower stereoselectivity control was observed using *para*- and *ortho*-substituted phenylthiols ((*3R*)-**3h**–(*3R*)-**3k**). The same observation was made when unsubstituted thiophenol **2g** was used ((*3R*)-**3g** vs (*3R*)-**3a**). Electron-rich and -deficient groups in the *para* position of the thiol aromatic ring had negligible influence on the enantioselectivity in both the benzyl and phenyl series (**3b–3e** and (*3R*)-**3h**–(*3R*)-**3j**). These groups changed the thiol reactivity, but with no influence on the stereoselectivity control. *o*-Methyl substitution of the aryl thiol induced an increased er, which was not observed using thiol **2f** ((*3R*)-**3k** vs **3f**). No enantioselectivity was obtained using 2-mercaptopyridine (**3l**). Furfuryl thiol, as a heterocyclic nucleophile, led to an excellent er ((*3R*)-**3m**). Butyl and isopropyl thiols led to good and moderate enantioselectivities, respectively ((*3R*)-**3n** and (*3R*)-**3o**). Finally, all β -thioethers in this study were obtained in good to excellent yields (up to 98%).

A variety of α,β -unsaturated carbonyl compounds (**1a–i**) were examined as substrates for the 1,4-addition of benzylthiol **2a**, under the optimal reaction conditions (Scheme 2). The electronic and steric effects of various R^1 groups on the enantioselectivity were studied. Among a small chosen set of α,β -unsaturated oxazolidin-2-ones, comprising electron-donating (**1a**, **1b**) and electron-withdrawing (**1c**, **1d**) groups, the highest er was obtained with $\text{R}^1 = \text{Me}$ ((*3R*)-**3a**). A major decrease of the enantioselectivity was observed when increasing the electron-withdrawing ability of R^1 from CH_3 to CF_3 ((*3R*)-**3a** vs **4d**), albeit a high level of er was maintained with $\text{R}^1 = \text{CO}_2\text{Et}$ (**4c**). Introducing a Me group at the α -position (R^2) instead of the β -position (R^1) caused the enantioselectivity to no longer be dependent on the *Re* addition face, but rather on the later protonation step. A low enantioselective α -protonation step by the chiral catalyst was highlighted by the 64:36 er obtained with (*2R*)-**4e**. A slightly reduced er was afforded using a 2-pyrrolidinone 5-membered cycle (**4f**). The nature of the chelating properties of R^3 was also examined. Pyridyl, phenyl, and pyridyl *N*-oxide as R^3 substituents were studied in regard to their different chelating structures; the enantioselectivity dropped dramatically in comparison with the oxazolidin-2-one

analogue (**4g–4i** vs (*3S*)-**4b**). The absence of a dicarbonyl chelating system did not lead to any reaction using α,β -unsaturated amide **1j** and ester **1k** (0% of **4j** and **4k**, recovered starting materials). Indeed, the dicarbonyl core of the Michael acceptor appeared to be essential for maintaining high levels of stereocontrol in the asymmetric 1,4-addition of thiols using $\text{Fe}^{\text{II}}/\text{L}^*$ system.

A catalytic cycle was postulated based on precedents gained on the coordination of Fe^{II} salt with L^* (Figure 1).^{16a–c} The bipyridine ligand is coordinated to the metal center in a tetradentate fashion via the coordination of two O and N atoms in the four equatorial sites of the octahedral $d^6 \text{Fe}^{\text{II}}$ center. MeCN molecules (noted as S) are coordinated to the axial sites as shown in I. As observed from previous crystallographic studies using Fe^{II} and L^* ,^{16a} the appearance of a fifth labile equatorial substituent arisen from electrostatic interactions, reveals the pentagonal bipyramidal geometry adopted by the chiral catalyst. After ligand exchange with substrate **1a**, both carbonyl groups chelated Fe^{II} to form complex II. This hypothesized structure of complex II is similar to the previously reported C_2 -symmetrical Fe^{III} /bis-(oxazoline) complex by Corey.²⁴ Then, the thiol would attack the more accessible *Re* face of the β -carbon of the α,β -unsaturated carbonyl compound to give III. Enantioselectivities were induced by the steric hindrance of the *t*Bu group of the ligand, which blocks the nucleophilic attack on the *Si* face of the substrate **1a**. Finally, a low enantioselective protonation on III (as noted with **4e**) generates the expected thioether adducts. The high enantioselectivities arising from the chiral induction in the β -position are in agreement with this speculated mechanism.

In the *endo* complex II depicted above, the $\text{C}=\text{C}$ bond of **1a** is oriented toward the bipyridine backbone, making its *Re* face the most accessible one for the thiol. Exchanging the equatorial and apical carbonyls would place the $\text{C}=\text{C}$ bond in the opposite direction, with the *Si* face being more accessible. Thus, the *endo*/*exo* orientation of the substrate is a critical feature, as it determines the absolute configuration of the product. To validate the *endo* configuration as the preferred one, DFT computations were carried out at the B3LYP/SDD(Fe)-cc-pVTZ (other elements)//B3LYP/SDD(Fe)-6-31+G(d) (other elements), as recently described for the mechanism of Fe^{II} -catalyzed asymmetric Mukaiyama aldol reaction.²⁵ Using MeCN as axial ligand, three isomers IIa–c could be optimized (Figure 2). In the *exo* complexes IIa and IIb, the oxazolidin-2-one carbonyl occupies the apical position. The second carbonyl is located at the equatorial position in IIa. In IIb, the second carbonyl is actually H-bonded to a hydroxyl group. In the *endo* series, no H-bonded isomers could be modeled, as they irretrievably collapse to IIc exhibiting the oxazolidin-2-one carbonyl at the equatorial position and the second carbonyl at the apical position. In agreement with the observed stereoselectivity of the title

reaction, the *endo* complex **IIc** is the most stable of the three (ΔG_{298} **IIc** (0.0); **IIa** (3.0); **IIb** (3.5)).

In summary, we have successfully developed an efficient asymmetric Michael addition of thiols. An $\text{Fe}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ conjointly used with Bolm's ligand has been shown to be an effective catalyst for the asymmetric Michael addition of thiols to α,β -unsaturated oxazolidin-2-ones. The $\text{Fe}^{\text{II}}/(\text{S,S})\text{-L}^*$ catalytic system was suitable for catalyzing asymmetric thia-Michael addition giving yields up to 98% and er's up to 96:4. The method is practical and cost-effective, and high enantioselectivities were obtained at room temperature. The chiral bipyridine ligand can be easily prepared and recycled in the purification process. A model has been proposed to support the high levels of stereoselection observed at the β -position. DFT calculations are in agreement with the postulated model. Further developments will be reported in due course.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: [10.1021/acs.orglett.7b03118](https://doi.org/10.1021/acs.orglett.7b03118).

Experimental details, characterization data, NMR spectra, and chromatograms (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: vincent.gandon@u-psud.fr.

*E-mail: thierry.ollevier@chm.ulaval.ca.

ORCID

Samuel Lauzon: 0000-0002-3672-3601

Vincent Gandon: 0000-0003-1108-9410

Thierry Ollevier: 0000-0002-6084-7954

Notes

The authors declare no competing financial interest.

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■ REFERENCES

- (1) (a) Bolm, C.; Legros, J.; Le Pailh, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217. (b) Darwish, M.; Wills, M. *Catal. Sci. Technol.* **2012**, *2*, 243. (c) Gopalaiah, K. *Chem. Rev.* **2013**, *113*, 3248. (d) Bauer, I.; Knölker, H.-J. *Chem. Rev.* **2015**, *115*, 3170.
- (2) (a) Enthaler, S.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3317. (b) Egorova, K. S.; Ananikov, V. P. *Angew. Chem., Int. Ed.* **2016**, *55*, 12150.
- (3) Bauer, E. In *Iron Catalysis II*; Bauer, E., Ed.; Springer: Berlin, 2015; Vol. 50, pp 1–18.
- (4) (a) Morris, R. H. *Chem. Soc. Rev.* **2009**, *38*, 2282. (b) Ollevier, T. *Catal. Sci. Technol.* **2016**, *6*, 41. (c) Ollevier, T.; Keipour, H. In *Iron Catalysis II*; Bauer, E., Ed.; Springer: Berlin, 2015; Vol. 50, pp 259–310. (d) Misal Castro, L. C.; Li, H.; Sortais, J.-B.; Darcel, C. *Green Chem.* **2015**, *17*, 2283. (e) Fingerhut, A.; Serdyuk, O. V.; Tsogoeva, S. B. *Green Chem.* **2015**, *17*, 2042. (f) Olivo, G.; Cussó, O.; Costas, M. *Chem. - Asian J.* **2016**, *11*, 3148.
- (5) (a) Legros, J.; Figadère, B. *Nat. Prod. Rep.* **2015**, *32*, 1541. (b) Roschangar, F.; Colberg, J.; Dunn, P. J.; Gallou, F.; Hayler, J. D.; Koenig, S. G.; Kopach, M. E.; Leahy, D. K.; Mergelsberg, I.; Tucker, J. L.; Sheldon, R. A.; Senanayake, C. H. *Green Chem.* **2017**, *19*, 281.
- (6) (a) Heravi, M. M.; Hajiabbasi, P. *Mol. Diversity* **2014**, *18*, 411. (b) Vicario, J. L.; Badia, D.; Carrillo, L. *Synthesis* **2007**, 2065.
- (7) (a) Yu, J.-S.; Huang, H.-M.; Ding, P.-G.; Hu, X.-S.; Zhou, F.; Zhou, J. *ACS Catal.* **2016**, *6*, 5319. (b) Dunbar, K. L.; Scharf, D. H.; Litomska, A.; Hertweck, C. *Chem. Rev.* **2017**, *117*, 5521. (c) Jackson, P. A.; Widen, J. C.; Harki, D. A.; Brummond, K. M. *J. Med. Chem.* **2017**, *60*, 839. (d) Shen, C.; Zhang, P. F.; Sun, Q.; Bai, S. Q.; Hor, T. S. A.; Liu, X. G. *Chem. Soc. Rev.* **2015**, *44*, 291.
- (8) (a) Enders, D.; Lutten, K.; Narine, A. A. *Synthesis* **2007**, 959. (b) Chauhan, P.; Mahajan, S.; Enders, D. *Chem. Rev.* **2014**, *114*, 8807.
- (9) (a) Zu, L. S.; Wang, J.; Li, H.; Xie, H. X.; Jiang, W.; Wang, W. *J. Am. Chem. Soc.* **2007**, *129*, 1036. (b) Rana, N. K.; Singh, V. K. *Org. Lett.* **2011**, *13*, 6520. (c) Liu, Y.; Sun, B.; Wang, B.; Wakem, M.; Deng, L. *J. Am. Chem. Soc.* **2009**, *131*, 418. (d) Dai, L.; Yang, H. J.; Chen, F. *Eur. J. Org. Chem.* **2011**, 5071. (e) Chen, W. C.; Jing, Z. Z.; Chin, K. F.; Qiao, B. K.; Zhao, Y.; Yan, L.; Tan, C. H.; Jiang, Z. Y. *Adv. Synth. Catal.* **2014**, *356*, 1292.
- (10) (a) Chen, J.; Meng, S.; Wang, L.; Tang, H.; Huang, Y. *Chem. Sci.* **2015**, *6*, 4184. (b) Yuan, P. F.; Meng, S. X.; Chen, J. A.; Huang, Y. *Synlett* **2016**, 27, 1068.
- (11) Kanemasa, S.; Oderaotoshi, Y.; Wada, E. *J. Am. Chem. Soc.* **1999**, *121*, 8675.
- (12) (a) Kobayashi, S.; Ogawa, C.; Kawamura, M.; Sugiura, M. *Synlett* **2001**, 983. (b) Matsumoto, K.; Watanabe, A.; Uchida, T.; Ogi, K.; Katsuki, T. *Tetrahedron Lett.* **2004**, *45*, 2385.
- (13) (a) Abe, A. M. M.; Sauerland, S. J. K.; Koskinen, A. M. P. *J. Org. Chem.* **2007**, *72*, 5411. (b) Kitanosono, T.; Sakai, M.; Ueno, M.; Kobayashi, S. *Org. Biomol. Chem.* **2012**, *10*, 7134.
- (14) Kawatsura, M.; Komatsu, Y.; Yamamoto, M.; Hayase, S.; Itoh, T. *Tetrahedron* **2008**, *64*, 3488.
- (15) (a) Kawatsura, M.; Komatsu, Y.; Yamamoto, M.; Hayase, S.; Itoh, T. *Tetrahedron Lett.* **2007**, *48*, 6480. (b) White, J. D.; Shaw, S. *Chem. Sci.* **2014**, *5*, 2200.
- (16) (a) Ollevier, T.; Plancq, B. *Chem. Commun.* **2012**, *48*, 2289. (b) Plancq, B.; Ollevier, T. *Chem. Commun.* **2012**, *48*, 3806. (c) Kitanosono, T.; Ollevier, T.; Kobayashi, S. *Chem. - Asian J.* **2013**, *8*, 3051. (d) Lafantaisie, M.; Mirabaud, A.; Plancq, B.; Ollevier, T. *ChemCatChem* **2014**, *6*, 2244. (e) Plancq, B.; Lafantaisie, M.; Companys, S.; Maroun, C.; Ollevier, T. *Org. Biomol. Chem.* **2013**, *11*, 7463. (f) Jalba, A.; Regnier, N.; Ollevier, T. *Eur. J. Org. Chem.* **2017**, 1628.
- (17) Based on the integration of the Me groups of **1a** and **3a**.
- (18) (a) Bolm, C.; Zehnder, M.; Bur, D. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 205. (b) Bolm, C.; Ewald, M.; Felder, M.; Schlingloff, G. *Chem. Ber.* **1992**, *125*, 1169. (c) Ishikawa, S.; Hamada, T.; Manabe, K.; Kobayashi, S. *Synthesis* **2005**, 2176.
- (19) Hong, L.; Sun, W.; Yang, D.; Li, G.; Wang, R. *Chem. Rev.* **2016**, *116*, 4006.
- (20) $\text{Fe}(\text{OTf})_2$: 93:7 er, 42% conv, 72 h vs 89:11 er, 40% conv, 48 h.
- (21) (a) Kobayashi, S.; Busujima, T.; Nagayama, S. *Chem. - Eur. J.* **2000**, *6*, 3491. (b) Huber, R.; Bigler, R.; Mezzetti, A. *Organometallics* **2015**, *34*, 3374. (c) Dyson, P. J.; Jessop, P. G. *Catal. Sci. Technol.* **2016**, *6*, 3302.
- (22) MeCN was also more effective using $\text{Fe}(\text{OTf})_2$: 95:5 er, 72% conv of **3a**. 12 mol % $\text{L}^*/10$ mol % $\text{Fe}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$: 91:9 er, 96% of **3a**. The er decreased when 20 mol % Pyr (34% conv, 75:25 er, 48 h) or 200 mol % K_2HPO_4 (95% conv, 51:49 er, 24 h) was used.
- (23) Reaction times using **2o**: 2 equiv, >130 h vs 5 equiv, 43 h.
- (24) (a) Corey, E. J.; Imai, N.; Zhang, H. Y. *J. Am. Chem. Soc.* **1991**, *113*, 728. (b) Corey, E. J.; Ishihara, K. *Tetrahedron Lett.* **1992**, *33*, 6807.
- (25) Sameera, W. M. C.; Hatanaka, M.; Kitanosono, T.; Kobayashi, S.; Morokuma, K. *J. Am. Chem. Soc.* **2015**, *137*, 11085.