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Chiral 2-Aryl Ferrocene Carboxylic Acids for the Catalytic Asymmetric C(sp^3)–H Activation of Thioamides

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ABSTRACT: Enantioselective C–H functionalization reactions using trivalent group 9 metals (Co, Rh, Ir) have been investigated mainly based on the development of well-designed chiral cyclopentadienyl (Cp) ligands. Although it has recently been demonstrated that chiral carboxylic acids combined with achiral Cp-type ligands can enable highly enantioselective C–H functionalization reactions, the structural diversity of the applied chiral acids remains limited. Here, we report that chiral 2-aryl ferrocene carboxylic acids, which are easily obtained from diastereoselective *ortho*-lithiation and Suzuki-Miyaura coupling, can serve as external chiral sources for the Cp*Co^{III}-catalyzed enantioselective C(sp^3)–H amidation of α-aryl thioamides using dioxazolones.

Since the seminal work on Cp*Rh^{III} catalysis by Satoh, Miura, and co-workers in 2007,[1] trivalent group 9 metal (Co, Rh, Ir) complexes with a pentamethylcyclopentadienyl (Cp*) or other Cp-type (Cp^x) ligand have been used for a wide variety of catalytic C–H functionalization reactions in organic synthesis[2,3] Such Cp*M^{III} catalysts are characterized by the particularly high reactivity, functional group compatibility, and robustness. More recently, the development of catalytic asymmetric C–H functionalization reactions[4] using these catalysts has attracted considerable attention, as controlling stereochemistry is crucial for the synthesis of complex molecules.[5–16] Cramer and co-workers,[5,6] as well as other groups[7] have demonstrated that well-designed chiral Cp^x ligands and their metal complexes provide a powerful and versatile platform for asymmetric C–H functionalization reactions. Engineered protein-conjugated chiral Cp^xRh catalysts also provide efficient chiral environments, as reported by Ward, Rovis, and co-workers.[8] Our group has focused on the combination of achiral Cp^xM^{III} complexes and chiral disulfonates[9] or chiral carboxylic acids[10] as an alternative approach to enantioselective C–H functionalization reactions. Chiral carboxylic acids participate in the C–H activation step as the external chiral source in a carboxylate-assisted concerted metalation-deprotonation mechanism, leading to the selective cleavage of enantiotopic C–H bonds (Figure 1a).[11-13] The groups of Ackermann[14] and Shi[15] have also reported the use of chiral carboxylic acids in enantioselective C–H functionalization reactions.[16] Although these approaches using chiral carboxylic acids are attractive in terms of the accessibility of the chiral catalytic components, the diversity of the applied chiral carboxylic acids therein is still limited compared to chiral Cp ligands[5-7,12] and bidentate ligands used in Pd^{II}-catalyzed asymmetric C–H functionalizations.[17,18] Further development of appropriate chiral carboxylic acids is highly demanded for expanding the scope of Cp*M^{III}-catalyzed enantioselective C–H functionalization reactions.

Unsymmetrically 1,2-disubstituted ferrocenes, which exhibit planar chirality, have been extensively explored in asymmetric catalysis.[19,20] Based on their unique but readily accessible chirality, a variety of chiral ligands and organocatalysts have been developed over the past few decades (Figure 1b). We anticipated that chiral carboxylic acids with a planar chiral ferrocene backbone could serve as external chiral sources for Cp^xM^{III}-catalyzed enantioselective C–H functionalization reactions, which would significantly expand catalyst diversity. Herein, we report the synthesis of chiral 2-aryl ferrocene carboxylic acids and their application to the enantioselective C(sp^3)–H amidation of α-aryl thioamides using a Cp*Co^{III} catalyst (Figure 1c).[10b,21-23] This synthetic route provides easy access to various derivatives, which is often necessary for optimization studies in asymmetric catalysis.

For the synthesis of the chiral ferrocene carboxylic acids, we initially subjected ferrocene oxazoline **1** to diastereoselective *ortho*-lithiation (Scheme S1 in Supporting Information) under previously reported conditions.[24] After quenching with 1,1,2,2-tetrabromoethane, bromide **2** was obtained as an almost single diastereomer. Partial hydrolysis of the oxazoline moiety, acetylation of the resulting primary amine,[25] and methanolysis of the ester intermediate led to the common precursor (**3**) in 76% yield over three steps. Chiral HPLC analysis of **3** indicated that an essentially pure enantiomer was obtained (99:1 er). Subsequently, we investigated cross-coupling reactions to synthesize various derivatives from **3**. Suzuki–Miyaura coupling reactions under Buchwald's conditions using SPhos[26] as a ligand proceeded smoothly to afford 2-aryl ferrocene carboxylic acids **4** (28–85% yield) after hydrolysis of the ester.

With several chiral carboxylic acids in hand (**4a**–**4d**), we investigated the cobalt-catalyzed enantioselective C(sp^3)–H amidation reaction of α-aryl thioamide **5a** using dioxazolone **6a** (Table 1). In our previous studies (Figure 1a), only α-alkyl and α-benzyl thioamides were examined as substrates.[10b]

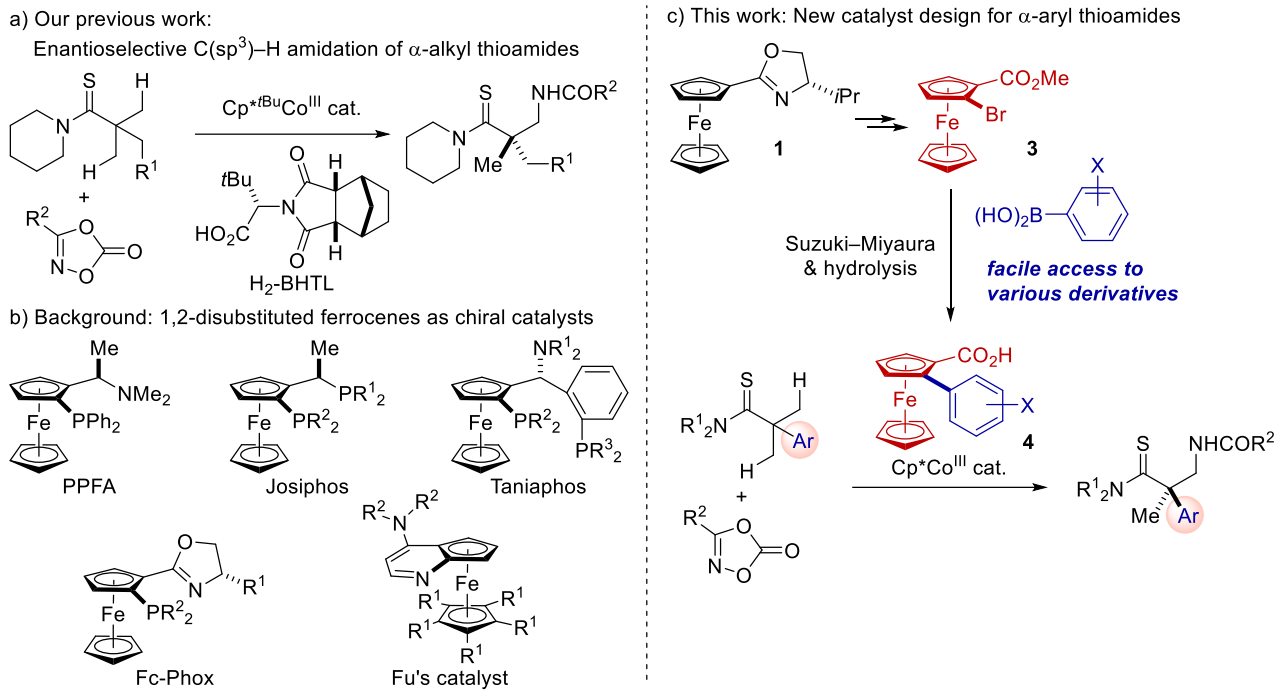
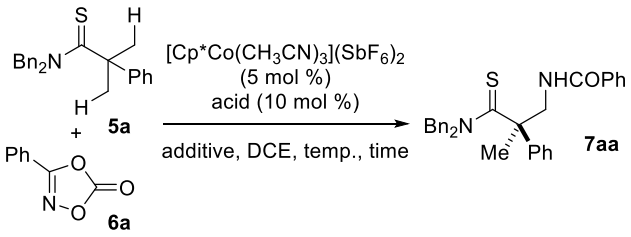


Figure 1. (a) Our previous work on enantioselective C(sp^3)–H amidation of α-alkyl thioamides (b) Representative examples of chiral 1,2-disubstituted ferrocenes used in asymmetric catalysis (c) Chiral ferrocene carboxylic acids for Cp*Co^{III}-catalyzed enantioselective C(sp^3)–H amidation of α-aryl thioamides (this work).

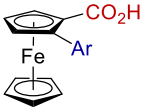
Considering the synthetic importance of this transformation to give chiral β-amino carbonyl building blocks, we decided to explore expanding the substrate scope using the newly synthesized chiral acids **4**. Our optimization studies started with screening the chiral acids **4** using [Cp*Co(CH_3CN)$_3$](SbF_6)$_2$ (entries 1–4). While **4a**–**4c** exhibited similar reactivity (57–62% yield) and selectivity (65:35–67:33 er), the most sterically hindered derivative (**4d**; Ar = 3,5-di-*tert*-butyl phenyl) led to higher conversion with higher enantioselectivity (84:16 er; entry 4). Since the reactivity was greatly enhanced by **4d**, lower reaction temperatures were then examined in order to improve the selectivity (entries 5–7). Although the reaction barely proceeded at 15 °C (entry 5), the addition of molecular sieves 13X (MS13X) significantly accelerated the reaction and provided a high yield with increased selectivity (entry 6). To our surprise, the reaction proceeded even at 4 °C, affording the product in 90% yield with 87:13 er after 72 h (entry 7).

The optimized reaction conditions using **4d** as the chiral source were then applied to other α-aryl thioamides **5** (Scheme 1). The electronic properties of the α-aryl group did not affect the enantioselectivity (**7aa**–**7ca**), albeit that the reactivity was somewhat deteriorated when a *p*Cl-phenyl-substituted substrate was used (**7ca**). 6-Methoxy-2-naphthyl-substituted thioamide (**5d**) also provided the corresponding product (**7da**) in 96% with 87:13 er. Changing the substituents at the thioamide moiety to *i*Bu groups had negligible influence on the reactivity and selectivity (**7ea**). We examined a range of dioxazolones **6** using thioamide **5a**. Aromatic, heteroaromatic, and aliphatic dioxazolones all provided the targeted products in good yield and enantioselectivity (**7ab**–**7af**). Steric hindrance around the dioxazolone functionality did not affect the reactions (**7ac** and **7af**). Finally, the reaction using **5a** and **6a** was carried out in 1.0 mmol scale, providing **7aa** in 92% yield with 85:15 er.

Table 1. Screening of chiral carboxylic acids 4 and optimization.[a]



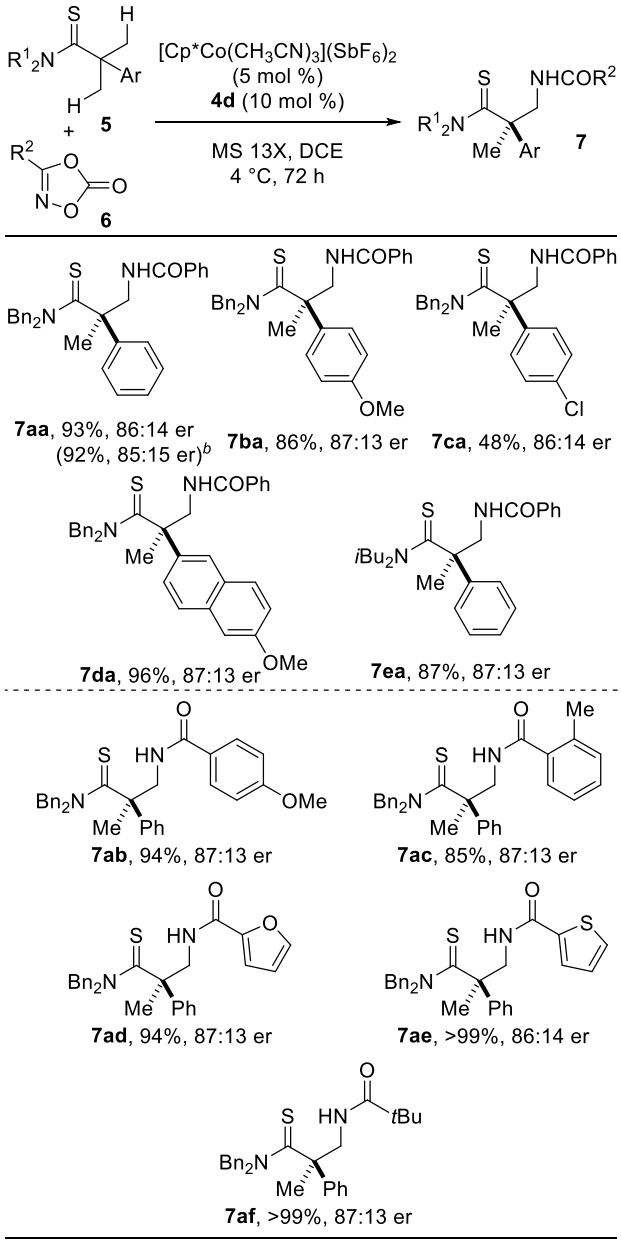
entry	acid	additive	temp. [°C]	time [h]	yield[b] [%]	er[c]
1	**4a**	none	30	24	59	66:34
2	**4b**	none	30	24	57	65:35
3	**4c**	none	30	24	62	67:33
4	**4d**	none	30	24	90	84:16
5	**4d**	none	15	24	5	85:15
6	**4d**	MS13X	15	24	90	86:14
7	**4d**	MS13X	4	72	90	87:13



4a, Ar = Ph
4b, Ar = 4-MeO-C_6H_4-
4c, Ar = 3,5-$(CF_3)_2$-C_6H_3-
4d, Ar = 3,5-$(t$Bu$)_2$-C_6H_3-

[a]Reactions were carried out using **5a** (0.050 mmol), **6a** (0.06 mmol), [Cp*Co(CH_3CN)$_3$](SbF_6)$_2$ (0.0025 mmol, 5 mol %), acid (0.005 mmol, 10 mol %), and additive (10 mg) in DCE (0.5 mL) unless otherwise noted. [b]Determined by ^{1}H NMR analysis of the crude mixture using 1,1,2,2-tetrachloroethane as the internal standard. [c]Determined by chiral HPLC analysis. Cp* = 1,2,3,4,5-pentamethylcyclopentadienyl.

Scheme 1. Substrate scope of the enantioselective C(sp^3)–H amidation of α-aryl thioamides 5 with dioxazolone 6.[a]



[a]Reactions were carried out using **5** (0.20 mmol), **6** (0.24 mmol), [Cp*Co(CH$_3$CN)$_3$](SbF$_6$)$_2$ (0.01 mmol, 5 mol %), **4d** (0.02 mmol, 10 mol %), and MS13X (40 mg) in DCE (2 mL). [b]1.0 mmol scale.

In order to rationalize the observed enantioselectivity using **4d**, we would like to propose qualitative stereochemical models in Figure 2.[27] Due to the piano-stool structure of Cp*Co^{III}L$_3$ complexes, the CoL$_3$ fragment constitutes a conical scaffold with concave and convex faces. The ferrocene moiety of **4d** would be aligned on the convex face to avoid the steric repulsion with the thioamide. Based on this assumption, four different transition states (TSs) for the C–H activation are possible. In **TS-(*S*)-1** and **TS-(*R*)-1**, the α-aryl group of the thioamide is located on the concave face, which would render these two TSs unfavorable. **TS-(*S*)-2** might be less favored than **TS-(*R*)-2** due to the steric repulsion between the 3,5-di-

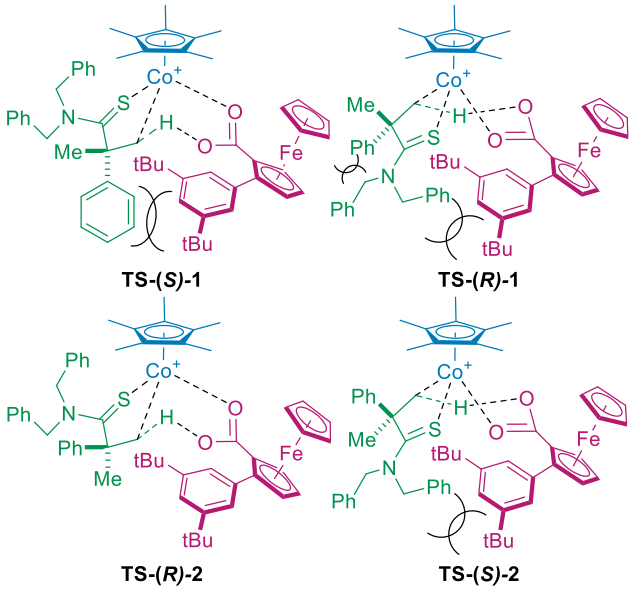


Figure 2. Stereochemical models for plausible transition states of the C–H activation to rationalize the observed enantioselectivity using chiral carboxylic acid **4d**.

tert-butyl-phenyl group of **4d** and the *N*-benzyl groups of the thioamide. Overall, **TS-(*R*)-2** is the most plausible transition state for the C–H activation, which selectively provides (*R*)-products.[28]

In summary, we have synthesized several chiral 2-aryl ferrocene carboxylic acids **4**, one of which exhibited good reactivity and enantioselectivity in cobalt-catalyzed C(sp^3)–H amidation reactions of α-aryl thioamides. These carboxylic acids can be easily synthesized and modified by changing the aryl substituent, which is introduced via a cross-coupling reaction in the late step of the synthesis. Investigation on catalytic enantioselective C–H functionalization using these carboxylic acids in combination with Cp*Co^{III} or Cp*Rh^{III} catalysts are currently in progress in our group.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedures, characterization data of the synthesized compounds, and copies of their NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Ueura, K.; Satoh, T.; Miura, M. An Efficient Waste-free Oxidative Coupling via Regioselective C–H Bond Cleavage: Rh/Cu-Catalyzed Reaction of Benzoic Acids with Alkynes and Acrylates under Air. *Org. Lett.* **2007**, *9*, 1407-1409.

(2) For selected general reviews on C–H functionalization reactions, see: (a) Shin, K.; Kim, H.; Chang, S. Transition-Metal-Catalyzed C-N Bond Forming Reactions Using Organic Azides as the Nitrogen Source: A Journey for the Mild and Versatile C–H Amination. *Acc. Chem. Res.* **2015**, *48*, 1040-1052. (b) Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. Mild Metal-catalyzed C–H Activation: Examples and Concepts. *Chem. Soc. Rev.* **2016**, *45*, 2900-2936. (c) He, J.; Wasa, M.; Chan, K. S. L.; Shao, Q.; Yu, J.-Q. Palladium-Catalyzed Transformations of Alkyl C–H Bonds. *Chem. Rev.* **2017**, *117*, 8754-8786. (d) Hummel, J. R.; Boerth, J. A.; Ellman, J. A. Transition-Metal-Catalyzed C–H Bond Addition to Carbonyls, Imines, and Related Polarized π Bonds. *Chem. Rev.* **2017**, *117*, 9163-9227. (e) Karimov, R. R.; Hartwig, J. F. Transition-Metal-Catalyzed Selective Functionalization of C(sp^3)–H Bonds in Natural Products. *Angew. Chem., Int. Ed.* **2018**, *57*, 4234-4241. (f) Sambiagio, C.; Schönbauer, D.; Blieck, R.; Dao-Huy, T.; Pototschnig, G.; Schaaf, P.; Wiesinger, T.; Zia, M. F.; Wencel-Delord, J.; Besset, T.; Maes, B. U. W.; Schnürch, M. A Comprehensive Overview of Directing Groups Applied in Metal-Catalysed C–H Functionalisation Chemistry. *Chem. Soc. Rev.* **2018**, *47*, 6603-6743. (g) Gandeepan, P.; Müller, T.; Zell, D.; Cera, G.; Warratz, S.; Ackermann, L. 3d Transition Metals for C–H Activation. *Chem. Rev.* **2019**, *119*, 2192-2452.

(3) For reviews on Cp*M^{III}-catalyzed C–H functionalization reactions, see: (a) Satoh, T.; Miura, M. Oxidative Coupling of Aromatic Substrates With Alkynes and Alkenes Under Rhodium Catalysis. *Chem. Eur. J.* **2010**, *16*, 11212-11222. (b) Kuhl, N.; Schröder, N.; Glorius, F. Formal S_N-Type Reactions in Rhodium(Iii)-Catalyzed C–H Bond Activation. *Adv. Synth. Catal.* **2014**, *356*, 1443-1460. (c) Song, G.; Li, X. Substrate Activation Strategies in Rhodium(III)-Catalyzed Selective Functionalization of Arenes. *Acc. Chem. Res.* **2015**, *48*, 1007-1020. (d) Yoshino, T.; Matsunaga, S. (Pentamethylcyclopentadienyl)cobalt(III)-Catalyzed C–H Bond Functionalization: From Discovery to Unique Reactivity and Selectivity. *Adv. Synth. Catal.* **2017**, *359*, 1245-1262. (e) Wang, S.; Chen, S.-Y.; Yu, X.-Q. C–H Functionalization by High-Valent Cp*Co(III) Catalysis. *Chem. Commun.* **2017**, *53*, 3165-3180. (f) Chirila, P. G.; Whiteoak, C. J. Recent Advances Using [Cp*Co(CO)I_2] Catalysts as a Powerful Tool for C–H Functionalisation. *Dalton Trans.* **2017**, *46*, 9721-9739. (g) Piou, T.; Rovis, T. Electronic and Steric Tuning of a Prototypical Piano Stool Complex: Rh(III) Catalysis for C–H Functionalization. *Acc. Chem. Res.* **2018**, *51*, 170-180. (h) Yoshino, T.; Matsunaga, S. Cp*Co^{III}-Catalyzed C–H Functionalization and Asymmetric Reactions Using External Chiral Sources. *Synlett* **2019**, *30*, 1384-1400.

(4) For reviews on enantioselective C–H functionalization reactions, see: (a) Newton, C. G.; Wang, S.-G.; Oliveira, C. C.; Cramer, N. Catalytic Enantioselective Transformations Involving C–H Bond Cleavage by Transition-Metal Complexes. *Chem. Rev.* **2017**, *117*, 8908-8976. (b) Saint-Denis, T. G.; Zhu, R.-Y.; Chen, G.; Wu, Q.-F.; Yu, J.-Q. Enantioselective C(sp^3)-H Bond Activation by Chiral Transition Metal Catalysts. *Science* **2018**, *359*, eaao4798.

(5) For selected examples, see: (a) Ye, B.; Cramer, N. Chiral Cyclopentadienyl Ligands as Stereocontrolling Element in Asymmetric C–H Functionalization. *Science* **2012**, *338*, 504-506. (b) Ye, B.; Cramer, N. A Tunable Class of Chiral Cp Ligands for Enantioselective Rhodium(III)-Catalyzed C–H Allylations of Benzamides. *J. Am. Chem. Soc.* **2013**, *135*, 636-639. (c) Sun, Y.; Cramer, N. Tailored Tri-substituted Chiral Cp^xRh(III) Catalysts for Kinetic Resolutions of Phosphinic Amides. *Chem. Sci.* **2018**, *9*, 2981-2985. (d) Ozols, K.; Jang, Y.-S.; Cramer, N. Chiral Cyclopentadienyl Cobalt(III) Complexes Enable Highly Enantioselective 3d-Metal-Catalyzed C–H Functionalizations. *J. Am. Chem. Soc.* **2019**, *141*, 5675-5680. Selected examples of asymmetric reactions using Cramer's chiral Cp^xRh^{III} complexes: (e) Potter, T. J.; Kamber, D. N.; Mercado, B. Q.; Ellman, J. A. Rh(III)-Catalyzed Aryl and Alkenyl C–H Bond Addition to Diverse Nitroalkenes. *ACS Catal.* **2017**, *7*, 150-153. (f) Yang, X.; Zheng, G.; Li, X. Rhodium(III)-Catalyzed Enantioselective Coupling of Indoles and 7-Azabenzonorbornadienes by C–H Activation/Desymmetrization. *Angew. Chem., Int. Ed.* **2019**, *58*, 322.

(6) (a) Ye, B.; Cramer, N. Chiral Cyclopentadienyls: Enabling Ligands for Asymmetric Rh(III)-Catalyzed C–H Functionalizations. *Acc. Chem. Res.* **2015**, *48*, 1308-1318. (b) Newton, C. G.; Kossler, D.; Cramer, N. Asymmetric Catalysis Powered by Chiral Cyclopentadienyl Ligands. *J. Am. Chem. Soc.* **2016**, *138*, 3935-3941.

(7) (a) Zheng, J.; Cui, W.-J.; Zheng, C.; You, S.-L. Synthesis and Application of Chiral Spiro Cp Ligands in Rhodium-Catalyzed Asymmetric Oxidative Coupling of Biaryl Compounds with Alkenes. *J. Am. Chem. Soc.* **2016**, *138*, 5242-5245. (b) Jia, Z.-J.; Merten, C.; Gontla, R.; Daniliuc, C. G.; Antonchick, A. P.; Waldmann, H. General Enantioselective C–H Activation with Efficiently Tunable Cyclopentadienyl Ligands. *Angew. Chem., Int. Ed.* **2017**, *56*, 2429-2434. (c) Trifonova, E. A.; Ankudinov, N. M.; Mikhaylov, A. A.; Chusov, D. A.; Nelyubina, Y. V.; Perekalin, D. S. A Planar-Chiral Rhodium(III) Catalyst with a Sterically Demanding Cyclopentadienyl Ligand and Its Application in The Enantioselective Synthesis of Dihydroisoquinolones. *Angew. Chem., Int. Ed.* **2018**, *57*, 7714-7718.

(8) Hyster, T. K.; Knörr, L.; Ward, T. R.; Rovis, T. Biotinylated Rh(III) Complexes in Engineered Streptavidin for Accelerated Asymmetric C–H Activation. *Science* **2012**, *338*, 500-503.

(9) Satake, S.; Kurihara, T.; Nishikawa, K.; Mochizuki, T.; Hatano, M.; Ishihara, K.; Yoshino, T.; Matsunaga, S. Pentamethylcyclopentadienyl Rhodium(III)–Chiral Disulfonate Hybrid Catalysis for Enantioselective C–H Bond Functionalization. *Nat. Catal.* **2018**, *1*, 585-591.

(10) (a) Lin, L.; Fukagawa, S.; Sekine, D.; Tomita, E.; Yoshino, T.; Matsunaga, S. Chiral Carboxylic Acid Enabled Achiral Rhodium(III)-Catalyzed Enantioselective C–H Functionalization. *Angew. Chem., Int. Ed.* **2018**, *57*, 12048-12052. (b). Fukagawa, S.; Kato, Y.; Tanaka, R.; Kojima, M.; Yoshino, T.; Matsunaga, S. Enantioselective C(sp^3)–H Amidation of Thioamides Catalyzed by a $Cobalt^{III}$/Chiral Carboxylic Acid Hybrid System. *Angew. Chem., Int. Ed.* **2019**, *58*, 1153-1157.

(11) For a preliminary report on chiral carboxylic acid-enabled enantioselective C–H bond cleavage, see: Gwon, D.; Park, S.; Chang, S. Dual Role of Carboxylic Acid Additive: Mechanistic Studies and Implication for the Asymmetric C–H Amidation. *Tetrahedron* **2015**, *71*, 4504-4511.

(12) Chiral CpM^{III}/chiral carboxylic acid cooperative systems have been reported by Cramer and co-workers: (a) Jang, Y.-S.; Dieckmann, M.; Cramer, N. Cooperative Effects Between Chiral Cp^x-Iridium(III) Catalysts and Chiral Carboxylic Acids in Enantioselective C–H Amidations of Phosphine Oxides. *Angew. Chem., Int. Ed.* **2017**, *56*, 15088-15092. (b) Jang, Y.-S.; Woźniak, Ł.; Pedroni, J.; Cramer, N. Access to P- and Axially Chiral Biaryl Phosphine Oxides by Enantioselective Cp^xIr^{III}-Catalyzed C–H Arylations. *Angew. Chem., Int. Ed.* **2018**, *57*, 12901-12905. (c) Sun, Y.; Cramer, N. Enantioselective Synthesis of Chiral-at-Sulfur 1,2-Benzothiazines by Cp^xRh^{III}-Catalyzed C–H Functionalization of Sulfoximines. *Angew. Chem., Int. Ed.* **2018**, *57*, 15539-15543. (d) Brauns, M.; Cramer, N. Efficient Kinetic Resolution of Sulfur-Stereogenic Sulfoximines Exploiting Cp^xRh^{III}-Catalyzed C–H Functionalization. *Angew. Chem., Int. Ed.* **2019**, *58*, 8902-8906.

(13) (a) Lapointe, D.; Fagnou, K. Overview of the Mechanistic Work on the Concerted Metallation–Deprotonation Pathway. *Chem. Lett.* **2010**, *39*, 1118-1126. (b) Ackermann, L. Carboxylate-Assisted Transition-Metal-Catalyzed C–H Bond Functionalizations: Mechanism and Scope. *Chem. Rev.* **2011**, *111*, 1315-1345. (c) Davies, D. L.; Macgregor, S. A.; McMullin, C. L. Computational Studies of Carboxylate-Assisted C–H Activation and Functionalization at Group 8-10 Transition Metal Centers. *Chem. Rev.* **2017**, *117*, 8649-8709.

(14) (a) Zell, D.; Bursch, M.; Müller, V.; Grimme, S.; Ackermann, L. Full Selectivity Control in Cobalt(III)-Catalyzed C–H Alkylations by Switching of the C–H Activation Mechanism. *Angew. Chem., Int. Ed.* **2017**, *56*, 10378-10382. (b) Pesciaioli, F.; Dhawa, U.; Oliveira, J. C. A.; Yin, R.; John, M.; Ackermann, L. Enantioselective Cobalt(III)-Catalyzed C–H Activation Enabled by Chiral Carboxylic Acid Cooperation. *Angew. Chem., Int. Ed.* **2018**, *57*, 15425-15429.

(15) Liu, Y.-H.; Li, P.-X.; Yao, Q.-J.; Zhang, Z.-Z.; Huang, D.-Y.; Le, M. D.; Song, H.; Liu, L.; Shi, B.-F. Cp*Co(III)/MPAA-Catalyzed Enantioselective Amidation of Ferrocenes Directed by Thioamides Under Mild Conditions. *Org. Lett.* **2019**, *21*, 1895-1899.

(16) Wang and co-workers reported a chiral transient directing group for Cp*Rh(III)-catalyzed enantioselective C–H functionalization: Li, G.; Jiang, J.; Xie, H.; Wang, J. Introducing the Chiral Transient Directing Group Strategy to Rhodium(III)-Catalyzed Asymmetric C–H Activation. *Chem. Eur. J.* **2019**, *25*, 4688-4694.

(17) For pioneering work on Pd/mono protected amino acid (MPAA) catalysts for enantioselective C–H functionalization reactions, see: (a) Shi, B.-F.; Maugel, N.; Zhang, Y.-H.; Yu, J.-Q. Pd^{II}-Catalyzed Enantioselective Activation of $C(sp^2)$–H and $C(sp^3)$–H Bonds Using Monoprotected Amino Acids as Chiral Ligands. *Angew. Chem., Int. Ed.* **2008**, *47*, 4882-4886. For selected recent work, see: (b) Chen, G.; Gong, W.; Zhuang, Z.; Andrä, M. S.; Chen, Y.-Q.; Hong, X.; Yang, Y.-F.; Liu, T.; Houk, K. N.; Yu, J.-Q. Ligand-Accelerated Enantioselective Methylene $C(sp^3)$–H Bond Activation. *Science* **2016**, *353*, 1023-1027. (c) Wu, Q.-F.; Shen, P.-X.; He, J.; Wang, X.-B.; Zhang, F.; Shao, Q.; Zhu, R.-Y.; Mapelli, C.; Qiao, J. X.; Poss, M. A.; Yu, J.-Q. Formation of α-Chiral Centers by Asymmetric β-$C(sp^3)$–H Arylation, Alkenylation, and Alkynylation. *Science* **2017**, *355*, 499-503. (d) Shao, Q.; Wu, Q.-F.; He, J.; Yu, J.-Q. Enantioselective γ-$C(sp^3)$–H Activation of Alkyl Amines via Pd(II)/Pd(0) Catalysis. *J. Am. Chem. Soc.* **2018**, *140*, 5322-5325. (e) Shen, P.-X.; Hu, L.; Shao, Q.; Hong, K.; Yu, J.-Q. Pd(II)-Catalyzed Enantioselective $C(sp^3)$–H Arylation of Free Carboxylic Acids. *J. Am. Chem. Soc.* **2018**, *140*, 6545-6549.

(18) Yang, Y.-F.; Hong, X.; Yu, J.-Q.; Houk, K. N. Experimental-Computational Synergy for Selective Pd(II)-Catalyzed C–H Activation of Aryl and Alkyl Groups. *Acc. Chem. Res.* **2017**, *50*, 2853-2860.

(19) For recent reviews on chiral ferrocene derivatives, see: (a) Gómez Arrayás, R.; Adrio, J.; Carretero, J. C. Recent Applications of Chiral Ferrocene Ligands in Asymmetric Catalysis. *Angew. Chem., Int. Ed.* **2006**, *45*, 7674-7715. (b) Schaarschmidt, D.; Lang, H. Selective Syntheses of Planar-Chiral Ferrocenes. *Organometallics* **2013**, *32*, 5668-5704. (c) Gao, D.-W.; Gu, Q.; Zheng, C.; You, S.-L. Synthesis of Planar Chiral Ferrocenes via Transition-Metal-Catalyzed Direct C−H Bond Functionalization. *Acc. Chem. Res.* **2017**, *50*, 351-365.

(20) For selected examples, see: (a) Hayashi, T.; Yamamoto, K.; Kumada, M. Asymmetric Catalytic Hydrosilylation of Ketones Preparation of Chiral Ferrocenylphosphines as Chiral Ligands. *Tetrahedron Lett.* **1974**, *15*, 4405-4408. (b) Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. A Novel Easily Accessible Chiral Ferrocenyldiphosphine for Highly Enantioselective Hydrogenation, Allylic Alkylation, and Hydroboration Reactions. *J. Am. Chem. Soc.* **1994**, *116*, 4062-4066. (c) Richards, C. J.; Damalidis, T.; Hibbs, D. E.; Hursthouse, M. B. Synthesis of 2-[2-(Diphenylphosphino)ferrocenyl]oxazoline Ligands. *Synlett* **1995**, 74-76. (d) Nishibayashi, Y.; Uemura, S. Asymmetric Synthesis and Highly Diastereoselective *ortho*-Lithiation of Oxazolinylferrocenes. *Synlett* **1995**, *1995*, 79-81. (e) Sawamura, M.; Hamashima, H.; Sugawara, M.; Kuwano, R.; Ito, Y. Synthesis and Structures of Trans-Chelating Chiral Diphosphine Ligands Bearing Aromatic P-Substituents, (*S*,*S*)-(*R*,*R*)- and (*R*,*R*)-(*S*,*S*)-2,2"-Bis[1-(diarylphosphino)ethyl]-1,1"-biferrocene (ArylTRAPs) and Their Transition Metal Complexes. *Organometallics* **1995**, *14*, 4549-4558. (f) Ruble, J. C.; Fu, G. C. Chiral π-Complexes of Heterocycles with Transition Metals: A Versatile New Family of Nucleophilic Catalysts. *J. Org. Chem.* **1996**, *61*, 7230-7231. (g) Hodous, B. L.; Ruble, J. C.; Fu, G. C. Enantioselective Addition of Alcohols to Ketenes Catalyzed by a Planar-Chiral Azaferrocene: Catalytic Asymmetric Synthesis of Arylpropionic Acids. *J. Am. Chem. Soc.* **1999**, *121*, 2637-2638. (h) Ireland, T.; Grossheimann, G.; Wieser-Jeunesse, C.; Knochel, P. Ferrocenyl Ligands with Two Phosphanyl Substituents in the α,ε Positions for the Transition Metal Catalyzed Asymmetric Hydrogenation of Functionalized Double Bonds. *Angew. Chem., Int. Ed.* **1999**, *38*, 3212-3215. (i) Bringmann, G.; Hinrichs, J.; Peters, K.; Peters, E.-M. Synthesis of a Chiral Aryl-Ferrocenyl Ligand, by Intramolecular Coupling to a Biaryl-Related Lactone. *J. Org. Chem.* **2001**, *66*, 629-632. (j) Ireland, T.; Tappe, K.; Grossheimann, G.; Knochel, P. Synthesis of a New Class of Chiral 1,5-Diphosphanylferrocene Ligands and Their Use in Enantioselective Hydrogenation. *Chem. Eur. J.* **2002**, *8*, 843-852. (k) Boaz, N. W.; Debenham, S. D.; Mackenzie, E. B.; Large, S. E. Phosphinoferrocenylaminophosphines as Novel and Practical Ligands for Asymmetric Catalysis. *Org. Lett.* **2002**, *4*, 2421-2424. (l) Garcia Mancheño, O.; Priego, J.; Cabrera, S.; Gómez Arrayás, R.; Llamas, T.; Carretero, J. C. 1-Phosphino-2-sulfenylferrocenes as Planar Chiral Ligands in Enantioselective Palladium-Catalyzed Allylic Substitutions. *J. Org. Chem.* **2003**, *68*, 3679-3686. (m) Jensen, J. F.; Johannsen, M. New Air-Stable Planar Chiral Ferrocenyl Monophosphine Ligands: Suzuki Cross-Coupling of Aryl Chlorides and Bromides. *Org. Lett.* **2003**, *5*, 3025-3028. (n) Spindler, F.; Malan, C.; Lotz, M.; Kesselgruber, M.; Pittelkow, U.; Rivas-Nass, A.; Briel, O.; Blaser, H.-U. Modular Chiral Ligands: The Profiling of the Mandyphos and Taniaphos Ligand Families. *Tetrahedron: Asymmetry* **2004**, *15*, 2299-2306.

(21) For general reviews on cobalt-catalyzed C–H functionalization reactions, see: (a) Gao, K.; Yoshikai, N. Low-Valent Cobalt Catalysis: New Opportunities for C–H Functionalization. *Acc. Chem. Res.* **2014**, *47*, 1208-1219. (b) Moselage, M.; Li, J.; Ackermann, L. Cobalt-Catalyzed C–H Activation. *ACS Catal.* **2016**, *6*, 498-525. (c) Usman, M.; Ren, Z.-H.; Wang, Y.-Y.; Guan, Z.-H. Recent Developments in Cobalt Catalyzed Carbon–Carbon and Carbon–Heteroatom Bond Formation via C–H Bond Functionalization. *Synthesis* **2017**, *49*, 1419-1443. (d) Yoshino, T.; Matsunaga, S. Cobalt-Catalyzed $C(sp^3)$−H Functionalization Reactions. *Asian J. Org. Chem.* **2018**, *7*, 1193-1205.

(22) For the racemic reactions, see: (a) Tan, P. W.; Mak, A. M.; Sullivan, M. B.; Dixon, D. J.; Seayad, J. Thioamide-Directed Cobalt(III)-Catalyzed Selective Amidation of $C(sp^3)$–H Bonds. *Angew. Chem., Int. Ed.* **2017**, *56*, 16550-16554. For selected examples for C–H amidation reactions using dioxazolones under Cp^*Co^{III} or Cp^*Rh^{III} catalysis: (b) Park, Y.; Park, K. T.; Kim, J. G.; Chang, S. Mechanistic Studies on the Rh(III)-Mediated Amido Transfer Process Leading to Robust C–H Amination with a New Type of Amidating Reagent. *J. Am. Chem. Soc.* **2015**, *137*, 4534-4542. (c) Park, J.; Chang, S. Comparative Catalytic Activity of Group 9 [Cp^*M^{III}] Complexes: Cobalt-Catalyzed C–H Amidation of Arenes with Dioxazolones as Amidating Reagents. *Angew. Chem., Int. Ed.* **2015**, *54*, 14103-10104. (d) Liang, Y.; Liang, Y-F.; Tang, C.; Yuan, Y.; Jiao, N. Cationic Cobalt(III)-Catalyzed Aryl and Alkenyl C‑H Amidation: A Mild Protocol for the Modification of Purine Derivatives. *Chem. Eur. J.* **2015**, *21*, 16395-16399. (e) Wang, H.; Lorion, M. M.; Ackermann, L. Overcoming the Limitations of C−H Activation with Strongly Coordinating *N*-Heterocycles by Cobalt Catalysis. *Angew. Chem., Int. Ed.* **2016**, *55*, 10386-10390. (f) Barsu, N.; Rahman, M. A.; Sen, M.; Sundararaju, B. Cp^*Co^{III}-Catalyzed $C(sp^3)$−H Bond Amidation of 8-Methylquinoline. *Chem. Eur. J.* **2016**, *22*, 9135-9138. (g) Wang, S.-B.; Gu, Q.; You, S.-L. Cp*Co(III)-Catalyzed *ortho* C–H Amidation of 2-Pyridinyl Ferrocenes with 1,4,2-Dioxazol-5-ones. *Journal of Catalysis* **2018**, *361*, 393-397.

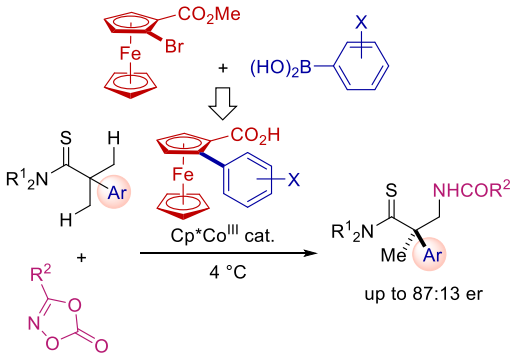
(23) For related Pd- and Rh^I-catalyzed enantioselective C–H functionalization reactions of thioamides, see: (a) Jain, P.; Verma, P.; Xia, G.; Yu, J.-Q. Enantioselective Amine α-Functionalization *via* Palladium-Catalysed C–H Arylation of Thioamides. *Nat. Chem.* **2017**, *9*, 140-144. (b) Greßies, S.; Klauck, F. J. R.; Kim, J. H.; Constantin G. Daniliuc, C. G.; Glorius, F. Ligand-Enabled Enantioselective C_{sp3} – H Activation of Tetrahydroquinolines and Saturated Aza-Heterocycles by Rh^I. *Angew. Chem., Int. Ed.* **2018**, *57*, 9950-9954. (c) Jiang, H.-J.; Zhong, X.-M.; Yu, J.; Zhang, Y.; Zhang, Z.; Wu, Y.-D. Gong, L.-Z. Assembling a Hybrid Pd Catalyst from a Chiral Anionic Co^{III} Complex and Ligand for Asymmetric $C(sp^3)$–H Functionalization. *Angew. Chem., Int. Ed.* **2019**, *58*, 1803-1807.

(24) (a) Herbert, S. A.; Castell, D. C.; Clayden, J.; Arnott, G. E. Manipulating the Diastereoselectivity of Ortholithiation in Planar Chiral Ferrocenes. *Org. Lett.* **2013**, *15*, 3334-3337. For original conditions, see: (b) Sammakia, T.; Latham, H. A.; Schaad, D. R. Highly Diastereoselective *ortho* Lithiations of Chiral Oxazoline-Substituted Ferrocenes. *J. Org. Chem.* **1995**, *60*, 10-11. (c) Sammakia, T.;

Latham, H. A. Ligand Effects on the Stereochemistry of the Metalation of Chiral Ferrocenyloxazolines. *J. Org. Chem.* **1995**, *60*, 6002-6003. See also refs. 20c and 20d.

(25) Gao, D.-W.; Shi, Y.-C.; Gu, Q.; Zhao, Z.-L.; You, S.-L. Enantioselective Synthesis of Planar Chiral Ferrocenes *via* Palladium-Catalyzed Direct Coupling with Arylboronic Acids. *J. Am. Chem. Soc.* **2013**, *135*, 86-89.

(26) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. Catalysts for Suzuki-Miyaura Coupling Processes: Scope and Studies of the Effect of Ligand Structure. *J. Am. Chem. Soc.* **2005**, *127*, 4685-4696.

(27) Although the external CMD mechanism in which two carboxylates are involved was proposed in the previous report based on quantum chemical calculations (ref. 22a), our own preliminary computational studies on the racemic model systems indicate that an internal CMD mechanism is more likely. See Supporting Information for the details.

(28) The absolute configuration of the products was determined to be (*R*) by the X-ray analysis of **7ba** (See Supporting Information).