Communication

Chiral Cyclopentadienyl Cobalt(III) Complexes Enable Highly Enantioselective 3d-Metal-Catalyzed C-H Functionalizations

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Chiral Cyclopentadienyl Cobalt(III) Complexes Enable Highly Enantioselective 3d-Metal-Catalyzed C-H Functionalizations

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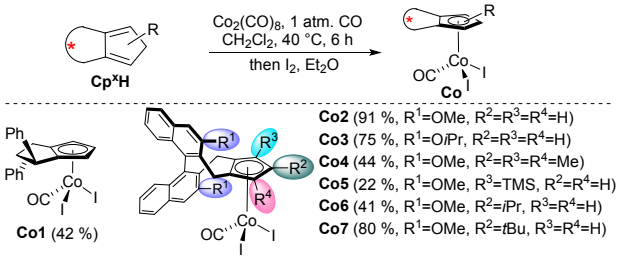
Supporting Information Placeholder

ABSTRACT: The synthesis of a set of cobalt(III)-complexes equipped with trisubstituted chiral cyclopentadienyl ligands is reported and their steric and electronic parameters are mapped. The application potential of these complexes for asymmetric C-H functionalizations with 3d-metals is shown by the synthesis of dihydroisoquinolones from *N*-chlorobenzamides with a broad range of alkenes. The transformation proceeds with excellent enantioselectivities of up to 99.5:0.5 *er* and high regioselectivities. The observed values outperform the best rhodium(III)-based methods for this reaction type. Moreover, challenging substrates such as alkyl alkenes also react with high regio- and enantioselectivities.

The rise of catalytic C-H functionalization has contributed to substantial changes in synthesis design and increases in synthetic efficiency.[1] Besides advances in chemo- and regioselectivity,[2] asymmetric reactions have been devised.[3] Most frequently, the underlying are catalyst systems precious-metal complexes and specifically tailored chiral ligands.[4] In recent years, a shift to more abundant 3d-metals as C-H functionalization catalysts is occuring.[5] While largely fueled by the price argument, it also creates new reactivity opportunities. 3d-Metal complexes often follow other mechanisms and offer complementary transformations and selectivities with respect to their heavier noble congeners.[6] However, enantioselective C-H functionalizations with abundant 3d-metals remain a highly challenging and underdeveloped research area.[5,7] Since the seminal work of Kanai/Matsunaga,[8] Cp*Co^{III}-catalyzed transformations emerged as a very versatile tool to complement Cp*Rh^{III} processes.[6,9] Despite the availability of chiral Cp^x-ligand bound Co^{III} complexes,[10] no application in asymmetric catalysis has been reported. Very recently, Ackermann reported an enantioselective indole alkylation with up to 93:7 *er*, using the achiral Cp*Co^{III} complex in conjunction with a chiral carboxylic acid, responsible for the enantioselective protonation.[11] Independently, Matsunaga/Yoshino disclosed an asymmetric thioamide-directed amidation with a bulky achiral Cp*Co^{III} catalyst, again together with a chiral carboxylic acid responsible for the enantiodetermining C-H activation with up to 94:6 *er*.[12] The seemingly most logical and straightforward strategy of using chiral Cp^x ligands[13,14] that have a proven performance with other metals[15] for corresponding tasks with cobalt(III) remains elusive. One might speculate that this void is linked to a low reactivity and unknown stability of Cp^{x}Co^{III} species. Complementary low-valent chiral indenyl Co^I complexes have been reported in 2004 for asymmetric [2+2+2]-cyclotrimerizations.[16] Herein, we report a trisubstituted chiral Cp^{x}Co^{III} complex and show its superior performance for the asymmetric C-H bond functionalization of *N*-chlorobenzamides providing access to a broad range of dihydroisoquinolones in excellent enantioselectivities.

The cobalt(III) complexes were designed based upon our robust Cp^x backbones[14b,14f] and one additional variable substitution on the Cp core[14c,17] (Scheme 1). In contrast to the complexation with precious metals,[10,14a,15a-b] the targeted complexes **Co1**-**Co7** were obtained by simply mixing Cp^{x}H with Co_2CO_8, followed by oxidation with I_2.[18] To boost the yields with respect to the Cp^x-ligands, one equivalent of Co_2CO_8 under a CO atmosphere was employed, significantly improving the previous procedure (see SI). All Co^{III} complexes are air- and moisture-stable solids and voluntarely crystallize to provide important structural information.

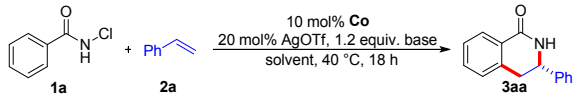
Scheme 1: Synthesis of the chiral Cp^{x}Co^{III} complexes.



The synthesized Co^{III} complexes were exploited as catalysts for enantioselective C-H functionalizations of chlorobenzamides to provide dihydroisoquinolones. Besides the synthetic relevance of them,[19] this reaction type became a benchmark transformation for chiral CpRh^{III}-catalysts.[14a,14d,14g,14h,17] Moreover, it is reported with achiral Cp*Co-catalysts[20] allowing to collect valuable data on reactivity/selectivity differences between Cp^{x}Co and Cp*Co, as well as between Cp^{x}Co and Cp^{x}Rh complexes. *N*-Chlorobenzamide (**1a**) and styrene (**2a**) were selected as model substrates (Table 1). While exposure to **Co1** complex did not yield desired product **3aa**, **Co2** with binaphthyl-derived Cp^x-ligand provided **3aa** in a modest yield

and poor enantioselectivity of 44:56 (entry 2). **Co3** having larger R^1 sidewalls (*i*PrO instead of MeO) resulted in 31.5:68.5 *er* (entry 3). A switch to **Co4** with a penta-substituted Cp^x reversed the enantioselectivity to 66:34 *er* (entry 4). Complex **Co5** with a trisubstituted Cp-ring (R^3=TMS) slightly improved the selectivity to 79:21 *er* (entry 5). Notably, **Co6**, having a isopropyl group as third substituent, gave superior reactivity and a massively improved enantioselectivity of 97:3 *er* (entry 6). Increasing the size of R^2 to a *tert*-butyl group (**Co7**) lowered the reactivity but simultaneously boosted the selectivity even further (entry 7), giving **3aa** in 99.5:0.5 *er*. Such an impressive selectivity level is uncommon for asymmetric C-H functionalizations. For comparison, the highest selectivity for **3aa** obtained by Rh^{III}-catalysis is 96:4 *er*.[17] Replacing TFE by HFIP and KOAc by CsOPiv substantially improved the reactivity, giving **3aa** in 90% yield and maintaining the outstanding enantioselectivity (entries 7-10). Lowering the catalyst loading to 5 mol% had no influence on the reaction performance (entry 11). In the absence of **Co7**, chloroamide **1a** is completely consumed by Hofmann-rearrangement leading to hexafluoropropan-2-yl phenylcarbamate (entry 12). Notably, silver triflate is not mandatory for the generation of the active catalyst (entry 13), although its omission slightly reduces the yield.

Table 1. Screen of Cp^xCo^{III} complexes and optimization[a]

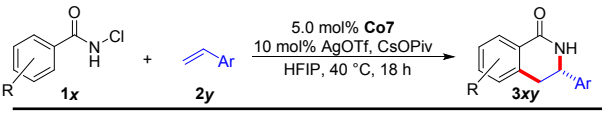


Entry	Co	solvent	base	% conv.[b]	% yield[b]	er[c]
1	**Co1**	TFE	KOAc	49	-	-
2	**Co2**	TFE	KOAc	70	27	44: 56
3	**Co3**	TFE	KOAc	58	28	31.5:68.5
4	**Co4**	TFE	KOAc	70	29	66:34
5	**Co5**	TFE	KOAc	70	33	79:21
6	**Co6**	TFE	KOAc	80	51	97:3
7	**Co7**	TFE	KOAc	72	26	99.5:0.5
8	**Co7**	HFIP	KOAc	100	51	99.5:0.5
9	**Co7**	HFIP	KOPiv	100	88	99.5:0.5
10	**Co7**	HFIP	CsOPiv	100	90	99.5:0.5
11[d]	**Co7**	HFIP	CsOPiv	100	96	99.5:0.5
12[d]	-	HFIP	CsOPiv	100	0	-
13[d,e]	**Co7**	HFIP	CsOPiv	100	73	99.5:0.5

[a] 50 µmol **1a**, 75 µmol **2a**, 5.0 µmol **Co**, 10 µmol AgOTf, 60 µmol base, 0.10 M at 40 °C for 18 h; [b] determined by ^{1}H-NMR; [c] determined by chiral HPLC; [d] 2.5 µmol **Co**, 5.0 µmol AgOTf; [e] no AgOTf.

With the optimized conditions, the scope of the reaction was investigated. The initial focus was set on variations of the chloroamide and the styrene acceptor. Both electron-deficient and electron-rich aryl groups on both reactants reliably delivered desired products **3**. Without any exception, the outstanding enantioselectivities were maintained and were largely independent of the substituents on both aryl groups. The parasitic Hofmann rearrangement is slightly more pronounced with *N*-chlorobenzamides bearing electron-donating substituents such as **1b-1d**, causing a slight reduction in yield (entries 2-4). The functionalization proceeded selectively at the least hindered *ortho*-C-H group, giving **3da** as a single regioisomer (entry 4).

Table 2. Scope of the Cp^xCo^{III}-catalyzed functionalization with respect to *N*-chlorobenzamides and styrenes[a]

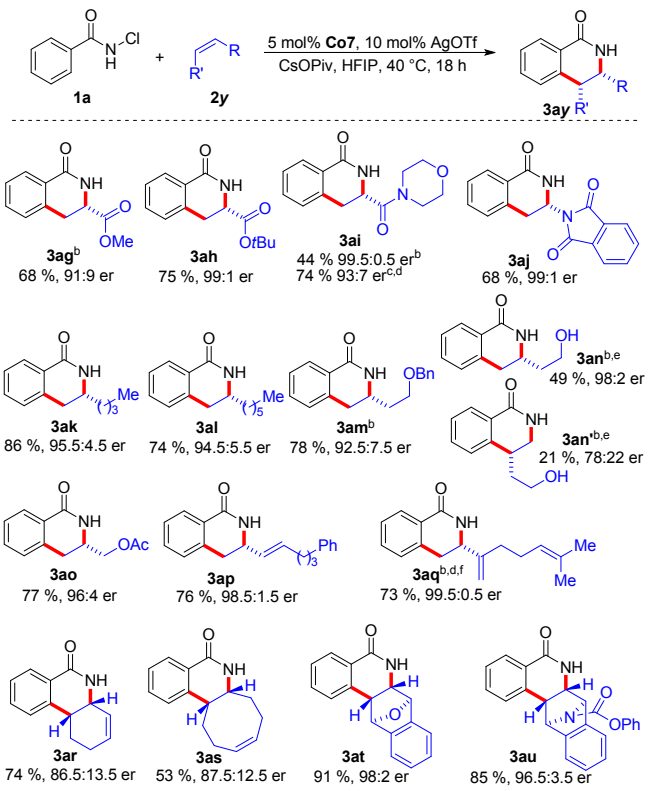


Entry	3xy	R	Ar	% yield[b]	er[c]
1	3aa	H	Ph	87	99.5:0.5
2[d]	3ba	4-OMe	Ph	61	99.0:1.0
3	3ca	4-Me	Ph	63	98.5:1.5
4	3da	3-Me	Ph	73	99.5:0.5
5	3ea	4-Br	Ph	89	98.5:1.5
6	3fa	4-Cl	Ph	82	99.5:0.5
7	3ga	4-F	Ph	87	99.5:0.5
8	3ab	H	4-MeO-C_6H_4	87	99.5:0.5
9	3ac	H	4-*t*Bu-C_6H_4	81	98.0:2.0
10	3ad	H	4-Me-C_6H_4	88	99.5:0.5
11	3ae	H	3-Me-C_6H_4	88	99.5:0.5
12	3af	H	4-F-C_6H_4	85	99.5:0.5

[a] 0.20 mmol **1*x***, 0.30 mmol **2*y***, 10 µmol **Co7**, 20 µmol AgOTf, 0.24 mmol CsOPiv, 0.10 M in HFIP at 40 °C for 18 h; [b] isolated yield; [c] determined by chiral HPLC; [d] 20 µmol **Co7**, 40 µmol AgOTf.

Next, more challenging olefin acceptors that are problematic for Cp^xRh^{III} catalysis were tested (Scheme 2). These suffer from at least one shortcoming such as poor enantioselectivity,[14a,14g] limited regio-control,[21] as well as low reactivity and scope limitations.[14g,14h] Pleasingly, acrylates reacted very well. For *tert*-butyl acrylate, product **3ah** was generated in 75% yield and 99:1 *er*. Hindered acryl amide **2i** reacted and yielded **3ai** in 99.5:0.5 *er*. Alternatively, less congested **Co6** provides an increased yield. Noteworthy, vinyl phthalimide as an example for a hetero atom-substituted olefin[23] provides access to **3aj** with an aminal stereogenic center as single regioisomer in 99:1 *er*. Simple olefins such as 1-hexene and 1-octene yield *single* regioisomers of **3ak** and **3al** with 95.5:4.5 *er*. These olefins react under Rh^{III}-catalysis in a notoriously low regio- and enantioselectivity. Noteworthy, bulky achiral $CpRh^{III}$ catalysts favor the *opposite regioisomer*.[21,22] The introduction of an oxygen atom in coordination distance influenced the enantioselectivity (**3am**) as well as the regioselectivity (**3an**). Allyl acetate delivered dihydroisoquinolone product **3ao** as a single regioisomer in 96:4 *er*. A linear conjugated diene (**2p**), as well as myrcene (**2q**) were suitable substrates giving excellent levels of enantioselectivity. Myrcene (**2q**) did not react under Cp^*Rh^{III} catalysis.[22] Cyclohexadiene and cyclooctadiene were competent, albeit with attenuated reactivity and selectivity.The excellent enantioselectivity was restored in strained bicyclic systems to afford products **3at** and **3au** as single diastereomers.

Scheme 2: Scope for miscellaneous olefins[a]



[a] 0.20 mmol **1a**, 0.30 mmol **2*y***, 10 µmol **Co7**, 20 µmol AgOTf, 0.24 mmol CsOPiv in HFIP (0.10 M) at 40 °C for 18 h; [b] 20 µmol **Co7**, 40 µmol AgOTf; [c] 20 µmol **Co6**, 40 µmol AgOTf [d] with 0.60 mmol alkene; [e] 0.36 mmol CsOPiv; [f] with 0.10 mmol Cs_2CO_3 additive in HFIP/DCE 2:1.

To gain insights into the dramatic performance difference between the cobalt complexes, X-ray and IR data were obtained for **Co2**, **Co4**, **Co6**, **Co7** along with $CpCo(CO)I_2$[24] and $Cp^*Co(CO)I_2$[18c] (Table 3). Despite its frequent use, no X-ray crystal structure data was available for $Cp^*Co(CO)I_2$. The CO-stretching frequencies decrease with the number of donating alkyl substituents on the Cp.[25] The best performing tri-substituted Cp^x are between Cp (2060 cm^{-1}) and Cp^* (2026 cm^{-1}). The Co-C bond length increases from 1.76 Å in $CpCo(CO)I_2$ to 1.80 Å in **Co4** (respective 1.86 Å in $Cp^*Co(CO)I_2$). The distance of the cobalt atom from the Cp-plane increases incrementally with the number and size of the Cp substituents and ranges from 1.68-1.72 Å. An important difference between the complexes is the influence of the remote substituents on the dihedral angle θ of the biaryl backbone of the Cp^x. For chiral biaryl phosphines, θ is well known for its influence on the chiral discrimination of catalysts.[26] The consequences of the change in the dihedral angle θ for the Cp^x complexes can be visualized straightforwardly by an overlay of the X-ray crystal structure of **Co2** and **Co7** (Figure 1). A larger dihedral angle slightly opens up the methoxy naphthyl portion of the pocket. A noteworthy feature setting the most selective complex **Co7** apart from the others, is the orientation of the CO ligand with respect to the chiral Cp^x backbone. For **Co2**, **Co4** and even **Co6**, the direction of CO bond is virtually completely parallel with the plane of the lower naphthyl ring. In contrast, the CO ligand of **Co7** swapped position with an iodide, indicating the significantly modulated chiral environment of this particular Cp^x ligand.

Table 3. Comparison of key analytical data of selected cyclopentadienyl $Co(CO)I_2$ complexes[a]

[Co]	ν(CO) (cm^{-1})[a]	Co-CO (Å)	Co-Cp (Å)	dihedral angle θ
$CpCo(CO)I_2$	2060	1.76[b]	1.68[b]	-
Co2	2061	1.79	1.69	69.6
Co6	2054	1.79	1.70	70.0
Co7	2054	1.79	1.71	76.5
Co4	2047	1.80	1.72	72.0
$Cp^*Co(CO)I_2$	2026	1.86	1.72	-

[a] ATR measurement; [b] reported values.[24]

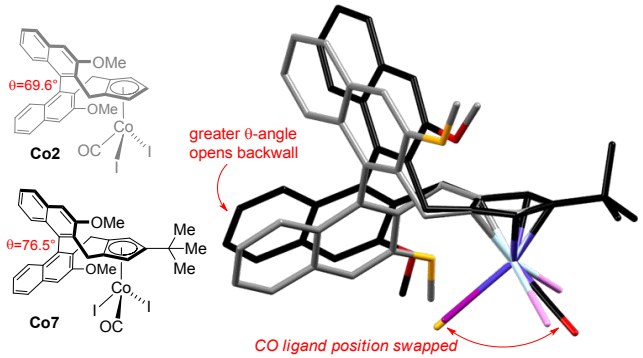


Figure 1. Comparison of **Co2** (grey C-atoms) and **Co7** (black C-atoms) by X-ray crystal structure overlay.

To foster further understanding of the ligand geometry/selectivity relationship, steric maps of the binding pocket were generated with the SambVca 2 tool (Figure 2).[27] The buried volume increase from 48.2% V_{Bur} of **Co2** (disubstituted Cp^x) to 52.0% V_{Bur} of **Co4** (pentasubstituted Cp^x). **Co6** and **Co7** (both trisubsituted Cp^x) range within 50.3% and 50.2% V_{Bur}. The steric maps along the Z-axis (Co-Cp) provide information of the chiral binding pockets around the metal. Comparing the steric heatmaps of **Co2** and **Co4** to **Co6** and **Co7**, the common feature is the naphthyl backbone, the „backwall“,[13a] generating significant bulk in the SW quadrant. For **Co2** and **Co4**, the remaining three quadrants are rather indifferent in their sterics. In contrast, the map for **Co7** reveals the massive bulk of the *tert*-butyl group. This diminishes access to the southern hemisphere, thus making the nothern trajectory most accessible. The present enantioselection falls into the double facial selectivity category. The backwall is responsible for the orientation and alignment of the metallocycle. The *tert*-butyl group then forces a specific orientation of the olefin, minimizing the steric interaction. The poor enantioselectivity of **Co2** can be attributed to a lack of this guiding interaction, leading to several possible approaches of the olefin.

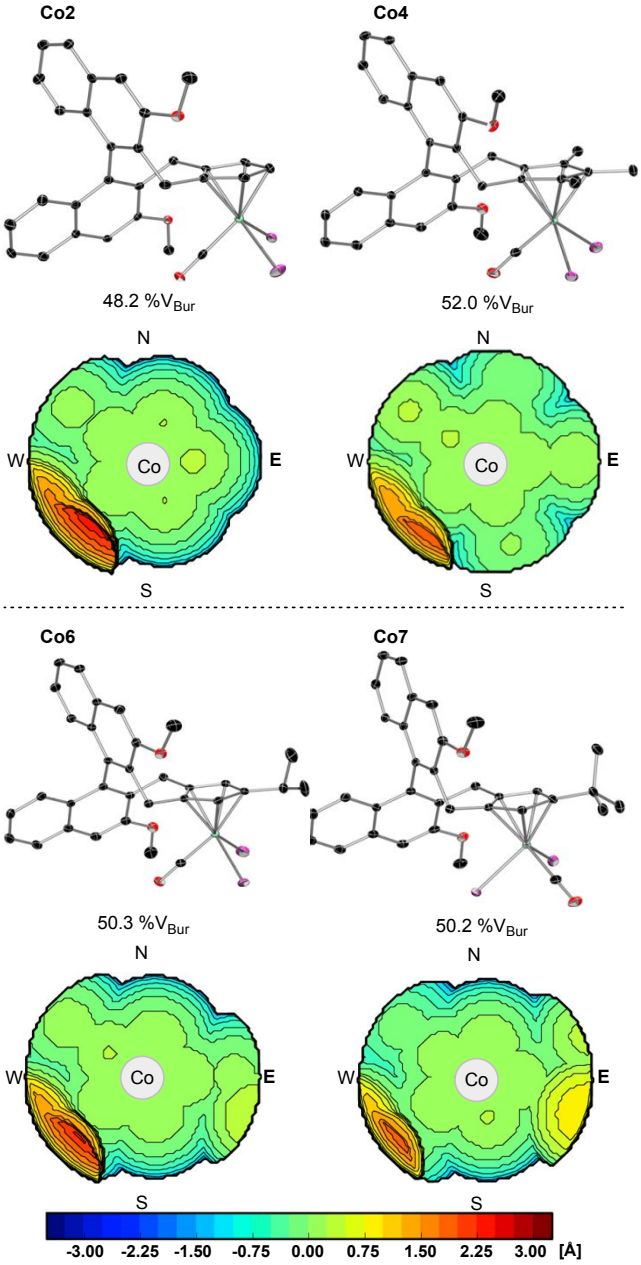


Figure 2: X-ray crystal structures of **Co2, Co4, Co6**[28] and **Co7,** buried volumes and corresponding steric maps.[27] Bondi radii scaled by 1.17, sphere radius: 3.5 Å, mesh spacing: 0.1 Å.

In summary, we disclosed Co^{III}-complexes equipped with trisubstituted chiral cyclopentadienyl ligands. Their catalytic potential for asymmetric C-H functionalizations was showcased with the synthesis of dihydroisoquinolones from *N*-chlorobenzamides and a large set of alkenes. Excellent enantioselectivities and regioselectivities were obtained, outperforming the corresponding Rh^{III}-catalyzed processes. Particularly noteworthy is the observed opposite regioselectivity of cobalt *vs* rhodium complexes alkyl alkenes. This makes the Cp^xCo complexes not just a cheaper and more abundant version of rhodium but a truly unique set of catalysts with complementary behavior and a bright future potential. Enlarging the application scope of this Cp^xCo^{III} complex class with further valuable transformations is currently being investigated in our laboratory.

ASSOCIATED CONTENT

Supporting Information

Synthetic procedures, characterization data for all new compounds. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

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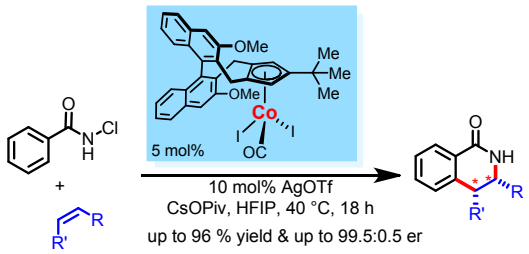
REFERENCES

(1) (a) Shilov, A. E.; Shul'pin, G. B. Activation of C−H Bonds by Metal Complexes *Chem. Rev.* **1997**, *97*, 2879; (b) Abrams, D. J.; Provencher, P. A.; Sorensen, E. J. Recent applications of C–H functionalization in complex natural product synthesis *Chem. Soc. Rev.* **2018**, *47*, 8925.
(2) *C-H Activation*; Yu, J.-Q.; Shi, Z., Eds.; Springer-Verlag: Berlin, Heidelberg, 2010.
(3) *Asymmetric Functionalization of C-H Bonds*; You, S.-L., Ed.; The Royal Society of Chemistry: Cambridge, 2015.
(4) *Organotransition Metal Chemistry: From Bonding to Catalysis*; Hartwig, J., Ed.; University Science Books: Sausalito, CA, 2010.
(5) Gandeepan, P.; Müller, T.; Zell, D.; Cera, G.; Warratz, S.; Ackermann, L. 3d Transition Metals for C–H Activation *Chem. Rev.* **2019**, *119*, 2192.
(6) (a) 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; (b) Park, J.; Chang, S. Comparison of the Reactivities and Selectivities of Group 9 [Cp^*M^{III}] Catalysts in C−H Functionalization Reactions *Chem. - Asian J.* **2018**, *13*, 1089.
(7) (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; (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.
(8) Yoshino, T.; Ikemoto, H.; Matsunaga, S.; Kanai, M. A Cationic High-Valent Cp^*Co^{III} Complex for the Catalytic Generation of Nucleophilic Organometallic Species: Directed C−H Bond Activation *Angew. Chem., Int. Ed.* **2013**, *52*, 2207.
(9) For reviews, see: (a) Loginov, D. A.; Shul'pina, L. S.; Muratov, D. V.; Shul'pin, G. B. Cyclopentadienyl cobalt(III) complexes: Synthetic and catalytic chemistry *Coord. Chem. Rev.* **2019**, *387*, 1; (b) Yoshino, T.; Matsunaga, S. Cobalt-Catalyzed C(sp^3)−H Functionalization Reactions *Asian J. Org. Chem.* **2018**, *7*, 1193; (c) Prakash, S.; Kuppusamy, R.; Cheng, C.-H. Cobalt-Catalyzed Annulation Reactions *via* C−H Bond Activation *ChemCatChem* **2018**, *10*, 683; (d) 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; (e) Wang, S.; Chen, S.-Y.; Yu, X.-Q. C–H Functionalization by high-valent Cp*Co(III) catalysis *Chem. Commun.* **2017**, *53*, 3165; (f) Pototschnig, G.; Maulide, N.; Schnürch, M. Direct Functionalization of C−H Bonds by Iron, Nickel, and Cobalt Catalysis *Chem. − Eur. J.* **2017**, *23*, 9206; (g) 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; (h) Moselage, M.; Li, J.; Ackermann, L. Cobalt-Catalyzed C–H Activation *ACS Catal.* **2016**, *6*, 498; (i) Wei, D.; Zhu, X.; Niu, J.-L.; Song, M.-P. High-Valent-Cobalt-Catalyzed C−H Functionalization Based on Concerted Metalation−Deprotonation and

Single-Electron-Transfer Mechanisms *ChemCatChem* **2016**, *8*, 1242; (j) Gao, K.; Yoshikai, N. Low-Valent Cobalt Catalysis: New Opportunities for C–H Functionalization *Acc. Chem. Res.* **2014**, *47*, 1208.
(10) Smits, G.; Audic, B.; Wodrich, M. D.; Corminboeuf, C.; Cramer, N. A β-Carbon elimination strategy for convenient *in situ* access to cyclopentadienyl metal complexes *Chem. Sci.* **2017**, *8*, 7174.
(11) 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.
(12) (a) 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. During manuscript drafting a related report appeared: (b) 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.
(13) For reviews, see: (a) Newton, C. G.; Kossler, D.; Cramer, N. Asymmetric Catalysis Powered by Chiral Cyclopentadienyl Ligands *J. Am. Chem. Soc.* **2016**, *138*, 3935; (b) Ye, B.; Cramer, N. Chiral Cyclopentadienyls: Enabling Ligands for Asymmetric Rh(III)-Catalyzed C–H Functionalizations *Acc. Chem. Res.* **2015**, *48*, 1308.
(14) For seminal reports of Cp^x ligand families, see: (a) 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; (b) Wang, S.-G.; Park, S. H.; Cramer, N. A Readily Accessible Class of Chiral Cp Ligands and their Application in Ru^{II}-Catalyzed Enantioselective Syntheses of Dihydrobenzoindoles *Angew. Chem., Int. Ed.* **2018**, *57*, 5459; (c) Sun, Y.; Cramer, N. Tailored trisubstituted chiral Cp^xRh^{III} catalysts for kinetic resolutions of phosphinic amides *Chem. Sci.* **2018**, *9*, 2981; (d) 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; (e) 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; (f) 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; (g) Ye, B.; Cramer, N. Chiral Cyclopentadienyl Ligands as Stereocontrolling Element in Asymmetric C–H Functionalization *Science* **2012**, *338*, 504; (h) 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.
(15) For seminal reports of catalytic enantioselective applications with additional metals, see: with Ir (a) Dieckmann, M.; Jang, Y.-S.; Cramer, N. Chiral Cyclopentadienyl Iridium(III) Complexes Promote Enantioselective Cycloisomerizations Giving Fused Cyclopropanes *Angew. Chem., Int. Ed.* **2015**, *54*, 12149; with Ru (b) Kossler, D.; Cramer, N. Chiral Cationic Cp^xRu(II) Complexes for Enantioselective Yne-Enone Cyclizations *J. Am. Chem. Soc.* **2015**, *137*, 12478; with Fe (c) Gajewski, P.; Renom-Carrasco, M.; Facchini, S. V.; Pignataro, L.; Lefort, L.; de Vries, J. G.; Ferraccioli, R.; Piarulli, U.; Gennari, C. Synthesis of (*R*)-BINOL-Derived (Cyclopentadienone)iron Complexes and Their Application in the Catalytic Asymmetric Hydrogenation of Ketones *Eur. J. Org. Chem.* **2015**, *2015*, 5526; with rare-earth metals and Sc (d) Song, G.; O, W. W. N.; Hou, Z. Enantioselective C–H Bond Addition of Pyridines to Alkenes Catalyzed by Chiral Half-Sandwich Rare-Earth Complexes *J. Am. Chem. Soc.* **2014**, *136*, 12209; (e) Teng, H.-L.; Luo, Y.; Wang, B.; Zhang, L.; Nishiura, M.; Hou, Z. Synthesis of Chiral Aminocyclopropanes by Rare-Earth-Metal-Catalyzed Cyclopropene Hydroamination *Angew. Chem., Int. Ed.* **2016**, *55*, 15406.
(16) (a) Gutnov, A.; Heller, B.; Fischer, C.; Drexler, H.-J.; Spannenberg, A.; Sundermann, B.; Sundermann, C. Cobalt(I)-Catalyzed Asymmetric [2+2+2] Cycloaddition of Alkynes and Nitriles: Synthesis of Enantiomerically Enriched Atropoisomers of 2-Arylpyridines *Angew. Chem., Int. Ed.* **2004**, *43*, 3795; (b) Gutnov, A.; Drexler, H.-J.; Spannenberg, A.; Oehme, G.; Heller, B. Syntheses of Chiral Nonracemic Half-Sandwich Cobalt Complexes with Menthyl-Derived Cyclopentadienyl, Indenyl, and Fluorenyl Ligands *Organometallics* **2004**, *23*, 1002.
(17) Audic, B.; Wodrich, M. D.; Cramer, N. Mild complexation protocol for chiral Cp^xRh and Ir complexes suitable for *in situ* catalysis *Chem. Sci.* **2019**, *10*, 781.
(18) (a) Heck, R. F. Dihalocarbonylcyclopentadienylcobalt Complexes *Inorg. Chem.* **1965**, *4*, 855; (b) King, R. B. Organometallic Chemistry of the Transition Metals. XI. Some New Cyclopentadienyl Derivatives of Cobalt and Rhodium *Inorg. Chem.* **1966**, *5*, 82; (c) Sun, B.; Yoshino, T.; Matsunaga, S.; Kanai, M. Air-Stable Carbonyl(pentamethylcyclopentadienyl)cobalt Diiodide Complex as a Precursor for Cationic (Pentamethylcyclopentadienyl)cobalt(III) Catalysis: Application for Directed C-2 Selective C–H Amidation of Indoles *Adv. Synth. Catal.* **2014**, *356*, 1491.
(19) (a) Amer, M. M.; Carrasco, A. C.; Leonard, D. J.; Ward, J. W.; Clayden, J. Substituted Dihydroisoquinolinones by Iodide-Promoted Cyclocarbonylation of Aromatic α-Amino Acids *Org. Lett.* **2018**, *20*, 7977; (b) Palmer, N.; Peakman, T. M.; Norton, D.; Rees, D. C. Design and synthesis of dihydroisoquinolones for fragment-based drug discovery (FBDD) *Org. Biomol. Chem.* **2016**, *14*, 1599.
(20) (a) Yu, X.; Chen, K.; Wang, Q.; Zhang, W.; Zhu, J. Co(III)-Catalyzed *N*-chloroamide-directed C–H activation for 3,4-dihydroisoquinolone synthesis *Org. Chem. Front.* **2018**, *5*, 994; (b) Muniraj, N.; Prabhu, K. R. Cobalt(III)-Catalyzed [4 + 2] Annulation of *N*-Chlorobenzamides with Maleimides *Org. Lett.* **2019**, *21*, 1068; (c) Yu, X.; Chen, K.; Guo, S.; Shi, P.; Song, C.; Zhu, J. Direct Access to Cobaltacycles *via* C–H Activation: *N*-Chloroamide-Enabled Room-Temperature Synthesis of Heterocycles *Org. Lett.* **2017**, *19*, 5348.
(21) (a) Hyster, T. K.; Dalton, D. M.; Rovis, T. Correction: Ligand design for Rh(III)-catalyzed C–H activation: an unsymmetrical cyclopentadienyl group enables a regioselective synthesis of dihydroisoquinolones *Chem. Sci.* **2018**, *9*, 8024; (b) Hyster, T. K.; Dalton, D. M.; Rovis, T. Ligand design for Rh(III)-catalyzed C–H activation: an unsymmetrical cyclopentadienyl group enables a regioselective synthesis of dihydroisoquinolones *Chem. Sci.* **2015**, *6*, 254.
(22) Trifonova, E. A.; Ankudinov, N. M.; Kozlov, M. V.; Sharipov, M. Y.; Nelyubina, Y. V.; Perekalin, D. S. Rhodium(III) Complex with a Bulky Cyclopentadienyl Ligand as a Catalyst for Regioselective Synthesis of Dihydroisoquinolones through C−H Activation of Arylhydroxamic Acids *Chem. − Eur. J.* **2018**, *24*, 16570.
(23) (a) Webb, N. J.; Marsden, S. P.; Raw, S. A. Rhodium(III)-Catalyzed C–H Activation/Annulation with Vinyl Esters as an Acetylene Equivalent *Org. Lett.* **2014**, *16*, 4718; (b) Sun, R.; Yang, X.; Chen, X.; Zhang, C.; Zhao, X.; Wang, X.; Zheng, X.; Yuan, M.; Fu, H.; Li, R.; Chen, H. Rh(III)-Catalyzed [4 + 2] Self-Annulation of *N*-Vinylarylamides *Org. Lett.* **2018**, *20*, 6755.
(24) Avilés, T.; Dinis, A.; Gonçalves, J. O.; Félix, V.; Calhorda, M. J.; Prazeres, Â.; Drew, M. G. B.; Alves, H.; Henriques, R. T.; da Gama, V.; Zanello, P.; Fontani, M. Synthesis, X-ray structures, electrochemistry, magnetic properties, and theoretical studies of the novel monomeric $[CoI_2(dppfO_2)]$ and polymeric chain $[CoI_2(\mu\text{-}dppfO_2)_n]$ *J. Chem. Soc., Dalton Trans.* **2002**, 4595.
(25) Piou, T.; Romanov-Michailidis, F.; Romanova-Michaelides, M.; Jackson, K. E.; Semakul, N.; Taggart, T. D.; Newell, B. S.; Rithner, C. D.; Paton, R. S.; Rovis, T. Correlating Reactivity and Selectivity to Cyclopentadienyl Ligand Properties in Rh(III)-Catalyzed C–H Activation Reactions: An Experimental and Computational Study *J. Am. Chem. Soc.* **2017**, *139*, 1296.
(26) (a) Jeulin, S.; de Paule, S. D.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Champion, N.; Dellis, P. Chiral biphenyl diphosphines for asymmetric catalysis: Stereoelectronic design and industrial perspectives *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5799; (b) Dierkes, P.; W. N. M. van Leeuwen, P. The bite angle makes the difference: a practical ligand parameter for diphosphine ligands *J. Chem. Soc., Dalton Trans.* **1999**, 1519.
(27) (a) Poater, A.; Ragone, F.; Mariz, R.; Dorta, R.; Cavallo, L. Comparing the Enantioselective Power of Steric and Electrostatic Effects in Transition-Metal-Catalyzed Asymmetric Synthesis *Chem. − Eur. J.* **2010**, *16*, 14348; (b) Poater, A.; Cosenza, B.; Correa, A.; Giudice, S.; Ragone, F.; Scarano, V.; Cavallo, L. SambVca: A Web Application for the Calculation of the Buried Volume of *N*-Heterocyclic Carbene Ligands *Eur. J. Inorg. Chem.* **2009**, *2009*, 1759; (c) Poater, A.; Ragone, F.; Giudice, S.; Costabile, C.; Dorta, R.; Nolan, S. P.; Cavallo, L. Thermodynamics of *N*-Heterocyclic Carbene Dimerization: The Balance of Sterics and Electronics *Organometallics* **2008**, *27*, 2679.
(28) The *i*Pr group of **Co6** may rotate free in solution and adopt a different conformation than in the solid state.


OMe
Me
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OC
5 mol%
10 mol% AgOTf
CsOPiv, HFIP, 40 °C, 18 h
up to 96 % yield & up to 99.5:0.5 er
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