OL Organic Letters

pubs.acs.org/OrgLett Letter

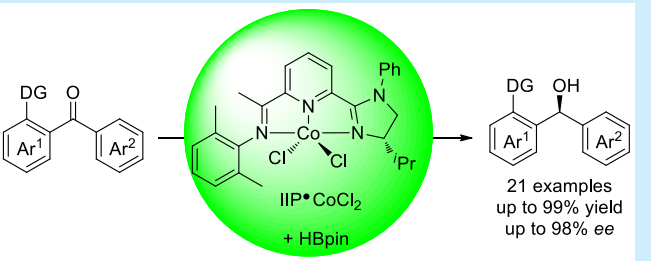
Highly Enantioselective Cobalt-Catalyzed Hydroboration of Diaryl Ketones

Wenbo Liu,[†] Jun Guo,[†] Shipei Xing, and Zhan Lu*

Cite This: https://dx.doi.org/10.1021/acs.orglett.0c00293 Read Online

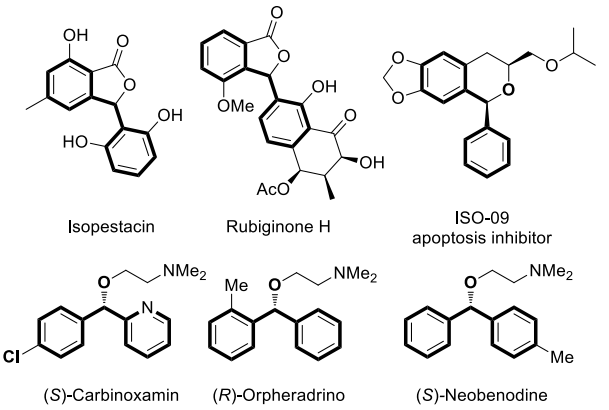
ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: A highly enantioselective cobalt-catalyzed hydroboration of diaryl ketones with pinacolborane was developed using chiral imidazole iminopyridine as a ligand to access chiral benzhydrols in good to excellent yields and ee. This protocol could be carried out in a gram scale under mild reaction conditions with good functional group tolerance. Chiral biologically active 3-substituted phthalide and (*S*)-neobenodine could be easily constructed through asymmetric hydroboration as a key step.



Chiral diaryl- and aryl heteroarylmethanols are present in a large number of natural products and biologically active compounds,[1] such as isopestacin, rubiginone H, (*S*)-carbinoxamin, (*R*)-orpheradrino, and (*S*)-neobenodine (Scheme 1).

Scheme 1. Selected Examples of Bioactive Molecules and Natural Products Derived from Diaryl- or Aryl(heteroaryl)methanols



Nowadays, several strategies have been developed for the catalytic asymmetric synthesis of diarylmethanols,[2] which could be divided into two categories: (1) the nucleophilic addition of organometallic reagents to aromatic aldehydes[3] and (2) the catalytic reduction of prochiral diaryl ketones. For asymmetric reduction of prochiral diaryl ketones, several reduction reagents, including lithium aluminum hydride modified with chiral amino alcohol derivatives,[4] silanes catalyzed by chiral rhodium[5] or copper complexes,[1c] boranes catalyzed by oxazaborolidine derivatives (CBS reduction),[6] hydrogen mediated by Ru,[7] Ir,[8] or Mn[9] complexes, and formic acid via asymmetric transfer hydrogenation,[10] have been explored. Compared with well-investigated asymmetric reduction of aryl alkyl ketones,[11] the counterpart of diaryl ketone is challenging for the difficulty to differentiate two structurally similar aryl groups in substrates.[9] Although some elegant works have been developed, it is still of great interest to both the academic community and the industrial sector to develop efficient and environmentally benign catalytic methodology for synthesis of chiral benzhydrols.

Over the past decade, due to the abundance and environmental friendliness, cobalt catalysis has emerged as a hot field of organic synthesis. Using cobalt to achieve the highly enantioselective reduction of diaryl ketones sounds desirable from both scientific and synthetic points of view. In 2005, using ketolminatocobalt complexes, the enantioselective borohydride reduction of benzophenones was achieved by Yamada with good to excellent enantioselectivity.[12] However, the substrates were strictly limited to *ortho*-fluorinated benzophenones, which restricted its synthetic utility. Additionally, in that case, functional group tolerance has not been investigated. It was not until 2015 that another cobalt-catalyzed enantioselective hydroboration reduction of diaryl ketones was developed by us using oxazoline iminopyridine (OIP) as a ligand; however, only two cases were reported.[13]

In the last 3 years, several types of chiral ligands[14] were designed and synthesized in our group, which gave us a new chance to reinvestigate the asymmetric hydroboration

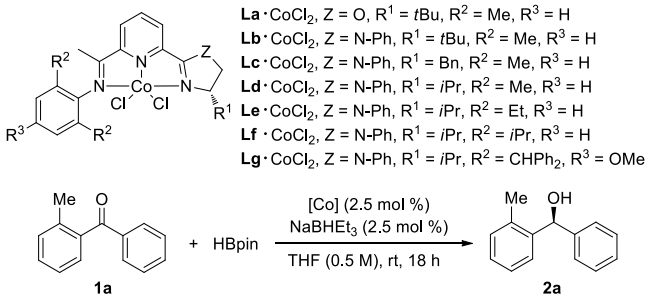
Received: January 20, 2020

https://dx.doi.org/10.1021/acs.orglett.0c00293
Org. Lett. XXXX, XXX, XXX−XXX

reduction of diaryl ketones. Initially, *ortho*-methyl benzophenone **1a** was chosen as the model substrate to test the activity and selectivity of different cobalt catalysts. First, the reaction of **1a** with pinacolborane (HBpin) using 2.5 mol % of La·$CoCl_2$ as catalyst and 2.5 mol % of $NaBHEt_3$ as activator in the solution of THF (0.5 M) was conducted at rt for 18 h, delivering chiral diarylmethanol **2a** in 99% yield with 87% ee (Table 1, entry 1). Using more electron-rich imidazoline iminopyridine (IIP)-ligated cobalt complex Lb·$CoCl_2$, **2a** was obtained in 85% yield with 90% ee (entry 2). Changing the *tert*-butyl group on imidazoline to benzyl gave a high yield, and the enantioselectivity was slightly increased (entry 3). When the R^1 was changed to isopropyl, **1a** could almost be converted completely into **2a** with the same enantioselectivity (entry 4). When steric bulky imide-derived catalysts were used, the ee values of **2a** were decreased to varying degrees (entries 5−7). In particular, when 2,6-di(diphenylmethyl)aniline-derived Lg·$CoCl_2$ was used, the yield and enantioselectivity of **2a** were sharply decreased (entry 7). Further investigation of the effect of counterion showed that the chloride was the best in terms of the enantioselectivity. It should be noted that the enantioselectivity was dramatically decreased when 2 or 3 equiv of $NaBHEt_3$ was used (entries 10 and 11), indicating the critical impact of the amount of reductant in this catalytic system. In addition, the reaction almost did not occur in the absence of reductant (entry 12), implying that Ld·$CoCl_2$ has no catalytic activity. The reductant itself was able to catalyze the hydroboration without the existence of a cobalt complex (entry 13) as a background reaction. The hydroboration did not occur when no base or cobalt complex was added (entry 14). Finally, the standard conditions were confirmed as **1a** (0.5 mmol), HBpin (0.6 mmol), Ld·$CoCl_2$ (2.5 mol %), and $NaBHEt_3$ (2.5 mol %) in THF (0.5 M) running at rt for 18 h.

With the optimized conditions in hand, the substrate scope of diaryl ketones was investigated and is shown in Scheme 2.

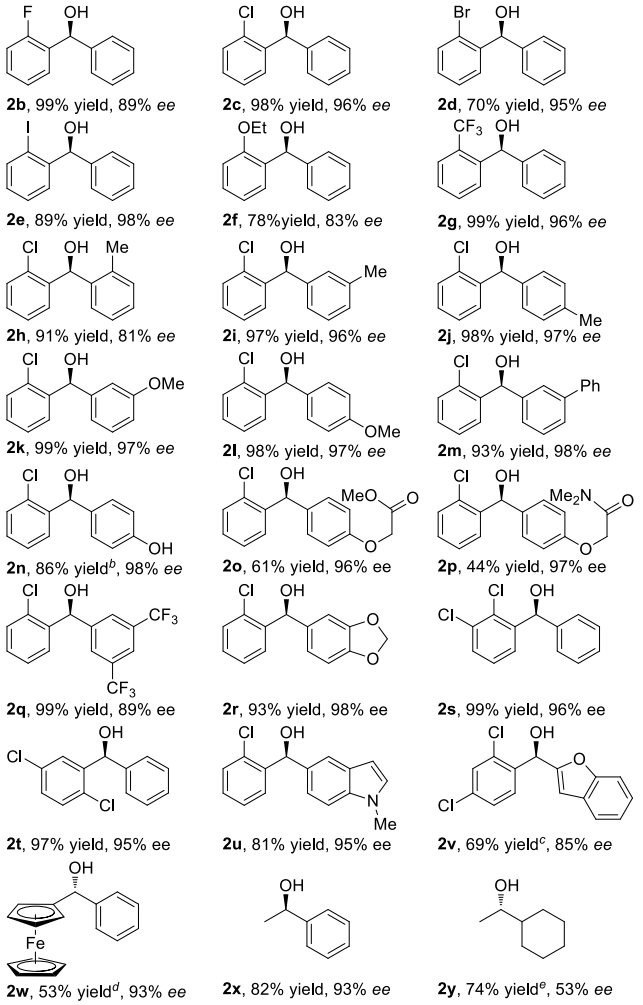
Table 1. Optimizations[a]



entry	[Co]	yield (%)	ee (%)[b]
1	La·$CoCl_2$	99	87
2	Lb·$CoCl_2$	85	90
3	Lc·$CoCl_2$	98	91
4	Ld·$CoCl_2$	99	91
5	Le·$CoCl_2$	77	87
6	Lf·$CoCl_2$	82	89
7	Lg·$CoCl_2$	48	28
8	Ld·$CoBr_2$	99	89
9	Ld·CoI_2	98	84
10[c]	Ld·$CoCl_2$	99	68
11[d]	Ld·$CoCl_2$	99	63
12[e]	Ld·$CoCl_2$	trace	
13[f]		72	
14[e,f]		ND	

[a]The reactions were conducted using **1a** (0.5 mmol), HBpin (0.6 mmol), cobalt complex (2.5 mol %), and $NaBHEt_3$ (2.5 mol %) in a solution of THF (1 mL) at rt under the atmosphere of nitrogen for 18 h. Yields were determined by ^{1}H NMR using 1,3,5-trimethylbenzene as an internal standard. [b]Enantiomeric excess value was determined by HPLC. [c]$NaBHEt_3$ (5 mol %). [d]$NaBHEt_3$ (7.5 mol %). [e]Without $NaBHEt_3$. [f]Without a cobalt complex.

Scheme 2. Substrate Scope[a]



[a]Standard conditions: unless otherwise noted, diaryl ketone (0.5 mmol), HBPin (1.2 equiv), Ld·$CoCl_2$ (2.5 mol %), $NaBHEt_3$ (2.5 mol %), THF (1 mL), rt, 18 h. Isolated yields. [b]HBpin (2 equiv). [c]Ld·$CoCl_2$ (5 mol %). [d]Diaryl ketone (0.25 mmol), HBPin (1.2 equiv), Ld·$CoCl_2$ (10 mol %), $NaBHEt_3$ (10 mol %), THF (1 mL), 0 °C, 48 h. [e]1-Cyclohexylethanone (1.0 mmol), THF (2 mL), 22 h.

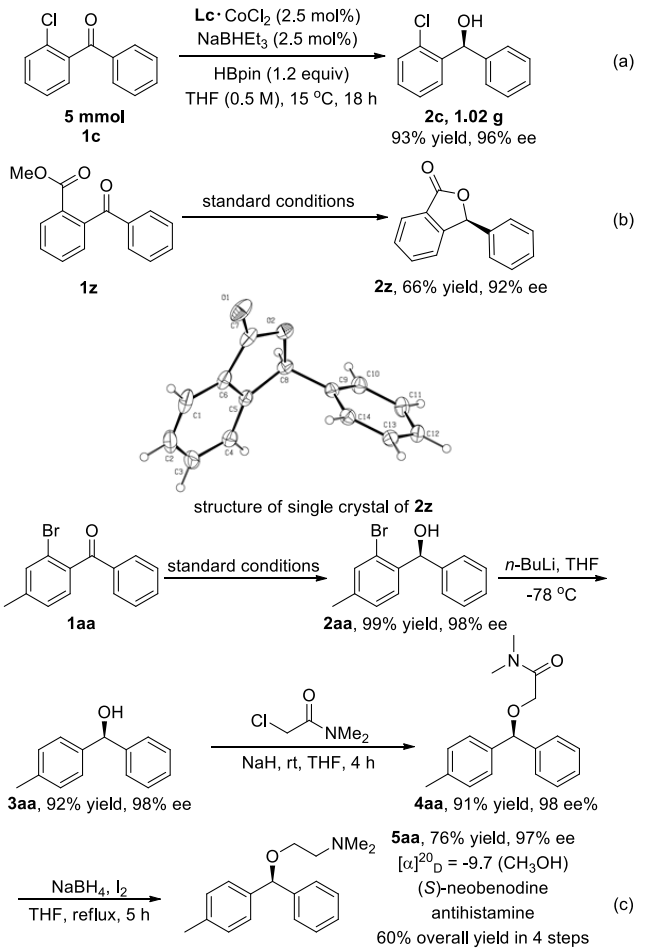
First, the *ortho*-substituents were examined. Halides, such as fluoro (**1b**), chloro (**1c**), bromo (**1d**), and even iodo (**1e**), which could easily undergo oxidative addition in noble metal catalysis, were tolerated well to afford the corresponding diaryl methanols **2b**−**2e** in 70−99% yields with 88−98% ee. It is worth noting that **2b**−**2e** could be easily functionalized through halide transformations, which demonstrated their synthetic utilities. Substrates containing electron-donating (2-OEt) or electron-withdrawing group (2-CF_3) participated to yield **2f** in 78% yield with 83% ee or **2g** in 99% yield with 96% ee. Next, using an *ortho*-chloro phenyl group as a partner,

https://dx.doi.org/10.1021/acs.orglett.0c00293
Org. Lett. XXXX, XXX, XXX−XXX

substituents at the other phenyl ring were also investigated. Usually, due to the challenge in differentiating the enantiotopic faces, it was difficult to achieve highly enantioselective reduction of a substrate having a nearly symmetric structure. To our delight, substrate **1h** containing 2-chloro and 2′-methyl on the two phenyl rings was afforded in excellent yield with a good enantioselectivity. Substrates containing substituents at the 3′- or 4′-position were suitable for this catalytic system, giving **2i**−**2m** in excellent yield and enantioselectivity. Phenol (**1n**), ester (**1o**), and amide (**1p**) could also be tolerated to deliver **2n**−**2p** in 44−86% yields and 96−98% ee. Substrates with disubstituents were good partners to give **2q**−**2t** in 93−99% yields with 89−98% ee. *N*-Methyl-protected indole could also be tolerated to obtain **2u** in 81% yield with 95% ee. Additionally, reaction of aryl heteroaryl ketones like **1v** and **1w** afforded corresponding heteroarylmethanols **2v** and **2w** in 69 and 53% yield and 85 and 93% ee, respectively, with increased catalyst loading. The absolute configurations of **2a**−**2d** and **2h** were verified by comparison of their optical rotation with previously reported data.[3f,15,16a] The configuration of **2z** was verified by X-ray diffraction, and other products were then assigned by analogy.

To showcase the utility of this transformation, a gram-scale reaction was carried out to give the corresponding chiral alcohol **2c** in 93% yield with 96% ee under the standard conditions (Scheme 3a). Chiral 3-substituted phthalide frameworks (1(3*H*)-isobenzofuranones) are versatile building blocks broadly present in many natural products and biologically active compounds.[1a,b,16] The *ortho*-methyl-ester-substituted diaryl ketone **1z** could smoothly undergo sequential asymmetric hydroboration/lactonization reactions to afford (*S*)-3-phenylisobenzofuran-1(3*H*)-one (**2z**) in 66% yield with 92% ee (Scheme 3b). The structure and absolute configuration of (*S*)-**2z** were determined via X-ray diffraction analysis.[17] Benzhydrol **2aa** can be obtained with 95% yield and 98% ee via hydroboration of **1aa** under standard conditions. Further debromination of **2aa** delivered **3aa** in 91% yield and 98% ee, which was used to synthesize the (*S*)-neobenodine in 60% overall yield and 97% ee.

Scheme 3. Gram-Scale Reaction and Further Derivatizations



Based on the previous work of Chirik,[18] we considered that it was cobalt chloride LCoCl that generated rather than cobalt hydride LCoH when 1 equiv of $NaBHEt_3$ was used as the activator. So the key catalytic species is LCoCl rather than LCoH, which is so common for catalysis based on cobalt. Meanwhile, given the possibility that LCoCl might undergo other transformations, such as oxidative addition, it could also be the precursor of real catalytic species. It should be noted that the actual chemical valence of cobalt is not confirmed. The IIP ligand is proposed as a redox-active ligand.[19] As mentioned in Table 1, excess $NaBHEt_3$ led to lower ee and higher yield. We owed that to the generation of IIP·Co(I)H when more than 1 equiv of $NaBHEt_3$ was used as IIP·Co(I)H might lead to another type of catalytic mechanism. This mechanism based on IIP·Co(I)H might be similar to that described by Gade's group in 2018, which was based on Mn[20] and resulted in lower ee in this case. Meanwhile, given that the isomerization of terminal alkene was observed under standard conditions when terminal alkene was contained in the substrate, the mechanism based on IIP·Co(I)H could not be simply ruled out.

In summary, a cobalt-catalyzed highly enantioselective hydroboration of diaryl ketones with pinacolborane was developed using chiral imidazole iminopyridine as a ligand to deliver chiral benzhydrols in good to excellent yield and ee. Various functional groups such as halides, ethers, phenol, esters, and amides are well-tolerated under the mild conditions. The developed methodology could also be utilized to construct the biologically active 3-substituted phthalide in an asymmetric hydroboration/lactonization sequence. Additionally, the asymmetric reduction could be easily carried out in a gram scale without any decrease in yield and ee. Further studies on the mechanism and asymmetric catalysis via ligand design are underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c00293.

Experimental procedures and characterization data for all compounds (PDF)

Accession Codes

CCDC 1962316 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

https://dx.doi.org/10.1021/acs.orglett.0c00293
Org. Lett. XXXX, XXX, XXX−XXX

AUTHOR INFORMATION

Corresponding Author

Zhan Lu − *Department of Chemistry, Zhejiang University, Hangzhou 310058, China;* orcid.org/0000-0002-3069-079X; Email: luzhan@zju.edu.cn

Authors

Wenbo Liu − *Department of Chemistry, Zhejiang University, Hangzhou 310058, China*

Jun Guo − *Department of Chemistry, Zhejiang University, Hangzhou 310058, China*

Shipei Xing − *Department of Chemistry, Zhejiang University, Hangzhou 310058, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c00293

Author Contributions

†W.L. and J.G. contributed equally.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

Financial support was provided by Zhejiang Provincial Natural Science Foundation of China (LR19B020001), NSFC (21772171), Center Chemistry for Frontier Technologies, and the Fundamental Research Funds for the Central Universities (2019QNA3008). Dr. Xu Chen, Mr. Xiang Ren, Mr. Tao Han, and Mr. Huangzhe Lu at Zhejiang University are thanked for the help with the synthesis of some starting materials. Prof. Longwu Ye at Xiamen University is thanked for helpful discussions.

REFERENCES

(1) (a) Beck, J. J.; Chou, S.-C. The Structural Diversity of Phthalides from the Apiaceae. *J. Nat. Prod.* **2007**, *70*, 891−900. (b) Knepper, K.; Ziegert, R. E.; Bräse, S. Solid-phase synthesis of isoindolinones and naturally-occurring benzobutyrolactones (phthalides) using a cyclative-cleavage approach. *Tetrahedron* **2004**, *60*, 8591−8603. (c) Sui, Y.; Zhang, X.; Wu, J.; Li, S.; Zhou, J.; Li, M.; Fang, W.; Chan, A. S. C.; Wu, J. Cu^{II}-Catalyzed Asymmetric Hydrosilylation of Diaryl- and Aryl Heteroaryl Ketones: Application in the Enantioselective Synthesis of Orphenadrine and Neobenodine. *Chem. - Eur. J.* **2012**, *18*, 7486−7492.

(2) Schmidt, F.; Stemmler, R. T.; Rudolph, J.; Bolm, C. Catalytic asymmetric approaches towards enantiomerically enriched diarylmethanols and diarylmethylamines. *Chem. Soc. Rev.* **2006**, *35*, 454−470.

(3) (a) Chaumont-Olive, P.; Rouen, M.; Barozzino-Consiglio, G.; Abdeladhim, A. B.; Maddaluno, J.; Harrison-Marchand, A. Chiral Lithium Amido Aryl Zincates: Simple and Efficient Chemo- and Enantio-Selective Aryl Transfer Reagents. *Angew. Chem., Int. Ed.* **2019**, *58*, 3193−3197. (b) Salvi, L.; Kim, J. G.; Walsh, P. J. Practical Catalytic Asymmetric Synthesis of Diaryl-, Aryl Heteroaryl-, and Diheteroarylmethanols. *J. Am. Chem. Soc.* **2009**, *131*, 12483−12493. (c) Jimeno, C.; Sayalero, S.; Fjermestad, T.; Colet, G.; Maseras, F.; Pericàs, M. A. Practical Implications of Boron-to-Zinc Transmetalation for the Catalytic Asymmetric Arylation of Aldehydes. *Angew. Chem., Int. Ed.* **2008**, *47*, 1098−1101. (d) Qin, Y.-C.; Pu, L. Highly Enantioselective Addition of Diphenylzinc to Aliphatic and Aromatic Aldehydes Catalyzed by a Readily Available H_8-Binol Derivative. *Angew. Chem., Int. Ed.* **2006**, *45*, 273−277. (e) Kim, J. G.; Walsh, P. J. From Aryl Bromides to Enantioenriched Benzylic Alcohols in a Single Flask: Catalytic Asymmetric Arylation of Aldehydes. *Angew. Chem., Int. Ed.* **2006**, *45*, 4175−4178. (f) Duan, H.-F.; Xie, J.-H.; Shi, W.-J.; Zhang, Q.; Zhou, Q.-L. Enantioselective Rhodium-Catalyzed Addition of Arylboronic Acids to Aldehydes Using Chiral Spiro Monophosphite Ligands. *Org. Lett.* **2006**, *8*, 1479−1481. (g) Bolm, C.; Kesselgruber, M.; Hermanns, N.; Hildebrand, J. P.; Raabe, G. Application of a Planar Chiral η^5-Cyclopentadienylrhenium(I)tricarbonyl Complex in Asymmetric Catalysis: Highly Enantioselective Phenyl Transfer to Aldehydes. *Angew. Chem., Int. Ed.* **2001**, *40*, 1488−1490.

(4) Brown, E.; Penfornis, A.; Bayma, J.; Touet, J. Asymmetric reductions of ketones using lithium aluminium hydride modified with *N*, *N*-dialkyl derivatives of (*R*)-(−)-2-aminobutan-1-ol. *Tetrahedron: Asymmetry* **1991**, *2*, 339−342.

(5) Peyronel, J.; Fiaud, H.; Kagan, H. J. *Chem. Res. Synop.* **1980**, *9*, 320−320.

(6) Corey, E. J.; Helal, C. J. Reduction of Carbonyl Compounds with Chiral Oxazaborolidine Catalysts: A New Paradigm for Enantioselective Catalysis and a Powerful New Synthetic Method. *Angew. Chem., Int. Ed.* **1998**, *37*, 1986−2012.

(7) (a) Ohkuma, T.; Koizumi, M.; Ikehira, H.; Yokozawa, T.; Noyori, R. Selective Hydrogenation of Benzophenones to Benzhydrols. Asymmetric Synthesis of Unsymmetrical Diarylmethanols. *Org. Lett.* **2000**, *2*, 659−662. (b) Chen, C.-Y.; Reamer, R. A.; Chilenski, J. R.; McWilliams, C. J. Highly Enantioselective Hydrogenation of Aromatic-Heteroaromatic Ketones. *Org. Lett.* **2003**, *5*, 5039−5042.

(8) Ling, F.; Nian, S.-F.; Chen, J.-C.; Luo, W.-J.; Wang, Z.; Lv, Y.-P.; Zhong, W.-H. Development of Ferrocene-Based Diamine-Phosphine-Sulfonamide Ligands for Iridium-Catalyzed Asymmetric Hydrogenation of Ketones. *J. Org. Chem.* **2018**, *83*, 10749−10761.

(9) (a) Zhang, L.-L.; Tang, Y.-T.; Han, Z.-B.; Ding, K.-L. Lutidine-Based Chiral Pincer Manganese Catalysts for Enantioselective Hydrogenation of Ketones. *Angew. Chem., Int. Ed.* **2019**, *58*, 4973−4977. (b) Ling, F.; Hou, H.; Chen, J.; Nian, S.; Yi, X.; Wang, Z.; Song, D.; Zhong, W. Highly Enantioselective Synthesis of Chiral Benzhydrols via Manganese Catalyzed Asymmetric Hydrogenation of Unsymmetrical Benzophenones Using an Imidazole-Based Chiral PNN Tridentate Ligand. *Org. Lett.* **2019**, *21*, 3937−3941.

(10) Touge, T.; Nara, H.; Fujiwhara, M.; Kayaki, Y.; Ikariya, T. Efficient Access to Chiral Benzhydrols via Asymmetric Transfer Hydrogenation of Unsymmetrical Benzophenones with Bifunctional Oxo-Tethered Ruthenium Catalysts. *J. Am. Chem. Soc.* **2016**, *138*, 10084−10087.

(11) For selected examples on noble metal catalysis, see: (a) Noyori, R.; Ohkuma, T. Asymmetric Catalysis by Architectural and Functional Molecular Engineering: Practical Chemo- and Stereoselective Hydrogenation of Ketones. *Angew. Chem., Int. Ed.* **2001**, *40*, 40−73. (b) Wu, J.; Ji, J.-X.; Guo, R.; Yeung, C.-H.; Chan, A. S. C. Chiral [$RuCl_2$(dipyridylphosphane)(1,2-diamine)] Catalysts: Applications in Asymmetric Hydrogenation of a Wide Range of Simple Ketones. *Chem. - Eur. J.* **2003**, *9*, 2963−2968. (c) Hamilton, R. J.; Leong, C. G.; Bigam, G.; Miskolzie, M.; Bergens, S. H. A Ruthenium-Dihydrogen Putative Intermediate in Ketone Hydrogenation. *J. Am. Chem. Soc.* **2005**, *127*, 4152−4153. (d) Abbel, R.; Abdur-Rashid, K.; Faatz, M.; Hadzovic, A.; Lough, A. J.; Morris, R. H. A Succession of Isomers of Ruthenium Dihydride Complexes. Which One Is the Ketone Hydrogenation Catalyst? *J. Am. Chem. Soc.* **2005**, *127*, 1870−1882. (e) Xu, Y.-J.; Clarkson, G. C.; Docherty, G.; North, C. L.; Woodward, G.; Wills, M. Ruthenium(II) Complexes of Monodonor Ligands: Efficient Reagents for Asymmetric Ketone Hydrogenation. *J. Org. Chem.* **2005**, *70*, 8079−8087. (f) Mikami, K.; Wakabayashi, K.; Aikawa, K. Achiral" Benzophenone Ligand for Highly Enantioselective Ru Catalysts in Ketone Hydrogenation. *Org. Lett.* **2006**, *8*, 1517−1519. (g) Hamilton, R. J.; Bergens, S. H. Direct Observations of the Metal-Ligand Bifunctional Addition Step in an Enantioselective Ketone Hydrogenation. *J. Am. Chem. Soc.* **2008**, *130*, 11979−11987. (h) Tian, C.; Gong, L.; Meggers, E. Chiral-at-metal iridium complex for efficient enantioselective transfer hydrogenation of ketones. *Chem. Commun.* **2016**, *52*, 4207−4210. (i) Wan, K. Y.; Sung, M. M. H.; Lough, A. J.; Morris, R. H. Half-Sandwich Ruthenium Catalyst Bearing an Enantiopure Primary Amine Tethered to an N-

Heterocyclic Carbene for Ketone Hydrogenation. *ACS Catal.* **2017**, *7*, 6827−6842. (j) Wang, Y.-Z.; Yang, G.-Q.; Xie, F.; Zhang, W.-B. A Ferrocene-Based NH-Free Phosphine-Oxazoline Ligand for Iridium-Catalyzed Asymmetric Hydrogenation of Ketones. *Org. Lett.* **2018**, *20*, 6135−6139. (k) Wu, J.; Ji, J.-X.; Chan, A. S. C. A remarkably effective copper(II)-dipyridylphosphine catalyst system for the asymmetric hydrosilylation of ketones in air. *Proc. Natl. Acad. Sci. U. S. A.* **2005**, *102*, 3570−3575. For selected examples on earth-abundant transition metal catalysis, see: (l) Shimizu, H.; Igarashi, D.; Kuriyama, W.; Yusa, Y.; Sayo, N.; Saito, T. Asymmetric Hydrogenation of Aryl Ketones Mediated by a Copper Catalyst. *Org. Lett.* **2007**, *9*, 1655−1657. (m) Shaikh, N. S.; Enthaler, S.; Junge, K.; Beller, M. Iron-Catalyzed Enantioselective Hydrosilylation of Ketones. *Angew. Chem., Int. Ed.* **2008**, *47*, 2497−2501. (n) Hamada, Y.; Koseki, Y.; Fujii, T.; Maeda, T.; Hibino, T.; Makino, K. Catalytic asymmetric hydrogenation of α-amino-β-keto ester hydrochlorides using homogeneous chiral nickel-bisphosphine complexes through DKR. *Chem. Commun.* **2008**, 6206−6208. (o) Lee, C.-T.; Lipshutz, B. H. Nonracemic Diarylmethanols From CuH-Catalyzed Hydrosilylation of Diaryl Ketones. *Org. Lett.* **2008**, *10*, 4187−1490. (p) Junge, K.; Wendt, B.; Addis, D.; Zhou, S.-L.; Das, S.; Fleischer, S.; Beller, M. Copper-Catalyzed Enantioselective Hydrogenation of Ketones. *Chem. - Eur. J.* **2011**, *17*, 101−105. (q) Berkessel, A.; Reichau, S.; von der Höh, A.; Leconte, N.; Neudörfl, J.-M. Light-Induced Enantioselective Hydrogenation Using Chiral Derivatives of Casey's Iron-Cyclopentadienone Catalyst. *Organometallics* **2011**, *30*, 3880−3887. (r) Krabbe, S. W.; Hatcher, M. A.; Bowman, R. K.; Mitchell, M. B.; McClure, M. S.; Johnson, J. S. Copper-Catalyzed Asymmetric Hydrogenation of Aryl and Heteroaryl Ketones. *Org. Lett.* **2013**, *15*, 4560−4563. (s) Li, Y.-Y.; Yu, S.-L.; Wu, X.-F.; Xiao, J.-J.; Shen, W.-Y.; Dong, Z.-R.; Gao, J.-X. Iron Catalyzed Asymmetric Hydrogenation of Ketones. *J. Am. Chem. Soc.* **2014**, *136*, 4031−4039. (t) Zuo, Z.-Q.; Zhang, L.; Leng, X.-B.; Huang, Z. Iron-catalyzed asymmetric hydrosilylation of ketones. *Chem. Commun.* **2015**, *51*, 5073−5076. (u) Hodgkinson, R.; Del Grosso, A.; Clarkson, G.; Wills, M. Iron cyclopentadienone complexes derived from C_2-symmetric bis-propargylic alcohols; preparation and applications to catalysis. *Dalton Trans.* **2016**, *45*, 3992−4005. (v) Ma, X.-C.; Zuo, Z.-Q.; Liu, G.-X.; Huang, Z. Manganese-Catalyzed Asymmetric Hydrosilylation of Aryl Ketones. *ACS Omega* **2017**, *2*, 4688−4692. (w) Blasius, C. K.; Vasilenko, V.; Gade, L. H. Ultrafast Iron-Catalyzed Reduction of Functionalized Ketones: Highly Enantioselective Synthesis of Halohydrines, Oxaheterocycles, and Enantioselective Synthesis of Halohydrines, Oxaheterocycles, and Amino-alcohols. *Angew. Chem., Int. Ed.* **2018**, *57*, 10231−10235. (x) Zatolochnaya, O. V.; Rodríguez, S.; Zhang, Y.-D.; Lao, K. S.; Tcyrulnikov, S.; Li, G.-S.; Wang, X.-J.; Qu, B.; Biswas, S.; Mangunuru, H. P. R.; Rivalti, D.; Sieber, J. D.; Desrosiers, J.-N.; Leung, J. C.; Grinberg, N.; Lee, H.; Haddad, N.; Yee, N. K.; Song, J. J.; Kozlowski, M. C.; Senanayake, C. H. Copper-catalyzed asymmetric hydrogenation of 2-substituted ketones via dynamic kinetic resolution. *Chem. Sci.* **2018**, *9*, 4505−4510. (y) Vasilenko, V.; Blasius, C. K.; Wadepohl, H.; Gade, L. H. Borohydride intermediates pave the way for magnesium-catalysed enantioselective ketone reduction. *Chem. Commun.* **2020**, *56*, 1203. (z) Lebedev, Y.; Polishchuk, I.; Maity, B.; Guerreiro, M. D. V.; Cavallo, L.; Rueping, M. Asymmetric Hydroboration of Heteroaryl Ketones by Aluminum Catalysis. *J. Am. Chem. Soc.* **2019**, *141*, 19415−19423. (aa) Falconnet, A.; Magre, M.; Maity, B.; Cavallo, L.; Rueping, M. Asymmetric Magnesium-Catalyzed Hydroboration by Metal-Ligand Cooperative Catalysis. *Angew. Chem., Int. Ed.* **2019**, *58*, 17567−17571. (bb) Bigler, R.; De Luca, L.; Huber, R.; Mezzetti, A. Asymmetric Reduction of Polar Double Bonds. In *Non-Noble Metal Catalysis: Molecular Approaches and Reactions*; Klein-Gebbink, R. J. M., Moret, M. E., Eds.; Wiley-VCH: Weinheim, Germany, 2020; pp 209−240.

(12) Kokura, A.; Tanaka, S.; Ikeno, T.; Yamada, T. Catalytic Enantioselective Borohydride Reduction of *Ortho*-Fluorinated Benzophenones. *Org. Lett.* **2006**, *8*, 3025−3027.

(13) It should be noted that the absolute configurations of **2a** and **2b** were assigned incorrectly in our previous work. See: Guo, J.; Chen, J.-H.; Lu, Z. Cobalt-catalyzed asymmetric hydroboration of aryl ketones with pinacolborane. *Chem. Commun.* **2015**, *51*, 5725−5727.

(14) Reviews in our group: (a) Chen, X.; Lu, Z. Recent advances in chiral imino-containing ligands for metal-catalyzed asymmetric transfomrations. *Org. Biomol. Chem.* **2017**, *15*, 2280−2306. (b) Chen, J.-H.; Lu, Z. Asymmetric hydrofunctionalization of minimally functionalized alkenes via earth abundant transition metal catalysis. *Org. Chem. Front.* **2018**, *5*, 260−272. (c) Chen, J.-H.; Guo, J.; Lu, Z. Recent Advances in Hydrometallation of Alkenes and Alkynes via the First Row Transition Metal Catalysis. *Chin. J. Chem.* **2018**, *36*, 1075−1109. (d) Cheng, B.; Liu, W.-B.; Lu, Z. Iron-Catalyzed Highly Enantioselective Hydrosilylation of Unactivated Terminal Alkenes. *J. Am. Chem. Soc.* **2018**, *140*, 5014−5017. For selected recent asymmetric reaction in our group, see: (e) Zhang, H.-Y.; Cheng, B.; Lu, Z. Enantioselective Cobalt-Catalyzed Sequential Nazarov Cyclization/Electrophilic Fluorination: Access to Chiral α-Fluorocyclopentenones. *Org. Lett.* **2018**, *20*, 4028−4031. (f) Chen, X.; Cheng, Z.-Y.; Guo, J.; Lu, Z. Asymmetric remote C-H borylation of internal alkenes via alkene isomerization. *Nat. Commun.* **2018**, *9*, 3939. (g) Chen, X.; Cheng, Z.; Lu, Z. Cobalt-Catalyzed Asymmetric Markovnikov Hydroboration of Styrenes. *ACS Catal.* **2019**, *9*, 4025−4029. (h) Cheng, Z.-Y.; Xing, S.-P.; Guo, J.; Cheng, B.; Hu, L.-F.; Zhang, X.-H.; Lu, Z. Highly Regioselective Sequential 1,1-Dihydrosilylation of Terminal Aliphatic Alkynes with Primary Silanes. *Chin. J. Chem.* **2019**, *37*, 457−461. (i) Guo, J.; Wang, H.-L.; Xing, S.-P.; Hong, X.; Lu, Z. Cobalt-Catalyzed Asymmetric Synthesis of gem-Bis(silyl)alkanes by Double Hydrosilylation of Aliphatic Terminal Alkynes. *Chem.* **2019**, *5*, 881−895. (j) Cheng, X.; Lu, H.-Z.; Lu, Z. Enantioselective benzylic C-H arylation via photoredox and nickel dual catalysis. *Nat. Commun.* **2019**, *10*, 3549.

(15) (a) Umeda, R.; Studer, A. Ag-Catalyzed Stereoselective Cyclohexadienyl Transfer: A Novel Entry into Arylphenylmethanols. *Org. Lett.* **2008**, *10*, 993−996. (b) Ohkuma, T.; Koizumi, M.; Ikehira, H.; Yokozawa, T.; Noyori, R. Selective Hydrogenation of Benzophenones to Benzhydrols. Asymmetric Synthesis of Unsymmetrical Diarylmethanols. *Org. Lett.* **2000**, *2*, 659−662.

(16) (a) Phan, D. H. T.; Kim, B.; Dong, V. M. Phthalides by Rhodium-Catalyzed Ketone Hydroacylation. *J. Am. Chem. Soc.* **2009**, *131*, 15608−15609. (b) Lu, B.; Zhao, M.-M.; Ding, G.-N.; Xie, X.-M.; Jiang, L.-L.; Ratovelomanana-Vidal, V.; Zhang, Z.-G. Ruthenium-Catalyzed Enantioselective Hydrogenation/ Lactonization of 2-Acylarylcarboxylates: Direct Access to Chiral 3-Substituted Phthalides. *ChemCatChem* **2017**, *9*, 3989−3996.

(17) Kalyani, V.; Vijayan, M. The Crystal and Molecular Structure of 3-(p-Bromophenyl)phthalide. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1969**, *25*, 1281−1288.

(18) Semproni, S. P.; Atienza, C. C. H.; Chirik, P. J. Oxidative addition and C-H activation chemistry with a PNP pincer-ligated cobalt complex. *Chem. Sci.* **2014**, *5*, 1956−1960.

(19) Chirik, P. J.; Wieghardt, K. Radical Ligands Confer Nobility on Base-Metal Catalysts. *Science* **2010**, *327*, 794−795.

(20) Vasilenko, V.; Blasius, C. K.; Gade, L. H. One-Pot Sequential Kinetic Profiling of a Highly Reactive Manganese Catalyst for Ketone Hydroboration: Leveraging σ-Bond Metathesis via Alkoxide Exchange Steps. *J. Am. Chem. Soc.* **2018**, *140*, 9244−9254.

https://dx.doi.org/10.1021/acs.orglett.0c00293
Org. Lett. XXXX, XXX, XXX−XXX