

Cite this: *Chem. Sci.*, 2023, 14, 4888

All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 30th January 2023
Accepted 13th March 2023

DOI: 10.1039/d3sc00491k

rsc.li/chemical-science

Facile access to chiral γ -butyrolactones via rhodium-catalysed asymmetric hydrogenation of γ -butenolides and γ -hydroxybutenolides†

Yuxuan Zhou,^{‡a} Siyuan Guo,^{‡a} Qiyuan Huang,^a Qiwei Lang,^{*a} Gen-Qiang Chen^{ab} and Xumu Zhang^{ab}

The highly efficient Rh/ZhaoPhos-catalysed asymmetric hydrogenation of γ -butenolides and γ -hydroxybutenolides was successfully developed. This protocol provides an efficient and practical approach to the synthesis of various chiral γ -butyrolactones, which are synthetically valuable building blocks of diverse natural products and therapeutic substances, with excellent results (up to >99% conversion and 99% ee). Further follow-up transformations have been revealed to accomplish creative and efficient synthetic routes for several enantiomerically enriched drugs *via* this catalytic methodology.

γ -Butyrolactone is an essential framework existing in large numbers of natural products¹ and pharmaceutical compounds² and shows unique and excellent biological activities (Fig. 1). Furthermore, enantiomerically pure γ -butyrolactones could serve as building blocks for the construction of a wide range of complex molecules,³ and diverse transformations have been developed,⁴ especially in the highly versatile furanone structure, to synthesize physiologically and therapeutically important reagents, for example brivaracetam,⁵ arctigenin,⁶ pilocarpine,⁷ etc.

As commercially available or easily accessible compounds, γ -butenolides⁸ are important synthetic precursors towards γ -butyrolactones, and an impressive range of transformations have been developed for the enantioselective construction of chiral γ -butyrolactones.⁹ With the advancement in the field of asymmetric metal catalysis, enantioselective 1,4-addition and reduction of γ -butenolides have been considered representative methodologies of preparing optically active γ -butyrolactones. In contrast to the well-developed asymmetric 1,4-additions¹⁰ (Scheme 1a), with transition metal-catalysed 1,4-reduction of γ -butenolides as an alternative it would be difficult to achieve satisfactory catalytic conversion and stereoselectivity as well as broad substrate scope because of the lack of efficient metal catalysts.¹¹ The Buchwald group reported a CuH-catalysed enantioselective conjugate reduction of γ -butenolides;¹²

however, the requirement of using high catalyst loading and a strong base additive could limit the application of this method in organic synthesis and the pharmaceutical industry. Recently, our group developed a bisphosphine-thiourea chiral ligand, ZhaoPhos,¹³ which exhibited extraordinary potential in rhodium¹⁴ and iridium-catalyzed¹⁵ asymmetric hydrogenation due to its powerful hydrogen-bonding and anion-binding ability resulting from the thiourea moiety. Inspired by this novel strategy, we herein demonstrated a Rh/ZhaoPhos catalysed asymmetric hydrogenation of easily accessible γ -butenolides and γ -hydroxybutenolides, which could be a straightforward method of approaching chiral γ -butyrolactones with excellent catalytic results (Scheme 1b).

We initiated our investigation with evaluation of various combinations of the rhodium precatalyst and different chiral phosphine ligands for the asymmetric hydrogenation of 4-phenylfuran-2(5*H*)-one **1a**. After examining a series of commonly used chiral phosphine ligands and using THF as the

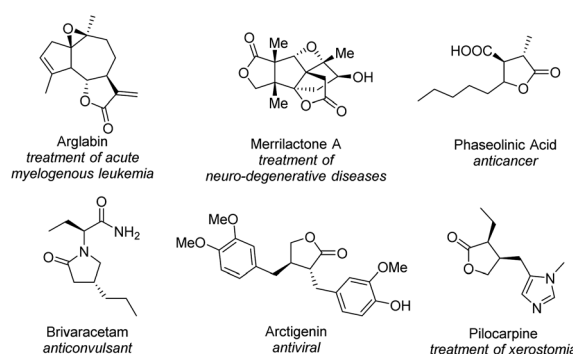


Fig. 1 Natural products containing the γ -butyrolactone core, and pharmaceutical compounds derived from γ -butyrolactones.

^aShenzhen Grubbs Institute, Department of Chemistry, and Medi-Pingshan, Southern University of Science and Technology, Shenzhen 518000, People's Republic of China. E-mail: langqw@sustech.edu.cn; chengq@sustech.edu.cn; zhangxm@sustech.edu.cn

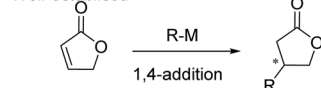
^bAcademy for Advanced Interdisciplinary Studies, Southern University of Science and Technology, Shenzhen 518000, People's Republic of China

† Electronic supplementary information (ESI) available. See DOI: <https://doi.org/10.1039/d3sc00491k>

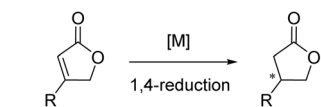
‡ Yuxuan Zhou and Siyuan Guo contributed equally to this work.

a. Current metal-catalyzed transformations of γ -butenolides to prepare chiral γ -butyrolactones.

Well-established

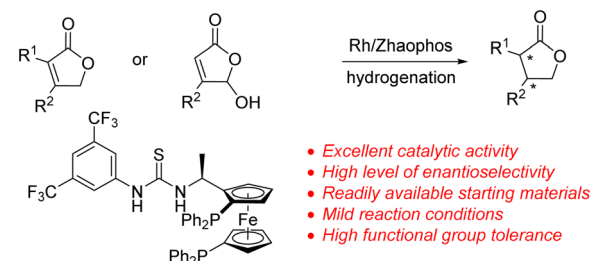


Problematic



- Poor conversion
- Low or moderate enantioselectivity
- Limited substrate scope
- Harsh reaction conditions
- Tedious work-up procedures

b. This work: Rh/Zhaophos-catalyzed hydrogenation of γ -butenolides.



Scheme 1 Current methods of preparing chiral γ -butyrolactones from γ -butenolides, and proposed Rh/Zhaophos-catalyzed hydrogenation.

solvent, very poor enantioselectivity was achieved with ligands such as DuanPhos, SegPhos, BINAP and so on (Table 1, entries 1–7). Employing ZhaoPhos as a ligand could facilitate the hydrogenation with a significantly improved enantioselective manner, and the desired product **2a** was obtained in 79% conversion and 97% ee under 50 atm of H_2 at room temperature within 24 hours (entry 8). Furthermore, the solvent was crucial to the control of the reaction rate, and by screening several protic and aprotic solvents (Table 2, entries 1–9), we found that by employing DCM as solvent complete hydrogenation could be achieved under standard conditions, which afforded **2a** with >99% conversion and in 98% ee (entry 8).

With optimized reaction conditions in hand, we then continued to investigate the substrate generality (Table 3). A considerable number of β -aryl substituents (**2a–l**) on γ -butenolides were investigated, and the hydrogenation proceeded smoothly to yield the desired products with excellent yields (95 ~ 99%) and in high enantioselectivities (97 ~ 98% ee), in which both electron-withdrawing (**2b–2d**) and electron-donating (**2e–2j**) substituents on the aryl ring at different positions were well tolerated. The hydrogenation of substrates with the bulky naphthyl moiety (**1k**) and heterocyclic unit (thienyl, **1l**) was feasible, giving the corresponding product with excellent results (95 ~ 99% yields and 98% ee). In addition, the alkyl substituents (**2m–n**) were explored as well, and it is noteworthy that α -methyl substituted lactone **2n** could be produced with 84% or 82% ee respectively from the substrates featuring either endo-(**1n**) or exocyclic (**1n'**) unsaturation, in which this transformation was rarely achieved with good yield and in acceptable enantioselectivity according to previous studies.¹⁶ The reactions of α,β -disubstituted γ -butenolides **1o** and **1p** were also conducted; however, no desired products were obtained.

Table 1 Ligand screening for the asymmetric hydrogenation of **1a**

Entry ^a	Ligand	Conv. ^b (%)	ee ^c (%)
1	(<i>R</i> _C , <i>S</i> _P)-DuanPhos	14	1
2	(<i>S</i>)-SegPhos	100	2
3	(<i>S</i>)-BINAP	78	0
4	(<i>R,S</i>)-JosiPhos	100	2
5	(<i>R</i>)-MeO-BIPHEP	13	10
6	WalPhos	31	16
7	(<i>R</i>)-C ₃ *-TunePhos	8	13
8	ZhaoPhos	79	97

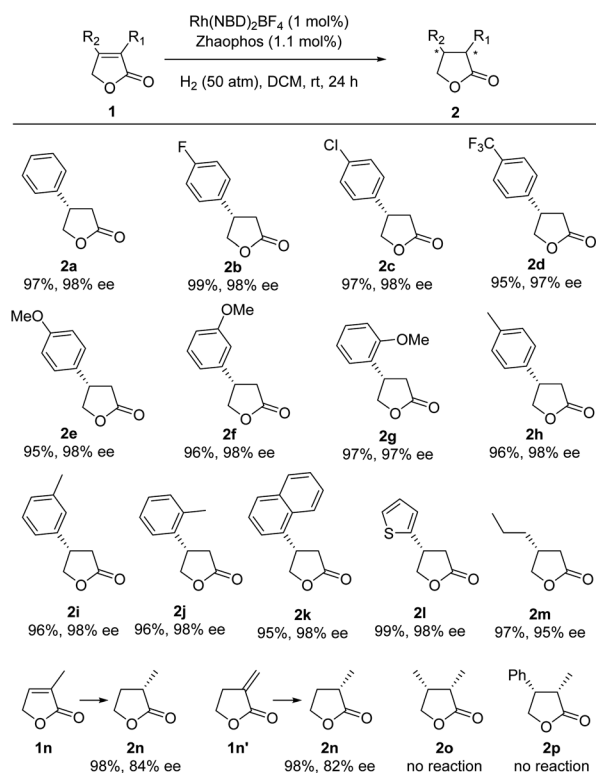
^a Unless otherwise noted, all hydrogenations were carried out with a [Rh(NBD)₂BF₄]/ligand/**1a** (0.1 mmol) ratio of 1 : 1.1 : 100 in 1.0 mL of THF under H_2 (50 atm) at room temperature for 24 h. ^b Determined by ¹H NMR. ^c Determined by HPLC analysis, and the absolute configuration of **2a** was determined as *S* by comparing the optical rotation data with the literature.

Apart from the hydrogenation of γ -butenolides, γ -hydroxybutenolides **3** were also successfully reduced under the same reaction conditions with CF₃COOH as an additive (see the ESI†)

Table 2 Solvent screening for the asymmetric hydrogenation of **1a**

Entry ^a	Solvent	Conv. ^b (%)	ee ^c (%)
1	MeOH	29	96
2	EtOH	19	97
3	CF ₃ CH ₂ OH	59	98
4	EtOAc	>99	97
5	Toluene	91	95
6	THF	79	97
7	1,4-Dioxane	30	16
8	DCM	>99	98
9	DCE	25	96

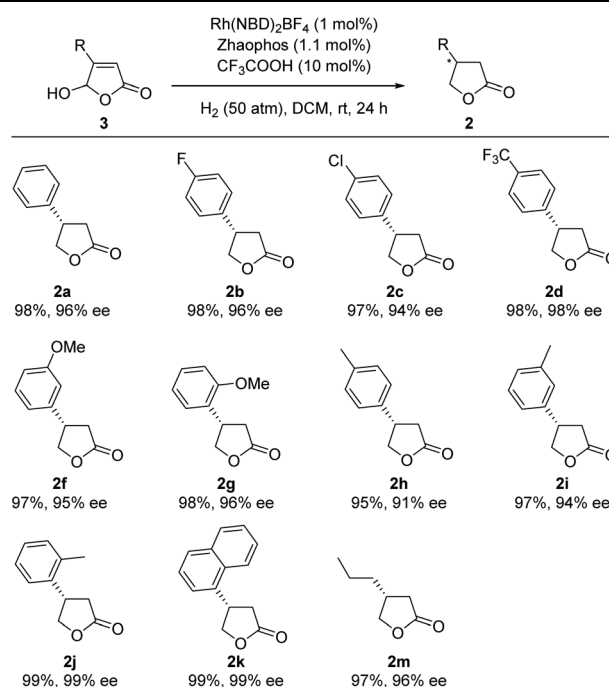
^a Unless otherwise noted, all hydrogenations were carried out with a [Rh(NBD)₂BF₄]/ligand/**1a** (0.1 mmol) ratio of 1 : 1.1 : 100 in 1.0 mL of solvent under H_2 (50 atm) at room temperature for 24 h. ^b Determined by ¹H NMR. ^c Determined by HPLC analysis, and the absolute configuration of **2a** was determined as *S* by comparing the optical rotation data with the literature.

Table 3 Substrate scope of the hydrogenation of γ -butenolides **1**^{a,b,c}

^a Unless otherwise noted, all hydrogenations were carried out with a $[\text{Rh(NBD)}_2\text{BF}_4]/\text{ligand}/\mathbf{1a}$ (0.1 mmol) ratio of 1 : 1.1 : 100 in 1.0 mL of DCM under H_2 (50 atm) at room temperature for 24 h. ^b Isolated yield. ^c Determined by HPLC analysis, and the absolute configuration was determined by comparing the optical rotation data with the literature.

for details), and consequently afforded γ -butyrolactones **2** directly in high yields (95 ~ 99%) and with excellent enantioselectivities (up to 99% ee) (Table 4). We suggested that $\text{CF}_3\text{-COOH}$ could activate the hydroxy group of lactol, which could be protonated to form an oxonium salt, and then hydrogenated by the catalyst.^{15e,f} γ -Hydroxybutenolides could be naturally occurring as well as easily prepared, and on account of realizing these transformations, the scope of the starting material for preparing chiral γ -butyrolactones was extremely expanded, which further improved the synthetic value of the Rh/ZhaPhos catalyst in the field of asymmetric hydrogenation.

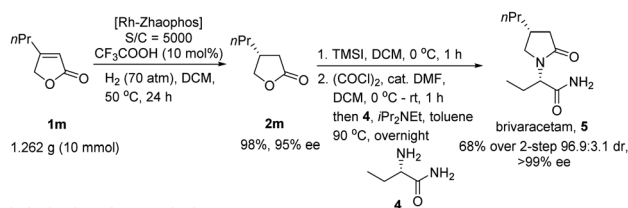
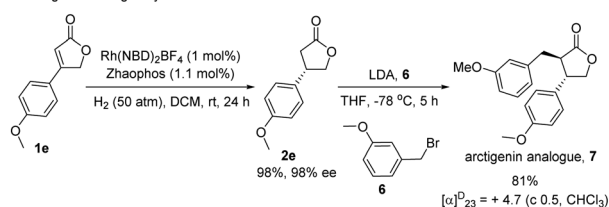
To demonstrate the synthetic utilities of this method, a gram-scale hydrogenation of substrate **1m** (Scheme 2a) was conducted with a low catalyst loading of 0.02 mol%. To our delight, the hydrogenation underwent smoothly under 70 atm of H_2 at 50 °C using CF_3COOH (10 mol%) as the additive (adding CF_3COOH could not only stabilize the cationic rhodium catalyst to increase the TON of the reaction, but also activate the carbonyl of α,β -unsaturated lactone to facilitate the hydrogenation), and the chiral γ -butyrolactone **2m** was afforded in 98% yield and with 95% ee. We further transformed this chiral building block *via* a ring-opening/recyclization strategy to achieve the total synthesis of brivaracetam in high optical purity

Table 4 Substrate scope of the hydrogenation of γ -hydroxybutenolides **3**^{a,b,c}

^a Unless otherwise noted, all hydrogenations were carried out with a $[\text{Rh(NBD)}_2\text{BF}_4]/\text{ligand}/\mathbf{1a}$ (0.1 mmol) ratio of 1 : 1.1 : 10 : 100 in 1.0 mL of DCM under H_2 (50 atm) at room temperature for 24 h. ^b Isolated yield. ^c Determined by HPLC analysis, and the absolute configuration was determined comparing the optical rotation data with the literature.

(96.9 : 3.1 dr and >99% ee) within only 3 steps (67% overall yield). Moreover, the 2-step synthesis of arctigenin analogue **7** was realized using γ -butenolide **1e** as the starting material (79% overall yield, Scheme 2b), which presented a shorter synthetic route compared to previous studies.^{6c}

In summary, we have developed a highly enantioselective Rh/ZhaPhos-catalyzed hydrogenation, providing a series of

a. Gram-scale hydrogenation of **1m** (S/C = 5000) and application in brivaracetam synthesis**b.** Arctigenin analogue synthesis**Scheme 2** Synthetic applications.

synthetically useful chiral γ -butyrolactones with readily available γ -butenolides and γ -hydroxybutenolides as starting materials. In addition, this strategy was applicable to the construction of various natural products and therapeutic substances, and scalable and concise syntheses of the pharmaceutical drugs brivaracetam and arctigenin were accomplished through this methodology, which demonstrated its practical utilities.

Data availability

All experimental procedures, characterization, and computational data for this study, can be found in the ESI.†

Author contributions

The manuscript was written through the contributions of all authors. All authors have approved the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

X. Zhang is indebted to the Southern University of Science and Technology (start-up fund), Shenzhen Science and Technology Innovation Committee (No. KQTD20150717103157174), Stable Support Plan Program of the Shenzhen Natural Science Fund (Program Contract No. 20200925161222002), Key-Area Research and Development Program of Guangdong Province (No. 2020B010188001), Innovative Team of Universities in Guangdong Province (No. 2020KCXTD016), and National Natural Science Foundation of China (No. 21991113). G.-Q. Chen gratefully acknowledges the National Natural Science Foundation of China (No. 22171129), the Guangdong Basic and Applied Basic Research Foundation (2022B1515020055) and Shenzhen Science and Technology Innovation Committee (JCYJ20210324104202007) for financial support. The authors acknowledge the assistance of SUSTech Core Research Facilities.

References

- (a) R. Haritakun, P. Rachtawee, R. Chanthaket, N. Boonyuen and M. Isaka, Butyrolactones from the fungus *Aspergillus terreus* BCC 4651, *Chem. Pharm. Bull.*, 2010, **58**, 1545–1548; (b) D. J. Faulkner, Marine natural products, *Nat. Prod. Rep.*, 2001, **18**, 1–49.
- (a) M. Yamawaki, K. Nishi, S. Nishimoto, S. Yamauchi, K. Akiyama, T. Kishida, M. Maruyama, H. Nishiwaki and T. Sugahara, Immunomodulatory effect of (–)-matairesinol in vivo and ex vivo, *Biosci., Biotechnol., Biochem.*, 2011, **75**, 859–863; (b) S. Ōmura, H. Tanaka, Y. Okada and H. Marumo, Isolation and structure of nanaomycin D, an enantiomer of the antibiotic kalafungin, *J. Chem. Soc., Chem. Commun.*, 1976, 320–321; (c) O. C. Snead III and K. M. Gibson, Gamma-hydroxybutyric acid, *N. Engl. J. Med.*, 2005, **352**, 2721–2732.
- J. Hur, J. Jang and J. Sim, A review of the pharmacological activities and recent synthetic advances of γ -butyrolactones, *Int. J. Mol. Sci.*, 2021, **22**, 2769.
- B. Mao, M. Fananas-Mastral and B. L. Feringa, Catalytic Asymmetric Synthesis of Butenolides and Butyrolactones, *Chem. Rev.*, 2017, **117**, 10502–10566.
- (a) M. Gayke, H. Narode, G. Eppa, R. S. Bhosale and J. S. Yadav, Synthetic Approaches toward the Synthesis of Brivaracetam: An Antiepileptic Drug, *ACS Omega*, 2022, **7**, 2486–2503; (b) S. Liao, H. Chen, G. Wang, S. Wu, Z. Yang, W. Luo, Z. Liu, X. Gao, J. Qin, C.-h. Li and Z. Wang, Identification, characterization, synthesis and strategy for minimization of potential impurities observed in the synthesis of brivaracetam, *Tetrahedron*, 2020, **76**, 131273; (c) S. P. Chavan, S. A. Kawale and P. N. Chavan, Formal synthesis of brivaracetam: a key to construct the pyrrolidone scaffold using Pd-catalyzed oxidative cyclization and ring-closing metathesis reaction, *Tetrahedron Lett.*, 2019, **60**, 151249.
- (a) S. Duan, S. Huang, J. Gong, Y. Shen, L. Zeng, Y. Feng, W. Ren, Y. Leng and Y. Hu, Design and synthesis of novel arctigenin analogues for the amelioration of metabolic disorders, *ACS Med. Chem. Lett.*, 2015, **6**, 386–391; (b) D. Wu, L. Jin, X. Huang, H. Deng, Q. K. Shen, Z. S. Quan, C. Zhang and H. Y. Guo, Arctigenin: pharmacology, total synthesis, and progress in structure modification, *J. Enzyme Inhib. Med. Chem.*, 2022, **37**, 2452–2477; (c) L. M. Recnik, R. J. Thatcher, S. Mallah, C. P. Butts, G. L. Collingridge, E. Molnar, D. E. Jane and C. L. Willis, Synthesis and pharmacological characterisation of arctigenin analogues as antagonists of AMPA and kainate receptors, *Org. Biomol. Chem.*, 2021, **19**, 9154–9162.
- (a) D. A. Horne, B. Fugmann, K. Yakushijin and G. Buchi, A synthesis of pilocarpine, *J. Org. Chem.*, 2002, **58**, 62–64; (b) T. Schmidt, N. Heise, K. Merzweiler, H. P. Deigner, A. Al-Harrasi and R. Csuk, Concise Synthesis of Both Enantiomers of Pilocarpine, *Molecules*, 2021, **26**, 3676; (c) S. G. Davies, P. M. Roberts, P. T. Stephenson, H. R. Storr and J. E. Thomson, A practical and scaleable total synthesis of the jaborandi alkaloid (+)-pilocarpine, *Tetrahedron*, 2009, **65**, 8283–8296.
- S. Chatterjee, R. Sahoo and S. Nanda, Recent reports on the synthesis of gamma-butenolide, gamma-alkylidenebutenolide frameworks, and related natural products, *Org. Biomol. Chem.*, 2021, **19**, 7298–7332.
- J. Y. Kato, N. Funa, H. Watanabe, Y. Ohnishi and S. Horinouchi, Biosynthesis of gamma-butyrolactone autoregulators that switch on secondary metabolism and morphological development in *Streptomyces*, *Proc. Natl. Acad. Sci. U. S. A.*, 2007, **104**, 2378–2383.
- (a) M. K. Brown, S. J. Degrado and A. H. Hoveyda, Highly enantioselective Cu-catalyzed conjugate additions of dialkylzinc reagents to unsaturated furanones and pyranones: preparation of air-stable and catalytically active Cu-peptide complexes, *Angew. Chem., Int. Ed.*, 2005, **44**,



- 5306–5310; (b) T. Gendrineau, O. Chuzel, H. Eijsberg, J. P. Genet and S. Darses, C1-symmetric monosubstituted chiral diene ligands in asymmetric rhodium-catalyzed 1,4-addition reactions, *Angew. Chem., Int. Ed.*, 2008, **47**, 7669–7672; (c) Y. Luo and A. J. Carnell, Chemoenzymatic synthesis and application of bicyclo[2.2.2]octadiene ligands: increased efficiency in rhodium-catalyzed asymmetric conjugate additions by electronic tuning, *Angew. Chem., Int. Ed.*, 2010, **49**, 2750–2754; (d) T. Hayashi and K. Yamasaki, Rhodium-catalyzed asymmetric 1,4-addition and its related asymmetric reactions, *Chem. Rev.*, 2003, **103**, 2829–2844; (e) H. J. Edwards, J. D. Hargrave, S. D. Penrose and C. G. Frost, Synthetic applications of rhodium catalysed conjugate addition, *Chem. Soc. Rev.*, 2010, **39**, 2093–2105; (f) G. Chen, N. Tokunaga and T. Hayashi, Rhodium-catalyzed asymmetric 1,4-addition of arylboronic acids to coumarins: asymmetric synthesis of (R)-tolterodine, *Org. Lett.*, 2005, **7**, 2285–2288.
- 11 (a) J. J. Verendel, J. Q. Li, X. Quan, B. Peters, T. Zhou, O. R. Gautun, T. Govender and P. G. Andersson, Chiral hetero- and carbocyclic compounds from the asymmetric hydrogenation of cyclic alkenes, *Chem.-Eur. J.*, 2012, **18**, 6507–6513; (b) T. Ohta, T. Miyake, N. Seido, H. Kumobayashi and H. Takaya, Asymmetric Hydrogenation of Olefins with Aprotic Oxygen Functionalities Catalyzed by BINAP-Ru(II) Complexes, *J. Org. Chem.*, 2002, **60**, 357–363; (c) P. M. Donate, D. Frederico, R. da Silva, M. G. Constantino, G. Del Ponte and P. S. Bonatto, Asymmetric synthesis of γ -butyrolactones by enantioselective hydrogenation of butenolides, *Tetrahedron: Asymmetry*, 2003, **14**, 3253–3256.
- 12 G. Hughes, M. Kimura and S. L. Buchwald, Catalytic enantioselective conjugate reduction of lactones and lactams, *J. Am. Chem. Soc.*, 2003, **125**, 11253–11258.
- 13 Q. Zhao, S. Li, K. Huang, R. Wang and X. Zhang, A novel chiral bisphosphine-thiourea ligand for asymmetric hydrogenation of beta,beta-disubstituted nitroalkenes, *Org. Lett.*, 2013, **15**, 4014–4017.
- 14 (a) Z. Zhang, Z. Han, G. Gu, X.-Q. Dong and X. Zhang, Enantioselective Synthesis of Chiral 3-Substituted-3-silylpropionic Esters via Rhodium/Bisphosphine-Thiourea-Catalyzed Asymmetric Hydrogenation, *Adv. Synth. Catal.*, 2017, **359**, 2585–2589; (b) G. Liu, Z. Han, X. Q. Dong and X. Zhang, Rh-Catalyzed Asymmetric Hydrogenation of beta-Substituted-beta-thio-alpha,beta-unsaturated Esters: Expedition Access to Chiral Organic Sulfides, *Org. Lett.*, 2018, **20**, 5636–5639; (c) X. Yin, Y. Huang, Z. Chen, Y. Hu, L. Tao, Q. Zhao, X. Q. Dong and X. Zhang, Enantioselective Access to Chiral 2-Substituted 2,3-Dihydrobenzo[1,4]dioxane Derivatives through Rh-Catalyzed Asymmetric Hydrogenation, *Org. Lett.*, 2018, **20**, 4173–4177; (d) Z. Han, G. Liu, R. Wang, X. Q. Dong and X. Zhang, Highly efficient Ir-catalyzed asymmetric hydrogenation of benzoxazinones and derivatives with a Bronsted acid cocatalyst, *Chem. Sci.*, 2019, **10**, 4328–4333; (e) C. Yin, T. Yang, Y. Pan, J. Wen and X. Zhang, Rh-Catalyzed Asymmetric Hydrogenation of Unsaturated Medium-Ring NH Lactams: Highly Enantioselective Synthesis of N-Unprotected 2,3-Dihydro-1,5-benzothiazepinones, *Org. Lett.*, 2020, **22**, 920–923; (f) Q. Zhao, C. Chen, J. Wen, X. Q. Dong and X. Zhang, Noncovalent Interaction-Assisted Ferrocenyl Phosphine Ligands in Asymmetric Catalysis, *Acc. Chem. Res.*, 2020, **53**, 1905–1921; (g) H. Yang, Y. Zhou, Z. Zhang, J. Wen and X. Zhang, Iridium-Catalyzed Hydroiodination and Formal Hydroamination of Olefins with N-Iodo Reagents and Molecular Hydrogen: An Umpolung Strategy, *Org. Lett.*, 2022, **24**, 1842–1847; (h) L. S. Zheng, C. Yin, F. Wang, G. Q. Chen and X. Zhang, Enantioselective synthesis of cis-hexahydro-gamma-carboline derivatives via Ir-catalyzed asymmetric hydrogenation, *Chem. Commun.*, 2022, **58**, 3286–3289.
- 15 (a) L.-S. Zheng, C. Yin, F. Wang, G.-Q. Chen and X. Zhang, Enantioselective synthesis of cis-hexahydro- γ -carboline derivatives via Ir-catalysed asymmetric hydrogenation, *Chem. Commun.*, 2022, **58**, 3286–3289; (b) F. Wang, Y. Chen, P. Yu, G.-Q. Chen and X. Zhang, Asymmetric Hydrogenation of Oximes Synergistically Assisted by Lewis and Bronsted Acids, *J. Am. Chem. Soc.*, 2022, **144**, 17763–17768; (c) G. Liu, L. Zheng, K. Tian, H. Wang, L. Wa Chung, X. Zhang and X.-Q. Dong, Ir-Catalyzed Asymmetric Hydrogenation of Unprotected Indoles: Scope Investigations and Mechanistic Studies, *CCS Chem.*, 2022, 1–13, DOI: [10.31635/ccschem.022.202101643](https://doi.org/10.31635/ccschem.022.202101643); (d) Z. Han, G. Liu, X. Yang, X.-Q. Dong and X. Zhang, Enantiodivergent Synthesis of Chiral Tetrahydroquinoline Derivatives via Ir-Catalyzed Asymmetric Hydrogenation: Solvent-Dependent Enantioselective Control and Mechanistic Investigations, *ACS Catal.*, 2021, **11**, 7281–7291; (e) T. Yang, Y. Sun, H. Wang, Z. Lin, J. Wen and X. Zhang, Iridium-Catalyzed Enantioselective Hydrogenation of Oxocarbenium Ions: A Case of Ionic Hydrogenation, *Angew. Chem., Int. Ed.*, 2020, **59**, 6108–6114; (f) Y. Sun, Q. Zhao, H. Wang, T. Yang, J. Wen and X. Zhang, Asymmetric Hydrogenation of Cationic Intermediates for the Synthesis of Chiral N,O-Acetals, *Chem.-Eur. J.*, 2020, **26**, 11470–11477; (g) T. Yang, X. Guo, Q. Yin and X. Zhang, Intramolecular asymmetric reductive amination: synthesis of enantioenriched dibenz[*c,e*]azepines, *Chem. Sci.*, 2019, **10**, 2473–2477; (h) Z. Han, G. Liu, R. Wang, X.-Q. Dong and X. Zhang, Highly efficient Ir-catalyzed asymmetric hydrogenation of benzoxazinones and derivatives with a Bronsted acid cocatalyst, *Chem. Sci.*, 2019, **10**, 4328–4333; (i) Z. Han, Y.-Q. Guan, G. Liu, R. Wang, X. Yin, Q. Zhao, H. Cong, X.-Q. Dong and X. Zhang, Iridium-Catalyzed Asymmetric Hydrogenation of Tetrasubstituted α -Fluoro- β -enamino Esters: Efficient Access to Chiral α -Fluoro- β -amino Esters with Two Adjacent Tertiary Stereocenters, *Org. Lett.*, 2018, **20**, 6349–6353.
- 16 Q. Lang, G. Gu, Y. Cheng, Q. Yin and X. Zhang, Highly Enantioselective Synthesis of Chiral γ -Lactams by Rh-Catalyzed Asymmetric Hydrogenation, *ACS Catal.*, 2018, **8**, 4824–4828.

