ChemComm

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2020, **56**, 5815

Received 18th January 2020,
Accepted 18th April 2020

DOI: 10.1039/d0cc00480d

rsc.li/chemcomm

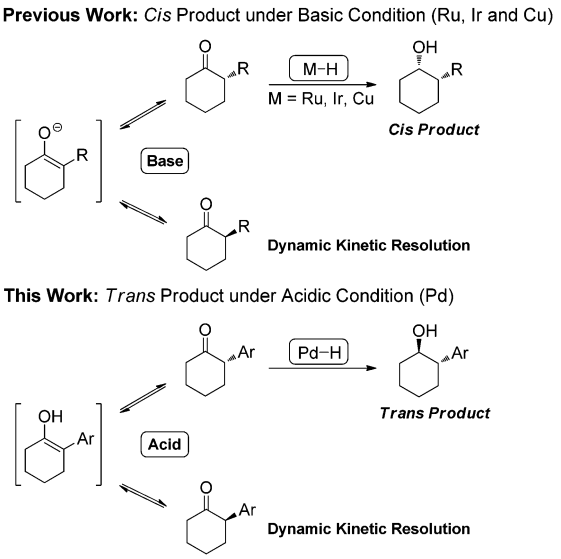
Palladium-catalyzed asymmetric hydrogenation of 2-aryl cyclic ketones for the synthesis of *trans* cycloalkanols through dynamic kinetic resolution under acidic conditions†

Xiang Li,[ab] Zi-Biao Zhao,[b] Mu-Wang Chen,[b] Bo Wu,[b] Han Wang,[a] Chang-Bin Yu *[b] and Yong-Gui Zhou *[ab]

The first efficient palladium-catalyzed asymmetric hydrogenation of 2-aryl cyclic ketones has been described through dynamic kinetic resolution under acidic conditions, providing a facile access to chiral *trans* cycloalkanol derivatives with excellent enantioselectivities.

The significance of chiral cycloalkanols with two contiguous stereocenters has been widely recognized in natural products, pharmaceuticals and other bioactive molecules.[1] Transition metal-catalyzed asymmetric hydrogenation of corresponding cyclic ketones is one of the most efficient and facile methods because of their high atom economy and environmental friendliness.[2] In the past decades, asymmetric hydrogenation of 2-substituted cyclic ketones was usually carried out under basic conditions using chiral metal complexes such as ruthenium[3–5] or iridium[6] or copper[7] *via* dynamic kinetic resolution (DKR),[8,9] and *cis* selective products were obtained due to the steric hindrance effect of the substituents (Scheme 1a). To the best of our knowledge, although the asymmetric hydrogenation of linear ketones to construct *anti* alkanols has obtained success,[10] there are rare examples for the synthesis of *trans* selective products through asymmetric hydrogenation of 2-substituted cyclic ketones except a directing ester group[11] in the 2-position. Therefore, the development of transition metal-catalyzed asymmetric hydrogenation to construct the chiral *trans* cycloalkanols through DKR is highly desired.

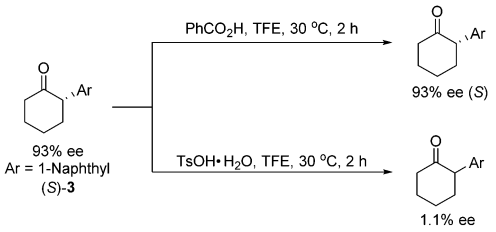
In recent years, our group has been working on palladium-catalyzed asymmetric hydrogenation.[2f,12] Lately, we disclosed a palladium-catalyzed asymmetric hydrogenative desymmetrization of 2-aryl-1,3-cyclopentanediones, giving the *trans* 2-aryl substituted β-hydroxy ketones, the possible reason ascribes to the interaction between palladium and aromatic ring during the hydrogenation transition state.[13] Thus, we envisioned whether the palladium/acid co-catalysis system could be used for the asymmetric hydrogenation of simple 2-aryl substituted cyclic ketones[14] to construct *trans* cycloalkanols through the interaction between the palladium and the aromatic ring (Scheme 1b). However, there are some challenges in this topic: (1) the interaction is very weak between metal palladium and aryl ring; (2) the racemization of 2-aryl cyclic ketones under acidic conditions is more difficult than that in basic conditions; (3) secondary alcohols are unstable in the presence of strong acid, which would be leading to dehydration. In order to verify the hypothesis, we firstly performed the racemization experiments of chiral ketone (*S*)-**3**. When benzoic acid was used, the ee value of ketone (*S*)-**3** was maintained. Almost racemic product was obtained in the presence of strong acidic TsOH·H_2O. The results of experiments showed that the ketones were able to fast racemize *via* an enol intermediate under strong acidic



Scheme 1 Metal-catalyzed asymmetric hydrogenation of 2-substituted cyclic ketones.

[a] *Zhang Dayu School of Chemistry, Dalian University of Technology, 2 Linggong Road, Dalian 116024, P. R. China. E-mail: ygzhou@dicp.ac.cn*
[b] *State Key Laboratory of Catalysis, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, P. R. China. E-mail: cbyu@dicp.ac.cn, ygzhou@dicp.ac.cn*

† Electronic supplementary information (ESI) available. See DOI: 10.1039/d0cc00480d

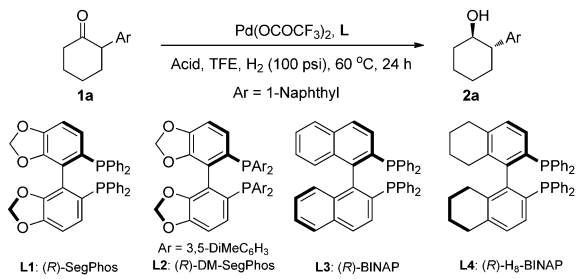


Scheme 2 Racemization experiments of chiral ketone (*S*)-**3**.

conditions (Scheme 2), which provide a prerequisite for the asymmetric hydrogenation of ketones through DKR. Herein, we report a palladium-catalyzed asymmetric hydrogenation of 2-aryl cyclic ketones to construct *trans* cycloalkanols through DKR under acidic conditions.

At the outset, 2-(naphthalen-1-yl)cyclohexan-1-one **1a** was chosen as a model substrate for condition optimization. We found that 81% yield of **2a** with 13% ee and 6 : 1 *trans*/*cis* ratio could be obtained when acid was not added (Table 1, entry 1). Considering the importance of acid for racemization, we turned our attention to the evaluation of acids. To our delight, the anticipated product **2a** was obtained with 83% ee and > 20 : 1 *trans*/*cis* ratio in the presence of $TsOH{\cdot}H_2O$ (entry 2). However, other acids including $Zn(OTf)_2$, $PhCO_2H$ and CF_3CO_2H, exhibited the lower stereoselectivities (entries 3–5). We further investigated the effect of the amount of acid (entries 6–7). Gratifyingly, increasing the amount of acid to 50 mol%, the ee value of the product was increased to 91% (entry 6). Subsequently, some commercially available chiral diphosphine ligands were screened. Among them, (*R*)-SegPhos **L1** proved to be a suitable ligand in view of yield and enantioselectivity (entries 8–10). To further improve enantioselectivity and yield, the effect of temperature was examined (entries 11–13). When the reaction was conducted at 30 °C, the desired product was obtained in 92% yield with 97% ee and >20 : 1 *trans*/*cis* ratio (entry 13). Therefore, the optimal conditions were established as $Pd(OCOCF_3)_2$ (5 mol%)/(*R*)-SegPhos (6 mol%)/$TsOH{\cdot}H_2O$ (50 mol%)/TFE/H_2 (100 psi)/30 °C. The absolute configuration of hydrogenation product **2a** was determined to be (1*R*,2*S*)-**2a** by comparison with the value of optical rotations reported in the literature.[15]

Table 1 Optimization of the reaction conditions[a]



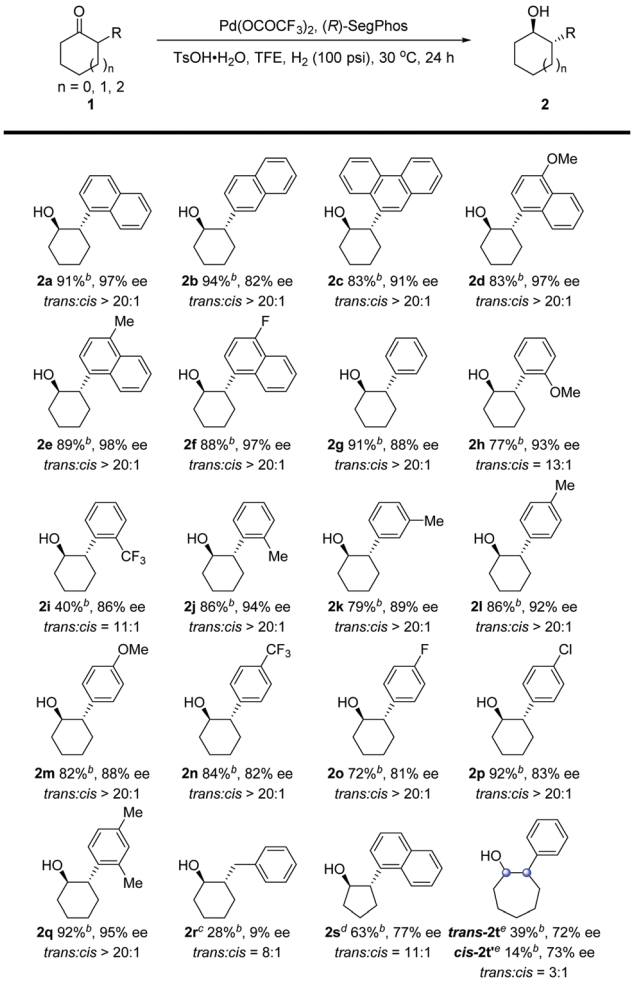
Entry	Acid	L	*trans* : *cis*[b]	**2a**[b] (%)	Ee[c] (%)
1	None	**L1**	6 : 1	81	13
2	$TsOH{\cdot}H_2O$	**L1**	>20 : 1	82	83
3	$Zn(OTf)_2$	**L1**	6 : 1	77	12
4	$PhCO_2H$	**L1**	4 : 1	80	21
5	CF_3CO_2H	**L1**	2 : 1	63	33
6[d]	$TsOH{\cdot}H_2O$	**L1**	>20 : 1	76	91
7[e]	$TsOH{\cdot}H_2O$	**L1**	>20 : 1	63	89
8[d]	$TsOH{\cdot}H_2O$	**L2**	>20 : 1	81	89
9[d]	$TsOH{\cdot}H_2O$	**L3**	>20 : 1	71	87
10[d]	$TsOH{\cdot}H_2O$	**L4**	>20 : 1	73	83
11[df]	$TsOH{\cdot}H_2O$	**L1**	>20 : 1	86	94
12[dg]	$TsOH{\cdot}H_2O$	**L1**	>20 : 1	90	95
13[dh]	$TsOH{\cdot}H_2O$	**L1**	>20 : 1	92 (91)[i]	97

[a] Reaction conditions: **1a** (0.2 mmol), $Pd(OCOCF_3)_2$ (5 mol%), **L** (6 mol%), acid (20 mol%), TFE (2.0 mL), 60 °C, H_2 (100 psi), 24 h. All the conversions >95%. [b] Determined by ^1H NMR analysis using the dibromomethane as the internal standard. [c] Determined by chiral HPLC analysis. [d] $TsOH{\cdot}H_2O$ (50 mol%). [e] $TsOH{\cdot}H_2O$ (100 mol%). [f] 50 °C. [g] 40 °C. [h] 30 °C. [i] Isolated yield.

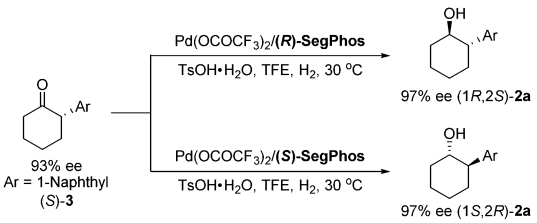
With the optimized reaction conditions established, we investigated the substrate scope of the reaction. The results were summarized in Scheme 3. Substrates **1b** and **1c** bearing polycyclic aryls exhibited comparable *trans* selectivities and yields with **1a** albeit with the lower enantioselectivities. Subsequently, we explored the effect of substituents on the naphthyl ring. Various groups at *para*-position including MeO–, Me–, and F– were compatible under the standard reaction conditions, furnishing the products with excellent yields and stereoselectivities (**2d–f**). Furthermore, phenyl substrate **1g** was favorable reaction partners, and the reaction proceeded smoothly in high yield and stereoselectivity (91% yield, 88% ee, > 20 : 1 *trans*/*cis* ratio). The presence of a MeO– or a CF_3– at *ortho*-position of phenyl ring, incomplete conversion and slightly lower diastereoselectivity were observed (**2h–i**). A methyl group at the *ortho*-, *meta*- or *para*-position of phenyl ring had a marginal effect on the reactivities and enantioselectivities (**2j–l**). Both electron-donating and electron-withdrawing groups at *para*-position were compatible, giving the desirable products in high yields and stereoselectivities (**2m–p**). In addition, it was also suitable to have two substituents on the phenyl ring (**2q**). When benzyl group was introduced, low conversion was observed, the stereoselectivity was also low, which indicated that the aryl on 2-position was very crucial to activity and enantioselectivity (**2r**). This catalytic system is not well compatible for the hydrogenation of 5-membered and 7-membered ketones. Although the desirable products could be successfully obtained under modified conditions, the yields were low due to incomplete conversion (**2s–t**).

To further illustrate the reaction process, asymmetric hydrogenation of chiral ketone (*S*)-**3** was performed by using ligands (*R*)- or (*S*)-SegPhos under the optimal conditions. The products with opposite configuration could be obtained with the same ee values (Scheme 4), respectively, indicating that the chiral ketone (*S*)-**3** was initially racemized *via* keto–enol tautomerism, and then further hydrogenated. The above experimental results showed that the asymmetric hydrogenation of 2-aryl substituted cyclic ketones undergoes dynamic kinetic resolution process under palladium/acid conditions.

This reaction could be also scaled up smoothly, when substrate **1a** and **1d** were conducted at 1.5 mmol scale, both activity and enantioselectivity maintained. Considering that hydroxyl group is versatile functional group, further transformations

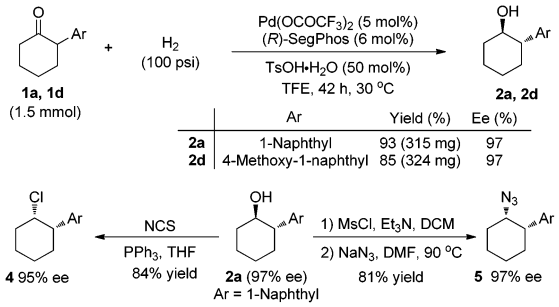


Scheme 3 Substrate scope of 2-substituted cyclic ketones.[a] [a] Reaction conditions: **1** (0.3 mmol), $Pd(OCOCF_3)_2$ (5 mol%), (*R*)-SegPhos (6 mol%), $TsOH{\cdot}H_2O$ (50 mol%), TFE (3.0 mL), 30 °C, H_2 (100 psi), 24 h. [b] Isolated yield. [c] 48 h. [d] The pentafluorobenzoic acid (200 mol%) was used instead of $TsOH{\cdot}H_2O$ and the reaction was run at 80 °C for 24 h. [e] The bis-(4-nitrophenyl)phosphate (200 mol%) was used instead of $TsOH{\cdot}H_2O$ and the reaction was runned at 60 °C for 48 h.



Scheme 4 The control experiments.

of chiral product **2a** was conducted (Scheme 5). Firstly, chlorination of cyclic alcohol **2a** using PPh_3-NCS afforded chloroalkane **4** with 84% yield and 95% ee. In addition, esterification of **2a** with methanesulfonyl chloride followed by a nucleophilic substitution with NaN_3 furnished the chiral azide product **5** (81% yield, 97% ee) without loss of optical purity, which can be further converted into amine or triazole derivatives.[16]



Scheme 5 Scale-up experiment and transformations of **2a**.

In summary, we have successfully developed the first palladium-catalyzed asymmetric hydrogenation of 2-aryl cyclic ketones *via* dynamic kinetic resolution under acidic conditions. A series of cyclic ketones were hydrogenated to construct chiral *trans* cycloalkanols with two contiguous stereocenters in high yields with excellent enantioselectivities and *trans* selectivities.[17] Notably, the Brønsted acids had a significant influence in the reaction and accelerated the racemization of the substrates. Further investigations on the asymmetric synthesis of *trans* cycloalkanol derivatives with multiple chiral stereocenters under acidic conditions are being performed.

Financial support from National Natural Science Foundation of China (21532006, 21690074) and Chinese Academy of Sciences (XDB17020300, QYZDJ-SSW-SLH035) is acknowledged.

Conflicts of interest

There are no conflicts to declare.

Notes and references

1 For selected reviews, see: (*a*) B. Heasley, *Eur. J. Org. Chem.*, 2009, 1477; (*b*) B. Heasley, *Curr. Org. Chem.*, 2014, **18**, 641; (*c*) S. P. Simeonov, J. P. M. Nunes, K. Guerra, V. B. Kurteva and C. A. M. Afonso, *Chem. Rev.*, 2016, **116**, 5744.

2 For selected reviews, see: (*a*) W. S. Knowles, *Angew. Chem., Int. Ed.*, 2002, **41**, 1998; (*b*) R. Noyori, *Angew. Chem., Int. Ed.*, 2002, **41**, 2008; (*c*) W. Tang and X. Zhang, *Chem. Rev.*, 2003, **103**, 3029; (*d*) J.-H. Xie, S.-F. Zhu and Q.-L. Zhou, *Chem. Rev.*, 2011, **111**, 1713; (*e*) Q.-A. Chen, Z.-S. Ye, Y. Duan and Y.-G. Zhou, *Chem. Soc. Rev.*, 2013, **42**, 497; (*f*) P. Etayo and A. Vidal-Ferran, *Chem. Soc. Rev.*, 2013, **42**, 728; (*g*) J. J. Verendel, O. Pàmies, M. Diéguez and P. G. Andersson, *Chem. Rev.*, 2014, **114**, 2130; (*h*) Z. Zhang, N. A. Butt and W. Zhang, *Chem. Rev.*, 2016, **116**, 14769; (*i*) Z. Zhang, N. Butt, M. Zhou, D. Liu and W. Zhang, *Chin. J. Chem.*, 2018, **36**, 443.

3 (*a*) T. Ohkuma, H. Ooka, M. Yamakawa, T. Ikariya and R. Noyori, *J. Org. Chem.*, 1996, **61**, 4872; (*b*) R. Noyori and T. Ohkuma, *Pure Appl. Chem*, 1999, **71**, 1493; (*c*) R. Noyori and T. Ohkuma, *Angew. Chem., Int. Ed.*, 2001, **40**, 40; (*d*) M. Scalone and P. Waldmeier, *Org. Process Res. Dev.*, 2003, **7**, 418; (*e*) T. Ohkuma, T. Hattori, H. Ooka, T. Inoue and R. Noyori, *Org. Lett.*, 2004, **6**, 2681.

4 (*a*) T. Ohkuma, J. Li and R. Noyori, *Synlett*, 2004, 1383; (*b*) J.-H. Xie, S. Liu, X.-H. Huo, X. Cheng, H.-F. Duan, B.-M. Fan, L.-X. Wang and Q.-L. Zhou, *J. Org. Chem.*, 2005, **70**, 2967; (*c*) L.-J. Cheng, J.-H. Xie, L.-X. Wang and Q.-L. Zhou, *Adv. Synth. Catal.*, 2012, **354**, 1105; (*d*) C. Liu, J.-H. Xie, Y.-L. Li, J.-Q. Chen and Q.-L. Zhou, *Angew. Chem., Int. Ed.*, 2013, **52**, 593; (*e*) L.-J. Cheng, J.-H. Xie, Y. Chen, L.-X. Wang and Q.-L. Zhou, *Org. Lett.*, 2013, **15**, 764; (*f*) G. Li, J.-H. Xie, J. Hou, S.-F. Zhu and Q.-L. Zhou, *Adv. Synth. Catal.*, 2013, **355**, 1597; (*g*) Y. Liu, L.-J. Cheng, H.-T. Yue, W. Che, J.-H. Xie and Q.-L. Zhou, *Chem. Sci.*, 2016, **7**, 4725.

5 (*a*) T. Matsumoto, T. Murayama, S. Mitsuhashi and T. Miura, *Tetrahedron Lett.*, 1999, **40**, 5043; (*b*) T. Ohkuma, D. Ishii, H. Takeno and R. Noyori, *J. Am. Chem. Soc.*, 2000, **122**, 6510; (*c*) S. Liu, J.-H. Xie, L.-X. Wang and Q.-L. Zhou, *Angew. Chem., Int. Ed.*, 2007, **46**, 7506; (*d*) S. Liu, J.-H. Xie, W. Li, W.-L. Kong, L.-X. Wang and Q.-L. Zhou, *Org. Lett.*, 2009, **11**, 4994; (*e*) W.-J. Bai, J.-H. Xie, Y.-L. Li, S. Liu and Q.-L. Zhou, *Adv. Synth. Catal.*, 2010, **352**, 81; (*f*) J.-Q. Chen, J.-H. Xie, D.-H. Bao, S. Liu and Q.-L. Zhou, *Org. Lett.*, 2012, **14**, 2714; (*g*) X.-F. Huang, S.-Y. Zhang, Z.-C. Geng, C.-Y. Kwok, P. Liu, H.-Y. Li and X.-W. Wang, *Adv. Synth. Catal.*, 2013, **355**, 2860.

6 (*a*) H. Lin, L.-J. Xiao, M.-J. Zhou, H.-M. Yu, J.-H. Xie and Q.-L. Zhou, *Org. Lett.*, 2016, **18**, 1434; (*b*) Y.-T. Liu, J.-Q. Chen, L.-P. Li, X.-Y. Shao, J.-H. Xie and Q.-L. Zhou, *Org. Lett.*, 2017, **19**, 3231; (*c*) Y.-T. Liu, L.-P. Li, J.-H. Xie and Q.-L. Zhou, *Angew. Chem., Int. Ed.*, 2017, **56**, 12708; (*d*) H.-Y. Bin, K. Wang, D. Yang, X.-H. Yang, J.-H. Xie and Q.-L. Zhou, *Angew. Chem., Int. Ed.*, 2019, **58**, 1174.

7 O. V. Zatolochnaya, S. Rodríguez, Y. Zhang, K. S. Lao, S. Tcyrulnikov, G. Li, X.-J. Wang, B. Qu, S. Biswas, H. P. R. Mangunuru, D. Rivalti, J. D. Sieber, J.-N. Desrosiers, J. C. Leung, N. Grinberg, H. Lee, N. Haddad, N. K. Yee, J. J. Song, M. C. Kozlowski and C. H. Senanayake, *Chem. Sci.*, 2018, **9**, 4505.

8 For selected reviews, see: (*a*) R. Noyori, M. Tokunaga and M. Kitamura, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 36; (*b*) S. Caddick and K. Jenkins, *Chem. Soc. Rev.*, 1996, **25**, 447; (*c*) F. F. Huerta, A. B. E. Minidis and J. E. Bäckvall, *Chem. Soc. Rev.*, 2001, **30**, 321.

9 (*a*) H. Pellissier, *Tetrahedron*, 2003, **59**, 8291; (*b*) E. Vedejs and M. Jure, *Angew. Chem., Int. Ed.*, 2005, **44**, 3974.

10 (*a*) K. Makino, T. Goto, Y. Hiroki and Y. Hamada, *Angew. Chem., Int. Ed.*, 2004, **43**, 882; (*b*) A. Lei, S. Wu, M. He and X. Zhang, *J. Am. Chem. Soc.*, 2004, **126**, 1626; (*c*) O. Labeeuw, P. Phansavath and J. P. Genêt, *Tetrahedron: Asymmetry*, 2004, **15**, 1899; (*d*) K. Makino, Y. Hiroki and Y. Hamada, *J. Am. Chem. Soc.*, 2005, **127**, 5784; (*e*) K. Makino, T. Fujii and Y. Hamada, *Tetrahedron: Asymmetry*, 2006, **17**, 481; (*f*) K. Makino, M. Iwasaki and Y. Hamada, *Org. Lett.*, 2006, **8**, 4573; (*g*) N. Arai, H. Ooka, K. Azuma, T. Yabuuchi, N. Kurono, T. Inoue and T. Ohkuma, *Org. Lett.*, 2007, **9**, 939; (*h*) Y. Hamada, Y. Koseki, T. Fujii, T. Maeda, T. Hibino and K. Makino, *Chem. Commun.*, 2008, 6206; (*i*) I. Plantan, M. Stephan, U. Urleb and B. Mohar, *Tetrahedron Lett.*, 2009, **50**, 2676; (*j*) T. Hibino, K. Makino, T. Sugiyama and Y. Hamada, *ChemCatChem*, 2009, **1**, 237.

11 (*a*) R. Noyori, T. Ikeda, T. Ohkuma, M. Widhalm, M. Kitamura, H. Takaya, S. Akutagawa, N. Sayo, T. Saito, T. Taketomi and H. Kumobayashi, *J. Am. Chem. Soc.*, 1989, **111**, 9134; (*b*) J. P. Genêt, C. Pinel, S. Mallart, S. Jugé, S. Thorimbert and J. A. Laffitte, *Tetrahedron: Asymmetry*, 1991, **2**, 555; (*c*) T. Benincori, E. Brenna, F. Sannicolò, L. Trimarco, P. Antognazza and E. Cesarotti, *J. Chem. Soc., Chem. Commun.*, 1995, 685; (*d*) M. J. Burk, T. G. P. Harper and C. S. Kalberg, *J. Am. Chem. Soc.*, 1995, **117**, 4423; (*e*) T. Ireland, G. Grossheimann, C. Wieser-Jeunesse and P. Knochel, *Angew. Chem., Int. Ed.*, 1999, **38**, 3212; (*f*) T. Yamano, N. Taya, M. Kawada, T. Huang and T. Imamoto, *Tetrahedron Lett.*, 1999, **40**, 2577; (*g*) T. Benincori, O. Piccolo, S. Rizzo and F. Sannicolò, *J. Org. Chem.*, 2000, **65**, 8340; (*h*) T. Ireland, K. Tappe, G. Grossheimann and P. Knochel, *Chem. – Eur. J.*, 2002, **8**, 843; (*i*) K. Tappe and P. Knochel, *Tetrahedron: Asymmetry*, 2004, **15**, 91; (*j*) M. T. Reetz and X. Li, *Adv. Synth. Catal.*, 2006, **348**, 1157; (*k*) S. Fukuzawa, H. Oki, M. Hosaka, J. Sugasawa and S. Kikuchi, *Org. Lett.*, 2007, **9**, 5557; (*l*) A. V. R. Madduri and A. J. Minnaard, *Chem. – Eur. J.*, 2010, **16**, 11726.

12 (*a*) D.-S. Wang, Q.-A. Chen, W. Li, C.-B. Yu, Y.-G. Zhou and X. Zhang, *J. Am. Chem. Soc.*, 2010, **132**, 8909; (*b*) M.-W. Chen, Y. Duan, Q.-A. Chen, D.-S. Wang, C.-B. Yu and Y.-G. Zhou, *Org. Lett.*, 2010, **12**, 5075; (*c*) C.-B. Yu, K. Gao, D.-S. Wang, L. Shi and Y.-G. Zhou, *Chem. Commun.*, 2011, **47**, 5052; (*d*) D.-S. Wang, Z.-S. Ye, Q.-A. Chen, Y.-G. Zhou, C.-B. Yu, H.-J. Fan and Y. Duan, *J. Am. Chem. Soc.*, 2011, **133**, 8866; (*e*) C.-B. Yu and Y.-G. Zhou, *Angew. Chem., Int. Ed.*, 2013, **52**, 13365; (*f*) Y. Duan, L. Li, M.-W. Chen, C.-B. Yu, H.-J. Fan and Y.-G. Zhou, *J. Am. Chem. Soc.*, 2014, **136**, 7688; (*g*) C.-B. Yu, W.-X. Huang, L. Shi, M.-W. Chen, B. Wu and Y.-G. Zhou, *J. Am. Chem. Soc.*, 2014, **136**, 15837; (*h*) B. Song, C.-B. Yu, W.-X. Huang, M.-W. Chen and Y.-G. Zhou, *Org. Lett.*, 2015, **17**, 190; (*i*) Z.-P. Chen, S.-B. Hu, J. Zhou and Y.-G. Zhou, *ACS Catal.*, 2015, **5**, 6086.

13 C.-B. Yu, H.-D. Wang, B. Song, H.-Q. Shen, H.-J. Fan and Y.-G. Zhou, *Sci. China: Chem.*, 2019, **62**, 215.

14 (*a*) H. Nishiyama, S.-B. Park and K. Itoh, *Tetrahedron: Asymmetry*, 1992, **3**, 1029; (*b*) L. Zhang, Y. Tang, Z. Han and K. Ding, *Angew. Chem., Int. Ed.*, 2019, **58**, 4973.

15 (*a*) E. Vrancken, A. Alexakis and P. Mangeney, *Eur. J. Org. Chem.*, 2005, 1354; (*b*) L. Wang, R. K. Akhani and S. L. Wiskur, *Org. Lett.*, 2015, **17**, 2408.

16 (*a*) K. Asano and S. Matsubara, *Org. Lett.*, 2010, **12**, 4988; (*b*) A. Kale, N. Medishetti, S. Kanugala, G. Kumar and K. Atmakur, *Org. Biomol. Chem.*, 2019, **17**, 3186.

17 Asymmetric hydrogenation of 2-(furan-2-yl)cyclohexan-1-one and 2-(6-methyl pyridin-2-yl)cyclohexan-1-one was tried under the standard condition, unfortunately, no desirable product was observed. In addition, low activity was also observed when using benzofused six-membered cyclic ketone (2-phenyl-3,4-dihydronaphthalen-1(2*H*)-one).

