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Synthesis of Chiral Fluorinated Hydrazines via Pd-Catalyzed Asymmetric Hydrogenation

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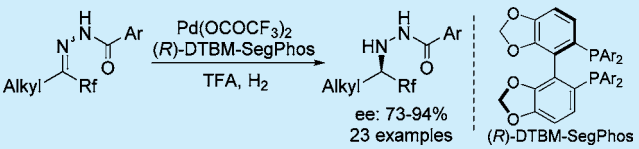
Supporting Information

ABSTRACT: An enantioselective hydrogenation of fluorinated hydrazones has been achieved by employing [Pd(*R*)-DTBM-SegPhos$(OCOCF_3)_2$] as the catalyst, providing a general and convenient method toward chiral fluorinated hydrazines. A broad substrate scope including β-aryl-, γ-aryl-, and alkyl-chain-substituted hydrazones worked efficiently in high yields and up to 94% of enantioselectivity. The reductive amination between trifluoromethyl-substituted ketones and benzohydrazides could also proceed smoothly.



Because electron-withdrawing fluorine atoms bestow various biologically vital properties on parent architectures, fluorinated compounds have attracted a great deal of interest over the past decades.[1] In addition, introduction of fluorine atoms or fluorine-containing groups into organics often has a strong impact on the lipophilicity, metabolic stability, and pharmacokinetic and pharmacodynamic properties, thus dramatically broadening their application abilities.[2] Today, an increasing number of fluorinated molecules have been developed as well-known drugs such as bicalutamide (anticancer agent), efavirenz (against HIV infection), fluoxetin (antidepressant), and fulvestrant (treatment of hormone receptor positive metastatic breast cancer).[3] Ascribing to the flourishing of organofluorine chemistry, systematic fluorine scans have emerged as a promising strategy in pharmaceutical and agrochemical discovery. Therefore, the development of synthetic methods for fluorinated compounds is very important in organic chemistry.

Enantioenriched compounds bearing a hydrazine moiety are omnipresent in many synthetic drugs, materials sciences, and agricultural industries.[4] As depicted in Figure 1, β-aryl hydrazine D-(+)-JB-516 is a potent inhibitor of monoamine oxidase of mouse brain,[5] and cyclic hydrazine **II** is an inhibitor of DPP-IV.[6]

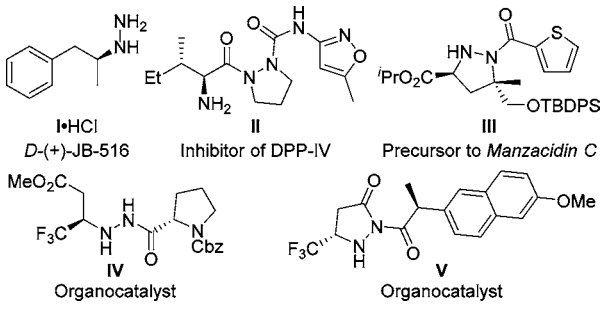


Figure 1. Examples of privileged hydrazine-based compounds.

In addition, chiral hydrazines are also crucial intermediates for construction of various complicated compounds and natural products, such as compound **III** (pivotal precursor to alkaloid manzacidin C).[7] In particular, the importance of fluorinated hydrazines has also been noticed by chemists. Funabiki and co-workers have demonstrated that chiral trifluoromethylated hydrazines could be conveniently transformed to an array of useful compounds.[8] Aside from organic synthesis, such hydrazines also showed great advantages in organocatalysis chemistry. Recently, *N*-acyl hydrazines **IV** and **V** have been reported as efficient catalysts to promote the asymmetric Diels–Alder reactions of inactivated cyclic dienes with β-aryl enals.[9]

Accordingly, the preponderance of chiral fluorinated hydrazines has compelled chemists to explore efficient and environmentally benign synthetic methods for their preparation. A frequently adopted method to fulfill this target is transformation from chiral starting materials. In 2001, Enders and Funabiki reported an asymmetric synthesis of α-trifluoromethyl-substituted hydrazines via nucleophilic 1,2-addition of alkyllithium reagents to chiral 1-amino-2-(methoxymethyl)pyrrolidine (SAMP) hydrazones.[10] Thereafter, Brigaud's group studied the addition of organolithium and Grignard reagents to (*R*)-phenylglycinol-derived trifluoromethylhydrazone, providing the corresponding chiral hydrazines with high stereoselectivity and moderate chemoselectivity.[11] Significantly, Shibata and co-workers developed the enantioselecive synthesis of trifluoromethylated hydrazines via trifluoromethylation of azomethine imines with $TMSCF_3$ and organocatalysis.[12]

Another alternative strategy to obtain optically active fluorinated hydrazines relies on the stereoselective hydrogenation of prochiral hydrazones.[13] Burk's group has developed an example of rhodium-catalyzed asymmetric hydrogenation of

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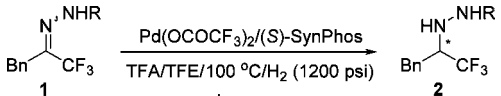
trifluoromethylated hydrazone.[14] However, only 50% ee was obtained with good activity. Very recently, Zhou and co-workers disclosed the nickel-catalyzed asymmetric transfer hydrogenation with HCOOH/Et_3N as hydride source to give one instance of trifluoromethylated hydrazine with good enantioselectivity.[15] Despite some progress in this area, the asymmetric hydrogenation of hydrazones remains a great challeng with many opportunities. To the best of our knowledge, only a few catalyst systems have been successfully introduced to this research field, and the substrate scope is limited.[16] The difficulty along the way is that hydrogenation of hydrazones often suffers from low activity and poor stereoselectivity, especially for hydrazones with alkyl-chain substituents.

In view of the constantly growing demand for new enantioenriched fluorine-containing hydrazines, we envisaged development of a general and efficient method for their preparation. As a result of our recent finding that palladium catalysts could promote asymmetric hydrogenation of α-aryl hydrazones,[17] the α-alkyl-substituted trifluoromethylated hydrazones became the subject of special interest in this context. Since alkyl-substituted hydrazines are important components found in various useful organics, development of an efficient method toward hydrogenation of alkyl-chain-substituted hydrazones is challenging and highly desirable. As such, we herein report the palladium-catalyzed asymmetric hydrogenation of fluorinated β-aryl-, γ-aryl-, and alkyl-chain-substituted hydrazones together with the direct asymmetric reductive amination between trifluoromethyl-substituted ketones and benzohydrazides.

At the beginning, the effect of the *N*-protecting groups of β-phenyl hydrazone on the reactivity and enantioselectivity of this hydrogenation was investigated. Three types of hydrazones have been synthesized and subjected to asymmetric hydrogenation with $Pd(OCOCF_3)_2$/(*S*)-SynPhos as catalyst (Scheme 1).[18] To

Scheme 1. Evaluation of Protecting Groups

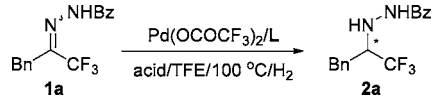


entry	R	conv	ee
1	Ph	95%	20% (-)
2	Ts	< 5%	--
3	Bz	35%	61% (-)

our disappointment, the hydrazone with a phenyl substituent was hydrogenated with low enantioselectivity albeit with good activity (entry 1). Hydrogenation of the substrate with tosyl as the protecting group failed to proceed (entry 2). To our delight, the exposure of *N*-Bz-protected hydrazone with trifluoroacetic acid (TFA) in 2,2,2-trifluoroethanol (TFE) furnished the desirable hydrazine with 61% ee and 35% conversion (entry 3). Subsequently, the effects of other acids including benzoic acid and L-(+)-tartaric acid were investigated (Table 1, entries 2 and 3). However, no other acid could present a better result than the initially employed acid TFA.

Further examinations were focused on ligand screening (Scheme 2). The commonly used chiral bisphosphine ligands **L2**–**L4** exhibited poor to moderate enantioselectivities and moderate reactivities (Table 1, entries 4–6). Electron-rich diphosphine ligands led to excellent conversion and moderate ee values (Table 1, entries 7–10). Utilizing TangPhos as ligand, almost full conversion with 76% ee was achieved (Table 1, entry 7). When chiral ferrocenyl ligands were employed, the reaction worked very well and gave the desired product with complete

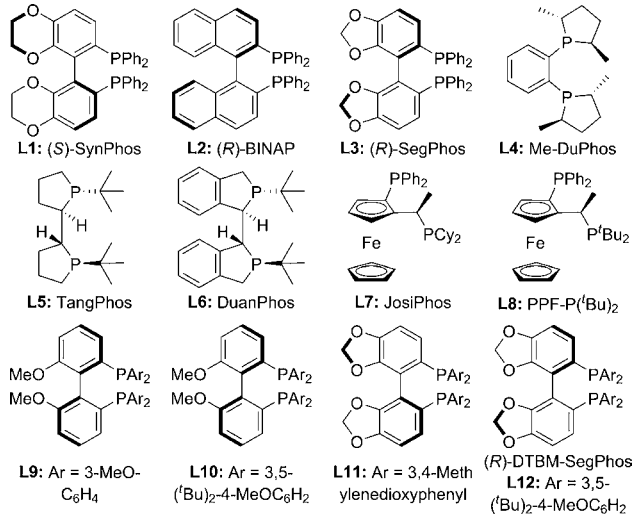
Table 1. Condition Optimization[a]



entry	acid	ligand	conv[b] (%)	ee[c] (%)
1	TFA	**L1**	35	61 (−)
2	benzoic acid	**L1**	4	58 (−)
3	L-(+)-tartaric acid	**L1**	5	60 (−)
4	TFA	**L2**	35	35 (+)
5	TFA	**L3**	20	74 (+)
6	TFA	**L4**	45	47 (+)
7	TFA	**L5**	>95	76 (+)
8	TFA	**L6**	>95	61 (+)
9	TFA	**L7**	>95	38 (−)
10	TFA	**L8**	>95	66 (+)
11	TFA	**L9**	61	62 (+)
12	TFA	**L10**	>95	71 (+)
13	TFA	**L11**	33	55 (−)
14	TFA	**L12**	>95	91 (+)
15[d]	TFA	**L12**	>95	92 (+)

[a]Reaction conditions: $Pd(OCOCF_3)_2$ (5 mol %), ligand (5.5 mol %), **1a** (0.2 mmol), H_2 (1200 psi), acid (0.2 mmol), TFE (3 mL), 100 °C, 48 h. [b]Determined by ^{1}H NMR spectroscopy. [c]Determined by HPLC. [d]80 °C.

Scheme 2. Structure of Phosphine Ligands



conversion, whereas the enantioselectivity failed to elevate even with bulky ligand **L8** (Table 1, entry 10). Based on these results, we envisaged that electron-rich ligands with sterically hindered substituents would give better results in this transformation. Therefore, a series of axial chiral bisphosphine ligands with an electron-donating group were investigated (entries 11–14). First, **L9** and **L10** were evaluated, and only up to 71% ee could be obtained (Table 1, entries 11 and 12). Then, ligands bearing a SegPhos moiety were examined. As expected, the DTBM-SegPhos **L12** with bulky aryl substituents at the phosphorus atom, which was developed by Saito and co-workers,[19] provided the best result of full conversion with 91% ee. When the reaction temperature was decreased to 80 °C, the enantioselectivity was further improved to 92% without loss of activity (Table 1, entry 15). Consequently, the optimized reaction conditions are $Pd(OCOCF_3)_2$, **L12**, TFA, 80 °C in TFE.

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After establishing the optimal conditions, substrate generality was carried out, and the results are summarized in Table 2.

Table 2. Asymmetric Hydrogenation of Fluorinated *N*-Acyl Hydrazones[a]

Rf = CF_3, C_2F_5, C_3F_7

entry	alkyl	Ar	yield[b] (%)	ee[c] (%)
1	$C_6H_5CH_2$	C_6H_5	98 (**2a**)	92 (+)
2	*o*-$MeC_6H_4CH_2$	C_6H_5	98 (**2b**)	92 (+)
3	*m*-$MeC_6H_4CH_2$	C_6H_5	96 (**2c**)	93 (+)
4	*p*-$MeC_6H_4CH_2$	C_6H_5	99 (**2d**)	93 (+)
5	*p*-$MeOC_6H_4CH_2$	C_6H_5	99 (**2e**)	92 (+)
6	*p*-$FC_6H_4CH_2$	C_6H_5	98 (**2f**)	90 (+)
7	*p*-$^tBuC_6H_4CH_2$	C_6H_5	98 (**2g**)	94 (+)
8	3,5-$Me_2C_6H_3CH_2$	C_6H_5	98 (**2h**)	92 (+)
9	$C_6H_5CH_2CH_2$	C_6H_5	96 (**2i**)	92 (+)
10	*c*-$HexCH_2$	C_6H_5	99 (**2j**)	90 (+)
11	Et	C_6H_5	98 (**2k**)	92 (+)
12	^{n}Pr	C_6H_5	96 (**2l**)	91 (*R*)
13	^{n}Bu	C_6H_5	97 (**2m**)	91 (+)
14	$Me(CH_2)_5$	C_6H_5	98 (**2n**)	91 (+)
15	$Me(CH_2)_6$	C_6H_5	96 (**2o**)	91 (+)
16	$Me_2CH(CH_2)_2$	C_6H_5	97 (**2p**)	91 (+)
17	$Me(CH_2)_{11}$	C_6H_5	98 (**2q**)	92 (+)
18	*c*-Hex	C_6H_5	98 (**2r**)	88 (+)
19	$C_6H_5CH_2$	*p*-$MeOC_6H_4$	98 (**2s**)	91 (+)
20	$C_6H_5CH_2$	*p*-ClC_6H_4	98 (**2t**)	91 (+)
21	$C_6H_5CH_2$	*m*-MeC_6H_4	98 (**2u**)	91 (+)
22[d]	$C_6H_5CH_2$	C_6H_5	99 (**2v**)	73 (+)
23[e]	$C_6H_5CH_2$	C_6H_5	98 (**2w**)	74 (+)

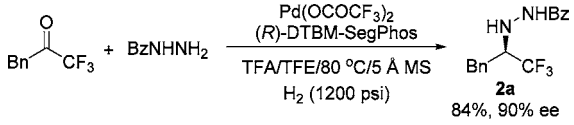
[a]Reaction conditions: $Pd(OCOCF_3)_2$ (5 mol %), **L12** (5.5 mol %), **1** (0.2 mmol), H_2 (1200 psi), TFA (0.2 mmol), TFE (3 mL), 80 °C, 48 h, Rf = CF_3. [b]Isolated yield. [c]Determined by HPLC. [d]Rf = C_2F_5. [e]Rf = C_3F_7.

Generally, a variety of *β*-aryl-substituted substrates were smoothly converted to the corresponding hydrazines with excellent enantioselectivities and activities (Table 2, entries 1−8). The position of the substituents in the aryl ring at the *β*-position of hydrazones barely affected the yields and ee values (Table 2, entries 2−4). In addition, the electronic properties of substituted groups at this place had little effect on the activities and enantioselectivities (Table 2, entry 5 vs entry 6). It was noted that the best result of 98% yield with 94% ee was obtained when the 4-*tert*-butylphenyl group was introduced (Table 2, entry 7). Moreover, *γ*-aryl- and *α*-alkyl-chain-substituted substrates could be hydrogenated successfully under the standard conditions, providing the trifluoromethylated hydrazines **2i−q** with 96−99% yields and 90−92% ee values (Table 2, entries 9−17). It is noteworthy that *α*-ethyl-substituted hydrazone **1k** has also been verified as a suitable substrate, providing hydrazine **2k** with 98% yield and 92% ee. Increasing the carbon number of alkyl chains has an inconspicuous influence on the yields and ee values. Hydrazones bearing a branched alkyl group (**1j**, **1p**) were hydrogenated without impediments. However, the slightly sterically hindered substrate **1r** resulted in relatively lower enantioselectivity (Table 2, entry 18). Notably, altering the electronic properties of substituents in the acyl protecting group almost marginally affected the hydrogenation performance (Table 2, entries 19−21). In order to further estimate the application possibility, hydrazones with longer perfluoroalkyl chains were also investigated (**1v,w**). To our delight, the hydrogenation reactions proceeded smoothly and provided the fluorinated hydrazines with high yields and moderate ee values (Table 2, entries 22 and 23).

After one step of recrystallization from the mixture solvent dichloromethane/*n*-hexane, enantiomerically pure product (+)-**2l** (>99% ee) was obtained as colorless crystals. Its absolute configuration was determined to be *R* on the basis of single-crystal X-ray diffraction analysis.[20] The configurations of other chiral products were assigned by analogy.

Metal-catalyzed asymmetric reductive amination is an operationally convenient and step-economic method for construction of chiral amines.[21] Although reductive amination of ketones with simple amines obtained good success, the reports on utilizing hydrazines as the nitrogen source are limited. Recently, Zhang's group developed the first iridium-catalyzed direct reductive amination of aromatic ketones with phenyl hydrazide as the nitrogen source.[22] Considering the direct transition-metal-catalyzed reductive amination of alkyl ketones was rare success and of great significance,[23] the catalytic asymmetric reductive amination of *β*-aryl-substituted trifluoromethylated ketones with benzohydrazide was subsequently investigated. To our delight, subjecting the mixture of 1,1,1-trifluoro-3-phenylpropan-2-one and benzohydrazide to hydrogenation could give the desired hydrazine **2a** with 90% ee and 79% yield. When 5 Å MS was used as additive, the yield could further increase to 84% without lost of enantioselectivity (Scheme 3).

Scheme 3. Asymmetric Reductive Amination



In summary, we have developed an efficient method for synthesis of linear chiral alkyl-substituted fluorinated hydrazines through palladium-catalyzed asymmetric hydrogention of *N*-acylhydrazones in excellent yields with up to 94% of enantioselectivity. A broad substrate scope was observed, including *β*-aryl-, *γ*-aryl-, and alkyl-chain-substituted hydrazones. The reductive amination between trifluoromethyl-substituted ketones and benzohydrazides was also achieved with slightly lower enantioselectivity. Further investigations on asymmetric hydrogenation of functionalized hydrazones are ongoing in our laboratories.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01118.

General procedures, X-ray crystallographic data, and NMR spectra of obtained compounds (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For reviews, see: (a) Prakash, G. K. S.; Yudin, A. K. *Chem. Rev.* **1997**, *97*, 757−786. (b) Ma, J.-A.; Cahard, D. *Chem. Rev.* **2004**, *104*, 6119−6146. (c) Shimizu, M.; Hiyama, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 214−231. (d) Schlosser, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5432−5446. (e) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320−330. (f) Ma, J.-A.; Cahard, D. *Chem. Rev.* **2008**, *108*, PR1−PR43. (g) Cahard, D.; Xu, X.; Couve-Bonnaire, S.; Pannecoucke, X. *Chem. Soc. Rev.* **2010**, *39*, 558−568. (h) Zheng, Y.; Ma, J.-A. *Adv. Synth. Catal.* **2010**, *352*, 2745−2750. (i) Nie, J.; Guo, H.-C.; Cahard, D.; Ma, J.-A. *Chem. Rev.* **2011**, *111*, 455−529. (j) Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475−4521. (k) Besset, T.; Schneider, C.; Cahard, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 5048−5050. (l) Wu, X.-F.; Neumann, H.; Beller, M. *Chem. - Asian J.* **2012**, *7*, 1744−1754. (m) Studer, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 8950−8958. (n) Macé, Y.; Magnier, E. *Eur. J. Org. Chem.* **2012**, *2012*, 2479−2494. (o) Liang, T.; Neumann, C. N.; Ritter, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 8214−8264. (p) Zhu, W.; Wang, J.; Wang, S.; Gu, Z.; Aceña, J. L.; Izawa, K.; Liu, H.; Soloshonok, V. A. *J. Fluorine Chem.* **2014**, *167*, 37−54.

(2) (a) Böhm, H.-J.; Banner, D.; Bendels, S.; Kansy, M.; Kuhn, B.; Müller, K.; Obst-Sander, U.; Stahl, M. *ChemBioChem* **2004**, *5*, 637−643. (b) Sani, M.; Volonterio, A.; Zanda, M. *ChemMedChem* **2007**, *2*, 1693−1700. (c) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881−1886. (d) Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature* **2011**, *473*, 470−477. (e) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; del Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. *Chem. Rev.* **2014**, *114*, 2432−2506.

(3) Robertson, J. F. R.; Come, S. E.; Jones, S. E.; Beex, F.; Kaufmann, M.; Makris, A.; Nortier, J. W. R.; Possinger, K.; Rutqvist, L.-E. *Eur. J. Cancer* **2005**, *41*, 346−356.

(4) (a) Rothgery, E. F. Hydrazine and its Derivatives. In *Kirk−Othmer Encylopedia Chemical Technology*, 5th ed.; Kirk, R. E., Othmer, D. F., Eds.; Wiley: New York, 2004; Vol. *13*, pp 1−896. (b) Yamashita, Y.; Kobayashi, S. *J. Am. Chem. Soc.* **2004**, *126*, 11279−11282. (c) Shirakawa, S.; Lombardi, P. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 9974−9975. (d) Giampietro, N. C.; Wolfe, J. P. *J. Am. Chem. Soc.* **2008**, *130*, 12907−12911. (e) Tran, K.; Lombardi, P. J.; Leighton, J. L. *Org. Lett.* **2008**, *10*, 3165−3167. (f) Coteron, J. M.; Catterick, D.; Castro, J.; Chaparro, M. J.; Diaz, B.; Fernandez, E.; Ferrer, S.; Gamo, F. J.; Gordo, M.; Gut, J.; de las Heras, L.; Legac, J.; Marco, M.; Miguel, J.; Munoz, V.; Porras, E.; de la Rosa, J. C.; Ruiz, J. R.; Sandoval, E.; Ventosa, P.; Rosenthal, P.; Fiandor, J. M. *J. Med. Chem.* **2010**, *53*, 6129−6152. (g) Geng, Z.-C.; Chen, J.; Li, N.; Huang, X.-F.; Zhang, Y.; Zhang, Y.-W.; Wang, X.-W. *Beilstein J. Org. Chem.* **2012**, *8*, 1710−1720. (h) Davis, L. O. *Org. Prep. Proced. Int.* **2013**, *45*, 437−464.

(5) Bernstein, J.; Losee, K. A.; Smith, C. I.; Rubin, B. *J. Am. Chem. Soc.* **1959**, *81*, 4433−4434.

(6) Cheon, H. G.; Kim, S.-S.; Kim, K.-R.; Rhee, S.-D.; Yang, S.-D.; Ahn, J. H.; Park, S.-D.; Lee, J. M.; Jung, W. H.; Lee, H. S.; Kim, H. Y. *Biochem. Pharmacol.* **2005**, *70*, 22−29.

(7) Tran, K.; Lombardi, P. J.; Leighton, J. L. *Org. Lett.* **2008**, *10*, 3165−3167.

(8) (a) Funabiki, K.; Nagamori, M.; Matsui, M.; Enders, D. *Synthesis* **2002**, 2585−2588. (b) Funabiki, K.; Nagamori, M.; Matsui, M. *J. Fluorine Chem.* **2004**, *125*, 1347−1350. (c) Funabiki, K.; Nagamori, M.; Matsui, M. *J. Fluorine Chem.* **2005**, *126*, 705.

(9) Gould, E.; Lebl, T.; Slawin, A. M. Z.; Reid, M.; Davies, T.; Smith, A. D. *Org. Biomol. Chem.* **2013**, *11*, 7877−7892.

(10) Enders, D.; Funabiki, K. *Org. Lett.* **2001**, *3*, 1575−1577.

(11) Fries, S.; Pytkowicz, J.; Brigaud, T. *Tetrahedron Lett.* **2005**, *46*, 4761−4764.

(12) Kawai, H.; Kusuda, A.; Nakamura, S.; Shiro, M.; Shibata, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 6324−6327.

(13) For selected reviews on homogeneous asymmetric hydrogenation, see: (a) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 40−73. (b) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029−3069. (c) Cui, X.; Burgess, K. *Chem. Rev.* **2005**, *105*, 3272−3296. (d) Zhou, Y.-G. *Acc. Chem. Res.* **2007**, *40*, 1357−1366. (e) Xie, J. H.; Zhu, S. F.; Zhou, Q. L. *Chem. Rev.* **2011**, *111*, 1713−1760. (f) Xie, J.-H.; Zhou, Q.-L. *Huaxue Xuebao* **2012**, *70*, 1427−1438. (g) Ager, D. J.; de Vries, A. H. M.; de Vries, J. G. *Chem. Soc. Rev.* **2012**, *41*, 3340−3380. (h) Wang, D.-S.; Chen, Q.-A.; Lu, S.-M.; Zhou, Y.-G. *Chem. Rev.* **2012**, *112*, 2557−2590. (i) Zhao, B.; Han, Z.; Ding, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 4744−4788. (j) Verendel, J. J.; Pàmies, O.; Diéguez, M.; Andersson, P. G. *Chem. Rev.* **2014**, *114*, 2130−2169.

(14) (a) Burk, M. J.; Feaster, J. E. *J. Am. Chem. Soc.* **1992**, *114*, 6266−6267. (b) Burk, M. J.; Martinez, J. P.; Feaster, J. E.; Cosford, N. *Tetrahedron* **1994**, *50*, 4399−4428.

(15) Xu, H.; Yang, P.; Chuanprasit, P.; Hirao, H.; Zhou, J. *Angew. Chem., Int. Ed.* **2015**, *54*, 5112−5116.

(16) (a) Tappe, K.; Knochel, P. *Tetrahedron: Asymmetry* **2004**, *15*, 91−102. (b) Yoshikawa, N.; Tan, L.; McWilliams, J. C.; Ramasamy, D.; Sheppard, R. *Org. Lett.* **2010**, *12*, 276−279. (c) Haddad, N.; Qu, B.; Rodriguez, S.; van der Veen, L.; Reeves, D. C.; Gonnella, N. C.; Lee, H.; Grinberg, N.; Ma, S.; Krishnamurthy, D.; Wunberg, T.; Senanayake, C. H. *Tetrahedron Lett.* **2011**, *52*, 3718−3722.

(17) Chen, Z.-P.; Hu, S.-B.; Zhou, J.; Zhou, Y.-G. *ACS Catal.* **2015**, *5*, 6086−6089.

(18) For reviews on Pd-catalyzed asymmetric hydrogenation, see: (a) Chen, Q.-A.; Ye, Z.-S.; Duan, Y.; Zhou, Y.-G. *Chem. Soc. Rev.* **2013**, *42*, 497−511. For selected reports on Pd-catalyzed asymmetric hydrogenation, see: (b) Li, C.; Chen, J.; Fu, G.; Liu, D.; Liu, Y.; Zhang, W. *Tetrahedron* **2013**, *69*, 6839−6844. (c) Chen, J.; Liu, D.; Butt, N.; Li, C.; Fan, D.; Liu, Y.; Zhang, W. *Angew. Chem., Int. Ed.* **2013**, *52*, 11632−11636. (d) Duan, Y.; Li, L.; Chen, M.-W.; Yu, C.-B.; Fan, H.-J.; Zhou, Y.-G. *J. Am. Chem. Soc.* **2014**, *136*, 7688−7700. (e) Yu, C.-B.; Huang, W.-X.; Shi, L.; Chen, M.-W.; Wu, B.; Zhou, Y.-G. *J. Am. Chem. Soc.* **2014**, *136*, 15837−15840. (f) Song, B.; Yu, C.-B.; Huang, W.-X.; Chen, M.-W.; Zhou, Y.-G. *Org. Lett.* **2015**, *17*, 190−193. (g) Chen, Z.-P.; Chen, M.-W.; Shi, L.; Yu, C.-B.; Zhou, Y.-G. *Chem. Sci.* **2015**, *6*, 3415−3419.

(19) Saito, T.; Yokozawa, T.; Ishizaki, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. *Adv. Synth. Catal.* **2001**, *343*, 264−267.

(20) CCDC 1457895 contains the supplementary crystallographic data for this paper. These can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(21) For selected reviews on metal-catalyzed asymmetric reductive amination, see: (a) Tararov, V. I.; Börner, A. *Synlett* **2005**, 203−211. (b) Nugent, T. C.; El-Shazly, M. *Adv. Synth. Catal.* **2010**, *352*, 753−819. (c) Wang, C.; Xiao, J. *Top. Curr. Chem.* **2013**, *343*, 261−282.

(22) Chang, M.; Liu, S.; Huang, K.; Zhang, X. *Org. Lett.* **2013**, *15*, 4354−4357.

(23) Huang, H.; Liu, X.; Zhou, L.; Chang, M.; Zhang, X. *Angew. Chem., Int. Ed.* **2016**, *55*, 5309−5312.

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