Received: 15 November 2020 | Revised: 6 December 2020 | Accepted: 11 January 2021
DOI: 10.1002/jccs.202000517

COMMUNICATION

JOURNAL OF THE CHINESE CHEMICAL SOCIETY

Silver catalyzed pyridine-directed acceptorless dehydrogenation of secondary alcohols

Xin Zhuang | **Jing Tao** | **Zhen Luo** | **Chuan-Ming Hong** | **Zheng-Qiang Liu** | **Qing-Hua Li** | **Li-Qing Ren** | **Qun-Li Luo** | **Tang-Lin Liu**

School of Chemistry and Chemical Engineering, Southwest University, Chongqing, 400715, China

Correspondence
Tang-Lin Liu and Qun-Li Luo, School of Chemistry and Chemical Engineering, Southwest University, Chongqing 400715, China.
Email: liuschop@swu.edu.cn (T.-L. L.) and qlluo@swu.edu.cn (Q.-L. L.)

Funding information
National Natural Science Foundation of China, Grant/Award Numbers: 21801209, 21801210; Venture & Innovation Support Program for Chongqing Overseas Returnees, Grant/Award Number: cx2018085; Fundamental Research Funds for the Central Universities, Grant/Award Numbers: SWU118028, SWU118117, XDJK2019AA003; Natural Science Foundation of Chongqing, China, Grant/Award Number: cstc2020jcyj-msxmX0130

Abstract

A silver catalyzed pyridine-directed acceptorless dehydrogenation of secondary benzyl alcohols was developed. This general procedure delivers ketones with high atom-economy and hydrogen was the sole byproduct. This dehydrogenation reaction has a good functional group tolerance and high efficiency (up to 90% yield and 10,000/1 substrates-to-catalyst ratio).

KEYWORDS
acceptorless dehydrogenation, atom-economy, silver catalyzed

1 | INTRODUCTION

The dehydrogenation of alcohols to carbonyl compounds is one of the most important reactions in organic chemistry, which also played an important role in industry.[1] The classical procedure employed the use of stoichiometric oxidants, which often produces large quantities of wastes.[2] As an important alternative, transition-metal catalyzed dehydrogenation in the presence of some acceptors[3] (aka transfer hydrogenation;[4] Scheme 1a) attracted much attention for several decades. These hydrogen acceptors, however, were usually loaded in stoichiometric or large excessive amounts, which may bring some negative environmental effects. Obviously, both stoichiometric oxidation and transfer hydrogenation have the drawback of low atom-economy. Recently, transition-metal catalyzed acceptorless dehydrogenation (CAD) has been well developed for its good atom economy, wherein hydrogen as the sole byproduct.[5] Several VIII group transition metals complexes such as iron,[6] rhodium,[7] ruthenium,[8] and iridium,[9] etc. have been developed for the dehydrogenation of alcohols to aldehydes or ketones (Scheme 1b).[10,11] This CAD strategy also found wide applications in biochemistry, material, and energy science, since it provided a unique way to release hydrogen under mild conditions from sustainable sources.[12]

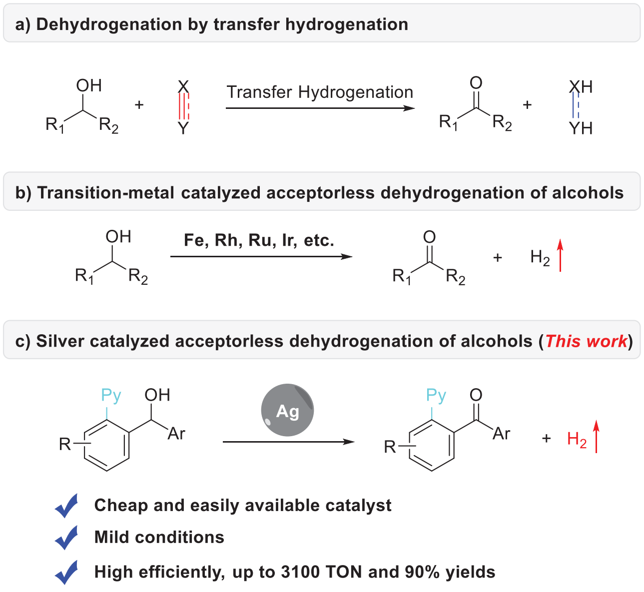
Silver is an easily available transition metal, which has often been used as stoichiometric oxidant.[13] The dehydrogen oxidation of alcohols catalyzed by nanoparticles supported silver have been developed,[14] while the catalytic oxidation with homogeneous silver has been rarely recorded. In 2014, a combination of silver(I) and NHC (N-heterocyclic carbene) has been successfully used for the catalytic aerobic oxidation of

---

Xin Zhuang and Jing Tao contributed equally to this study.

© 2021 The Chemical Society Located in Taipei & Wiley-VCH GmbH

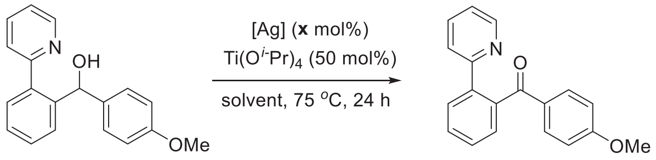
primary alcohol to aldehydes,[15] carboxylic acids could also be achieved by silver catalyzed dihydrogen oxidation of primary alcohols.[16] Li and co-workers reported the silver-catalyzed aerobic oxidation of aldehydes to carboxylic acids in 2015.[17] They also developed the silver(I)-catalyzed aerobic cleavage of 1,2-diols to form the corresponding ketones or carboxylic acids.[18] Silver catalytic oxidation of alcohols to carbonyl compounds in the presence of oxygen[19] and the oxidant-free alcohols dehydrogenation to aldehydes or ketones catalyzed by hydrotalcite-supported silver nanoparticle catalyst[14a] have been developed. Of note, no precedential examples of CAD of alcohols with homogeneous silver catalyst have been reported. Herein, we developed a silver catalyzed anaerobic acceptorless dehydrogenation of secondary alcohols to ketones with high yields and release hydrogen as the sole side product (Scheme 1c).



SCHEME 1 The dehydrogenation of alcohols to carbonyl compounds

Initially, we selected (4-methoxyphenyl)(2-[pyridin-2-yl]phenyl)methanol **1a**[20] as the model substrate and metallic silvers as the catalyst to optimize the reaction conditions (Table 1). Some common silver(I) salts like CF_3CO_2Ag, Ag_2CO_3, AgF, and $AgNO_3$ were ineffective for this catalytic dehydrogenation (see Supporting Information). Encouragingly, the corresponding ketone **2a** was obtained with 77% yield when $AgSbF_6$ was applied (entry 1). Further improvement in the yield was observed when $AgPF_6$ and AgOTf were used (81%, entry 2, 3). Finally, AgOTf was selected as the optimal catalyst since

TABLE 1 Optimization of reaction conditions in the Ag-catalyzed dehydrogenation of **1a**[a]



1a **2a**

Entry	[Ag]	*x*	Solvent	Yield (%)[b]
1	$AgSbF_6$	20	DCM	77
2	$AgPF_6$	20	DCM	81
3	AgOTf	20	DCM	81
4	AgOTf	20	PhMe	NR
5	AgOTf	20	$CHCl_3$	58
6	AgOTf	20	CH_3CN	70
7	AgOTf	20	TBME	82
8	AgOTf	5	TBME	65
9	AgOTf	1	TBME	64
10	AgOTf	0.1	TBME	43
11	AgOTf	0.01	TBME	31
12	—	—	TBME	Trace
13[c]	AgOTf	20	TBME	Trace

[a] The reaction was carried out with 0.1 mmol of **1a**, 20 mol% [Ag], and 50 mol% Lewis acid in 0.5 ml of solvent at 75°C for 24 hr.

[b] Isolated yield.

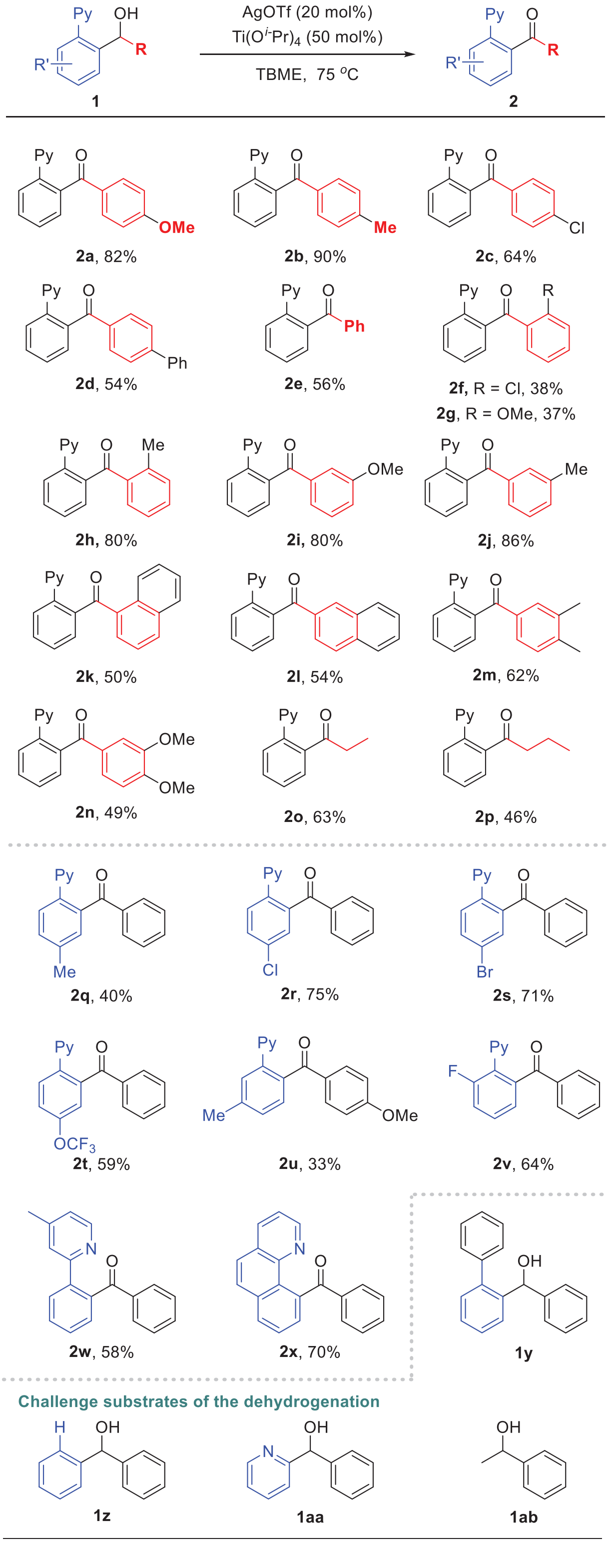
[c] The reaction was carried out in the absence of Ti(O^{i}Pr)$_4$. TBME = Methyl tert-butyl ether.

the lower cost. Then, the effect of solvent was tested. No target product was detected when the dehydrogenation reaction was carried out in toluene (entry 4). The model reaction in other polar solvents like $CHCl_3$ and CH_3CN delivered 58 and 70% yield, respectively (entry 5–6). The highest yield of 82% was achieved in TBME (entry 7).

Reducing the catalyst loading led to a lower yield (entry 8–11), of the desire product. When 5 or 1 mol% of the catalyst was used, the yields were 65 and 64%, respectively (Table 1, entries 8 and 9). The catalyst loading could be further lowered to 0.01 mol% (S/C = 10,000), and the dehydrogenation went smoothly and delivered the product with 31% yield (TON = 3,100) (Table 1, entry 11). The control experiments indicated that both silver and titanium were indispensable, since no **2a** was detected in the absence of sliver or titanium (Table 1, entries 12 and 13).

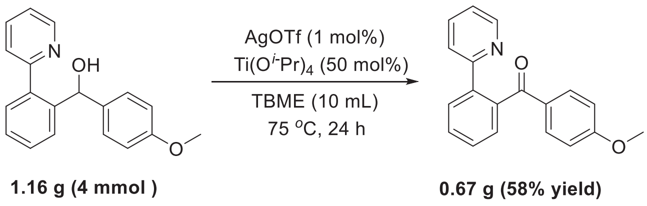
With the optimal reaction in hands, we next investigated the scope and limitation of diaryl methanols for this silver CAD (Scheme 2). We then tested the substitutes with electron-donating, electron-neutral, and the electron-withdrawing groups in place of the *para*-methoxyl of the phenyl group (Scheme 2,2b–e). All of them reacted smoothly to afford the desire ketones. The substrates bearing electron-donating group gave a higher yield than those with electron-neutral and electron-withdrawing groups (82 and 90% vs 54–64%). The *ortho* chloro (**1f**) or methoxy (**1h**) substituted substrates deliver the corresponding ketones (**2f** and **2g**) with lower yields. However, a high yield of 85% was achieved with ortho methyl substituent (**2h**). CH_3 (**2i**) and OCH_3 (**2j**) groups in the meta position were well-tolerated, and the yields were 80 and 86%, respectively. The substrates with electron-neutral aromatic groups such as 1-naphthyl and 2-naphthyl, also went smoothly to afford **2k** and **2l** in moderate yields. The aryl groups of the diaryl methanols could also tolerate multiple substituents (**2m** and **2n**).

Besides, the aryl alkyl methanols like 1-(2-[pyridin-2-yl]phenyl)propan-1-ol (**1o**) and 1-(2-[pyridin-2-yl]phenyl)butan-1-ol (**1p**) could also undergo dehydrogenation under the optimal reaction condition, furnishing corresponding ketones 63 and 46% yields, respectively.



SCHEME 2 The scope of diaryl methanols

Further evaluation of the scope of pyridine directed diaryl methanols to this silver CAD revealed that a variety of substituted 2-(pyridin-2-yl)phenyl groups could be tolerated, affording the corresponding diaryl ketones in moderate to good yields. 2-(Pyridin-2-yl)phenyl groups bearing electron-withdrawing groups, such as 5-Cl (**2r**), 5-Br (**2s**), 5-OCF_3 (**2t**), and 3-F (**2v**) or electron-donating groups, such as 5–CH_3 (**2q**) and 4-Me (**2u**) were subjected to the dehydrogenation, and proceed smoothly. Surprisingly, when the substitutes were on the 6-position of 2-(pyridin-2-yl)phenyl groups, neither the electron-withdrawing nor the electron-donating groups can realize in this transformation, probably because of steric hindrance (not shown in Scheme 2). Use of diaryl methanol with pyridine-2-yl group bearing a methyl substituent



SCHEME 3 Gram scale reaction

(**1w**) showed good yield. Benzo[h]quinolin-10-yl(phenyl) methanol (**1x**) was tested, and the desired product **2x** was obtained in 70% yield. By contrast, the substrates without any nitrogen-containing directing groups (**1y-1ab**) were submitted to the standard reaction conditions, no desire products were achieved, which indicated that the directing groups were indispensable.

To further demonstrate the potential and the practicality of this silver-catalyzed dehydrogenation, a gram-scale reaction was performed. When the reaction was conducted at 4.0 mmol (1.16 g), diaryl methanone **2a** could be prepared in 58% yield with 1 mol% of silver catalyst (Scheme 3).

2 | CONCLUSIONS

In summary, we have developed a novel catalytic acceptorless dehydrogenation of secondary alcohols catalyzed by silver under mild reaction conditions. High atom-efficiency was observed considering that hydrogen is the sole byproduct in this reaction. A wide range of aryl pyridinyl methanols was tolerated and the corresponding ketones were achieved with moderate to good yields. Study of the sliver-CAD with traceless directing groups is in progress and will be reported in due course.

ACKNOWLEDGMENTS

We are grateful for the financial support provided by the National Natural Science Foundation of China (21801209 and 21801210), the Fundamental Research Funds for the Central Universities (SWU118117, SWU118028, and XDJK2019AA003), and Venture and Innovation Support Program for Chongqing Overseas Returnees (cx2018085).

ORCID

Qun-Li Luo https://orcid.org/0000-0002-9724-5674
Tang-Lin Liu https://orcid.org/0000-0002-7318-4520

REFERENCES

[1] (a) G. Tojo, M. Fernandez, *Oxidation of Alcohols to Aldehydes and Ketones*, Springer, New York **2006**. (b) R. A. Sheldon, I. W. C. E. Arends, A. Dijksman, *Catal. Today* **2000**, *57*, 157. (c) T. Mallat, A. Baiker, *Chem. Rev.* **2004**, *104*, 3037. (d) G. E. Dobereiner, R. H. Crabtree, *Chem. Rev.* **2010**, *110*, 681. (e) J. Choi, A. H. MacArthur, M. Brookhart, A. S. Goldman, *Chem. Rev.* **2011**, *111*, 1761. (f) S. E. Allen, R. R. Walvoord, R. Padilla-Salinas, M. C. Kozlowski, *Chem. Rev.* **2013**, *113*, 6234. (g) C. Wang, J. Xiao, *Chem. Commun.* **2017**, *53*, 3399.

[2] (a) J. D. Albright, L. Goldman, *J. Am. Chem. Soc.* **1969**, *91*, 4317. (b) R. J. Sundberg, D. Eugene Rearick, H. F. Russell, *J. Pharm. Sci.* **1977**, *66*, 263. (c) D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155. (d) O. Dann, H. Char, P. Fleischmann, H. Fricke, *Liebigs Ann. Chem.* **1986**, *1986*, 438. (e) E. M. Beccalli, G. Broggini, A. Farina, L. Malpezzi, A. Terraneo, G. Zecchi, *Eur. J. Org. Chem.* **2002**, *2002*, 2080. (f) S. Palaniappan, C. Kumar, C. Devi, V. Rao, *Synlett* **2008**, *2008*, 2023. (g) J. Liu, S. Ma, *Org. Biomol. Chem.* **2013**, *11*, 4186.

[3] (a) D. Morales-Morales, R. Redón, Z. Wang, D. W. Lee, C. Yung, K. Magnuson, C. M. Jensen, *Can. J. Chem.* **2001**, *79*, 823. (b) T. Suzuki, K. Morita, M. Tsuchida, K. Hiroi, *J. Org. Chem.* **2003**, *68*, 1601. (c) A. N. Ajjou, J.-L. Pinet, *Can. J. Chem.* **2005**, *83*, 702. (d) M. Königsmann, N. Donati, D. Stein, H. Schönberg, J. Harmer, A. Sreekanth, H. Grützmacher, *Angew. Chem., Int. Ed.* **2007**, *46*, 3567. (e) B. Jiang, Y. Feng, E. A. Ison, *J. Am. Chem. Soc.* **2008**, *130*, 14462. (f) R. Levy, C. Azerraf, D. Gelman, K. Rueck-Braun, P. N. Kapoor, *Catal. Commun.* **2009**, *11*, 298. (g) A. Prades, E. Peris, M. Albrecht, *Organometallics* **2011**, *30*, 1162. (h) G. Giachi, M. Frediani, W. Oberhauser, E. Passaglia, *J. Polym. Sci. A Polym. Chem.* **2012**, *50*, 2725. (i) S. Gowrisankar, H. Neumann, D. Gordes, K. Thurow, H. Jiao, M. Beller, *Chem. Eur. J.* **2013**, *19*, 15979. (j) K. Chung, S. M. Banik, A. G. De Crisci, D. M. Pearson, T. R. Blake, J. V. Olsson, A. J. Ingram, R. N. Zare, R. M. Waymouth, *J. Am. Chem. Soc.* **2013**, *135*, 7593. (k) A. J. Ingram, D. Solis-Ibarra, R. N. Zare, R. M. Waymouth, *Angew. Chem. Int. Ed.* **2014**, *53*, 5648. (l) D. Sengupta, R. Bhattacharjee, R. Pramanick, S. P. Rath, N. Saha Chowdhury, A. Datta, S. Goswami, *Inorg. Chem.* **2016**, *55*, 9602. (m) R. Pramanick, R. Bhattacharjee, D. Sengupta, A. Datta, S. Goswami, *Inorg. Chem.* **2018**, *57*, 6816. (n) D. Ye, Z. Liu, J. L. Sessler, C. Lei, *Chem. Commun.* **2020**, *56*, 11811.

[4] (a) F. Alonso, P. Riente, M. Yus, *Acc. Chem. Res.* **2011**, *44*, 379. (b) D. Wang, D. Astruc, *Chem. Rev.* **2015**, *115*, 6621. (c) A. Quintard, J. Rodriguez, *Chem. Commun.* **2016**, *52*, 10456.

[5] (a) A. Friedrich, S. Schneider, *ChemCatChem* **2009**, *1*, 72. (b) T. C. Johnson, D. J. Morris, M. Wills, *Chem. Soc. Rev.* **2010**, *39*, 81. (c) C. Gunanathan, D. Milstein, *Science* **2013**, *341*, 1229712. (d) B. Zhou, Y. Hu, C. Wang, *Angew. Chem. Int. Ed.* **2015**, *54*, 13659. (e) R. H. Crabtree, *Chem. Rev.* **2017**, *117*, 9228. (f) K. Sordakis, C. Tang, L. K. Vogt, H. Junge, P. J. Dyson, M. Beller, G. Laurenczy, *Chem. Rev.* **2018**, *118*, 372.

[6] (a) H. Song, B. Kang, S. H. Hong, *ACS Catal.* **2014**, *4*, 2889. (b) E. A. Bielinski, P. O. Lagaditis, Y. Zhang, B. Q. Mercado, C. Würtele, W. H. Bernskoetter, N. Hazari, S. Schneider, *J. Am. Chem. Soc.* **2014**, *136*, 10234. (c) T. Zell, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2014**, *53*, 4685.

[7] (a) A. J. Blacker, E. Clot, S. B. Duckett, O. Eisenstein, J. Grace, A. Nova, R. N. Perutz, D. J. Taylor, A. C. Whitwood, *Chem. Commun.* **2009**, *2009*, 6801. (b) T. P. Brewster, A. J. M. Miller, D. M. Heinekey, K. I. Goldberg, *J. Am. Chem. Soc.* **2013**, *135*, 16022.

[8] (a) M. Matsumoto, N. Watanabe, *J. Org. Chem.* **1984**, *49*, 3435. (b) P. E. Morris, D. E. Kiely, *J. Org. Chem.* **1987**, *52*, 1149. (c) G. Barak, J. Dakka, Y. Sasson, *J. Org. Chem.* **1988**, *53*, 3553. (d) M. L. S. Almeida, M. Beller, G.-Z. Wang, J.-E. Bäckvall, *Chem. Eur. J.* **1996**, *2*, 1533. (e) R. Noyori, T. Ohkuma, *Angew. Chem. Int. Ed.* **2001**, *40*, 40. (f) J. Zhang, M. Gandelman, L. J. W. Shimon, H. Rozenberg, D. Milstein, *Organometallics* **2004**, *23*, 4026. (g) J. van Buijtenen, J. Meuldijk, J. A. J. M. Vekemans, L. A. Hulshof, H. Kooijman, A. L. Spek, *Organometallics* **2006**, *25*, 873. (h) H. Mizoguchi, T. Uchida, K. Ishida, T. Katsuki, *Tetrahedron Lett.* **2009**, *50*, 3432. (i) A. Taketoshi, X. N. Beh, J. Kuwabara, T.-a. Koizumi, T. Kanbara, *Tetrahedron Lett.* **2012**, *53*, 3573. (j) S.-S. Wang, J. Zhang, C.-L. Zhou, G. Vo-Thanh, Y. Liu, *Catal. Commun.* **2012**, *28*, 152. (k) S. Manzini, C. A. Urbina-Blanco, S. P. Nolan, *Organometallics* **2013**, *32*, 660.

[9] (a) K.-i. Fujita, N. Tanino, R. Yamaguchi, *Org. Lett.* **2007**, *9*, 109. (b) K.-i. Fujita, T. Yoshida, Y. Imori, R. Yamaguchi, *Org. Lett.* **2011**, *13*, 2278. (c) S. Musa, I. Shaposhnikov, S. Cohen, D. Gelman, *Angew. Chem., Int. Ed.* **2011**, *50*, 3533. (d) R. Kawahara, K. Fujita, R. Yamaguchi, *J. Am. Chem. Soc.* **2012**, *134*, 3643. (e) W. Tang, S. Johnston, J. A. Iggo, N. G. Berry, M. Phelan, L. Lian, J. Bacsa, J. Xiao, *Angew. Chem. Int. Ed.* **2013**, *52*, 1668. (f) A. H. Ngo, M. J. Adams, L. H. Do, *Organometallics* **2014**, *33*, 6742. (g) K.-i. Fujita, R. Tamura, Y. Tanaka, M. Yoshida, M. Onoda, R. Yamaguchi, *ACS Catal.* **2017**, *7*, 7226.

[10] (a) K. Shimizu, K. Sugino, K. Sawabe, A. Satsuma, *Chem. Eur. J.* **2009**, *15*, 2341. (b) G. Zhang, S. K. Hanson, *Org. Lett.* **2013**, *15*, 650. (c) S. Chakraborty, P. O. Lagaditis, M. Förster, E. A. Bielinski, N. Hazari, M. C. Holthausen, W. D. Jones, S. Schneider, *ACS Catal.* **2014**, *4*, 3994. (d) H. Fuse, H. Mitsunuma, M. Kanai, *J. Am. Chem. Soc.* **2020**, *142*, 4493.

[11] (a) J. G. West, D. Huang, E. J. Sorensen, *Nat. Commun.* **2015**, *6*, 10093. (b) Z. Chai, T.-T. Zeng, Q. Li, L.-Q. Lu, W.-J. Xiao, D. Xu, *J. Am. Chem. Soc.* **2016**, *138*, 10128. (c) H. Kasap, C. A. Caputo, B. C. M. Martindale, R. Godin, V. W.-h. Lau, B. V. Lotsch, J. R. Durrant, E. Reisner, J. Am, *Chem. Soc.* **2016**, *138*, 9183. (d) L.-M. Zhao, Q.-Y. Meng, X.-B. Fan, C. Ye, X.-B. Li, B. Chen, V. Ramamurthy, C.-H. Tung, L.-Z. Wu, *Angew. Chem. Int. Ed.* **2017**, *56*, 3020. (e) J.-J. Zhong, W.-P. To, Y. Liu, W. Lu, C.-M. Che, *Chem. Sci.* **2019**, *10*, 4883. (f) X.-J. Yang, Y.-W. Zheng, L.-Q. Zheng, L.-Z. Wu, C.-H. Tung, B. Chen, *Green Chem.* **2019**, *21*, 1401.

[12] (a) H. Junge, B. Loges, M. Beller, *Chem. Commun.* **2007**, *2007*, 522. (b) M. Nielsen, A. Kammer, D. Cozzula, H. Junge, S. Gladiali, M. Beller, *Angew. Chem. Int. Ed.* **2011**, *50*, 9593. (c) M. Trincado, D. Banerjee, H. Grützmacher, *Energy Environ. Sci.* **2014**, *7*, 2464. (d) S. Waiba, B. Maji, *ChemCatChem* **2020**, *12*, 1891. (e) K. R. Rohit, S. Radhika, S. Saranya, G. Anilkumar, *Adv. Synth. Catal.* **2020**, *362*, 1602.

[13] K. Oshima, B. Tollens, *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 1425.

[14] (a) T. Mitsudome, Y. Mikami, H. Funai, T. Mizugaki, K. Jitsukawa, K. Kaneda, *Angew. Chem., Int. Ed.* **2008**, *47*, 138. (b) E. Yazdani, A. Heydari, *J. Organomet. Chem* **2020**, *924*, 121453.

[15] L. Han, P. Xing, B. Jiang, *Org. Lett.* **2014**, *16*, 3428.

[16] H. G. Ghalehshahi, R. Madsen, *Chem. Eur. J.* **2017**, *23*, 11920.

[17] M. Liu, H. Wang, H. Zeng, C.-J. Li, *Sci. Adv.* **2015**, *1*, e1500020.

[18] Z. Z. Zhou, M. Liu, L. Lv, C. J. Li, *Angew. Chem. Int. Ed.* **2018**, *57*, 2616.

[19] (a) M. J. Beier, T. W. Hansen, J.-D. Grunwaldt, *J. Catal.* **2009**, *266*, 320. (b) J. Wang, Y. Li, Y. Peng, G. Song, *J. Chin. Chem. Soc.* **2014**, *61*, 517.

[20] (a) H. Li, Y. Li, X. S. Zhang, K. Chen, X. Wang, Z. J. Shi, *J. Am. Chem. Soc.* **2011**, *133*, 15244. (b) H. Wang, I. Choi, T. Rogge, N. Kaplaneris, L. Ackermann, *Nat. Catal.* **2018**, *1*, 993. (c) Y. Qiu, A. Scheremetjew, L. Ackermann, *J. Am. Chem. Soc.* **2019**, *141*, 2731.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Zhuang X, Tao J, Luo Z, et al. Silver catalyzed pyridine-directed acceptorless dehydrogenation of secondary alcohols. *J Chin Chem Soc*. 2021;68:245–249. https://doi.org/10.1002/jccs.202000517