OL Organic Letters

pubs.acs.org/OrgLett Letter

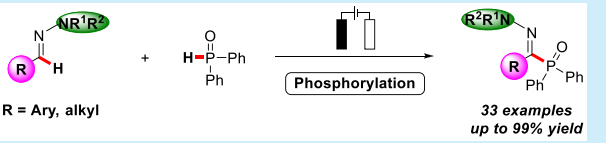
Electrochemical Oxidative Phosphorylation of Aldehyde Hydrazones

Zhongnan Xu,[§] Yueheng Li,[§] Guangquan Mo,[§] Yucheng Zheng, Shaogao Zeng, Ping-Hua Sun,* and Zhixiong Ruan*

Cite This: https://dx.doi.org/10.1021/acs.orglett.0c01343 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: The electrochemical phosphorylation of aldehyde hydrazones has been developed under exogenous oxidant-free conditions. The strategy provides expedient access to highly functionalized α-iminophosphine oxides with ample scope and broad functional group tolerance by means of mild, user-friendly electrolysis, in an undivided cell.

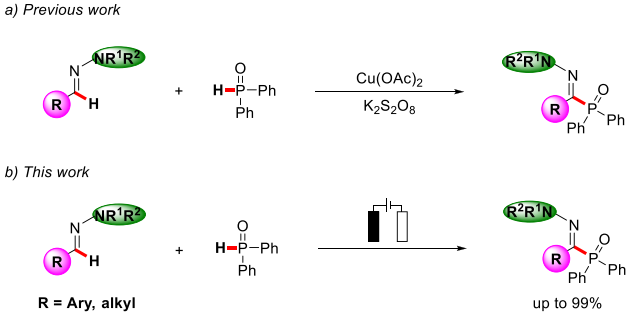


Organophosphorus compounds are of great importance since they are widely found in organic catalysis, medicinal chemistry, material science, and agriculture science.[1] As a consequence, there is a continued strong demand for the development of phosphorus-containing compounds using synthetic methods via step-economical C−P bond formation.[2] Although significant advances have been made in C−H phosphorylation by employing transition metal catalysis[3] and photoredox catalysis[4] for the construction of various C−P bonds, it is difficult to obviate the use of precious transition metals or stoichiometric chemical redox reagents. As a result, a direct C−H phosphorylation of quinoxalin-2(1*H*)-ones under transition-metal-free conditions was developed by Cui and coworkers,[5] to access functionalized heterocycles bearing α-iminophosphine oxide skeletons. Imine derivatives, especially aldehyde hydrazones, are crucial intermediates in synthetic organic chemistry.[6] Recently, Zhu's group reported a copper-mediated oxidative C−H phosphorylation of aldehyde hydrazones with diphenylphosphine oxide for the preparation of α-iminophosphine oxide by using an excess amount of $K_2S_2O_8$ as a chemical oxidant inevitably (Scheme 1a).[7]

Additionally, organic electrochemistry has been established as an increasingly powerful strategy for molecular synthesis, with transformative power for replacing sacrificial oxidizing or reducing reagents.[8] In this context, considerable progress has been accomplished in C−H functionalization by electrochemical anodic oxidation, such as C−H amination,[9] alkylation,[10] oxygenation,[11] and thiolation.[12] In spite of undisputed advances, the electrochemical oxidative C−H phosphorylation is still underdeveloped.[13] Anodic oxidative phosphonation of arenes as an early example was reported by Effenberger and Kottmann.[14] However, for nearly three decades, only a few elegant examples of electrochemical C−H phosphorylation have been explored, including aryl C−H phosphorylation by palladium[15] or rhodium catalysis[16] and electron-deficient heteroaromatic C−H phosphonation reactions.[17] Herein, within our program on electrochemical transformation,[18] we have now uncovered an unprecedented electrochemical phosphorylation of aldehyde hydrazones under external oxidant-free conditions (Scheme 1b). Notable features of our findings include (a) exceedingly mild reaction conditions at 23 °C in an undivided cell under ambient air, (b) avoiding the utilization of chemical oxidizing reagents, and (c) ample scope toward α-iminophosphine oxides with broad functional group tolerance.

Our studies were initiated by probing various reaction conditions for the envisioned electrochemical phosphorylation of aldehyde hydrazone **1a** with diphenylphosphine oxide (**2a**) under constant current electrolysis conditions (see Table 1). After extensive optimization, the optimal results were obtained when substrates **1a** and **2a** were electrolyzed at a constant current in an electrolyte solution of Et_4NClO_4 in MeCN at room temperature under atmospheric conditions with a catalytic amount of $MnBr_2{\cdot}H_2O$. Under these conditions, the

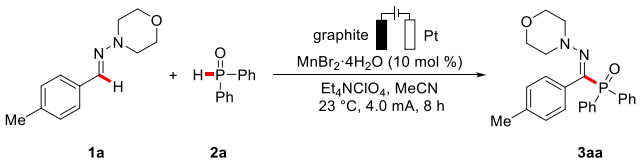
Scheme 1. Conventional and Electrochemical Phosphorylation of Aldehyde Hydrazones



Received: April 17, 2020

https://dx.doi.org/10.1021/acs.orglett.0c01343
Org. Lett. XXXX, XXX, XXX−XXX

Table 1. Optimization of Reaction Conditions[a]



entry	deviation from standard conditions	yield (%)[b]
1	none	85
2	no Et_4NClO_4	0
3	*n*-Bu_4NBF_4 instead of Et_4NClO_4	21
4	*n*-Bu_4NPF_6 instead of Et_4NClO_4	26
5	$LiClO_4$ instead of Et_4NClO_4	13
6	no $MnBr_2{\cdot}4H_2O$	76
7	$Mn(OAc)_3{\cdot}3H_2O$ instead of $MnBr_2{\cdot}4H_2O$	59
8	$Cu(OAc)_2$ instead of $MnBr_2{\cdot}4H_2O$	73
9	Cp_2Fe instead of $MnBr_2{\cdot}4H_2O$	80
10	MeOH instead of MeCN	70
11	MeCN/MeOH (2/1) instead of MeCN	73
12	MeCN/H_2O (2/1) instead of MeCN	36
13	no electricity	0

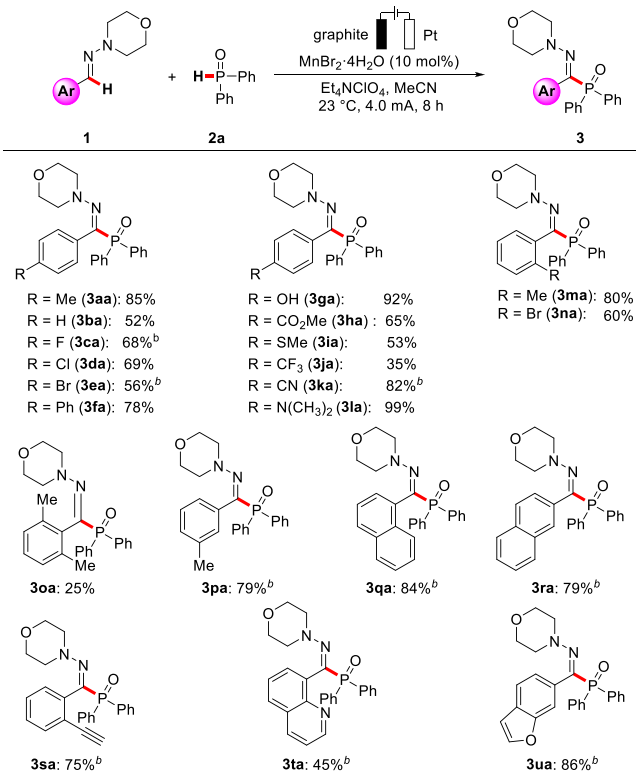
[a]Reaction conditions: undivided cell, graphite anode, Pt cathode, **1a** (0.5 mmol), **2a** (1.0 mmol), $MnBr_2{\cdot}4H_2O$ (10 mol %), Et_4NClO_4 (0.5 mmol), MeCN (5.0 mL), constant current = 4.0 mA, 8 h (2.6 F·mol^{-1}), under air, 23 °C. [b]Yield of isolated products.

desired α-iminophosphine oxide **3aa** was achieved in 85% isolated yield (Table 1, entry 1). The Et_4NClO_4 salt was found to be essential for the phosphorylation reaction (entry 2), while other electrolytes such as *n*-Bu_4NBF_4, *n*-Bu_4NPF_6, and $LiClO_4$ showed poor performance (entries 3−5). Control experiment in the absence of manganese salt resulted in a slightly lower yield of **3aa**, demonstrating that the additive of manganese salt might probably promote the C−H transformation. In contrast, other transition metal mediators were found to be less efficient (entries 7−9). Additionally, protic solvents, such as MeOH and other mixed solvents, were less efficient than the aprotic solvent (MeCN) (entries 10−12). Further control experiments verified the essential nature of the external electricity (entry 13).

With the optimal reaction conditions in hand, we next explored its versatility with a set of representative aldehyde hydrazones **1** (Scheme 2). Thereby, the electrochemical phosphorylation manifold proved amenable to both electron-rich and electron-deficient substituents. Thus, the robust nature of the electrooxidative transformation was reflected by fully tolerating a wealth of synthetically useful functionalities, including chloro, bromo, phenolic hydroxyl, ester, and cyano, as well as terminal alkynyl groups, which could serve as a handle for further late-stage modifications. The electrochemical C−H phosphorylation smoothly proceeded with various sterically hindered substituted substrates (**1m−1p**), albeit **1o** was in lower yield. Besides, the naphthalene substrates (**1q** and **1r**) could well convert to the desired products in good yields. Notably, the reaction could also be performed with heterocyclic aldehyde-derived hydrazones (**1t** and **1u**).

Furthermore, encouraged by these exciting results, we next investigated the compatibility with various substituted phosphorus coupling partners in the electrochemical C−H phosphorylation approach (Scheme 3). Hence, with *p*-tolualdehyde hydrazone **1a** as the C−H donor, the reaction

Scheme 2. Electrochemical Phosphorylation of Arylaldehyde Hydrazones with 2a[a]



[a]Reaction conditions: undivided cell, graphite anode, Pt cathode, **1** (0.5 mmol), **2a** (1.0 mmol), $MnBr_2{\cdot}4H_2O$ (10 mol %), Et_4NClO_4 (0.5 mmol), MeCN (5.0 mL), constant current = 4.0 mA, 8 h, under air, 23 °C. Isolated yields were given. [b]50 °C.

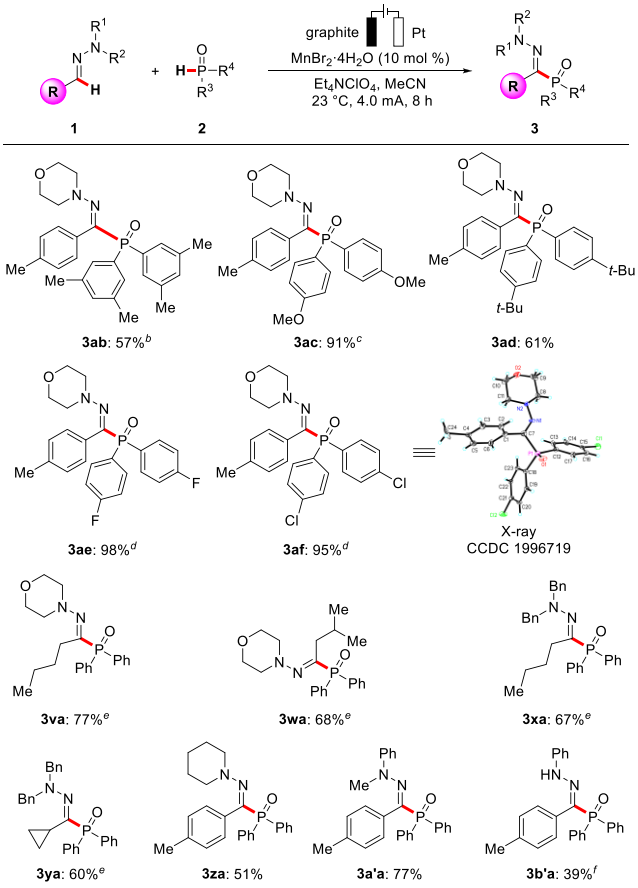
tolerated a diverse array of diphenylphosphine oxides bearing two functionalized aryl groups at the *meta*- or *para*-position, such as methyl, methoxyl, *tert*-butyl, fluoro, and chloro substituents (**2b−2f**). It is noteworthy that the aliphatic aldehyde-derived hydrazones also proved to be suitable substrates for the electrochemical phosphorylation and furnished the desired products with moderate yields (**3va−3ya**). The structure of compound **3af** was further definitely determined by X-ray single-crystal diffraction. To our delight, the electrochemical transformation was not just restricted to morpholine- and piperidinyl-derived hydrazones; the other *N*,*N*-disubstituted hydrazones with acyclic amino groups, such as dibenzylhydrazone and 1-methyl-1-phenylhydrazone, were also tolerated for this electrooxidative phosphorylation (**1x−1a′**). Notably, the phenylamine-derived hydrazone **1b′** with free NH was also suitable for the C−H transformation, albeit in lower conversion.

To further demonstrate the practical utility of this electrochemical protocol, a gram-scale synthesis of α-iminophosphine oxides **3aa** was carried out under standard conditions (Scheme 4). This electrolysis was performed with graphite as the anode and platinum as the cathode, at a higher constant current (20 mA), and obtained in 80% isolated yield, without appreciable loss in efficacy.

In consideration of the remarkable performance of the electrooxidative phosphorylation, we became intrigued with delineating its mode of action. To this end, intermolecular competition experiment between electronically discriminated

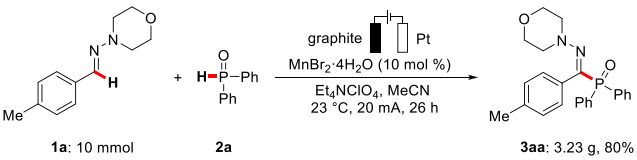
https://dx.doi.org/10.1021/acs.orglett.0c01343
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 3. Electrochemical Phosphorylation of Aldehyde Hydrazones with Diarylphosphine Oxide 2[a]



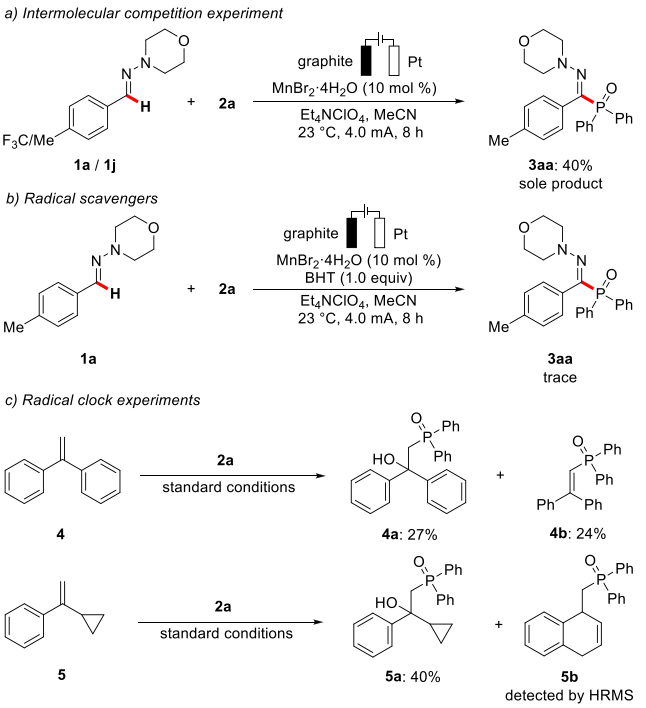
[a]Reaction conditions: undivided cell, graphite anode, Pt cathode, **1** (0.5 mmol), **2a** (1.0 mmol), $MnBr_2{\cdot}4H_2O$ (10 mol %), Et_4NClO_4 (0.5 mmol), MeCN (5.0 mL), constant current = 4.0 mA, 8 h, under air, 23 °C. Isolated yields were given. [b]8.0 mA. [c]10 h. [d]11 h. [e]7 h, under argon. [f]50 °C.

Scheme 4. Gram-Scale Reaction



substrates **1** revealed that electron-rich aldehyde hydrazones were inherently more reactive (Scheme 5a). In addition, 2,4-di-*tert*-butyl-4-methylphenol (BHT) was selected as a typical radical trapping reagent since its oxidative onset potential was higher than that of substrate **1a** (see Figure S2). Thus, the phosphorylation of substrate **1a** was fully suppressed upon the addition of the radical scavenger BHT with a trace of the desired product formed, being suggestive of involving a radical process (Scheme 5b). Gratifyingly, when 1,1-diphenylethene (**4**) was subjected to electrolysis with diphenylphosphine oxide (**2a**) under the standard conditions, the addition products **4a** and **4b** were isolated separately. This result indicated the involvement of a radical pathway, which was further demonstrated by the detection of adduct **5a** and ring-opening product **5b** from the radical clock reaction of 1-(1-

Scheme 5. Summary of Key Mechanistic Findings



cyclopropylvinyl)benzene (**5**) with **2a** under the standard electrochemical conditions (Scheme 5c).

The cyclic voltammetric (CV) analysis was also performed to reveal key mechanistic insights into the electrochemical functionalization (Figure 1 and Figures S1–S4). It was found

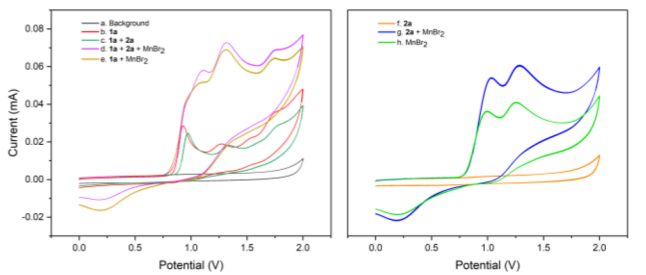


Figure 1. Cyclic voltammograms of **1a**, **2a**, and $MnBr_2{\cdot}4H_2O$. Conditions: a glassy carbon working electrode, a Ag/AgCl (3 M KCl) reference electrode, and a platinum wire counter electrode, Et_4NClO_4 (0.1 M in MeCN), 100 mV/s scan rate with (a) background; (b) **1a** (1 mM); (c) **1a** (1 mM) + **2a** (1 mM); (d) **1a** (1 mM) + **2a** (1 mM) + $MnBr_2{\cdot}4H_2O$ (1 mM); (e) **1a** (1 mM) + $MnBr_2{\cdot}4H_2O$ (1 mM); (f) **2a** (1 mM); (g) **2a** (1 mM) + $MnBr_2{\cdot}4H_2O$ (1 mM); and (h) $MnBr_2{\cdot}4H_2O$ (1 mM).

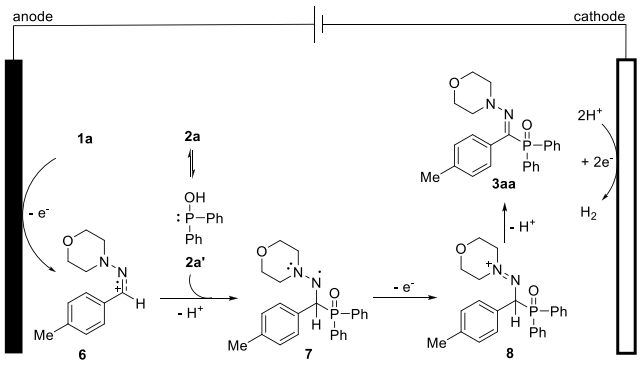
that **1a** could be oxidized at a low potential ($E_{p/2}$ = 0.89 V vs Ag/AgCl), which was even lower than the oxidation potential of phosphine oxide **2a** ($E_{p/2}$ > 1 V vs Ag/AgCl). This observation was different from the previous report.[7] Notably, the additive of $MnBr_2$ could somewhat promote the electro-oxidation of **1a** or the mixture of **1a** and **2a** with a lower onset potential and high oxidation current response. However, it is currently unclear whether the catalysis of $MnBr_2$ is from single Br^- or the synergistic effect of Mn^{2+} and Br^-.[19]

Based on related literature reports[6c,16,17,20] and our studies, a plausible mechanistic scenario was proposed for the electrochemical oxidative phosphorylation of aldehyde hydrazones in

https://dx.doi.org/10.1021/acs.orglett.0c01343
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 6 based on the direct electrochemical initiation model,[8r] omitting the effect of $MnBr_2$. Due to the much lower

Scheme 6. Proposed Mechanism



oxidative potential of aldehyde hydrazone **1a** than **2a**, the substrate **1a** is initially oxidized to carbocation intermediate **6**, which then reacts with **2a′** to form the C−N bond, generating the aminyl radical intermediate **7**. Further anodic oxidation of **7** produces the cation **8**, followed by deprotonation, giving the desired product **3aa**. At the cathode, protons are concurrently reduced to release molecular hydrogen.

In summary, we have developed a mild and efficient method for the preparation of functionalized α-iminophosphine oxides with ample scope and high functional group tolerance, by user-friendly, electrochemical oxidative phosphorylation of aldehyde hydrazones under external oxidant-free conditions. Importantly, this protocol could be easily conducted on a gram-scale reaction. Detailed mechanistic studies provided strong support for a diverse radical process compared with the previous report.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c01343.

Experimental procedures, characterization data, and ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra for all products (PDF)

Accession Codes

CCDC 1996719 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.

■ AUTHOR INFORMATION

Corresponding Authors

Zhixiong Ruan − *Key Laboratory of Molecular Target & Clinical Pharmacology and the State Key Laboratory of Respiratory Disease, School of Pharmaceutical Sciences & the Fifth Affiliated Hospital, Guangzhou Medical University, Guangzhou 511436, P.R. China;* orcid.org/0000-0002-5433-2460; Email: zruan@gzhmu.edu.cn

Ping-Hua Sun − *International Cooperative Laboratory of Traditional Chinese Medicine Modernization and Innovative Drug Development of Chinese Ministry of Education, College of Pharmacy, Jinan University, Guangzhou 510632, P.R. China;* Email: pinghuasunny@163.com

Authors

Zhongnan Xu − *Key Laboratory of Molecular Target & Clinical Pharmacology and the State Key Laboratory of Respiratory Disease, School of Pharmaceutical Sciences & the Fifth Affiliated Hospital, Guangzhou Medical University, Guangzhou 511436, P.R. China*

Yueheng Li − *Key Laboratory of Molecular Target & Clinical Pharmacology and the State Key Laboratory of Respiratory Disease, School of Pharmaceutical Sciences & the Fifth Affiliated Hospital, Guangzhou Medical University, Guangzhou 511436, P.R. China*

Guangquan Mo − *Key Laboratory of Molecular Target & Clinical Pharmacology and the State Key Laboratory of Respiratory Disease, School of Pharmaceutical Sciences & the Fifth Affiliated Hospital, Guangzhou Medical University, Guangzhou 511436, P.R. China*

Yucheng Zheng − *Key Laboratory of Molecular Target & Clinical Pharmacology and the State Key Laboratory of Respiratory Disease, School of Pharmaceutical Sciences & the Fifth Affiliated Hospital, Guangzhou Medical University, Guangzhou 511436, P.R. China*

Shaogao Zeng − *International Cooperative Laboratory of Traditional Chinese Medicine Modernization and Innovative Drug Development of Chinese Ministry of Education, College of Pharmacy, Jinan University, Guangzhou 510632, P.R. China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c01343

Author Contributions

[§]Z.X., Y.L., and G.M. contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Support by the National Natural Science Foundation of China (21901052), the Guangdong Province Universities and Colleges Pearl River Scholar Funded Scheme (2019), the Guangzhou Education Bureau University Scientific Research Project (201831845), Guangdong Basic and Applied Basic Research Foundation (2020A1515010722), the National Natural Science Fundation of China (81872759 to P.-H. S.), and Guangzhou City Key Laboratory of Precision Chemical Drug Development (201805010007 to P.-H. S.) is most gratefully acknowledged.

■ REFERENCES

(1) (a) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029. (b) Wydysh, E. A.; Medghalchi, S. M.; Vadlamudi, A.; Townsend, C. A. *J. Med. Chem.* **2009**, *52*, 3317. (c) Dang, Q.; Liu, Y.; Cashion, D. K.; Kasibhatla, S. R.; Jiang, T.; Taplin, F.; Jacintho, J. D.; Li, H.; Sun, Z.; Fan, Y.; DaRe, J.; Tian, F.; Li, W.; Gibson, T.; Lemus, R.; van Poelje, P. D.; Potter, S. C.; Erion, M. D. *J. Med. Chem.* **2011**, *54*, 153. (d) Demmer, C. S.; Krogsgaard-Larsen, N.; Bunch, L. *Chem. Rev.* **2011**, *111*, 7981. (e) Gagnon, K. J.; Perry, H. P.; Clearfield, A. *Chem. Rev.* **2012**, *112*, 1034. (f) Queffélec, C.; Petit, M.; Janvier, P.; Knight, D. A.; Bujoli, B. *Chem. Rev.* **2012**, *112*, 3777. (g) Carroll, M. P.; Guiry, P. J. *Chem. Soc. Rev.* **2014**, *43*, 819. (h) Montchamp, J.-L. *Acc. Chem. Res.* **2014**, *47*, 77.

(2) (a) Goulioukina, N. S.; Bondarenko, G. N.; Lyubimov, S. E.; Davankov, V. A.; Gavrilov, K. N.; Beletskaya, I. P. *Adv. Synth. Catal.*

https://dx.doi.org/10.1021/acs.orglett.0c01343
Org. Lett. XXXX, XXX, XXX−XXX

2008, *350*, 482. (b) Petro, P. O. k.; Yuliya, V. R.; Anatoly, D. S. *Curr. Org. Chem.* **2008**, *12*, 2. (c) Motevalli, S.; Iranpoor, N.; Etemadi-Davan, E.; Moghadam, K. R. *RSC Adv.* **2015**, *5*, 100070. (d) Jia, X.; Liu, X.; Shao, Y.; Yuan, Y.; Zhu, Y.; Hou, W.; Zhang, X. *Adv. Synth. Catal.* **2017**, *359*, 4399. (e) Palacios, F.; Vicario, J.; Maliszewska, A.; Aparicio, D. *J. Org. Chem.* **2007**, *72*, 2682.

(3) (a) Hirai, T.; Han, L.-B. *J. Am. Chem. Soc.* **2006**, *128*, 7422. (b) Xie, J.; Li, H.; Xue, Q.; Cheng, Y.; Zhu, C. *Adv. Synth. Catal.* **2012**, *354*, 1646. (c) Feng, C.-G.; Ye, M.; Xiao, K.-J.; Li, S.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 9322. (d) Wang, S.; Guo, R.; Wang, G.; Chen, S.-Y.; Yu, X.-Q. *Chem. Commun.* **2014**, *50*, 12718. (e) Yang, B.; Zhang, H.-Y.; Yang, S.-D. *Org. Biomol. Chem.* **2015**, *13*, 3561.

(4) (a) Shaikh, R. S.; Ghosh, I.; König, B. *Chem. - Eur. J.* **2017**, *23*, 12120. (b) Cai, B.-G.; Xuan, J.; Xiao, W.-J. *Sci. Bull.* **2019**, *64*, 337.

(5) Gao, M.; Li, Y.; Xie, L.; Chauvin, R.; Cui, X. *Chem. Commun.* **2016**, *52*, 2846.

(6) (a) Lazny, R.; Nodzewska, A. *Chem. Rev.* **2010**, *110*, 1386. (b) Xu, P.; Li, W.; Xie, J.; Zhu, C. *Acc. Chem. Res.* **2018**, *51*, 484. (c) Ye, Z.; Wang, F.; Li, Y.; Zhang, F. *Green Chem.* **2018**, *20*, 5271. (d) Wang, Z.; Liu, Q.; Ji, X.; Deng, G.-J.; Huang, H. *ACS Catal.* **2020**, *10*, 154.

(7) Xu, P.; Wu, Z.; Zhou, N.; Zhu, C. *Org. Lett.* **2016**, *18*, 1143.

(8) (a) Jutand, A. *Chem. Rev.* **2008**, *108*, 2300. (b) Yoshida, J.-i.; Kataoka, K.; Horcajada, R.; Nagaki, A. *Chem. Rev.* **2008**, *108*, 2265. (c) Horn, E. J.; Rosen, B. R.; Baran, P. S. *ACS Cent. Sci.* **2016**, *2*, 302. (d) Hou, Z.-W.; Mao, Z.-Y.; Xu, H.-C. *Synlett* **2017**, *28*, 1867. (e) Sambiagio, C.; Sterckx, H.; Maes, B. U. W. *ACS Cent. Sci.* **2017**, *3*, 686. (f) Sauermann, N.; Meyer, T. H.; Ackermann, L. *Chem. - Eur. J.* **2018**, *24*, 16209. (g) Sauermann, N.; Meyer, T. H.; Qiu, Y.; Ackermann, L. *ACS Catal.* **2018**, *8*, 7086. (h) Tang, S.; Liu, Y.; Lei, A. *Chem.* **2018**, *4*, 27. (i) Yang, Q. L.; Fang, P.; Mei, T. S. *Chin. J. Chem.* **2018**, *36*, 338. (j) Yan, M.; Kawamata, Y.; Baran, P. S. *Chem. Rev.* **2017**, *117*, 13230. (k) Jiang, Y.; Xu, K.; Zeng, C. *Chem. Rev.* **2018**, *118*, 4485. (l) Moeller, K. D. *Chem. Rev.* **2018**, *118*, 4817. (m) Möhle, S.; Zirbes, M.; Rodrigo, E.; Gieshoff, T.; Wiebe, A.; Waldvogel, S. R. *Angew. Chem., Int. Ed.* **2018**, *57*, 6018. (n) Nutting, J. E.; Rafiee, M.; Stahl, S. S. *Chem. Rev.* **2018**, *118*, 4834. (o) Sauer, G. S.; Lin, S. *ACS Catal.* **2018**, *8*, 5175. (p) Waldvogel, S. R.; Lips, S.; Selt, M.; Riehl, B.; Kampf, C. *Chem. Rev.* **2018**, *118*, 6706. (q) Wiebe, A.; Gieshoff, T.; Möhle, S.; Rodrigo, E.; Zirbes, M.; Waldvogel, S. R. *Angew. Chem., Int. Ed.* **2018**, *57*, 5594. (r) Yang, Q.-L.; Fang, P.; Mei, T.-S. *Chin. J. Chem.* **2018**, *36*, 338. (s) Yoshida, J.-i.; Shimizu, A.; Hayashi, R. *Chem. Rev.* **2018**, *118*, 4702. (t) Elsherbini, M.; Wirth, T. *Acc. Chem. Res.* **2019**, *52*, 3287. (u) Marken, F.; Wadhawan, J. D. *Acc. Chem. Res.* **2019**, *52*, 3325. (v) Wang, H.; Gao, X.; Lv, Z.; Abdelilah, T.; Lei, A. *Chem. Rev.* **2019**, *119*, 6769. (w) Xiong, P.; Xu, H.-C. *Acc. Chem. Res.* **2019**, *52*, 3339. (x) Yuan, Y.; Lei, A. *Acc. Chem. Res.* **2019**, *52*, 3309. (y) Ackermann, L. *Acc. Chem. Res.* **2020**, *53*, 84.

(9) (a) Yu, Y.; Yuan, Y.; Liu, H.; He, M.; Yang, M.; Liu, P.; Yu, B.; Dong, X.; Lei, A. *Chem. Commun.* **2019**, *55*, 1809. (b) Wang, H.; Shi, J.; Tan, J.; Xu, W.; Zhang, S.; Xu, K. *Org. Lett.* **2019**, *21*, 9430. (c) Wang, F.; Stahl, S. S. *Angew. Chem., Int. Ed.* **2019**, *58*, 6385. (d) Liu, S.; Li, J.; Wang, D.; Liu, F.; Liu, X.; Gao, Y.; Jie, D.; Cheng, X. *Chin. J. Chem.* **2019**, *37*, 570. (e) Zhang, S.-K.; Samanta, R. C.; Sauermann, N.; Ackermann, L. *Chem. - Eur. J.* **2018**, *24*, 19166. (f) Yang, Q.-L.; Wang, X.-Y.; Lu, J.-Y.; Zhang, L.-P.; Fang, P.; Mei, T.-S. *J. Am. Chem. Soc.* **2018**, *140*, 11487. (g) Tang, S.; Wang, S.; Liu, Y.; Cong, H.; Lei, A.; Lei, A. *Angew. Chem., Int. Ed.* **2018**, *57*, 4737. (h) Tang, S.; Wang, S.; Liu, Y.; Cong, H.; Lei, A. *Angew. Chem., Int. Ed.* **2018**, *57*, 4737. (i) Sauermann, N.; Mei, R.; Ackermann, L. *Angew. Chem., Int. Ed.* **2018**, *57*, 5090. (j) Qiu, Y.; Struwe, J.; Meyer, T. H.; Oliveira, J. C. A.; Ackermann, L. *Chem. - Eur. J.* **2018**, *24*, 12784. (k) Mei, R.; Sauermann, N.; Oliveira, J. C. A.; Ackermann, L. *J. Am. Chem. Soc.* **2018**, *140*, 7913. (l) Hu, X.; Zhang, G.; Bu, F.; Nie, L.; Lei, A. *ACS Catal.* **2018**, *8*, 9370. (m) Herold, S.; Bafaluy, D.; Muniz, K. *Green Chem.* **2018**, *20*, 3191. (n) Gao, X.; Wang, P.; Zeng, L.; Tang, S.; Lei, A. *J. Am. Chem. Soc.* **2018**, *140*, 4195. (o) Hayashi, R.; Shimizu, A.; Song, Y.; Ashikari, Y.; Nokami, T.; Yoshida, J.-i. *Chem. - Eur. J.* **2017**, *23*, 61. (p) Morofuji, T.; Shimizu, A.; Yoshida, J.-i. *J. Am. Chem. Soc.* **2013**, *135*, 5000.

(10) (a) Yuan, K.; Liu, C.; Xiao, Z.; Wu, S.; Shen, Y.; Ding, Y. *ChemSusChem* **2020**, *13*, 1997. (b) Qiu, Y.; Scheremetjew, A.; Finger, L. H.; Ackermann, L. *Chem. - Eur. J.* **2020**, *26*, 3241. (c) Zhang, Q.; Chang, X.; Peng, L.; Guo, C. *Angew. Chem., Int. Ed.* **2019**, *58*, 6999. (d) Yang, Q.-L.; Li, C.-Z.; Zhang, L.-W.; Li, Y.-Y.; Tong, X.; Wu, X.-Y.; Mei, T.-S. *Organometallics* **2019**, *38*, 1208. (e) Wu, Z.-J.; Li, S.-R.; Long, H.; Xu, H.-C. *Chem. Commun.* **2018**, *54*, 4601. (f) Wu, Z.-J.; Xu, H.-C. *Angew. Chem., Int. Ed.* **2017**, *56*, 4734. (g) Ma, C.; Zhao, C.-Q.; Li, Y.-Q.; Zhang, L.-P.; Xu, X.-T.; Zhang, K.; Mei, T.-S. *Chem. Commun.* **2017**, *53*, 12189. (h) Fu, N.; Li, L.; Yang, Q.; Luo, S. *Org. Lett.* **2017**, *19*, 2122. (i) Gao, H.; Zha, Z.; Zhang, Z.; Ma, H.; Wang, Z. *Chem. Commun.* **2014**, *50*, 5034. (j) Dudkina, Y. B.; Mikhaylov, D. Y.; Gryaznova, T. V.; Sinyashin, O. G.; Vicic, D. A.; Budnikova, Y. H. *Eur. J. Org. Chem.* **2012**, *2012*, 2114. (k) Zakurin, N. V.; Denisovich, L. I.; Gubin, S. P. *J. Organomet. Chem.* **1977**, *129*, 203.

(11) (a) Zhang, S.-K.; Struwe, J.; Hu, L.; Ackermann, L. *Angew. Chem., Int. Ed.* **2020**, *59*, 3178. (b) Massignan, L.; Tan, X.; Meyer, T. H.; Kuniyil, R.; Messinis, A. M.; Ackermann, L. *Angew. Chem., Int. Ed.* **2020**, *59*, 3184. (c) Zhang, S.; Li, L.; Wang, H.; Li, Q.; Liu, W.; Xu, K.; Zeng, C. *Org. Lett.* **2018**, *20*, 252. (d) Wang, F.; Rafiee, M.; Stahl, S. S. *Angew. Chem., Int. Ed.* **2018**, *57*, 6686. (e) Yang, Q.-L.; Li, Y.-Q.; Ma, C.; Fang, P.; Zhang, X.-J.; Mei, T.-S. *J. Am. Chem. Soc.* **2017**, *139*, 3293. (f) Xu, F.; Qian, X.-Y.; Li, Y.-J.; Xu, H.-C. *Org. Lett.* **2017**, *19*, 6332. (g) Sauermann, N.; Meyer, T. H.; Tian, C.; Ackermann, L. *J. Am. Chem. Soc.* **2017**, *139*, 18452.

(12) (a) Mo, Z.-Y.; Zhang, Y.-Z.; Huang, G.-b.; Wang, X.-Y.; Pan, Y.-m.; Tang, H.-T. *Adv. Synth. Catal.* **2020**, DOI: 10.1002/adsc.201901607. (b) Yuan, Y.; Cao, Y.; Qiao, J.; Lin, Y.; Jiang, X.; Weng, Y.; Tang, S.; Lei, A. *Chin. J. Chem.* **2019**, *37*, 49. (c) Yuan, Y.; Yu, Y.; Qiao, J.; Liu, P.; Yu, B.; Zhang, W.; Liu, H.; He, M.; Huang, Z.; Lei, A. *Chem. Commun.* **2018**, *54*, 11471. (d) Wang, P.; Tang, S.; Huang, P.; Lei, A. *Angew. Chem., Int. Ed.* **2017**, *56*, 3009. (e) Qian, X.-Y.; Li, S.-Q.; Song, J.; Xu, H.-C. *ACS Catal.* **2017**, *7*, 2730.

(13) Budnikova, Y. H.; Dudkina, Y. B. Phosphorus, Sulfur Silicon Relat. *Phosphorus, Sulfur Silicon Relat. Elem.* **2019**, *194*, 415.

(14) Effenberger, F.; Kottmann, H. *Tetrahedron* **1985**, *41*, 4171.

(15) (a) Grayaznova, T. V.; Dudkina, Y. B.; Islamov, D. R.; Kataeva, O. N.; Sinyashin, O. G.; Vicic, D. A.; Budnikova, Y. H. *J. Organomet. Chem.* **2015**, *785*, 68. (b) Yu, B. D.; Tatyana, V. G.; Olga, K.; Yu, H. B.; Oleg, G. S. *Russ. Chem. Bull.* **2014**, *63*, 2641.

(16) Wu, Z.-J.; Su, F.; Lin, W.; Song, J.; Wen, T.-B.; Zhang, H.-J.; Xu, H.-C. *Angew. Chem., Int. Ed.* **2019**, *58*, 16770.

(17) (a) Yuan, Y.; Qiao, J.; Cao, Y.; Tang, J.; Wang, M.; Ke, G.; Lu, Y.; Liu, X.; Lei, A. *Chem. Commun.* **2019**, *55*, 4230. (b) Li, K.-J.; Jiang, Y.-Y.; Xu, K.; Zeng, C.-C.; Sun, B.-G. *Green Chem.* **2019**, *21*, 4412.

(18) (a) Ruan, Z.; Huang, Z.; Xu, Z.; Mo, G.; Tian, X.; Yu, X.-Y.; Ackermann, L. *Org. Lett.* **2019**, *21*, 1237. (b) Xu, Z.; Huang, Z.; Li, Y.; Kuniyil, R.; Zhang, C.; Ackermann, L.; Ruan, Z. *Green Chem.* **2020**, *22*, 1099.

(19) The redox potentials of substrates and additives were given in the Supporting Information, and for the electrochemical transformaiton involving manganese, see: (a) Fu, N.; Sauer, G. S.; Saha, A.; Loo, A.; Lin, S. *Science* **2017**, *357*, 575. (b) Sauer, G. S.; Lin, S. *ACS Catal.* **2018**, *8*, 5175. (c) Zhang, Z.; Zhang, L.; Cao, Y.; Li, F.; Bai, G.; Liu, G.; Yang, Y.; Mo, F. *Org. Lett.* **2019**, *21*, 762.

(20) Ke, M.; Song, Q. *J. Org. Chem.* **2016**, *81*, 3654.

https://dx.doi.org/10.1021/acs.orglett.0c01343
Org. Lett. XXXX, XXX, XXX−XXX