Electrochemically driven regioselective C–H phosphorylation of group 8 metallocenes

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Metallocenes are privileged backbones for synthesis and catalysis. However, the direct dehydrogenative C–H functionalization of unsymmetric metallocenes suffers from reactivity and selectivity issues. Herein, we report an electrochemically driven regioselective C–H phosphorylation of group 8 metallocenes. Mechanistic investigations indicate this dehydrogenative cross coupling occurs through an electrophilic radical substitution of the metallocene with a phosphoryl radical, facilitated by the metallocene itself. This work not only offers an efficient and divergent synthesis of phosphorylated metallocenes, but also provides a guide to interpret the reactivity and regioselectivity for the C–H functionalization of unsymmetric metallocenes.
Since its discovery in the early 1950s, ferrocene and its metallocene derivatives have received widespread attention owing to their broad applications in physics, polymer science, and medicine. With regard to organic synthesis and catalysis, metallocene-based phosphines have proven to be privileged ligands or catalysts. Although there are well-established methods for the synthesis of simple and unsubstituted metallocenes, the construction of substituted metallocene derivatives remains a challenge. Two general approaches have been used for the synthesis of substituted metallocenes. The first strategy is the coordination of substituted cyclopentadienyl precursors with the corresponding metal complex. While reliable, this approach usually requires the multi-step synthesis of substituted cyclopentadienyl precursors and stoichiometric amounts of strong bases. The second strategy involves the C—H functionalization of the metallocene. The latter exhibits a better step economy but relies on strong bases or preinstalled directing groups. Therefore, it is of great importance to address the challenges in developing an efficient and concise protocol for the construction of substituted metallocenes.

**Fig. 1 Synthesis of metallocene phosphine ligands.**

**a)** Representative metallocenes and their derivatives

Ferrocene  Ruthenocen  DPPF  PPFA  mono-RuPHOX  Ophos

**b)** General strategies for selectively synthesizing substituted metallocenes and their derivatives

Base then M—Ln

Base = R—Li, Na—H, etc.

**c)** Regioselectivity challenges in the direct dehydrogenative functionalization of unsymmetric metallocenes

Site-selective differentiation of six similar sp² C—H bonds?

And other potential regioisomers...

**d)** This work: Electrochemically driven regioselective C—H phosphorylation of group 8 metallocenes

Compared with the biscyclopentadienyl complex, the direct C—H functionalization of indenyl metallocenes poses an additional challenge in regiocontrol. Bearing six similar sp² C—H bonds on indenyl moiety, the 4-substituted indenyl metallocene is a representative unsymmetric substrate for C—H functionalization. Theoretical, six possible regioisomers would be expected to form. We propose to develop a system to control the regioselectivity through site-selective differentiation of the six similar sp² C—H bonds. Based on the principle of mass conservation, this direct C—H functionalization will generate one molar equivalent of hydrogen gas or an associated byproduct. Usually, an external oxidant is required as a hydrogen scavenger. Meanwhile, electrochemical synthesis has emerged as a powerful method to facilitate oxidative cross-coupling reactions under external-oxidant-free conditions through anodic oxidation. Especially, electrochemical phosphorylation has emerged as a complementary approach to conventional methods for forming C—P bonds.

Here, we report an efficient regioselective C—H phosphorylation of group 8 metallocenes. This oxidative cross-coupling
Table 1 Optimization of reaction conditions.

| Entry | Deviation from standard conditions | Yield (%) |
|-------|-----------------------------------|-----------|
|       |                                   | 3a  | 4a  | 5a  | 6a  |
| 1     | None                              | 79 (73<sup>b</sup>) | 1   | 3   | 8   |
| 2     | without electricity               | 0   | 0   | 0   | 0   |
| 3     | C rod as anode                    | 59  | 2   | 3   | 6   |
| 4     | Pt plate as anode                 | 62  | 3   | 2   | 3   |
| 5     | 4a as electrolyte                 | 47  | 0   | 0   | 10  |
| 6     | LiClO<sub>4</sub>·3H<sub>2</sub>O as electrolyte | 45  | 2   | 4   | 15  |
| 7     | 3.0 mA                             | 32  | 5   | 6   | 33  |
| 8     | 5.0 mA                             | 12  | 9   | 3   | 28  |
| 9     | without Et<sub>3</sub>N           | 39  | 0   | 2   | 3   |
| 10    | NaOAc as base                     | 61  | 1   | 2   | 4   |
| 11    | K<sub>3</sub>PO<sub>4</sub> as base | 49  | 0   | 7   | 3   |
| 12    | TFE as solvent                    | 16  | 3   | 1   | 4   |
| 13    | DCE as solvent                    | 24  | 3   | 1   | 1   |
| 14    | MeCN as solvent                   | 38  | 0   | 4   | 0   |
| 15    | RT instead of 50 °C               | 52  | 1   | 2   | 4   |

TFE, trifluoroethanol; DCE, 1,2-dichloroethane.

<sup>a</sup>Conditions: Undivided cell, constant current (2.0 mA), 1a (0.20 mmol), 2a (0.40 mmol), Bu<sub>4</sub>NNOAc (0.20 mmol), Et<sub>3</sub>N (0.40 mmol), MeOH (4.0 mL), 50 °C, under N<sub>2</sub>, 6 h, 2.2 F/mol. Yields were determined by <sup>1</sup>H NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard.

<sup>b</sup>Isolated yield.

Protocol features broad substrate scope and mild conditions while avoiding the use of directing groups and external oxidants.

**Results**

**Reaction optimization.** Initially, under electrolysis conditions, benzoferrocene 1a and diphenyl phosphine oxide 2a were selected as model substrates to optimize the reaction. The reaction was conducted under constant current in an undivided cell equipped with a reticulated vitreous carbon (RVC) anode and a platinum plate cathode (Table 1). Using Bu<sub>4</sub>NOAc as the electrolyte, monophosphorylated product 3a was obtained in high regioselectivity and 73% yield in MeOH (entry 1). It is notable that small amounts of over phosphorylated products (4a, 5a, and 6a) were obtained. No desired reaction occurred in the absence of current (entry 2). Other electrode materials, including Pt and graphite anode, were found to be less effective in terms of reactivity (entries 3 and 4). The use of an alternative electrolyte, such as Bu<sub>4</sub>NBF<sub>4</sub> or LiClO<sub>4</sub>·3H<sub>2</sub>O lowered reaction efficiency (entries 5 and 6). Increasing the current to 3.0 or 5.0 mA had a negative effect on selectivities and favored the formation of bisphosphorylated products 4a–6a (entries 7 and 8). On the other hand, conducting the electrolysis without Et<sub>3</sub>N resulted in a lower yield (entry 9). Other basic additives such as NaOAc and K<sub>3</sub>PO<sub>4</sub> failed to give better results (entries 10 and 11). Solvents such as TFE (Trifluoroethanol), DCE (1,2-Dichloroethane), and MeCN were screened as well, but lower yields were obtained (entries 12–14). Notably, the electrochemical reaction could also be performed at RT (room temperature), although with a slight decrease in yield (entry 15). And the use of stoichiometric oxidants (e.g., AgF, MnO<sub>2</sub>, and DDQ (1,2-Dichloro-4,5-Dicyanobenzoquinone), etc.) for this phosphorylation gave low yields (See Supplementary Table 1 in Supporting Information).

**Substrate scope.** Having identified optimized conditions, we next evaluated the phosphorylation of different benzoferrocenes with diphenyl phosphine oxide 2a (Fig. 2a). The presence of a Br, Me, or Ph group at the α-position of the aryl ring of 1-methylbenzoferrocenes were all well tolerated to afford the phosphorylated products in decent yields (3a–3c). It should be noted that even when either Cp (cyclopentadienyl) or phenyl rings on the benzoferrocene substrates were naked, the phosphorylation still occurred at the α-position of phenyl ring (3d–3f). Some of the relatively low yields (3d and 3e) were due to low conversion or decomposition of substrates rather than regioselective issues. These results suggest that the Br atom on model substrate 1a does not act as an activating or directing group in this protocol. Due to its electron deficiency, theaza-benzoferrocene substrate was not applicable in this case (3g).

Subsequently, we turned our attention to the investigation of the scope of phosphine oxides with Br-substituted benzoferrocenes, which was good for further derivatization. As shown in Fig. 2b, phosphine oxides containing electron-donating or electron-withdrawing groups, such as Me, Bu, Ph, OCF<sub>3</sub>, Cl, and F, at the para position of the aryl components, all resulted in good yields (3h–3m). Likewise, substrates with substituents at the meta-position of the aryl components also exhibited good reactivities and delivered the corresponding products in 60–75% yields (3n–3q). Delightfully, the reaction also demonstrated good tolerance for the phosphine oxide bearing a heterocyclic 2-thiophenyl group (3r) which is usually problematic under transition metal catalysis. To our surprise, the desired reactions also worked when benzoferrocenes with the α-positions of the aryl components blocked were subjected to the standard conditions (Fig. 2c, 3s–3w). Less than 10% of the corresponding 2-phosphorylated products could be observed for these substrates. Meanwhile, over phosphorylations and
decomposition of substrates resulted in the relatively low yields (3s–3w). The regioselectivity and molecular structures of 3q and 3v were unambiguously determined by single-crystal X-ray diffraction analysis.

Additionally, the current electrochemical protocol was also suitable for the phosphorylation of simple ferrocene substrates (Fig. 3a). Substrates bearing either electron-donating or electron-withdrawing groups at the phenyl rings of phosphine oxides were all tolerated and gave the phosphorylated products in 48–75% yields (8a–8g). 1-Naphthylphosphine oxide was applicable to the standard condition as well (8h), while subjecting 2-thiophenyl phosphate oxides to the reaction could only deliver the desired product in a 38% yield (8i). For the substrate 1,1′-dibenzyferrocene, the products of o-phosphorylation and m-phosphorylation were isolated respectively in 1:2.8 ratio. Next, pentamethylferrocene and their analogs were tested with various phosphine oxides (Fig. 3b). These reactions proceeded successfully and all occurred at the bare Cp rings, leading to products in 36–75% yields (8k–8y). Unfortunately, the phosphorylation of ruthenocene initially failed due to its low solubility in MeOH. To overcome this drawback, DCE was chosen as solvent and LiClO4+3H2O was selected as an electrolyte in this case. Under the modified condition, ruthenocene reacted with a series of phosphine oxides smoothly and delivered products in decent yields (10a–10g), which further highlights the generality of the current strategy. The structure of ruthenocenyl phosphate oxide 10e was also further confirmed by single-crystal X-ray diffraction analysis.
Mechanistic investigations. To probe the mechanism of this electrochemically enabled C−H phosphorylation of metallocenes, preliminary mechanistic investigations have been conducted (Fig. 4). The addition of radical scavengers TEMPO (2,2,6,6-tetramethylpiperidinox) to the reaction mixture almost suppressed the reactivity (Fig. 4a, entry 2 vs 1). Using BHT (butylated hydroxytoluene) and 1,2-diphenylethylene as a radical scavenger, the phosphorylated products 12a and 12b were isolated in 25 and
Fig. 4 Mechanistic investigations. a Radical inhibition and capture experiments. b Control experiments of ferrocenium. c Kinetic studies. d Catalytic C–H phosphorylation of naphthalene facilitated by ferrocene. e Cyclic voltammograms (CVs).
18% yield respectively (entries 3–4)\textsuperscript{71}. Besides, radical clock reaction with 2 equiv. of (1-cyclopropylvinyl)benzene (11c) led to the ring-opened product 12c (entry 5)\textsuperscript{72}. The above experiments are strongly suggestive of a phosphinyl radical species being involved in this reaction.

In order to get insight into this electrochemical process, control experiments of ferrocenium were carried out (Fig. 4b). Conducting electrolysis by replacing ferrocene with ferrocenium 13a under the standard conditions gave a 50% yield of 8a accompanied by 7a (entry 1). Notably, an 18% yield of 8a could be obtained without electricity. A similar phenomenon was also observed in the control experiments with 7d (entries 3–4). Interestingly, some amount of phosphorylation product 8r was still obtained in the absence of electricity. These results suggest that this phosphorylation may undergo through the ferrocenium species. Kinetic studies on the coupling of 7a with 2a showed phosphorylation product 8a was generated continuously at the first 4h (Fig. 4c).

Surprisingly, a small amount of 16 was observed when the kinetic studies of phosphorylation of 7a were performed using naphthalene as the internal standard (Fig. 4c, d). Only 2% phosphorylated naphthalene could be obtained without 7a under standard conditions (Fig. 4d, entry 1). The addition of a catalytic amount of ferrocene 7a or ferrocenium 13a helped the formation of 16 (entries 2 and 3). Through rough optimization with ferrocene as a redox catalyst, the yield of 16 was improved to 54% (entries 4 and 5). Therefore, the above experiments suggested that the ferrocene could act as a redox catalyst in phosphorylation.

Next, cyclic voltammograms (CVs) of 7a were conducted under different conditions to gain mechanistic insight (Fig. 4e). The oxidation potential of ferrocene 7a was 0.44 V (curve I). Although compound 2a exhibited no apparent peak from 0 to 1.6 V (Supplementary Fig. 1, curve V, Supporting Information)\textsuperscript{50}, \textsuperscript{65}, \textsuperscript{69}, \textsuperscript{2a} showed an oxidative potential at 1.25 V in the presence of the base NaOMe (Supplementary Fig. 1, curve V1, Supporting Information). No significant change on the CVs of 7a was observed in the presence of 2a (curve II) and adding Et3N had no remarkable change (curve III). However, a catalytic current could be observed when 7a was mixed with 2a and NaOMe (curve IV)\textsuperscript{59}. A comparison of curves IV and V1 (Fig. S1), the voltammogram of the conjugate base of 2a, suggested that the current increase of curve IV did not result from the oxidation of phosphine oxide anion. The above results suggest that the addition of NaOMe facilitates the oxidation of 2a with ferrocenium. Notably, MeO– is assumed to be generated at the cathode through the reduction of MeOH. Based on the CVs of the metallocene substrates and products, the observed oxidation potentials could account for the reactivity difference between electron-rich and electron-deficient metallocenes (Fig. 4e).

Based on the experimental results above and literature precedent, a proposed mechanism is shown in Fig. 5. The electrolytic process begins with the anodic oxidation of 7a that produces ferrocenium ion B. Meanwhile, the addition of Et3N facilitates deprotonation of 2 for the formation of anion A. A first single-electron transfer (SET) between anion A and ferrocenium ion B generates phosphinyl radical C and ferrocene 7a. Subsequently, the in situ formed phosphinyl radical C adds to ferrocene 7a to yield radical species D. A second SET between radical D and ferrocenium ion B delivers the desired phosphorylation product 8 and regenerates ferrocene 7a for the next cycle. The hydrogen is released at the cathode. Therefore, an external oxidant is not required in this cross dehydrogenative phosphorylation.

In order to interpret the unexpected high regioselectivity in the phosphorylation of benzoferrocenes 1, the structural properties of 1e and 1h have been shown in Fig. 5b. Some important bond lengths are given according to the single-crystal X-ray diffraction analysis. For these substrates, the bond lengths of C(5)=C(6) and C(7)=C(8) are between 1.35–1.37 Å which are shorter than that of benzene (1.39 Å). The bond lengths for the rest of the C–C bonds on the indenyl motif are ~1.42 Å. These results suggest higher electron density is located around C(5)=C(6) and C(7)=C(8) and makes them more nucleophilic. Taking 1a as the example for regioselectivity interpretation, the four most likely radical species D (D1–D4 of 1a) will be expected to form via the reaction of phosphinyl radical C with benzoferrocene 1a. Based on the distribution of electron density on the indenyl motif, D1-1a is the least favored species to generate. Owing to the steric hindrance of the bromine atom, the formation of D4-1a is not preferred. Stronger ability on the stabilizing the allylic radical species make D2-1a preferentially yielded over D3-1a. The electron density distribution on the indenyl motif also results in the formation of 6a as the major bisphosphorylated side product.

Fig. 5 Proposed mechanism. a Proposed mechanism. b Regioselectivity interpretation.
Finally, gram-scale preparations of 8a (1.02 g) and 3a (1.74 g) were carried out to demonstrate the efficacy of this protocol (Fig. 6a, b). Further synthetic elaborations of these materials were conducted to show the synthetic utility. For instance, a strong single-electron oxidant 17 could be synthesized through the oxidation of 8a with BQ (1,4-Benzoquinone) in the presence of HPF6. Meanwhile, ferrocene-based phosphine 18 could be prepared via reduction of 8a with HSiCl3. Through a selective sp2 C−H activation, amination product 19 was produced under Ir catalysis. Besides, 1,1′-disubstituted ferrocenyl phosphine oxide 20 could be obtained with high regioselectivity through Friedel−Crafts acylation of 8a. Further reduction of 20 with LiAlH4 delivered alcohol 21. For the reduction of 3a, phosphine product 22 was isolated with a bromine atom intact. Additionally, 3b could be obtained via Ni-catalyzed Kumuda coupling reaction. Interestingly, with nBu4NPF6 as the electrolyte, a selective sp3 C−H etherification of 3a occurred efficiently in MeOH to deliver product 23. Furthermore, another different phosphinyl moiety can be installed on benzoferrocenes to obtain highly functionalized 24, which would otherwise be challenging to synthesize via traditional means.

Fig. 6 Scale-up preparations and synthetic transformations. a Scale-up preparation and synthetic transformation of 8a. b Scale-up preparation and synthetic transformation of 3a.
In this work, we have developed an electrochemically driven regioselective cross-coupling of group 8 metalloccenes with phosphine oxides. Without preinstalled directing groups or pyrophoric alkyl lithium reagent, over 60 examples of phosphorylated (benzo)ferrocenes and ruthenocene are easily accessed through this intramolecular dehydrogenative C–H phosphorylation. Mechanistic studies suggest that the desired C–P bond is constructed through a radical substitution between phosphoryl radical and metallic core. Meanwhile, the metalloccene acts as a single-electron transfer reagent for radical generation and quenching. The high regioselectivity for the C–H phosphorylation of benzoferrocenes is a consequence of the unequal electron density distribution on the indenyl motif.

Methods

General procedures for electrochemically driven C–H phosphorylation of ferrocenes or benzoferrocenes. (Method A): In an oven-dried undivided three-necked flask equipped with a stir bar, ferrocenes or benzoferrocenes (0.20 mmol), diphenyl phosphate oxide (0.40 mmol), Et,N (0.40 mmol), *Bu,N,Ac (0.20 mmol), and MeOH (4 mL) were combined. The flask was equipped with PVC (100 PPI, 15 mm × 10 mm × 5 mm) as the anode and platinum plate (10 mm × 10 mm × 0.3 mm) as the cathode under inert atmosphere in a nitrogen glove box. The flask was capped with a septum. The reaction mixture was stirred and electrolyzed at a constant current of 2.0 mA at 50 °C for 6–12 h. Upon reaction completion, the reaction crude was washed with water and the product was extracted with dichloromethane (10 × 3 mL). The organic layers were combined, dried over Na₂SO₄, and concentrated. The pure product was obtained after flash column chromatography on silica gel (petroleum: ethyl acetate = 1:1–4:1).

General procedures for electrochemically driven C–H phosphorylation of ruthenocene. (Method B): In an oven-dried undivided three-necked flask equipped with a stir bar, ruthenocenes (0.20 mmol), diphenyl phosphate oxide (0.40 mmol), Bu,N (0.40 mmol), LiClO₄·H₂O (0.30 mmol), and DCE (4 mL) were combined. The flask was also equipped with PVC (100 PPI, 15 mm × 10 mm × 5 mm) as the anode and platinum plate (10 mm × 10 mm × 0.3 mm) as the cathode under inert atmosphere in a nitrogen glove box. The flask was capped with a septum. The reaction mixture was stirred and electrolyzed at a constant current of 6.0 mA at 50 °C for 10 h. Upon reaction completion, the reaction crude was washed with water and the product was extracted with dichloromethane (10 mL × 3). The organic layers were combined, dried over Na₂SO₄, and concentrated. The pure product was obtained after flash column chromatography on silica gel (petroleum: ethyl acetate = 1:1–4:1).

Data availability

The X-ray crystallographic data for compounds 1, 1h, 3q, 3‘v, 8a, 8i, 10e, and 24 have been deposited in the Cambridge Crystallographic Data Centre (CCDC), under deposition numbers CCDC 2122111, CCDC 2123434, CCDC 2122916, CCDC 2124274, CCDC 2122023, CCDC 212026, CCDC 212018, and CCDC 2124271, respectively [www.ccdc.cam.ac.uk/data_request/cif]. The data that supports the findings of this study, including experimental details and compound characterization, are available within the manuscript and its Supplementary Information files. All data are available from the corresponding author upon request.

Received: 25 January 2022; Accepted: 1 June 2022; Published online: 17 June 2022

References

1. Kealy, T. J. & Pauson, P. L. A new type of organo-iron compound. *J. Am. Chem. Soc.* 72, 4971–4973 (1952).
2. Miller, S. A., Tebboh, J. A. & Tremaine, J. F. Dicyclopentadienyliron. *J. Chem. Soc.* 632–635 (1952).
3. Dunietz, J. D. & Orgel, L. E. Bis-cyclopentadienyl iron: a molecular sandwich. *Nature* 171, 121–122 (1953).
4. Dunietz, J. D., Orgel, L. E. & Rich, A. The crystal structure of ferrocene. *Acta Crystallogr.* 9, 373–375 (1956).
5. Takahashi, S. & Anzai, J.-i Recent progress in ferrocene-modified thin films and nanoparticles for biosensors. *Materials* 6, 5742–5762 (2013).
6. Peterschmig, R. Polymers with pendant ferrocenes. *Chem. Soc. Rev.* 45, 5216–5231 (2016).
37. Liu, L., Song, H., Liu, Y. H., Wu, L. S. & Shi, B. F. Achiral (Cp1=Ir)-x(III)/chiral carboxylic acid catalyzed enantioselective C–H amidation of ferrocenes under oxidative conditions. Acc. Catal. 10, 7117–7122 (2020).

38. Lou, S. J., Zhuo, Q. D., Nishura, M., Luo, G. & Hou, Z. M. Enantioselective C–H alkenylation of ferrocenes with alkenes by half-sandwich scandium catalyst. J. Am. Chem. Soc. 134, 2470–2476 (2021).

39. Zhu, L. et al. Electrocatalytic generation of amide radicals for olefin hydroamination: Use of solvent effects to enable anilide oxidation. Angew. Chem. Int. Ed. 55, 2226–2229 (2016).

40. Yan, M., Kawamata, Y. & Baran, P. S. Synthetic organic electrochemical methods since 2000: On the verge of a renaissance. Chem. Rev. 117, 13230–13319 (2017).

41. Tang, S., Liu, Y. & Lei, A. Electrochemical oxidative cross-coupling with hydrogen evolution: a green and sustainable way for bond formation. Chem 4, 27–45 (2018).

42. Yang, Q.-L., Fang, P. & Mei, T.-S. Recent advances in organic electrochemical C–H functionalization. Chin. J. Chem. 36, 338–352 (2018).

43. Wang, H., Gao, X., Lv, Z., Abdellah, T. & Lei, A. Recent advances in oxidative R1–H/R2–H cross-coupling with hydrogen evolution via photo-/electrochemistry. Chem. Rev. 119, 6769–6787 (2019).

44. Xiong, P. & Xu, H. C. Chemistry with electrochemically generated N-centered radicals. Acc. Chem. Res. 52, 3339–3350 (2019).

45. Yuan, Y. & Lei, A. Electrochemical oxidative cross-coupling with hydrogen evolution reactions. Acc. Chem. Res. 52, 3309–3324 (2019).

46. Yuan, Y. et al. Exogenous-oxidant-free electrochemical oxidative C–H phosphorylation with hydrogen evolution. Chem. Commun. 55, 4230–4233 (2019).

47. Chang, X., Zhang, Q. & Guo, C. Asymmetric electrochemical transformations. Angew. Chem. Int. Ed. 59, 12612–12622 (2020).

48. Jiao, K. J., Xing, Y. K., Yang, Q. L., Qiu, H. & Mei, T. S. Site-selective C–H functionalization via synergistic use of electrochemistry and transition metal catalysis. Acc. Chem. Res. 53, 300–310 (2020).

49. Meyer, T. H., Choi, I., Tian, C. & Ackermann, L. Powering the future: how can electrochemistry make a difference in organic synthesis? Chem. Sci. 6, 2484–2496 (2020).

50. Kurimoto, Y., Yamashita, J., Mitsudo, K., Sato, E. & Saga, S. Electrolysis of phosphaalkanes via dehydrogenation of C–P bond formation using DABCO as a mediator. Org. Lett. 23, 3120–3124 (2021).

51. Zhu, C., Ang, N. W. J., Meyer, T. H., Qiu, Y. & Ackermann, L. Organic electrochemistry: molecular syntheses with potential. ACS Cent. Sci. 7, 415–431 (2021).

52. Zhao, Y. et al. Oxidative cross-coupling through double transmetallation: Surprisingly high selectivity for palladium-catalyzed cross-coupling of alkylzinc and alkynyllanthanides. J. Am. Chem. Soc. 128, 15048–15049 (2006).

53. Li, C. J. Cross-dehydrogenative coupling (CDC): exploring C–C bond formations beyond functional group transformations. Acc. Chem. Res. 42, 335–344 (2009).

54. Chen, M., Zheng, X. L., Li, W. Q., He, J. & Lei, A. W. Palladium-catalyzed aerobic oxidation of alkynes with terminal alkynes by alkylzinc reagents. J. Am. Chem. Soc. 132, 4101–4103 (2010).

55. Le Bras, J. & Muzzart, J. Intermolecular dehydrogenative Heck reactions. Chem. Rev. 111, 1170–1214 (2011).

56. Liu, C., Zhang, H., Shi, W. & Lei, A. Bond formations between two nucleophiles: transition metal catalyzed oxidative cross-coupling reactions. Chem. Rev. 111, 1780–1824 (2011).

57. Yeung, C. S. & Dong, V. M. Catalytic dehydrogenative cross-coupling: beyond functional group transformations. Acc. Chem. Res. 49, 1440–1448 (2016).

58. Deng, Y. et al. Electrochemical regioselective phosphorylation of nitrogen-containing heterocycles and related derivatives. Adv. Synth. Catal. 363, 464–469 (2021).

59. Sei, N., Martins, G. M., Shirinfar, B. & Ahmed, N. Electrochemical phosphorylation of organic molecules. Chem. Rev. 20, 1530–1552 (2020).

60. Long, H. et al. Electrochemical C–H phosphorylation of amines in continuous flow suitable for late-stage functionalization. Nat. Commun. 12, 6629 (2021).

61. Lu, L., Li, H. & Lei, A. Oxidative cross-coupling reactions between two nucleophiles. Chin. J. Chem. 40, 256–266 (2021).

62. Wang, S., Xue, Q., Guan, Z., Ye & Lei, A. Mn-catalyzed electrooxidative undirected C–H/P–H cross-coupling between aromatics and diphenyl phosphine oxides. ACS Catal. 11, 4245–4250 (2021).

63. Zhu, P.-W., Yang, Y.-T., Li, Y., Zhu, J. & Wu, L. Electrochemical oxidative C–H phosphorylation of thiourea derivatives in ambient conditions. Mol. Catal. 517, 112022 (2022).

64. Qiu, X. et al. Visible-light-induced ligand-free RuCl3 catalyzed C–H phosphorylation in water. Chem. Commun. 56, 4704–4707 (2020).

65. Lei, T. et al. Cobaloxime catalysis for enamine phosphorylation with hydrogen evolution. Org. Lett. 22, 5385–5389 (2020).

66. Khorbradage, D. A. et al. Acceptor-substituted ferrocenium salts as strong, single-electron oxidants: synthesis, electrochemistry, theoretical investigations, and initial synthetic application. Chem. Eur. J. 18, 12267–12277 (2012).

67. Gwon, D., Park, S. & Chang, S. Dual role of carboxylic acid additive: mechanistic studies and implication for the asymmetric C–H amidation. Tetrahedron 71, 4504–4515 (2015).

68. Xiong, P. et al. Site-selective electrooxidation of methyalenes to aromatic acetics. Nat. Commun. 11, 2706 (2020).

Acknowledgements
We thank Prof. Kevin G. M. Kou (UCR), Prof. Hai-Chao Xu (Xiamen University), and Prof. Zhi-Shi Ye (DUT) for helpful discussions and manuscript revisions. Financial support from the Dalian Institute of Chemical Physics (DICP201902, Q.-A.C.), Dalian Outstanding Young Scientific Talent (2020RJ-05, Q.-A.C.), and the National Natural Science Foundation of China (20271239, Q.-A.C.) is acknowledged.

Author contributions
Q.-A.C. conceived and supervised the project. Q.-A.C. and H.Z. designed the experiments and analyzed the data. All authors discussed the results and commented on the manuscript.

Competing interests
The authors declare no competing interests.

Additional information
Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41467-022-31178-7.

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Peer review information Nature Communications thanks Yulia H. Budnikova and the anonymous reviewer(s) for their contribution to the peer review of this work.

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