Non-Directed Pd-Catalyzed Electrooxidative Olefination of Arenes

Subir Panja,^a Salman Ahsan,^b Tanay Pal,^a Simon Kolb,^c Wajid Ali,^a Sulekha Sharma,^b Chandan Das,^a Jagrit Grover,^a Arnab Dutta,^{a,*} Daniel B. Werz,^{c,*}, Amit Paul,^{b,*} and Debabrata Maiti ^{a,*}

^aIIT Bombay, Department of Chemistry, Powai, Mumbai 400076, India, E-mail: dmaiti@iitb.ac.in (DM); arnabdutta@chem.iitb.ac.in(AD) ^bIndian Institute of Science Education and Research (IISER) Bhopal, Department of Chemistry, Bhopal, Madhya Pradesh 462066, India, E-mail: apaul@iiserb.ac.in

^cTechnische Universität Braunschweig, Institute of Organic Chemistry, Hagenring 30, 38106 Braunschweig, Germany, E-mail: d.werz@tu-braunschweig.de

ABSTRACT: The Fujiwara-Moritani reaction is a powerful tool for the olefination of arenes by Pd-catalyzed C–H activation. However, the need for superstoichiometric amounts of toxic chemical oxidants makes the reaction unattractive from an environmental and atom-economical view. Herein, we report the first non-directed and regioselective olefination of simple arenes *via* an electrooxidative Fujiwara-Moritani reaction. The versatility of this operator-friendly approach was demonstrated by a broad substrate scope that includes arenes, heteroarenes and a variety of olefins. Electroanalytic studies suggest the involvement of a Pd(II)/Pd(IV) catalytic cycle *via* a Pd(III) intermediate.

KEYWORDS: C-H activation • Pd catalysis • olefination • synthetic electrochemistry • Pd(III) intermediate

Transition metal-catalyzed C-H functionalization reactions have increasingly gained importance over the last few decades since they allow direct and rapid installation of functionality. Regardless of the undeniable synthetic value of such transformations, the need for superstoichiometric quantities of expensive and hazardous oxidants (e.g., silver and copper salts) remains a major drawback from a sustainable chemistry perspective.^{1,2} Additionally, chemical oxidants often lead to the formation of byproducts, hindering purification and decreasing atom economy. To make chemical processes and transformations intrinsically sustainable, organic chemists re-discovered synthetic electrochemistry as an environmental friendly approach.³⁻⁶ Electroorganic synthesis utilizes electric current to realize redox processes and thereby avoids the use of dangerous, expensive, and polluting chemical oxidizing or reducing agents. Precise control of electrochemical reaction parameters often leads to commendable reactivity and chemoselectivity, and hence to an improved atom economy. In addition, electrochemical processes fulfil the expectations of sustainability since electricity can be generated from renewable energy sources, such as wind, sunlight or biomass. Recent efforts in the field of electrochemical C-H activation resulted in significant progress towards efficient C-C and C-heteroatom bond formations.7-10 Hence, the utilization of electric current as an alternative oxidant in Pd-catalyzed C-H functionalizations is emerging as an attractive alternative to stoichiometric reagents.¹¹⁻¹³

The Fujiwara-Moritani reaction is one of the earliest known examples of Pd-catalyzed oxidative C–H functionalizations for C–C bond formation.¹⁴ This extraordinary $C(sp^2)$ –H alkenylation reaction avoids the use of prefunctionalized starting materials; however, it suffers from the drawbacks of regioselectivity, reactivity and use of excess arenes.¹⁵ Since its development, a number of modified strategies have been reported by different research groups to address the issue of reactivity and selectivity.¹⁶⁻²¹ In recent time, the ligand assisted oxidative C–H alkenylation of arenes without directing substituents has been established as one of the major strategies to overcome the reactivity issue and to elaborate the substrate scope.

Scheme 1. Recent approaches to sustainable C–H alkenylation reactions.



However, the regioselectivity for most of the sterically and electronically unbiased arenes is still not up to the mark. The most recent studies on the non-directed oxidative C–H olefination of arenes were reported independently by Yu and van Gemmeren (Scheme 1). The Yu group employed electron-deficient 2-pyridone as a X-type ligand for the olefination of both electron-rich and electron-poor arenes including heteroarenes as the limiting reagent (Scheme 1a).¹⁸ The pyridone ligand improves the selectivity in a non-directed approach as comparable to directed C–H olefination reaction by enhancing the influence of steric effects.

On the other hand, the van Gemmeren group utilizes two complimentary ligands *N*-Ac-Gly-OH and a 6-methylpyridine derivative in a 1:1 ratio to accomplish the non-directed olefination reaction of arenes (Scheme 1b).²⁰ Despite the indisputable advances made by these research groups in the area of non-directed oxidative C–H olefination of arenes, the use of superstoichiometric amounts of toxic and waste generating oxidants (Ag salts) deciphers into a strong call for an environmentally responsive and atom-economic protocol.

In 2007, Jutand reported the directing group assisted Pd-electrocatalyzed ortho-olefination of acetyl protected aniline in a divided cell by utilizing catalytic amounts of benzoquinone as a redox mediator (Scheme 1c).^{22a} A Rh-catalyzed ortho-C-H olefination of benzamide was developed through an electrooxidative pathway by the Ackermann group (Scheme 1d).^{22b} Simple arenes that bear no directing groups are cheap, easily available and very desirable starting materials. However, such arenes are significantly more challenging for selective functionalization as transformations often result in the formation of complex product mixtures. With no report of an electrooxidative Pd-catalyzed $C(sp^2)$ -H alkenylation of simple arenes present, we wish to present such a variant of the Fujiwara-Moritani reaction (Scheme 1e). The developed method proceeds through a nondirected pathway and is controlled by stereoelectronic factors. This protocol does not require additional chemical oxidizing agents and is executed using an operator-friendly undivided cell setup.

 Table 1. Optimization of the non-directed Pd-catalyzed electrooxidative olefination of simple arenes^a

+	O''Bu Pd(OAc) ₂ (10 md	>	\bigcirc		
	TBAPF ₆ (0.5 equiv.), DC <i>j</i> = 2.5 mA/cm ² , rt,	E (3 mL) 15 h	1 [β:α >25:1]		
Entry	Alteration from	Yield	Selectivity		
	standard conditions	of 1	(β :α)		
		(%)			
1	none	70	>25:1		
2	Co(OAc)2•4H2O in-	9	1:1		
	stead of Pd(OAc) ₂				
3	[Ru(p-cymene)Cl ₂] ₂	NR			
	instead of Pd(OAc) ₂				
4	$Pd(OAc)_2 (5 mol\%)$	51	>25:1		
5	$Pd(OAc)_2$ (20 mol%)	71	>25:1		
6	L2 instead of L1	45	8:1		
7	L3 instead of L1	59	20:1		
8	L4 instead of L1	19	5:1		
9	L5 instead of L1	8	1:1		
10	Benzoquinone	68	>25:1		
	(10 mol%)				
11	PivOH (1.0 equiv.)	61	20:1		
12	Ni foam instead of Pt	64	>25:1		

13	GF instead of Pt	49	15:1
14	Steel instead of Pt	31	13:1
15	6 mA/cm ² instead of	27	11:1
	2.5 mA/cm^2		
16	24 h reaction time	47	20:1
17	12 h reaction time	56	21:1
18	no electricity	NR	-
19	no Pd(OAc) ₂	NR	-
	² Me NO ₂ I OH		
L1	L2 L3	L4	L5

^{*a*} Standard reaction conditions: undivided cell, GF anode, Pt cathode, $j = 2.5 \text{ mA/cm}^2$, naphthalene (0.2 mmol), *n*-butyl acrylate (0.5 mmol), Pd(OAc)₂ (10 mol%), **L1** (20 mol%), TBAPF₆ (0.5 equiv.), DCE (3 mL), 15 h, under air. ^{*b*} Yield determined by ¹H-NMR. NR = no reaction; TBAPF₆ = tetra-*n*-butylammonium hexafluorophosphate. GF = graphite felt. Surface area of electrodes dipped in solution = 0.7 cm x 0.7 cm, current = 1.225 mA and current density = 2.5 mA/ cm² (electrochemical surface area = 1.23 cm²).

To start our study, naphthalene was chosen as a challenging substrate because of its ability to form α - and β -products. We examined various reaction conditions for the desired Pd-catalyzed electrooxidative C-H alkenylation in a simple undivided cell setup (Table 1, and see Supporting Information Tables S1-S8) with *n*-butyl acrylate acting as the coupling partner. After rigorous optimization, we found that naphthalene reacts with nbutyl acrylate in dichloroethane (DCE) in the presence of $Pd(OAc)_2$ (10 mol%), ligand L1 (20 mol%), and the electrolyte tetra-*n*-butylammonium hexafluorophosphate (TBAPF₆, 0.5equiv.) while employing a graphite felt anode and a platinum cathode maintaining constant current electrolytic conditions $(i = 2.5 \text{ mA/cm}^2, \text{ Table 1, entry 1})$. The desired β -olefinated product was formed in 70% yield and with > 25:1 regioselectivity $(\beta; \alpha)$. Other transition metal catalysts such as $Co(OAc)_2 \cdot 4H_2O$ or $[Ru(p-cymene)Cl_2]_2$ as substitutes for $Pd(OAc)_2$ were found to be completely ineffective (entries 2) and 3). Changes in the catalyst loading were not found to be beneficial (entries 4 and 5).

Notably, in the present transformation the ligand has a major influence on the reactivity and selectivity aspects (see Supporting Information, Table S4). After studying a series of 2-pyridone, pyridine and amino acid-based ligands L2-L5 it was found that L1 is the optimal ligand since it provided superior yield and selectivity (entries 6–9). Addition of catalytic amounts of *p*-benzoquinone as a redox mediator (entry 10) or pivalic acid as an additive (entry 11, Table 1) had minimal influence on the reaction outcome. While nickel foam as cathode material shows similar efficiency, the use of a carbon felt or a steel cathode led to lower reactivity and selectivity

Scheme 2. Evaluation of simple arenes and heteroarenes in the electrochemical olefination^{*a*}



^aReaction conditions: undivided cell, GF anode, Pt cathode, j = 2.5 mA/cm² or j = 1.5 mA/cm², corresponding arenes or heteroarenes (0.2 mmol), *n*-butyl acrylate (0.5 mmol), Pd(OAc)₂ (10 mol%), L1 (20 mol%), TBAPF₆ (0.5 equiv.), DCE (3 mL) or 5:1 ration of dichloroethane (DCE) and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), 15 h, under air. ^bYields of isolated products are reported.

(entries 12–14). Increasing the electric current density ($j = 6 \text{ mA/cm}^2$) was detrimental since it provided the desired product in low yield (27%) and with decreased β : α -selectivity (11:1; entry 15). Additionally, longer and shorter reaction times resulted

in lower yields of the olefinated product **1** (entries 16 and 17). Finally, control experiments confirmed that both electric potential and $Pd(OAc)_2$ are essential to furnish the reaction products (entries 18 and 19, Table 1).

With optimized reaction conditions in hand, reaction generality was explored by testing a range of substituted arenes and heteroarenes with n-butyl acrylate (Scheme 2). Following the olefination of naphthalene (69%, > 25:1 β : α selectivity), 1,2,3,4tetrahydronaphthalene was successfully reacted (52%, 11:1 β : α -selectivity). Next, we applied our standard reaction conditions to benzene and found them not to be equally effective as only 25% of the olefinated product 3 was obtained. As a result, further optimizations of electric current density and solvent were carried out to enhance the yield (see Supporting Information, Table S9). To our satisfaction, the yield of product 3 increased to 63% when the electrolysis was carried out with an electric current density of $j = 1.5 \text{ mA/cm}^2$ and in a solvent mixture of DCE/HFIP (5:1). These modified reaction conditions were applied for the electrosynthesis of all other olefinated products 4-22 (Scheme 2). The olefination of 1,3,5-trimethoxybenzene and mesitylene with n-butyl acrylate proceeded smoothly under the revised reaction conditions to afford products 4-6 in up to 65% yield. The regioselectivity issue was more prominent for arenes bearing two or more electronically similar C-H bonds. (e.g., electron-rich arenes: ortho vs. para). Dimethoxy benzene gives β -selective olefinated product **6** (β : α ; 7:1). While toluene was converted with para-selectivity (7:1) to 7, phenol afforded olefinated product 8 with ortho-selectivity (o:others; 9:1, Scheme 2). On the other hand, subjecting TBDMS (tert-butyldimethylsilyl) protected phenol to the established protocol furnished 9 with 8:1 para-selectivity (Scheme 2). The TBDPS (tert-butyldiphenylsilyl) protected phenol afforded exclusively the *para*-olefinated product **10** which might be due to the steric repulsion caused by the bulky protecting group. Conversion of 2,6-diiso-propylphenol provided olefinated product 11 as a single para-olefinated isomer with 67% yield. Anisole and ethoxybenzene both reacted smoothly to produce 12 (72%, 15:1) and 13 (70%, 10:1) with ortho-selectivity (Scheme 2). The compatibility of the present transformation was further showcased by the olefination of N,N-dimethyl aniline in 70% yield (14) and 8:1 ortho-selectivity. Similarly, methyl ferrocene carboxylate and biologically active caffeine reacted smoothly with n-butyl acrylate to produce olefinated products 15 and 16 in good yields (Scheme 2). Moderately electron-withdrawing arenes such as a phenyl acetic acid derivative (17, 51%, o: others = 7:1), a homoveratric acid derivative (18, 12%)48%, o:others = 15:1) or 4-methoxy acetophenone (19, 59%, m:others = 7:1) gave the corresponding products in satisfactory yields. The coupling of unsubstituted thiophene and furan with *n*-butyl acrylate afforded the olefinated products 20 and 21 (64% and 68%) with synthetically useful C2 and C3 selectivity, respectively (C2:others; 18:1 and C3:others; 19:1, Scheme 2). In contrast, thiophenes bearing a substituent in C2 position such as 2-phenylthiophene and 1-(4-(thien-2-yl)phenyl)ethan-1-one reacted with high C5-selectivity (> 25:1) to the arylated α,β -unsaturated esters 22 and 23 (76% and 73% yield). Conversion of 2-(2-nitrophenyl)thiophene delivered the desired product 24 in 64% yield with exclusive C5-selectivity. A C3-substituted thiophene also reacted with the acrylate to 25 in 72% yield (C5:others; 6:1 selectivity). Heteroarenes bearing electronwithdrawing substituents such as 2-acetyl thiophene (26) afforded the C5-olefinated product in moderate yield and selectivity (64%, C5:others = 8:1). However, aromatic ring bearing

strong electron-withdrawing groups (-NO₂, -CHO, -CF₃, -F etc.) are not compatible under our present reaction conditions.





^aReaction conditions: undivided cell, GF anode, Pt cathode, j = 2.5 mA/cm² or j = 1.5 mA/cm², corresponding arenes or heteroarenes (0.2 mmol), activated olefins (0.5 mmol), Pd(OAc)₂ (10 mol%), L1 (20 mol%), TBAPF₆ (0.5 equiv.), DCE (3 mL) or 5:1 ratio of dichloroethane (DCE) and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), 15 h, under air. ^bYields of isolated products are reported.

Next, we investigated the applicability of other olefins by reacting them with simple arenes (Scheme 3). In addition to other acrylates (methyl 27, ethyl 28 and tert-butyl 29), acrylic acid was successfully converted with naphthalene to its arylated product 30. Moderate yields (54-60%) and moderate to high β :a-selectivities (up to >25:1) were obtained for all reactions. Coupling of methyl acrylate with benzene under adjusted electrochemical conditions ($j = 1.5 \text{ mA/cm}^2$; DCE/HFIP mixtures) gave 62% of olefinated product 31. Other activated olefins such as methyl vinyl sulfone, and acrylonitrile were also amenable to the present olefination protocol. Subjecting these substrates in combination with different arenes to our protocol led to a variety of arylated products 32-35 in good yields and regioselectivities. α,β -Unsaturated ester derivatives of bioactive molecules such as δ -tocopherol and cholesterol were efficiently reacted with naphthalene to the arylated products 36-37 in moderate yields. To further elaborate the scope of present protocol unactivated olefins such as aliphatic olefins and styrene derivatives were tested. However, none of them afford olefinated products under our reaction conditions. To monitor the scalability of the present transformation, two reactions were performed with the model reaction at scales of 0.504 g (46%, β : α = 7:1) and 1.08 g (41%, β : α = 7:1; see Supporting Information 4.2).

To gain insights into the catalytic mode of action, electrochemical and spectroelectrochemical experiments were performed. Cyclic voltammetry (CV) on Pd(OAc)₂ in DCE revealed two oxidation waves at +1.42 V vs. NHE (Normal Hydrogen Electrode) and at +2.47 V vs. NHE (Figure 1a) which might refer to the redox conversion of Pd(II/III) and Pd(III/IV).²³ Figure 1b shows CVs of naphthalene (substrate), ligand L1, n-butyl acrylate, and Pd(OAc)₂. In comparison to the Pd(II/III) redox pair, a significantly higher oxidation potential (+2.16 V vs. NHE) was observed for naphthalene, which suggests that substrate activation is potentially induced by a Pd species with an oxidation state greater than +II (Figure 1b). CVs of other substrates followed the same pattern (see Supporting Information, Figure S2). According to an electrochemical study on approximate ranges of standard redox potentials for Pd intermediates in catalytic reactions, the oxidation of Pd(II) to Pd(IV) is usually observed in the range of +1.00 - 2.00 V (vs. Fc/Fc⁺ = Ferrocene) or 1.63 - 2.63 V (vs. NHE).²³ The CV profile of Pd(OAc)₂ in the negative scan revealed two reduction waves at -0.23 V and at -1.06 V vs NHE (Figure S6) which might refer to the redox conversion of Pd(II/I) and Pd(I/0). Taking these results into account, involvement of a Pd(II/IV) catalytic cycle during the present transformation appears to be likely as the negative scan rules out a Pd(II/0) cycle.23d, 23e

In order to obtain further evidence for this hypothesis, we examined the reaction mixture at a constant potential of +2.61 V (vs. NHE) spectroelectrochemically (SEC) to check any changes in optical features during the reaction. This *in-situ* UV-Visible analysis of the reaction mixture revealed the gradual decrease of an absorption band at 379 nm and a new peak (~350 nm) appeared over time (Figure 1c). Similar behavior was observed for the Pd-ligand complex as a blue shift of optical bands was found from 368 nm to 352 nm under the same potential of +2.61 V (vs. NHE, Figure 1d). The differences in the observed UV-vis peak positions are presumably due to a change in the geometry of the Pd-complex upon oxidation in the analyzed reaction mixtures.

To further consolidate this hypothesis, the same SEC experiment was repeated with only Pd(OAc)₂ which showed an absorption peak at 404 nm (Figure S3). Electrolysis of Pd(OAc)₂ at +2.61 V (vs. NHE) also resulted in a blue shift with a new peak appearing at almost the same wavelength of 349 nm (Figure S4). All these results led us to postulate that the new peak was associated with a change in oxidation state of the Pd(II) center. In order to further understand the nature of intermediates involved in the catalytic cycle, a series of electron paramagnetic resonance (EPR) experiments of the reaction mixture were conducted at different time intervals employing optimized reaction conditions. The EPR spectra (273 K) after 1 h showed a strong peak at g = 2.005 which was presumably due to the formation of an organic radical (Figure 2a), however no naphthalene homo-coupled product was detected after different time intervals or under different conditions. At longer time intervals (4 h and 7 h), weak peaks at $g_x = 2.139$, $g_y = 2.081$



Figure 1. (a) Cyclic voltammogram of $Pd(OAc)_2$ and L1- $Pd(OAc)_2$ (1 mM, 100 mVs⁻¹ scan rate, glassy carbon, potential vs. NHE, 0.1 M TBAPF₆ in DCE); (b) Cyclic voltammogram of reactants (1 mM, 100 mVs⁻¹ scan rate, glassy carbon, potential vs. NHE, 0.1 M TBAPF₆ in DCE); (c) *In-situ* UV-vis spectroelectrochemical spectra of the reaction mixture during bulk electrolysis at +2.61 V vs. NHE; (d) *In-situ* UV-vis spectroelectrochemical spectra of the Pd-ligand complex during bulk electrolysis at +2.61 V vs. NHE.

and $g_z = 2.055$ arose due to the asymmetry of the electronic distribution. The appearance of rhombic signals suggested the formation of a Pd(III) intermediate having a d⁷ center (Figure 2a).²⁴ An enlarged version of the spectra for Pd(III) after 7 h is shown with simulated data in Figure 2b. Time-dependent EPR spectra highlight that the build-up of Pd(III) was concomitant with the

decreased formation of an organic radical ($Pd^{II}-R$ to $Pd^{II}R^*$) as the corresponding peak diminished. This implied that the catalytically active Pd(III) species got accumulated as the reaction approached towards completion. Furthermore, the EPR data in the absence of *n*-butyl acrylate (after 2 h) also revealed a very



Figure 2. (a) EPR spectrum of the reaction mixture under the standard reaction conditions at different time intervals (273 K); **(b)** Enlarged EPR spectra of Pd(III) after 7 h of experiment at 273 K (experimental vs. simulated).

strong peak at g = 2.005, hence the formation of a radical species from the olefin was ruled out (Figure S5).

Additionally, radical quenching experiments with TEMPO did not show any effects under the standard reaction conditions. Furthermore, electrochemical arene oxidation to generate organic radicals has been well reported in the literature.^{5f} All these control experiments suggest that a phenoxy radical from L1 (C') might be formed from intermediate C (Scheme 4).

All of the performed experiments give a strong indication that a Pd(II)/Pd(IV) cycle is involved in this electrochemical variant of the Fujiwara-Moritani reaction. Also, a palladium complex $Pd^{II}(\mathbf{L1})_4$ was synthesized and characterized by X-ray crystallography (Figure 3). This $Pd^{II}(\mathbf{L1})_4$ complex was found to be a competent intermediate for the Pd-catalyzed electrooxidative olefination of arenes.



Figure 3. Single X-ray crystal structure of Pd-complex [Pd(L1)₄].²⁵

Based on these results and literature precedence,²³ a plausible Pd(II/IV)-catalytic cycle is proposed for the electro-oxidative olefination of simple arenes (Scheme 4). The catalytic cycle starts with the anodic oxidation of the Pd(II) catalyst **A** to form a Pd (III) intermediate **B**. Arene C(*sp*²)–H bond activation delivers the organopalladium complex **C** which is converted to the Pd(IV) species **D** by anodic oxidation. Next, olefin coordination to form **E** followed by migratory insertion results in the formation of another organopalladium intermediate **F**. Finally, β -hydride elimination followed by reduction of Pd furnishes the olefinated product **1** and the Pd(II) catalyst **A** is regenerated.

Scheme 4. Proposed catalytic cycle for the electrooxidative olefination of arenes



In summary, we have demonstrated the first Pd-catalyzed electrooxidative non-directed olefination of simple arenes. The developed transformation provides an alternative route to conventional Fujiwara-Moritani reactions by substituting toxic chemical oxidants with electric current. The applicability of this nondirected approach was proven by broad substrate scopes and high regioselectivities. Preliminary mechanistic investigations suggested the involvement of a Pd(II)/Pd(IV) catalytic cycle via a Pd(III) intermediate. Further investigations to expand the understanding of the reaction mechanism are currently underway in our laboratory.

ASSOCIATED CONTENT

Supporting information contains the experimental details including optimization details, crystal details, spectroelectrochemical study, characterization data, ¹H, ¹³C NMR spectra of all the isolated compounds.

AUTHOR INFORMATION

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no conflict of interest.

ACKNOWLEDGMENT

Financial support received from SERB India is gratefully acknowledged (CRG/2018/003951, CRG/2020/002493). Financial support dareceived from CSIR-India (fellowship to C.D.), PMRF-India (fellowship to T.P., J.G.), UGC-India (fellowship to S.S), IISER Bhopal (S.A.), and IIT Bombay (S.P., W.A.) is gratefully acknowledged. Anjana S.S. is greatly acknowledged for her help with Pd^{II}(L1)₄ synthesis. D.M. and D.B.W. are grateful to the Alexander von Humboldt Foundation (Humboldt Research Fellowship for Experienced Researchers to D.M.). We thank G. A. Oliver for proof-reading the manuscript and Mr. Lalit Mohan Jha of CIF Facility, IISER Bhopal for helping us in EPR measurements.

REFERENCES

(1) (a) Woźniak, Ł.; Tan, J.-F.; Nguyen, A. Q.-H.; Vigné, Madron du; Smal, V.; Cao, Y.-X.; Cramer, N. Catalytic Enantioselective Functionalizations of C-H Bonds by Chiral Iridium Complexes. Chem. Rev. 2020, 120, 10516-10543. (b) Rej, S.; Ano, Y.; Chatani, N. Bidentate Directing Groups: An Efficient Tool in C-H Bond Functionalization Chemistry for the Expedient Construction of C-C Bonds. Chem. Rev. 2020, 120, 1788-1887. (c) Gandeepan, P.; Müller, T.; Zell, D.; Cera, G.; Warratz, S.; Ackermann, L. 3d Transition Metals for C-H Activation. Chem. Rev. 2019, 119, 2192-2452. (d) Park, Y.; Kim, Y.; Chang, S. Transition Metal-Catalyzed C-H Amination: Scope, Mechanism, and Applications. Chem. Rev. 2017, 117, 9247-9301. (e) He, J.; Wasa, M.; Chan, K. S. L.; Shao, Q.; Yu, J.-Q. Palladium-Catalyzed Transformations of Alkyl C-H Bonds. Chem. Rev. 2017, 117, 8754-8786. (f) Wencel-Delord, J.; Glorius, F. C-H Bond Activation Enables the Rapid Construction and Late-Stage Diversification of Functional Molecules. Nat. Chem. 2013, 5, 369–375. (g) Li, B.; Dixneuf, P. H. sp² C–H Bond Activation in Water and Catalytic Cross-Coupling Reactions. Chem. Soc. Rev. 2013, 42, 5744-5767. (h) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. Rhodium Catalyzed Chelation-Assisted C-H Bond Functionalization Reactions. Acc. Chem. Res. 2012, 45, 814-825. (i) Goswami, N.; Bhattacharya, T.; Maiti, D. Transient Directing Ligands for Selective Metal-Catalysed C-H Activation. Nat. Rev. Chem. 2021, 5, 646-659. (j) Dey, A.; Sinha, S. K.; Achar, T. K.; Maiti, D. Game of Directors: Accessing Remote Meta- and Para-C-H Bonds with Covalently Attached Directing Groups. Angew. Chem. 2019, 131, 10934-10958; Angew. Chem. Int. Ed. 2019, 58, 10820-10843. (k) Liu, Y.; Yi, H.; Lei, A. Oxidation-Induced C-H Functionalization: A Formal Way for C-H Activation. Chin. J. Chem. 2018, 36, 692-697.

(2) (a) Sinha, S. K.; Guin, S.; Maiti, S.; Biswas, J. P.; Porey, S.; Maiti, D. Toolbox for Distal C-H Bond Functionalizations in Organic Molecules. Chem. Rev. 2021, org/10.1021/acs.chemrev.1c00220. (b) Ali, W.; Prakash, G.; Maiti, D. Recent Development in Transition Metal-Catalysed C-H Olefination. Chem. Sci. 2021, 12, 2735-2759. (c) Dutta, U.; Maiti, S.; Bhattacharya, T.; Maiti, D. Arene Diversification Through Distal C(sp²)-H Functionalization. Science 2021, 372, 701-717. (d) Wencel-Delord, J.; Dröge, T.; Liu, F.; Glorius, F. Towards Mild Metal-Catalyzed C-H Bond Activation. Chem. Soc. Rev. 2011, 40, 4740-4761. (e) McMurray, L.; O'Hara, F.; Gaunt, M. J. Recent Developments in Natural Product Synthesis Using Metal-Catalysed C-H Bond Functionalization. Chem. Soc. Rev. 2011, 40, 1885-1898. (f) Zhao, Y.; Wang, H.; Hou, X.; Hu, Y.; Lei, A.; Zhang, H.; Zhu, L. Oxidative Cross-Coupling through Double Transmetallation: Surprisingly High Selectivity for Palladium-Catalyzed Cross-Coupling of Alkylzinc and Alkynylstannanes. J. Am. Chem. Soc. 2006, 128, 15048-15049. (g) Chen, M.; Zheng, X.; Li, W.; He, J.; Lei, A. Palladium-Catalyzed Aerobic Oxidative Cross-Coupling Reactions of Terminal Alkynes with Alkylzinc Reagents. J. Am. Chem. Soc. 2010, 132, 4101-4103. (h) Lu, L.; Li, H.; Lei, A. Oxidative Cross-Coupling Reactions between Two Nucleophiles. Chin. J. Chem. 2022, 40, 256-266.

(3) (a) Ma, C.; Fang, P.; Liu, D.; Jiao, K.-J.; Gao, P.-S.; Qiu, H.; Mei, T.-S. Transition Metal-Catalyzed Organic Reactions in Undivided Electrochemical Cells. *Chem. Sci.* **2021**, *12*, 12866–12873. (b) Chen, Z.; Villani, E.; Inagi, S. Recent Progress in Bipolar Electropolymerization Methods Toward One-Dimensional Conducting Polymer Structures. *Curr. Opin. Electrochem.* **2021**, *28*, 100702. (c) Zhu, C.; Ang, N. W. J.; Meyer, T. H.; Qiu, Y.; Ackermann, L. rganic Electrochemistry: Molecular Syntheses with Potential. *ACS Cent. Sci.* **2021**, *7*, 415–431. (4) (a) Novaes, L. F. T.; Liu, J.; Shen, Y.; Lu, L.; Meinhardt, J. M.; Lin, S. Electrocatalysis as an Enabling Technology for Organic synthesis. *Chem. Soc. Rev.* **2021**, *50*, 7941–8002. (b) Siu, J. C.; Fu, N.; Lin, S. Catalyzing Electrosynthesis: A Homogeneous Electrocatalytic Approach to Reaction Discovery. *Acc. Chem. Res.* **2020**, *53*, 547–560. (c) Yamamoto, K.; Kuriyama, M.; Onomura, O. Anodic Oxidation for the Stereoselective Synthesis of Heterocycles. *Acc. Chem. Res.* **2020**, *53*, 105–120. (d) Liu, J.; Lu, L.; Wood, D.; Lin, S. New Redox Strategies in Organic Synthesis by Means of Electrochemistry and Photochemistry. *ACS Cent. Sci.* **2020**, *6*, 1317–1340. (e) Xiong, P.; Xu, H.-C. Chemistry with Electrochemically Generated N-Centered Radicals. *Acc. Chem. Res.* **2019**, *52*, 3339–3350.

(5) (a) Sauer, G. S.; Lin, S. An Electrocatalytic Approach to the Radical Difunctionalization of Alkenes. *ACS Catal.* **2018**, *8*, 5175–5187. (b) Moeller, K. D. Using Physical Organic Chemistry To Shape the Course of Electrochemical Reactions. *Chem. Rev.* **2018**, *118*, 4817– 4833. (c) Kärkäs, M. D. Electrochemical strategies for C–H functionalization and C–N bond formation. *Chem. Soc. Rev.* **2018**, *47*, 5786– 5865. (d) Yan, M.; Kawamata, Y.; Baran, P. S. Synthetic Organic Electrochemical Methods Since 2000: On the Verge of a Renaissance. *Chem. Rev.* **2017**, *117*, 13230–13319. (e) Liu, S. T. Y.; Lei, A. Electrochemical Oxidative Cross-coupling with Hydrogen Evolution: A Green and Sustainable Way for Bond Formation. *Chem* **2018**, *4*, 27–45. (f) Waldvogel, S. R.; Lips, S.; Selt, M.; Riehl, B.; Kampf, C. J. Electrochemical Arylation Reaction. *Chem. Rev.* **2018**, *118*, 6706–6765.

(6) (a) Francke, R.; Little, R. D. Redox Catalysis in Organic Electrosynthesis: Basic Principles and Recent Developments. *Chem. Soc. Rev.* **2014**, *43*, 2492–2521. (b) Gosmini, C.; Begouin, J.-M.; Moncomble, A. Cobalt-Catalyzed Cross-Coupling Reactions. *Chem. Commun.* **2008**, 3221–3233. (c) Herold, S.; Mohle, S.; Zirbes, M.; Richter, F.; Nefzger, H.; Waldvogel, S. R. Electrochemical Amination of Less-Activated Alkylated Arenes Using Boron-Doped Diamond Anodes. *Eur. J. Org. Chem.* **2016**, 1274–1278. (d) Kehl, A.; Schollmeyer, D.; Moeller, K. D.; Waldvogel, S. R. Insights into the Mechanism of Anodic N–N Bond Formation by Dehydrogenative Coupling. *J. Am. Chem. Soc.* **2017**, *139*, 12317–12324.

(7) (a) Meyer, T. H.; Choi, I.; Tian, C.; Ackermann, L. Powering the Future: How Can Electrochemistry Make a Difference in Organic Synthesis? *Chem.* **2020**, *6*, 2484–2496. (b) 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.* **2020**, *53*, 300–310. (c) Gandeepan, P.; Finger, L. H.; Meyer, T. H.; Ackermann, L. 3d Metallaelectrocatalysis for Resource Economical Syntheses. *Chem. Soc. Rev.* **2020**, *49*, 4254–4272. (d) Saito, F.; Aiso, H.; Kochi, T.; Kakiuchi, F. Palladium-Catalyzed Regioselective Homocoupling of Arenes Using Anodic Oxidation: Formal Electrolysis of Aromatic Carbon–Hydrogen Bonds. *Organometallics* **2014**, *33*, 6704–6707.

(8) (a) Meyer, T. H.; Finger, L. H.; Gandeepan, P.; Ackermann, L. Resource Economy by Metallaelectrocatalysis: Merging Electrochemistry and CH Activation. *Trends Chem.* **2019**, *1*, 63–76. (b) Yuan, Y.; Lei, A. Electrochemical Oxidative Cross-Coupling with Hydrogen Evolution Reactions. *Acc. Chem. Res.* **2019**, *52*, 3309–3324. (c) Liu, K.; Tang, S.; Huang, P.; Lei, A. External Oxidant-Free Electrooxidative [3+2] Annulation between Phenol and Indole Derivatives. *Nat.Commun.* **2017**, *8*, 775.

(9) (a) Yang, Q.-L.; Fang, P.; Mei, T.-S. Recent Advances in Organic Electrochemical C-H Functionalization. *Chin. J. Chem.* **2018**, *36*, 338–352. (b) Ma, C.; Fang, P.; Mei, T.-S. Recent Advances in C–H Functionalization Using Electrochemical Transition Metal Catalysis. *ACS Catal.* **2018**, *8*, 7179–7189. (c) Wang, H.; Gao, X.; Lv, Z.; Abdelilah, T.; Lei, A. Recent Advances in Oxidative R¹-H/R²-H Cross-Coupling with Hydrogen Evolution via Photo-/Electrochemistry. *Chem. Rev.* **2019**, *119*, 6769–6787.

(10) (a) Sauermann, N.; Meyer, T. H.; Qiu, Y.; Ackermann, L. Electrocatalytic C–H Activation. *ACS Catal.* **2018**, *8*, 7086–7103. (b) Wang, P.; Tang, S.; Huang, P.; Lei, A. Electrocatalytic Oxidant-Free Dehydrogenative C–H/S–H Cross-Coupling. *Angew. Chem.* **2017**, *129*, 3055–3059; *Angew. Chem. Int. Ed.* **2017**, *56*, 3009–3013. (c) Ka-

kiuchi, F.; Kochi, T. New Strategy for Catalytic Oxidative C–H Functionalization: Efficient Combination of Transition-metal Catalyst and Electrochemical Oxidation. *Chem. Lett.* **2020**, *49*, 1256–1269.

(11) (a) Dhawa, U.; Tian, C.; Wdowik, T.; Oliveira, J. C. A.; Hao, J.; Ackermann, L. Enantioselective Pallada-Electrocatalyzed C-H Activation by Transient Directing Groups: Expedient Access to Helicenes. *Angew. Chem.* **2020**, *132*, 13553–13559; *Angew. Chem. Int. Ed.* **2020**, *59*, 13451–13457. (b) Li, Q.-L.; Yang, C.-Z.; Zhang, L.-W.; Li, Y.-Y.; Tong, X.; Wu, X.-Y.; Mei, T.-S. Palladium-Catalyzed Electrochemical C–H Alkylation of Arenes. *Organometallics* **2019**, *38*, 1208–1212. (c) Yang, Q.-L.; Li, Y.-Q.; Ma, C.; Fang, P.; Zhang, X.-J.; Mei, T.-S. Palladium-Catalyzed C(sp3)—H Oxygenation via Electrochemical Oxidation. *J. Am. Chem. Soc.* **2017**, *139*, 3293–3298.

(12) (a) Ma, C.; Zhao, C.-Q.; Li, Y.-Q.; Zhang, L.-P.; Xu, X.-T.; Zhang, K.; Mei, T.-S. Palladium-Catalyzed C–H Activation/C–C Cross-Coupling Reactions via Electrochemistry. *Chem. Commun.* **2017**, *53*, 12189–12192. (b) Konishi, M.; Tsuchida, K.; Sano, K.; Kochi, T.; Kakiuchi, F. Palladium-Catalyzed ortho-Selective C-H Chlorination of Benzamide Derivatives under Anodic Oxidation Conditions. *J. Org. Chem.* **2017**, *82*, 8716–8724. (c) Dudkina, Y. B.; Mikhaylov, D. Y.; Gryaznova, T. V.; Tufatullin, A. I.; Kataeva, O. N.; Vicic, D. A. Budnikova, Y. H. Electrochemical Ortho Functionalization of 2-Phenylpyridine with Perfluorocarboxylic Acids Catalyzed by Palladium in Higher Oxidation States. *Organometallics* **2013**, *32*, 4785– 4792.

(13) (a) Kakiuchi, F.; Kochi, T.; Mutsutani, H.; Kobayashi, N.; Urano, S.; Sato, M.; Nishiyama, S.; Tanabe, T. Palladium-Catalyzed Aromatic C–H Halogenation with Hydrogen Halides by Means of Electrochemical Oxidation. J. Am. Chem. Soc. 2009, 131, 11310– 11311. (b) Shi, R.; Lu, L.; Zhang, H.; Chen, B.; Sha, Y.; Liu, C.; Lei, A. Palladium/Copper-Catalyzed Oxidative C–H Alkenylation/N-Dealkylative Carbonylation of Tertiary Anilines. Angew. Chem. 2013, 125, 10776–10779; Angew. Chem. Int. Ed. 2013, 52, 10582–10585. (c) Kakiuchi, F.; Kochi, T. Palladium-Catalyzed Aromatic C-H Functionalizations Utilizing Electrochemical Oxidations. Chem. Rec. 2021, 21, 2320–2331.

(14) Moritani, I.; Fujiwara, Y. Aromatic Substitution of Styrene-Palladium Chloride Complex. *Tetrahedron Lett.* **1967**, *8*, 1119–1122.

(15) Le Bras, J.; Muzart, J. Intermolecular Dehydrogenative Heck Reactions. *Chem. Rev.* **2011**, *111*, 1170–1214.

(16) (a) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. Pd(II)-Catalyzed Olefination of Electron-Deficient Arenes Using 2,6-Dialkylpyridine Ligands. J. Am. Chem. Soc. **2009**, *131*, 5072–5074. (b) Zhang, S.; Shi, L.; Ding, Y. Theoretical Analysis of the Mechanism of Palladium(II) Acetate-Catalyzed Oxidative Heck Coupling of Electron-Deficient Arenes with Alkenes: Effects of the Pyridine-Type Ancillary Ligand and Origins of the meta-Regioselectivity. J. Am. Chem. Soc. **2011**, *133*, 20218–20229. (c) Patureau, F. W.; Nimphius, C.; Glorius, F. Rh Catalyzed C–H Activation and Oxidative Olefination without Chelate Assistance: On the Reactivity of Bromoarenes. Org. Lett. **2011**, *13*, 6346– 6349. (d) Kubota, A.; Emmert, M. H.; Sanford, M. S. Pyridine Ligands as Promoters in Pd^{II/0}-Catalyzed C–H Olefination Reactions. Org. Lett. **2012**, *14*, 1760–1763.

(17) (a) Vora, H. U.; Silvestri, A. P.; Engelin, C. J.; Yu, J.-Q. Rhodium(II)-Catalyzed Nondirected Oxidative Alkenylation of Arenes: Arene Loading at One Equivalent. Angew. Chem. 2014, 126, 2721-2724; Angew. Chem., Int. Ed. 2014, 53, 2683-2686. (b) Ying, C.-H.; Yan, S.-B.; Duan, W.-L. 2-Hydroxy-1,10-phenanthroline vs 1,10-Phenanthroline: Significant Ligand Acceleration Effects in the Palladium-Catalyzed Oxidative Heck Reaction of Arenes. Org. Lett. 2014, 16, 500-503. (c) Naksomboon, K.; Valderas, C.; Gómez-Martînez, M.; Álvarez-Casao, Y.; Fernández-Ibáñez, M. A. S,O-Ligand-Promoted Palladium-Catalyzed C-H Functionalization Reactions of Nondirected Arenes. ACS Catal. 2017, 7, 6342-6346. (d) Naksomboon, K.; Poater, J.; Bickelhaupt, F. M.; Fernández- Ibáñez, M. A. para-Selective C-H Olefination of Aniline Derivatives via Pd/S,O-Ligand Catalysis. J. Am. Chem. Soc. 2019, 141, 6719-6725. (e) Panja, S.; Maity, S.; Majhi, B.; Ranu, B. C. Palladium-Catalyzed Olefination of 4H-Benzo[d][1,3]oxazin-4-one Derivatives with Activated Alkenes via Preferential Cyclic Imine-N-Directed Aryl C-H Activation. Eur. J. Org. Chem. 2019, 5777-5786.

(18) Wang, P.; Verma, P.; Xia, G.; Shi, J.; Qiao, J. X.; Tao, S.; Cheng, P. T. W.; Poss, M. A.; Farmer, M. E.; Yeung, K.-S.; Yu, J.-Q. Ligand-Accelerated Non-Directed C-H Functionalization of Arenes. *Nature* **2017**, *551*, 489–493.

(19) Yin, B.; Fu, M.; Wang, L.; Liu, J.; Zhu, Q. Dual Ligand-Promoted Palladium-Catalyzed Nondirected C–H Alkenylation of Aryl Ethers. *Chem. Commun.* **2020**, *56*, 3293–3296.

(20) Chen, H.; Wedi, P.; Meyer, T.; Tavakoli, G.; van Gemmeren, M. Dual Ligand-Enabled Nondirected C–H Olefination of Arenes. *Angew. Chem.* **2018**, *130*, 2523–2527; *Angew. Chem., Int. Ed.* **2018**, *57*, 2497–2501.

(21) (a) Saha, A.; Guin, S.; Ali, W.; Bhattacharya, T.; Sasmal, S.; Goswami, N.; Prakash, G.; Sinha, S. K.; Chandrashekar, H. B.; Panda, S.; Anjana, S. S.; Maiti, D. Photoinduced Regioselective Olefination of Arenes at Proximal and Distal Sites. *J. Am. Chem. Soc.* **2022**, *4*, 1929–1940. (b) Hu, X.; Zhang, G.; Bu, F.; Luo, X.; Yi, K.; Zhang, H.; Lei, A. Photoinduced Oxidative Activation of Electron-Rich Arenes: Alkenylation with H₂ Evolution Under External Oxidant-Free Conditions. *Chem. Sci.* **2018**, *9*, 1521–1526.

(22) (a) Amatore, C.; Cammoun, C.; Jutand, A. Electrochemical Recycling of Benzoquinone in the Pd/Benzoquinone-Catalyzed Heck-Type Reactions from Arenes. *Adv. Synth. Catal.* 2007, *349*, 292–296.
(b) Zhang, Y.; Struwe, J.; Ackermann, L. Rhodium-Catalyzed Electrooxidative C–H Olefination of Benzamides. *Angew. Chem. Int. Ed.* 2020, *59*, 15076–15080.

(23) (a) Budnikova, Y. H.; Dudkina, Y. B.; Khrizanforov, M. N. Redox-Induced Aromatic C–H Bond Functionalization in Metal Complex Catalysis from the Electrochemical Point of View. *Inorganics* **2017**, *5*, 70-87. (b) Zhanga, D.; Yanga, D.; Wanga, S.; Zenga, L.; Xina, J.;

Zhang, H.; Lei, A. The Real Structure of Pd(OAc)2 in Various Solvents. Chin. J. Chem. 2021, 39, 307-311. (c) Wang, L.; Yang, D.; Alhumade, H.; Yi, H.; Qi, X.; Lei, A. Revealing the Solution Structure of Pd(OAc)2 with Halide Additives. Chin. J. Chem. 2021, DOI: https://doi.org/10.1002/cjoc.202100790. (d) Wu, Y.; Zeng, L.; Li, H.; Cao, Y.; Hu, J.; Xu, M.; Shi, R.; Yi, H.; Lei, A. Electrochemical Palladium-Catalyzed Oxidative Sonogashira Carbonylation of Arylhydrazines and Alkynes to Ynones. J. Am. Chem. Soc. 2021, 143, 12460-12466. (e) Zeng, L.; Li, H.; Hu, J.; Zhang, D.; Hu, J.; Peng, P.; Wang, S.; Shi, R.; Peng, J.; Pao, C. -W.; Chen, J. -L.; Lee, J. -F.; Zhang, H.; Chen, Y.-H.; Lei, A. Electrochemical Oxidative Aminocarbonylation of Terminal Alkynes. Nat. Catal. 2020, 3, 438-445. (f) Yuan, K.; Doucet, H. Benzenesulfonyl Chlorides: New Reagents for Access to Alternative Regioisomers in Palladium-Catalysed Direct Arylations of Thiophenes. Chem. Sci., 2014, 5, 392-396. (g) Sadowski, B.; Yuan, B.; Lin, Z.; Ackermann, L. Rhodaelectro-catalyzed peri-Selective Direct Alkenylations with Weak O-Coordination Enabled by the Hydrogen Evolution Reaction (HER). Angew. Chem. Int. Ed. 2022, e202117188. DOI: https://doi.org/10.1002/anie.202117188.

(24) Ruhs, N. P.; Khusnutdinova, J. R.; Rath, N. P.; Mirica, L. M. Mononuclear Organometallic Pd(II), Pd(III), and Pd(IV) Complexes Stabilized by a Pyridinophane Ligand with a C-Donor Group. *Organometallics* **2019**, *38*, 3834–3843.

(25) Deposition number 2120828 contains the supplementary crystallographic data for this paper. These data are provided free of charge by the Cambridge Crystallographic Data Centre www.ccdc.cam.ac.uk/structures.

Entry for the Table of Contents

