Enantioselective Alkylarylation of Olefins with Aliphatic C–H Bo nds via Asymmetric Paired Oxidative and Reductive Catalysis

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ABSTRACT: Enantioselective transformations of hydrocarbons to three-dimensional chiral molecules remain a significant challenge in synthetic chemistry. This study uses asymmetric paired oxidative and reductive catalysis (APORC) to promote the enantioselective alkylarylation of olefins through the functionalization of $C(sp^3)$ -H bonds in alkanes. This asymmetric photoelectrocatalytic approach enables the facile construction of a wide range of enantioenriched *a*-aryl carbonyls with excellent enantioselectivity (up to 96% ee) from readily accessible starting materials. Notably, aryl bromides, aryl iodides, and even aryl chlorides were compatible with the developed catalytic system. Mechanistic studies reveal that alkanes and electrophiles are simultaneously activated on the electrodes.

Photoelectrochemistry has been harnessed for diverse transformations ever since Xu and co-workers reported the photoelectrochemical C-H alkylation of heteroarenes with organotrifluoroborates in 2019.^{1,2} However, the inherently energetic and reactive intermediates (e.g., radicals and radical ions) generated during electrolysis make it challenging to ensure enantioselective control.³ Moreover, it is difficult to compatibility between the photocatalytic, maintain electrocatalytic, and asymmetric catalytic systems in a single cell. As a result, reports of asymmetric photoelectrocatalysis are scarce.⁴ In 2022, the Xu group and the Liu group independently established photoelectrochemical asymmetric catalysis by merging electrophoto- and copper catalysis,^{4f, 4g} which enabled enantioselective cyanation of benzylic C-H bonds, decarboxylative cyanation, and heteroarylcyanation of alkenes.^{4a,} ^{4b, 4d-g} More recently, Meggers et al. developed a photoelectrochemical asymmetric dehydrogenative [2+2] cycloaddition reaction involving cooperation between a chiral rhodium catalyst and ferrocene.^{4c} These systems all used single half-electrode reactions, where H₂ evolution at the cathode was required to ensure electroneutrality (Figure 1a). Merging asymmetric paired electrocatalysis with photochemistry should enhance the synthetic utility of such systems by promoting energy efficiency and atom economy, while stimulating further development of asymmetric synthesis.^{5,6}

Catalytic multicomponent reactions (MCRs) represent a versatile and powerful strategy for assembling complex molecular motifs from readily accessible materials via a single operation, thereby providing elegant retrosynthetic strategies to access natural products, drugs, and functionalized polymers.⁷ In particular, radical-based catalytic MCRs exhibit complementary reactivity and selectivity patterns compared with classical two-electron MCRs,⁸ which has highlighted new synthetic opportunities. However, the exceptionally high reactivity of radical species is notoriously difficult to handle in enantioselective processes, and therefore, catalytic asymmetric

radical MCRs still remain underexploited.⁹ To date, the limited examples of enantioselective three-component dicarbofunctionalization of alkenes typically rely on prefunctionalized alkylmetal or organohalide feedstocks,¹⁰ which leads to poor atom and step economies. In contrast, facile direct functionalization of ubiquitous $C(sp^3)$ –H bonds in inert hydrocarbons (e.g., alkanes) is an ambitious goal in synthetic chemistry that would revolutionize the field.¹¹



- Asymmetric paired electrocatalysis
 Asymmetric photoelectrocatalysis
- Catalytic multicomponent reactions
 C(sp³)-H functionalization of alkanes
 Figure 1. Asymmetric photoelectrocatalysis enabled C(sp³)-H

functionalization. (a) Single half-electrode reaction. (b) Asymmetric paired oxidative and reductive catalysis.

To date, the direct use of abundant alkanes as sp³-hybridized carbon radical precursors that could participate in the catalytic enantioselective functionalization of alkenes remains elusive,¹²

likely because of the following challenges: (1) the nonpolar alkyl C–H bonds in alkanes have high bond-dissociation energies, and harsh conditions are often required under thermal conditions;¹³ (2) a highly electrophilic radicals is needed to activate alkanes, but the target reactivity is in competition with undesired side reactions; (3) the carbon-centered radicals generated in situ are prone to oxidation to carbocations under oxidative conditions resulting in compromised enantio- and chemo-selectivity; (4) competition between two-component and three-component reactions reduces selectivity.¹⁴ and ratematching is vital for high reaction selectivity.

Our group's interest in electrosynthesis and recent success with paired oxidative and reductive catalysis for alkane functionalization inspired the current study.¹⁴⁻¹⁵ Herein, we present the photoelectrochemical alkylarylation of olefins via $C(sp^3)$ -H functionalization of alkanes to afford chiral α -aryl carbonyls with good to excellent enantioselectivity. Anodic photoelectrocatalysis was used to activate alkanes via ligand-tometal charge transfer (LMCT) to yield alkyl radicals, while cathodic transition metal catalysis was used to activate aryl halides to afford the corresponding aryl-Ni^{II} species. The crosscoupling of the two half-electrode reactions with an olefin as a linkage enabled enantioselective three-component reactions (Figure 1b). The key features of this approach include the following: (1) abundantly available alkanes were used as alkylating reactants to generate valuable chiral molecules revolutionizes the way in which prefunctionalized alkyl radical precursors were employed; (2) the photocatalytic and electrocatalytic processes remained relatively independent and could be modulated individually by adjusting the light source and the current/electrode potential, thus ensuring ratematching paired electrocatalysis; 3) ultra-low oxidative potential was required to recycle of Fe²⁺ to Fe³⁺,^{14,15a} which enabled mild redox-neutral electrosynthesis, suppressed undesirable over-oxidation, and promoted reaction selectivity.

To explore the feasibility of the proposed system, photoelectrochemically-driven three-component reactions involving cyclohexane (1a), 4'-bromoacetophenone (2a), and tert-butyl acrylate (3a) were carried out in the presence of commercially available FeCl₃ and Ni(NO₃)₂·6H₂O under irradiation with purple light emitting diodes (LEDs). As shown in Table 1, extensive experimentation and evaluation of key parameters (e.g., catalyst, solvent, electrolyte, current density, light source, ligand) revealed that the desired product 1 could be isolated in 82% yield with 91% ee (entry 1). Low yields of the desired product were detected when Ni(NO₃)₂•6H₂O was replaced with other Ni(II) precatalysts containing different counterions (entries 2-3), whereas changing the anodic catalyst (entries 4-5) reduced reaction efficiency. The solvent and electrolyte played key roles in promoting the reaction efficiency. For example, the reaction efficiency decreased dramatically when MeCN or a chlorine-free electrolyte was employed (entries 6-7). As expected, rate-matching between the anodic and cathodic reactions was crucial for this transformation. The tuning of the light source and current intensity, which influenced the anodic and cathodic reaction rates, significantly impacted the reaction efficiency and enantioselectivity (entries 8-10). Chiral biimidazoline (BiIm) ligands were the optimal ligands because they afforded the desired product in good yield with excellent enantioselectivity (entry 11). Notably, the

electronic nature of the BiIm ligands had a dramatic effect on the reaction efficiency and enantioselectivity, such that more electron-rich BiIm ligands gave better results (entry 1 vs 11). In contrast, chiral bioxazoline (Biox) ligand, pyrox ligand and chiral oxazoline ligand led to lower enantioselectivities and yields (entry 11; additional details are provided in the Supporting Information, Table S1). Control experiments indicated that paired catalysts, purple light, and the electrical current are all essential because reactions performed in their absence provided poor results (entries 12-13).

Table 1. Optimization of the reaction conditions.^a

•	Br + O'Bu		GF(+) GF(-), FeCl ₃ (10 mol %) Ni(NO ₃) ₂ 6H ₂ O (10 mol%), L1 (10 mol%) ^f Bu LiCl, Acetone, 25 mA, 12 h undivided cell, 20 W 390 - 392 nm		Cy
1a	2a	3a			1
Entry	Variation from standard conditions			Yield (%) ^{b}	ee (%) ^c
1	none			82	91
2	NiCl ₂ instead of Ni(NO ₃) ₂ GH_2O			52	90
3	NiBr ₂ instead of Ni(NO ₃) ₂ 6H ₂ O			47	89
4	$CuCl_2$ instead of FeCl ₃			7	90
5	$CeCl_3$ instead of $FeCl_3$			n.d.	
6	MeCN instead of Acetone			61	82
7	"Bu4NPF6 instead of LiCl			7	90
8	I = 10 mA			57	83
9	10 W 390-392 nm			55	90
10	20 W 395-400 nm			70	88
11	L2–L8 instead of L1			7-81	7-80
12	w/o FeCl ₃ or Ni(NO ₃) ₂ ·6H ₂ O			n.d.	
13	w/o electricity or light			n.d.	
	Ar Ar	_			о _{л г}



"Reaction conditions: 1a (9 mmol), 2a (0.9 mmol), 3a (1.8 mmol), FeCl₃ (10 mol%), electrolyte (2.0 equiv.), catalyst (10 mol%), ligand (10 mol%), solvent (6.0 mL), light, 25 mA, 12 h, argon, graphite felt (GF) as electrodes, undivided cell. ^bGC yields using biphenyl as an internal standard. ^cThe ee values were determined by HPLC on a chiral stationary phase. n.d. = not detected.

After establishing the optimal reaction conditions, we explored the scope of the photoelectrochemical asymmetric alkylarylation of olefins with respect to different alkanes (Figure 2). Cycloalkanes with various ring sizes (five to eight carbon atoms) were effective coupling partners, affording the corresponding desired products 1-5 in 71%-82% yields with good enantioselectivity (up to 92% ee). However, the reaction enantioselectivity decreased appreciably when other hydrocarbon compounds were employed. For example, acyclic alkanes (e.g., pivalonitrile) served as a suitable coupling partner in this reaction, producing product 6 in 52% yield but with moderate ee.



Figure 2. Substrate scope. Unless otherwise specified, all reactions were performed under standard conditions. For details, see the Supplementary Information. "L5 was used as the Ligand. ^bConstant cathodic potential = -2.0 V vs Ag/AgCl.

Additionally, the reaction scope was explored with respect to the aryl bromide. As shown in Figure 2, a variety of aryl bromides bearing electron-withdrawing groups (R = carbonyl, formyl, Ms) and electron-donating (R = SMe) substituents on the aromatic ring, were viable in this transformation, furnishing the corresponding products in 43%-75% yields, with good to excellent enantioselectivities (up to 96% ee). Compared with electron-deficient aryl bromides, electron-rich substrates exhibited slightly lower enantioselectivities (e.g., 15, 81% ee). Notably, the absolute configuration of coupling product 7 was unambiguously assigned by single-crystal X-ray diffraction (additional details are provided in the Supporting Information, Table S6). The described approach could also be applied to heteroaryl bromides (e.g., bromo-pyridines, benzothiophene. 17-20; 43%-67% yields; up to 88% ee). Certain functional groups that are typically sensitive to electroreductive conditions (e.g., carbonyl, formyl, sulfone, and heteroarenes) were well tolerated in this transformation. These results highlight the utility of this very mild redox-neutral asymmetric photoelectrocatalysis.

In addition to tert-butyl acrylate, a series of acrylates with various substituents were also compatible and yielded the corresponding products (21-26) in 44%-66% yields with 78%-87% ee. These results indicate that both the structure of the alkanes and the substituents on the acrylates are crucial for achieving high enantioselectivity. From a synthetic perspective, this asymmetric paired redox system offers a modular synthetic route for the enantioselective functionalization of inert $C(sp^3)$ -H bonds. Delightfully, this catalytic system can be further applied to aryl chlorides, and the corresponding products can be obtained with moderate yields and excellent enantioselectivities (up to 94% ee). Moreover, iodobenzenes were also coupled with cyclohexane and tert-butyl acrylate to provide the corresponding products in moderate yields and good enantioselectivities (up to 90% ee). The practicality of this methodology was further exemplified by a 9 mmol-scale experiment, after which product 7 was isolated in 61% yield, with 94% ee. These results highlight the potential synthetic applicability of this asymmetric paired oxidative and reductive catalytic system.

A series of experiments were conducted to gain insights into the reaction mechanism. First, 1-chloromethyl naphthalene 29, which can be generated via chlorination of the benzylic radical, was obtained in 27% yield when the reaction was performed using 1-methylnaphthalene as the substrate in the absence of a nickel catalyst (Figure 3a). The potential selected for this experiment was more negative than that needed for the direct oxidation of 1-methylnaphthalene, but it was sufficient to oxidize Fe²⁺ to Fe³⁺. This result reveals that a highly electrophilic chloride radical is formed in situ via an anodic LMCT process, which effectively activates $C(sp^3)$ -H bonds through hydrogen abstraction to afford the corresponding carbon radical. In addition, alkyl chlorides were detected as a major by-product via GC-MS analysis after the standard reaction. However, the desired product was not observed when alkyl chloride replaced the alkane (Figure 3b). Moreover, only product 1 was observed when chlorocycloheptane and cyclohexane were simultaneously added to the standard reaction conditions (Figure 3c). These results exclude the involvement of alkyl chlorides as key intermediates during the reaction.



Figure 3. Control experiments. (a) Radical trapping experiment. (b-c) Use of alkyl chloride as a reactant. (d) Reaction with an Ar-Ni(II)-Br complex.

An Ac-C₆H₄-Ni(II)-Br complex was prepared in situ and introduced to react with cyclohexane and *tert*-butyl acrylate (3a) in the presence of stoichiometric FeCl₃ under light irradiation (Figure 3d). The desired product 1 was obtained in 31% yield with 91% ee. Next, the electrode voltage was monitored over the course of the electrolysis for the model reaction using 4 mA. Anodic oxidation was maintained at approximately 0.28 V vs. Ag/AgCl, while cathodic reduction was maintained at approximately -0.83 V vs. Ag/AgCl (Figure 4a). These results are consistent with the Fe(II)/Fe(III) oxidative catalysis at the anode. The cathodic potential was sufficient to reduce ArNi^{III} to ArNi^{II} (e.g., for ArNi^{III} (Mebpy)Br₂, Ar = 4-CF₃C₆H₄; calc. E_{red} \approx -0.5 V vs. Ag/AgNO₃)¹⁶ but not enough to reduce ArNi^{II} to ArNi^I (e.g., for *p*-TolylNi^{II}(bpy)Br, $E_{red} \approx -1.8$ V vs. Ag/AgNO₃).¹⁷ These results suggest that the aryl-Ni(II) species is a productive intermediates in this transformation.

Next, we investigated the nonlinear effects. A nonlinear relationship was observed between product 1 and the enantiopurities of L1 (Figure 4b), suggesting that the involvement of at least two chiral BiIm ligands (L1) in the enantioselectivity-determining step.¹⁸ Moreover, the observed ee of product 1 remained constant over time, indicating that the reaction followed a unified stereo-convergent transformation process, thus ruling out the product deracemization pathway (Figure 4c). Subsequently, we evaluated the dependence of the average reaction rate on the current. The reaction exhibited a first-order dependence on the current (Figure 4d), which confirmed that electron transfer at the electrodes was the rate-determining step at the current applied in this reaction.

On the basis of the results presented herein, a plausible mechanism is proposed (Figure 4e). The process begins with electrophilic chloride-radical formation via LMCT of the excited $[FeCl_4]^{-}$.¹⁹ This chlorine radical is converted into alkyl radical E via hydrogen abstraction from the alkane. The resulting alkyl radical E is then added to the alkene, affording radical species F. Concomitantly, the catalyst precursor of Ni^{II} is reduced at the cathode, affording Ni^I species G. This Ni^I species

undergoes further oxidative addition with an aryl halide to generate an aryl-Ni^{III} complex, which is subsequently electrochemically reduced to an aryl-Ni^{II} species. The aryl-Ni^{II} species I intercept the radical species F to yield the

 $Ni^{III}(aryl)(alkyl)$ species J. Finally, J undergoes reductive elimination to furnish the cross-coupling products and regenerate the Ni^{I} catalyst.



Figure 4. Mechanistic studies. a) Electrode voltage over the course of electrolysis. b) Nonlinear effects for the standard reaction. c) The enantiopurity of product 1 hardly varied during the reaction. d)Plot showing first-order rate dependence on current. e) Possible mechanism.

In summary, we have demonstrated the first example of enantioselective alkylarylation of olefins with aliphatic C–H bonds via asymmetric paired oxidative and reductive catalysis. This protocol employs a binary catalytic system based on earth-abundant iron and nickel in an undivided cell. The key features of this asymmetric photoelectrocatalytic approach include excellent enantioselectivity, utilization of hydrocarbon feedstocks as coupling regents, and a broad aryl halide substrate scope. Ongoing efforts in our laboratory are focused on applying this catalytic platform (APORC) to other enantioselective multicomponent reactions.

ASSOCIATED CONTENT

Supporting Information

Experimental procedure, characterization data, and copies of 1 H and 13 C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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

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REFERENCES

1. Yan, H.; Hou, Z.-W.; Xu, H.-C., Photoelectrochemical C–H Alkylation of Heteroarenes with Organotrifluoroborates. *Angew. Chem. Int. Ed.* 2019, 58, 4592.

2. (a) Wu, S.; Kaur, J.; Karl, T. A.; Tian, X.; Barham, J. P., Synthetic Molecular Photoelectrochemistry: New Frontiers in Synthetic Applications, Mechanistic Insights and Scalability. Angew. Chem. Int. Ed. 2022, 61, e202107811; (b) Huang, H.; Steiniger, K. A.; Lambert, T. H., Electrophotocatalysis: Combining Light and Electricity to Catalyze Reactions. J. Am. Chem. Soc. 2022, 144, 12567; (c) Hardwick, T.; Ahmed, N.. C-H Functionalization via Electrophotocatalysis and Photoelectrochemistry: Complementary Synthetic Approach. ACS Sustainable Chem. Eng. 2021, 9, 4324; (d) Yu, Y.; Guo, P.; Zhong, J.-S.; Yuan, Y.; Ye, K.-Y., Merging Photochemistry with Electrochemistry in Organic Synthesis. Org. Chem. Front. 2020, 7, 131.

3. (a) Jiao, K.-J.; Wang, Z.-H.; Ma, C.; Liu, H.-L.; Cheng, B.; Mei, T.-S.,

The Applications of Electrochemical Synthesis in Asymmetric Catalysis. Chem Catal. 2022, 2, 3019; (b) Wang X.-Y.; Wang Z.-H.;, Fang P, Mei T.-S.;, Advances in Asymmetric Organotransition Metal-Catalyzed Electrochemistry. Chin. J. Org. Chem. 2020, 40, 3738; (c) Chang, X.; Zhang, Q.; Guo, C., Asymmetric Electrochemical Transformations. Angew. Chem. Int. Ed. 2020, 59, 12612; (d) Lin, Q.; Li, L.; Luo, S., Asymmetric Electrochemical Catalysis. Chem. Eur. J. 2019, 25, 10033; (e) Ghosh, M.; Shinde, V. S.; Rueping, M., A Review of Asymmetric Synthetic Organic Electrochemistry and Electrocatalysis: Concepts, Applications, Recent Developments and Future Directions. Beilstein J. Org. Chem. 2019, 15, 2710. 4. (a) Yuan, Y.; Yang, J.; Zhang, J., Cu-Catalyzed Enantioselective Decarboxylative Cyanation via the Synergistic Merger of Photocatalysis and Electrochemistry. Chem. Sci. 2023, 14, 705; (b) Yang, K.; Wang, Y.; Luo, S.; Fu, N., Electrophotochemical Metal-Catalyzed Enantioselective Decarboxylative Cyanation. Chem. Eur. J. 2023, 29, e202203962; (c) Xiong, P.; Ivlev, S. I.; Meggers, E., Photoelectrochemical Asymmetric Dehydrogenative [2 + 2] Cycloaddition Between C-C Single and Double Bonds via the Activation of Two C(sp3)-H Bonds. Nat. Catal. 2023, 6, 1186; (d) Lai, X.-L.; Xu, H.-C., Photoelectrochemical Asymmetric Catalysis Enables Enantioselective Heteroarylcyanation of Alkenes via C-H Functionalization. J. Am. Chem. Soc. 2023, 145, 18753; (e) Lai, X.-L.; Chen, M.; Wang, Y.; Song, J.; Xu, H.-C., Photoelectrochemical Asymmetric Catalysis Enables Direct and Enantioselective Decarboxylative Cyanation. J. Am. Chem. Soc. 2022, 144, 20201; (f) Fan, W.; Zhao, X.; Deng, Y.; Chen, P.; Wang, F.; Liu, G., Electrophotocatalytic Decoupled Radical Relay Enables Highly Efficient and Enantioselective Benzylic C-H Functionalization. J. Am. Chem. Soc. 2022, 144, 21674; (g) Cai, C.-Y.; Lai, X.-L.; Wang, Y.; Hu, H.-H.; Song, J.; Yang, Y.; Wang, C.; Xu, H.-C., Photoelectrochemical Asymmetric Catalysis Enables Site- and Enantioselective Cyanation of Benzylic C-H Bonds. Nat. Catal. 2022, 5, 943.

5. (a) Wu, T.; Moeller, K. D., Science of Synthesis: Electrochemistry in Organic Synthesis. Thieme Chem. 2021, 1, 481; (b) Wu, T.; Moeller, K. D., Organic Electrochemistry: Expanding the Scope of Paired Reactions. Angew. Chem. Int. Ed. 2021, 60, 12883.

6. Liu, D.; Liu, Z.-R.; Wang, Z.-H.; Ma, C.; Herbert, S.; Schirok, H.; Mei, T.-S., Paired Electrolysis-Enabled Nickel-Catalyzed Enantioselective Reductive Cross-Coupling Between *a*-Chloroesters and Aryl Bromides. *Nat. Commun.* 2022, *13*, 7318.

7. (a) Reguera, L.; Rivera, D. G., Multicomponent Reaction Toolbox for Peptide Macrocyclization and Stapling. *Chem. Rev.* 2019, *119*, 9836; (b) Rotstein, B. H.; Zaretsky, S.; Rai, V.; Yudin, A. K., Small Heterocycles in Multicomponent Reactions. *Chem. Rev.* 2014, *114*, 8323; (c) Touré, B. B.; Hall, D. G., Natural Product Synthesis Using Multicomponent Reaction Strategies. *Chem. Rev.* 2009, *109*, 4439.

8. (a) Zhu, S.; Zhao, X.; Li, H.; Chu, L., Catalytic Three-Component Dicarbofunctionalization Reactions Involving Radical Capture by Nickel. *Chem. Soc. Rev.* **2021**, *50*, 10836; (b) Plesniak, M. P.; Huang, H.-M.; Procter, D. J., Radical Cascade Reactions Triggered by Single Electron Transfer. *Nat. Rev. Chem.* **2017**, *1*, 0077; (c) Garbarino, S.; Ravelli, D.; Protti, S.; Basso, A., Photoinduced Multicomponent Reactions. *Angew. Chem. Int. Ed.* **2016**, *55*, 15476; (d) Godineau, E.; Landais, Y., Radical and Radical-Ionic Multicomponent Processes. *Chem. Eur. J.* **2009**, *15*, 3044.

9. (a) Lipp, A.; Badir, S. O.; Molander, G. A., Stereoinduction in Metallaphotoredox Catalysis. *Angew. Chem. Int. Ed.* **2021**, *60*, 1714; (b) Proctor, R. S. J.; Colgan, A. C.; Phipps, R. J., Exploiting Attractive Non-Covalent Interactions for the Enantioselective Catalysis of Reactions Involving Radical Intermediates. *Nat. Chem.* **2020**, *12*, 990; (c) Sibi, M. P.; Manyem, S.; Zimmerman, J., Enantioselective Radical Processes. *Chem. Rev.* **2003**, *103*, 3263.

10. (a) Wang, Y.-Z.; Sun, B.; Zhu, X.-Y.; Gu, Y.-C.; Ma, C.; Mei, T.-S., Enantioselective Reductive Cross-Couplings of Olefins by Merging Electrochemistry with Nickel Catalysis. J. Am. Chem. Soc. 2023, 145, 23901; (b) Li, X.; Yuan, M.; Chen, F.; Huang, Z.; Qing, F.-L.; Gutierrez, O.; Chu, L., Three-Component Enantioselective Alkenylation of Organophosphonates via Nickel Metallaphotoredox Catalysis. Chem. 2023, 9, 154; (c) Xi, Y.; Huang, W.; Wang, C.; Ding, H.; Xia, T.; Wu, L.; Fang, K.; Qu, J.; Chen, Y., Catalytic Asymmetric Diarylation of Internal Acyclic Styrenes and Enamides. J. Am. Chem. Soc. 2022, 144, 8389; (d) Liu, C.-F.; Wang, Z.-C.; Luo, X.; Lu, J.; Ko, C. H. M.; Shi, S.-L.; Koh, M. J., Synthesis of Tri- and Tetrasubstituted Stereocentres by Nickel-Catalysed Enantioselective Olefin Cross-Couplings. Nat. Catal. 2022, 5, 934; (e) Apolinar, O.; Kang, T.; Alturaifi, T. M.; Bedekar, P. G.; Rubel, C. Z.; Derosa, J.; Sanchez, B. B.; Wong, Q. N.; Sturgell, E. J.; Chen, J. S.; Wisniewski, S. R.; Liu, P.; Engle, K. M., Three-Component Asymmetric Ni-Catalyzed 1,2-Dicarbofunctionalization of Unactivated Alkenes via Stereoselective Migratory Insertion. J. Am. Chem. Soc. 2022, 144, 19337; (f) Qiao, J.-B.; Zhang, Y.-Q.; Yao, Q.-W.; Zhao, Z.-Z.; Peng, X.; Shu, X.-Z., Enantioselective Reductive Divinylation of Unactivated Alkenes by Nickel-Catalyzed Cyclization Coupling Reaction. J. Am. Chem. Soc. 2021, 143, 12961; (g) Qian, P.; Guan, H.; Wang, Y.-E.; Lu, Q.; Zhang, F.; Xiong, D.; Walsh, P. J.; Mao, J., Catalytic Enantioselective Reductive Domino Alkyl Arylation of Acrylates via Nickel/Photoredox Catalysis. Nat. Commun. 2021, 12, 6613; (h) Lu, F.-D.; Lu, L.-Q.; He, G.-F.; Bai, J.-C.; Xiao, W.-J., Enantioselective Radical Carbocyanation of 1,3-Dienes via Photocatalytic Generation of Allylcopper Complexes. J. Am. Chem. Soc. 2021, 143, 4168; (i) Zhang, Y.; Sun, Y.; Chen, B.; Xu, M.; Li, C.; Zhang, D.; Zhang, G., Copper-Catalyzed Photoinduced Enantioselective Dual Carbofunctionalization of Alkenes. Org. Lett. 2020, 22, 1490; (j) Wei, X.; Shu, W.; García-Domínguez, A.; Merino, E.; Nevado, C., Asymmetric Ni-Catalyzed Radical Relayed Reductive Coupling. J. Am. Chem. Soc. 2020, 142, 13515; (k) Tu, H.-Y.; Wang, F.; Huo, L.; Li, Y.; Zhu, S.; Zhao, X.; Li, H.; Qing, F.-L.; Chu, L., Enantioselective Three-Component Fluoroalkylarylation of Unactivated Olefins through Nickel-Catalyzed Cross-Electrophile Coupling. J. Am. Chem. Soc. 2020, 142, 9604; (1) Guo, L.; Yuan, M.; Zhang, Y.; Wang, F.; Zhu, S.; Gutierrez, O.; Chu, L., General Method for Enantioselective Three-Component Carboarylation of Alkenes Enabled by Visible-Light Dual Photoredox/Nickel Catalysis. J. Am. Chem. Soc. 2020, 142, 20390; (m) Chierchia, M.; Xu, P.; Lovinger, G. J.; Morken, J. P., Enantioselective Radical Addition/Cross-Coupling of Organozinc Reagents, Alkyl Iodides, and Alkenyl Boron Reagents. Angew. Chem. Int. Ed. 2019, 58, 14245; (n) Anthony, D.; Lin, Q.; Baudet, J.; Diao, T., Nickel-Catalyzed Asymmetric Reductive Diarylation of Vinylarenes. Angew. Chem. Int. Ed. 2019, 58, 3198; (o) Sha, W.; Deng, L.; Ni, S.; Mei, H.; Han, J.; Pan, Y., Merging Photoredox and Copper Catalysis: Enantioselective Radical Cyanoalkylation of Styrenes. ACS Catal. 2018, 8, 7489; (p) Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P., Catalytic Conjunctive Cross-Coupling Enabled by Metal-Induced Metallate Rearrangement. Science. 2016, 351, 70; (q) Wang, F.; Wang, D.; Wan, X.; Wu, L.; Chen, P.; G., Enantioselective Copper-Catalyzed Intermolecular Liu, Cyanotrifluoromethylation of Alkenes via Radical Process. J. Am. Chem. Soc. 2016, 138, 15547; (r) Wu, X.; Lin, H.-C.; Li, M.-L.; Li, L.-L.; Han, Z.-Y.; Gong, L.-Z., Enantioselective 1,2-Difunctionalization of Dienes Enabled by Chiral Palladium Complex-Catalyzed Cascade Arylation/Allylic Alkylation Reaction. J. Am. Chem. Soc. 2015, 137, 13476.

11. (a) Xu, S.; Chen, H.; Zhou, Z.; Kong, W., Three-Component Alkene Difunctionalization by Direct and Selective Activation of Aliphatic C–H Bonds. *Angew. Chem. Int. Ed.* **2021**, *60*, 7405; (b) Campbell, M. W.; Yuan, M.; Polites, V. C.; Gutierrez, O.; Molander, G. A., Photochemical C–H Activation Enables Nickel-Catalyzed Olefin Dicarbofunctionalization. J. Am. Chem. Soc. **2021**, *143*, 3901; (c) Ouyang, X.-H.; Li, Y.; Song, R.-J.; Hu, M.; Luo, S.; Li, J.-H., Intermolecular Dialkylation of Alkenes with Two Distinct C–H Bonds Enabled by Synergistic Photoredox Catalysis and Iron Catalysis. *Sci. Adv.* **2019**, *5*, 9839.

12. Fan, L.-F.; Liu, R.; Ruan, X.-Y.; Wang, P.-S.; Gong, L.-Z., Asymmetric 1,2-Oxidative Alkylation of Conjugated Dienes via Aliphatic C-H Bond Activation. *Nat. Syn.* 2022, 1, 946.

13. Qin, Y.; Zhu, L.; Luo, S., Organocatalysis in Inert C-H Bond Functionalization. Chem. Rev. 2017, 117, 9433.

14. Zou, L.; Xiang, S.; Sun, R.; Lu, Q., Selective C(sp³)-H Arylation/Alkylation of Alkanes Enabled by Paired Electrocatalysis. *Nat. Commun.* 2023, 14, 7992.

15. (a) Zou, L.; Wang, X.; Xiang, S.; Zheng, W.; Lu, Q., Paired Oxidative and Reductive Catalysis: Breaking the Potential Barrier of Electrochemical C(sp³)-H Alkenylation. *Angew. Chem. Int. Ed.* **2023**, *62*, e202301026; (b) Zheng, X.; Peng, P.; Huang, C.; Lu, Q., Reversing Conventional Siteselectivity: Electrochemically Driven C(sp²)-H/C(sp³)-H Coupling with H₂ Evolution. *CCS Chem.* **2023**, *5*, 1086; (c) Wang, B.; Zhang, X.; Cao, Y.; Zou, L.; Qi, X.; Lu, Q., Electrooxidative Activation of B-B Bond in B₂cat₂: Access to gem-Diborylalkanes via Paired Electrolysis. *Angew. Chem. Int. Ed.* **2023**, *62*, e202218179; (d) Tao, Y.; Huang, C.; Lu, Q., Cycloaddition with Asymmetric Photoelectrocatalysis. *Nat. Catal.* **2023**, *6*, 1107; (e) Peng, P.; Zhong, Y.; Zhou, C.; Tao, Y.; Li, D.; Lu, Q., Unlocking the Nucleophilicity of Strong Alkyl C-H Bonds via Cu/Cr Catalysis. *ACS Cent. Sci.* **2023**, *9*, 756; (f) Huang, C.; Tao, Y.; Cao, X.; Zhou, C.; Lu, Q., Asymmetric Paired Electrocatalysis: Enantioselective Olefin-Sulfonylimine Coupling. J. Am. Chem. Soc. 2024, 146, 1984.; (g) Huang, C.; Ma, W.; Zheng, X.; Xu, M.; Qi, X.; Lu, Q., Epoxide Electroreduction. J. Am. Chem. Soc. 2022, 144, 1389; (h) Wang, B.; Peng, P.; Ma, W.; Liu, Z.; Huang, C.; Cao, Y.; Hu, P.; Qi, X.; Lu, Q., Electrochemical Borylation of Alkyl Halides: Fast, Scalable Access to Alkyl Boronic Esters. J. Am. Chem. Soc. 2021, 143, 12985.

16. Kawamata, Y.; Vantourout, J. C.; Hickey, D. P.; Bai, P.; Chen, L.; Hou, Q.; Qiao, W.; Barman, K.; Edwards, M. A.; Garrido-Castro, A. F.; deGruyter, J. N.; Nakamura, H.; Knouse, K.; Qin, C.; Clay, K. J.; Bao, D.; Li, C.; Starr, J. T.; Garcia-Irizarry, C.; Sach, N.; White, H. S.; Neurock, M.; Minteer, S. D.; Baran, P. S., Electrochemically Driven, Ni-Catalyzed Aryl Amination: Scope, Mechanism, and Applications. J. Am. Chem. Soc. 2019, 141, 6392.

17. Budnikova, Y. H.; Perichon, J.; Yakhvarov, D. G.; Kargin, Y. M.; Sinyashin, O. G., Highly Reactive σ -Organonickel Complexes in Electrocatalytic Processes. J. Organomet. Chem. 2001, 630, 185.

18. Satyanarayana, T.; Abraham, S.; Kagan, H. B., Nonlinear Effects in Asymmetric Catalysis. Angew. Chem. Int. Ed. 2009, 48, 456.

19. (a) Juliá, F., Ligand-to-Metal Charge Transfer (LMCT) Photochemistry at 3d-Metal Complexes: An Emerging Tool for Sustainable Organic Synthesis. *ChemCatChem* 2022, 14, e202200916; (b) Abderrazak, Y.; Bhattacharyya, A.; Reiser, O., Visible-Light-Induced Homolysis of Earth-Abundant Metal-Substrate Complexes: A Complementary Activation Strategy in Photoredox Catalysis. *Angew. Chem. Int. Ed.* 2021, 60, 21100.



