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Article

Electrochemical Synergistic Ni/Co-Catalyzed Carbonylative Cross-Electrophile Coupling of Aryl and Alkyl Halides with CO

Published as part of JACS Au special issue "Advances in Small Molecule Activation Towards Sustainable Chemical Transformations".

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Cite This: JACS Au 2025, 5, 1413−1420

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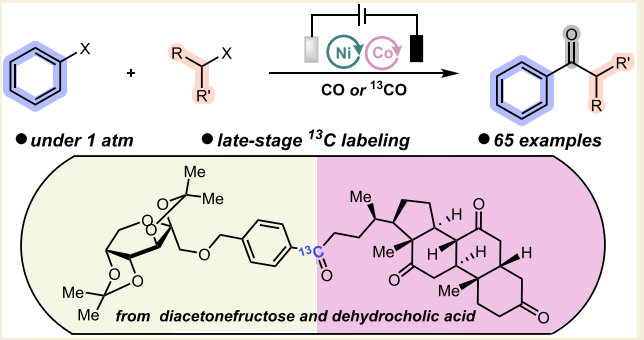
ABSTRACT: Accessing unsymmetric ketones and achieving their carbon isotope labeling are crucial yet challenging tasks in both synthetic and medicinal chemistry. We report here an efficient electrochemical nickel-/cobalt-catalyzed carbonylative cross-electrophile coupling reaction. This method allows for the modular synthesis of a library of unsymmetric ketones from simple building blocks, including aryl halides, alkyl halides, and gaseous CO. The simultaneous use of nickel and cobalt salts as concerted catalysts ensures the high efficiency of this three-component carbonylative coupling. Furthermore, electrochemical reduction avoids the use of stoichiometric reductants, making this protocol more sustainable and attractive. The broad substrate scope and late-stage ^{13}C isotope labeling of complex molecules derived from biologically active compounds highlight the practicality of this method.



KEYWORDS: *carbonylation, cross-electrophile coupling, electrochemistry, ketone, isotope label*

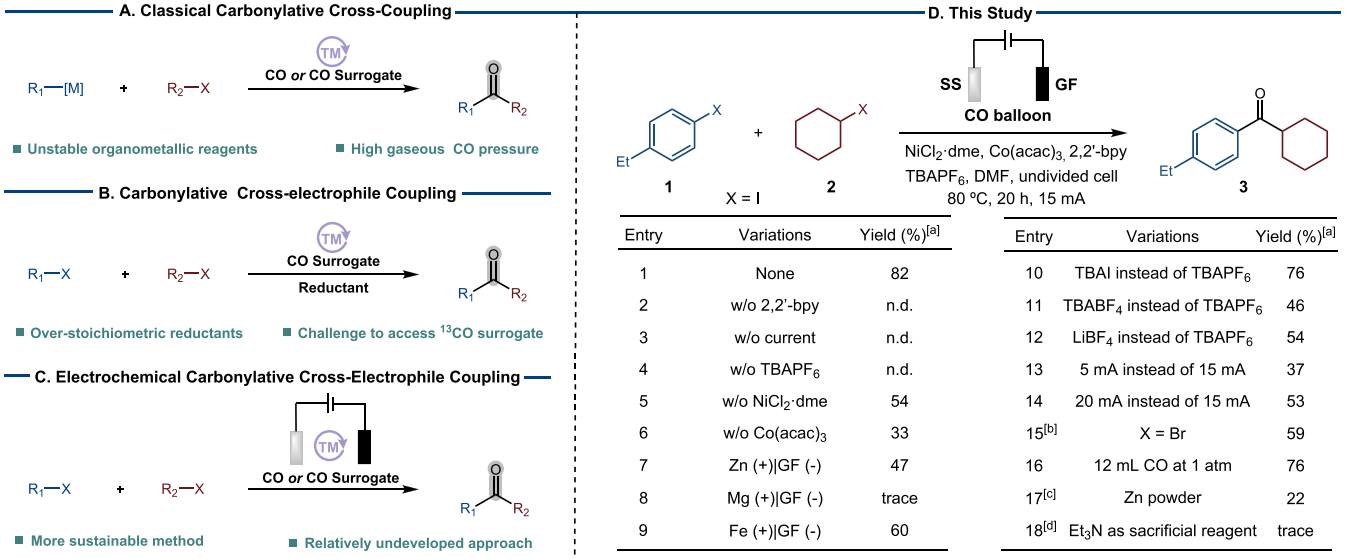
INTRODUCTION

Carbon isotope labeling of biologically active molecules is frequently used to trace metabolic pathways, study pharmacokinetics, and elucidate mechanisms of action, making it a powerful tool in drug discovery and development.[1−3] Consequently, the development of efficient methods to access ^{13}C-labeled compounds has been a long-standing focus of synthetic chemists. Among various approaches,[4−14] isotope labeling of the carbon atom in ketone scaffolds is particularly attractive,[15−19] as ketones are among the most versatile functional groups in medicinal chemistry and possess a characteristic ^{13}C NMR chemical shift over 200 ppm. Therefore, new strategies are needed not only to enable the synthesis of ketones, particularly unsymmetric ketones, but also to achieve effective carbon isotope labeling.

In this context, transition metal-catalyzed carbonylative cross-coupling reactions using cost-effective gaseous CO or its surrogates have emerged as a valuable platform for the synthesis of unsymmetric ketones.[20−22] These reactions typically require an electrophile, often an aryl or alkyl halide, along with a preprepared nucleophile, such as organometallic or organoboron reagents (Figure 1A). While this approach has enabled a variety of carbonylative coupling reactions, including Suzuki,[23−32] Stille,[33−35] Negishi,[36−43] and other couplings,[44−47] it is often burdened with the inherent instability of preprepared nucleophiles and the challenges in their preparation, thus limiting the substrate scope. To overcome these issues, carbonylative cross-electrophile coupling (XEC) was developed as an elegant alternative,[48−56] allowing two distinct, commercially available or easily accessible electrophiles to assemble with CO surrogates to generate unsymmetric ketones (Figure 1B).

The pioneering work by Troupel and co-workers demonstrated that $Fe(CO)_5$ could serve as an effective carbonylation reagent in electrochemical nickel-catalyzed carbonylative XEC reactions with aryl and benzyl electrophiles, enabling the synthesis of unsymmetric ketones.[57] However, the protocol showed a limited tolerance for alkyl electrophiles. Subsequently, the research groups of Weix,[58] Gosmini,[59] Hu,[60] Rueping,[61] Koh,[62] Shi,[63−65] and Wu[66,67] independently revealed the use of $Fe(CO)_5$, $Mo(CO)_6$, chloroformates,

Received: January 13, 2025
Revised: February 25, 2025
Accepted: February 27, 2025
Published: March 5, 2025



Entry	Variations	Yield (%)[a]
1	None	82
2	w/o 2,2'-bpy	n.d.
3	w/o current	n.d.
4	w/o $TBAPF_6$	n.d.
5	w/o $NiCl_2$·dme	54
6	w/o $Co(acac)_3$	33
7	Zn (+)|GF (-)	47
8	Mg (+)|GF (-)	trace
9	Fe (+)|GF (-)	60
10	TBAI instead of $TBAPF_6$	76
11	$TBABF_4$ instead of $TBAPF_6$	46
12	$LiBF_4$ instead of $TBAPF_6$	54
13	5 mA instead of 15 mA	37
14	20 mA instead of 15 mA	53
15[b]	X = Br	59
16	12 mL CO at 1 atm	76
17[c]	Zn powder	22
18[d]	Et_3N as sacrificial reagent	trace

Figure 1. Transition metal-catalyzed carbonylative cross-coupling for the synthesis of ketones. Standard conditions: **1** (0.25 mmol), **2** (0.50 mmol), CO balloon, $NiCl_2$·dme (0.0125 mmol), $Co(acac)_3$ (0.05 mmol), 2,2′-bpy (0.075 mmol), $TBAPF_6$ (0.30 mmol), DMF (3 mL), 80 °C, 20 h, undivided cell, 15 mA constant current, stainless steel (SS) anode, graphite felt (GF) cathode. (a) Isolated yield. (b) For X = Br: NaI (1.0 mmol) instead of $TBAPF_6$ as supporting electrolyte. (c) 1 mmol Zn was used instead of electrochemical devices. (d) 1 mmol Et_3N was used with GF as the anode. acac = acetylacetonate. bpy = bipyridine. dme = 1,2-dimethoxyethane. DMF = *N*,*N*-dimethylformamide. TBA = tetrabutylammonium.

oxalyl chloride, and phenyl formate[68] as carbonylation reagents in nickel-catalyzed carbonylative XEC reactions for ketone formation. In these protocols, overstoichiometric reductants are often required to ensure the catalytic cycle, and isotope labeling of CO surrogates was not incorporated due to the lack of established methods to access such reagents. Hence, more sustainable methods utilizing cost-effective gaseous CO or ^{13}CO at standard atmospheric pressure in carbonylative XEC reactions are highly desired for further exploration.

Electrochemical synthesis has emerged as a more sustainable approach to organic synthesis, eliminating the need for stoichiometric reductants or oxidants.[57,69−78] Moreover, it allows for precise control over electron transfer in catalytic transformations, such as between the electrodes and catalytic species or substrates. Herein, we report our efforts on electrochemical dual nickel/cobalt-catalyzed carbonylative cross-electrophile coupling for the formation of aryl−alkyl ketones under 1 atm of CO gas, providing a straightforward method for the preparation of aryl−alkyl ketones (Figure 1C). This approach is notable for its broad substrate scope and its ability to facilitate late-stage ^{13}C isotope labeling of complex and pharmaceutically relevant molecules.

RESULTS AND DISCUSSION

After substantial optimization (see the Supporting Information, Tables S1−S8), 1-ethyl-4-iodobenzene (**1**) coupled with iodocyclohexane (**2**) and CO (1 atm) in the presence of $NiCl_2$·dme, $Co(acac)_3$, 2,2′-bpy, and $TBAPF_6$ in DMF at 80 °C under 15 mA constant current electrolysis in an undivided cell equipped with a stainless steel sheet (SS) anode and graphite felt (GF) cathode, affording aryl−alkyl ketone **3** in 82% isolated yield (Figure 1D, entry 1). Blank experiments demonstrated that ligand, electrolyte, and current are essential (entries 2−4), while the simultaneous use of nickel and cobalt salts as synergistic catalysts significantly suppressed the major aryl−alkyl coupling side reaction (entries 5 and 6). Control experiments using either Ni or Co salts alone, even at higher loadings, did not significantly improve the coupling efficiency (Table S1), suggesting the synergistic role of Ni and Co catalysts. Changing the electrodes led to either reduced yields or only trace amounts of the products (entries 7−9). $TBAPF_6$ as an electrolyte proved generally superior to other ammonium and metal salts in the coupling reaction (entries 10−12). A constant current of 15 mA was found to be more effective than either lower or higher currents (entries 13 and 14). Different leaving groups were also examined. Aryl and alkyl chlorides did not react, while the corresponding bromides reacted with CO to give ketone **3** in 59% yield, using NaI as the supporting electrolyte (entry 15). The use of NaI might also enhance the coupling efficiency by facilitating *in situ* conversion of the alkyl bromide to the alkyl iodide. Control experiments conducted in a 15 mL tube filled with 12 mL of CO at 1 atm produced **3** in a 76% yield, indicating that approximately **2** equivalents of CO are sufficient to achieve optimal coupling efficiency (entry 16). As for alkyl iodides, 2 equivalents were required to maintain coupling efficiency, as homocoupled alkanes and ketones were generally observed as side products. When Zn powder was used as the reductant instead of the electrochemical devices, product **3** was obtained in 22% yield (entry 17). Only trace products were obtained when Et_3N was employed as the sacrificial reagent, with GF as the anode (entry 18).

With the optimized reaction conditions in hand, we proceeded to examine the scope of aryl iodides in this electrochemical coupling with CO and iodocyclohexane (Figure 2A). A wide series of aryl iodides with substituents at the *para*-position was first investigated. Electron-rich and -neutral iodobenzenes converted into the corresponding ketones in good yields (**3**−**8**, **16**), whereas electron-deficient ones reacted less efficiently with the formation of phenylalkyl byproducts (**9**−**13**). This may be attributed to the mechanistic hypothesis that the corresponding aryl acyl−Ni^{II} species is thermodynamically more stable.[64] Sensitive functional groups, such as free hydroxyl (**14**) and amine (**15**) groups, were also tolerated under the reaction conditions. Notably, this approach exhibited excellent chemoselective cleavage of the C−I bond

https://doi.org/10.1021/jacsau.5c00031
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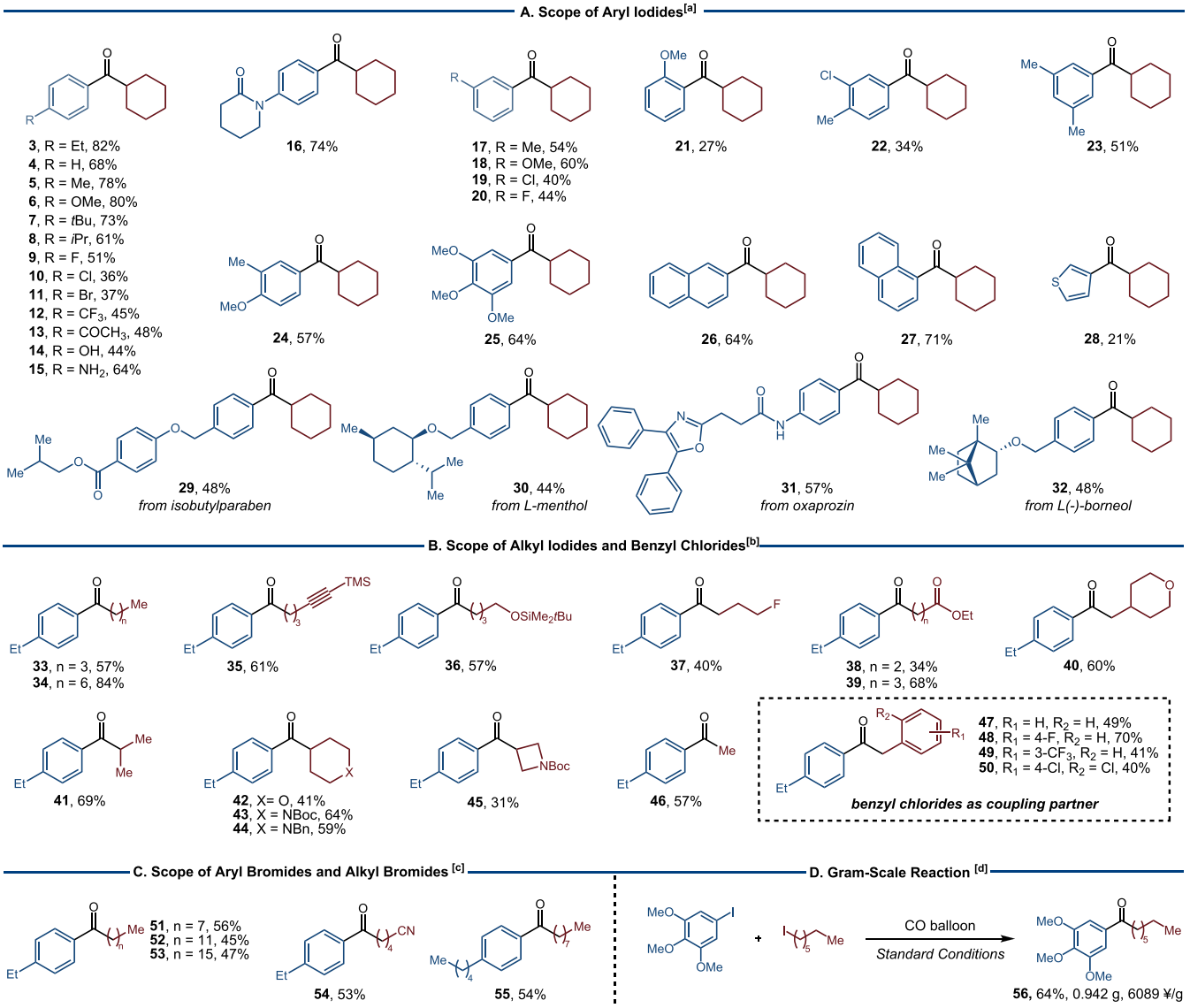

Figure 2. Substrate scope of aryl and alkyl halides. Reactions were performed on a 0.25 mmol scale unless otherwise stated. (a) Iodocyclohexane was used as the alkyl electrophile. (b) 1-Ethyl-4-iodobenzene was used as the aryl electrophile. (c) Both electrophiles were bromides, and NaI was used as the supporting electrolyte instead of $TBAPF_6$. (d) The reaction was performed on a 5.0 mmol scale.

over the C−Br and C−Cl bonds, as observed in the formation of **10** and **11**. Iodobenzenes bearing substituents at the *meta*-position coupled moderately (**17**−**20**), whereas *ortho*-substituents resulted in lower yields (**21**), likely due to steric hindrance. Likewise, disubstituted and trisubstituted iodobenzenes also proved to be suitable coupling partners, yielding the corresponding products in moderate yields (**22**−**25**). Likewise, iodopolyarenes (**26** and **27**), iodoheteroarene (**28**), as well as structurally more complex iodobenzenes derived from isobutylparaben (**29**), menthol (**30**), oxaprozin (**31**), and borneol (**32**) were also well tolerated, demonstrating the excellent functional group tolerance of this protocol.

We further investigated the applicability of a rich array of alkyl iodides in carbonylative coupling with iodobenzene **1** and CO (Figure 2B). Primary alkyl iodides displayed good reactivity under standard conditions, with functional groups such as alkyne, siloxane, ester, ether, and fluorine being tolerated (**33**−**40**). In addition to the model substrate **2**, both acyclic (**41**) and heterocyclic (**42**−**45**) secondary iodides were also compatible with this method, producing the corresponding ketones with moderate success. It is worth noting that iodomethane effectively participated in the coupling event, producing an arylmethyl ketone **46** in 57% yield.[79] Furthermore, when primary benzyl chlorides were subjected to the standard conditions for coupling with **1** and CO, the resulting ketones (**47**−**50**) were obtained in moderate to good yields. However, the method was not applicable to sterically hindered tertiary alkyl iodides.[80]

The electrochemical reductive coupling of aryl and alkyl bromides with CO was also tested. Besides secondary bromocyclohexane (Figure 1D, entry 15), primary alkyl bromides were good candidates, producing the desired ketones, albeit with slightly lower yields (Figure 2C, **51**−**55**). In a gram-scale reaction, high-value-added ketone **56** formed in 64% yield, highlighting the practicality of this method (Figure 2D).

Encouraged by the broad substrate scope of this electrochemical XEC protocol, we next turned our attention to the ^{13}C isotope labeling of biologically relevant compounds, a key goal of this research (Figure 3).[1] With respect to naturally

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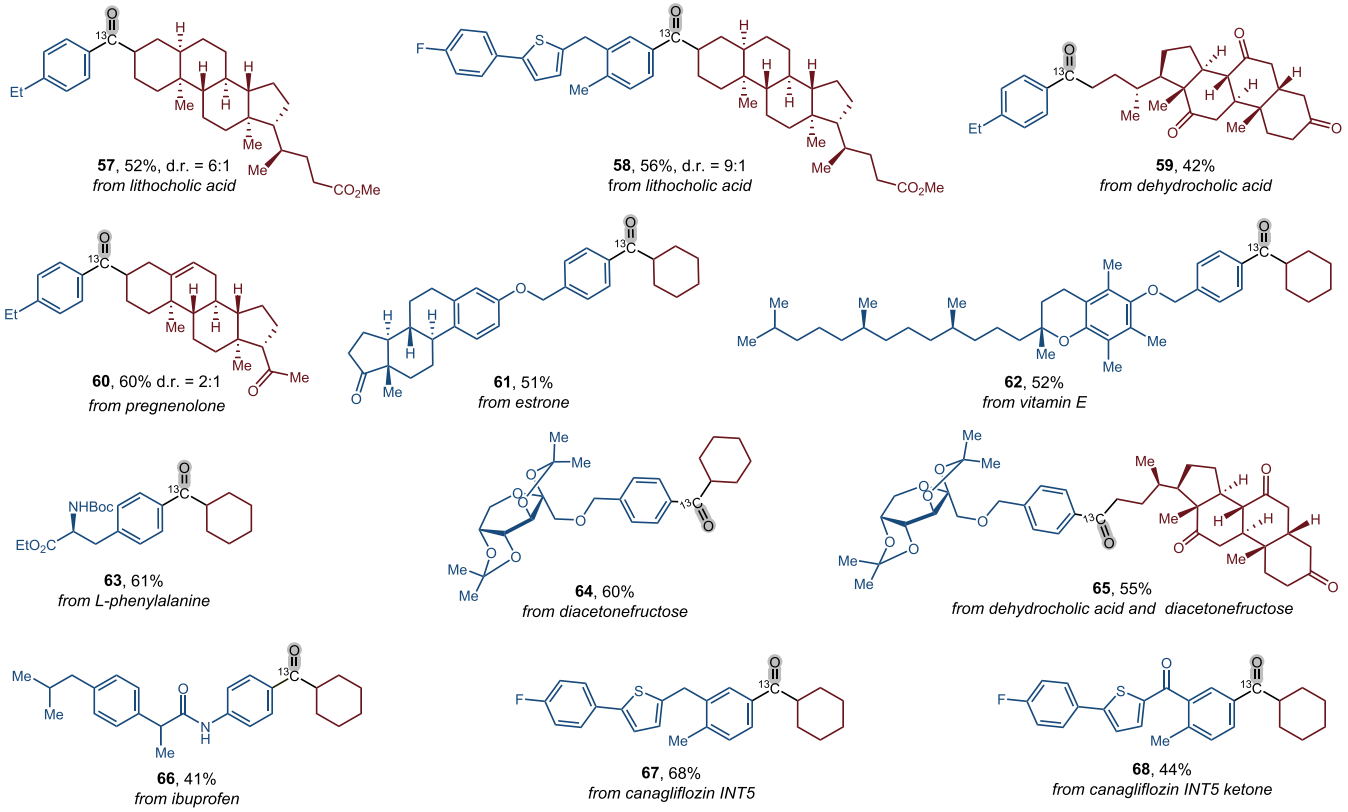

Figure 3. ^{13}C isotope labeling of biologically relevant compounds. Reactions were performed on a 0.25 mmol scale unless otherwise stated.

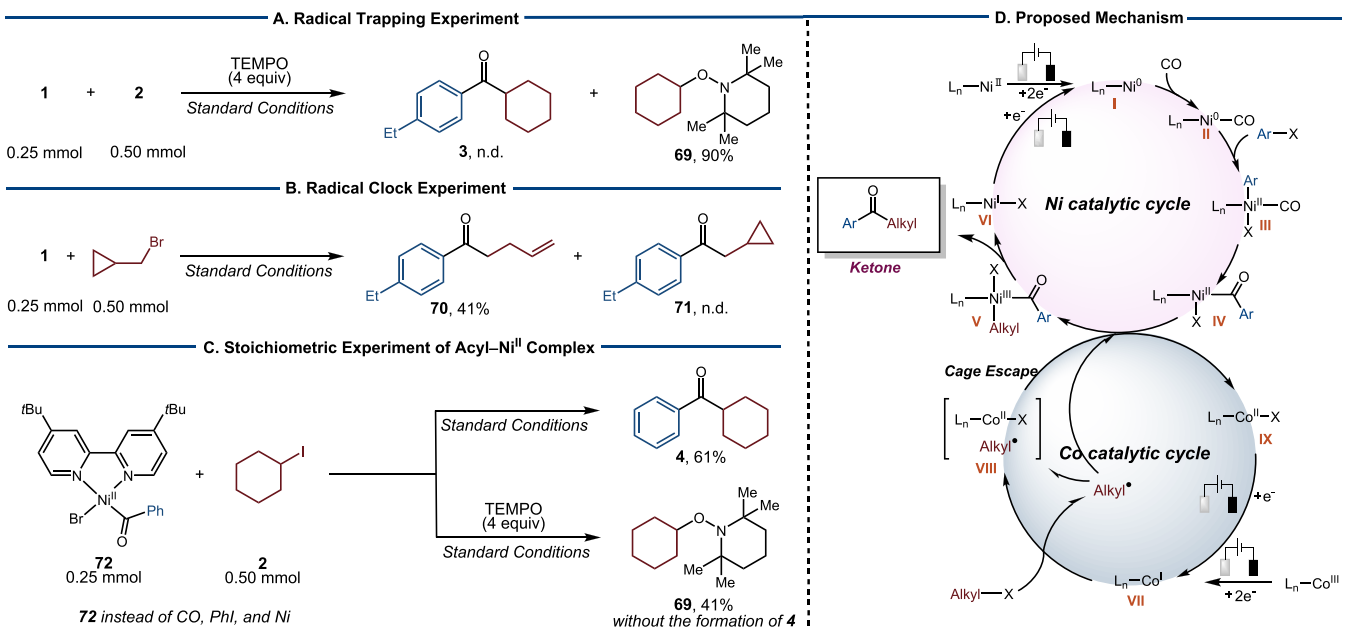

Figure 4. Preliminary mechanistic investigations and the proposed reaction mechanism.

occurring compounds, their derived aryl or alkyl iodides reacted moderately with ^{13}CO, forming ^{13}C-labeled ketones starting from lithocholic acid, dehydrocholic acid, pregnenolone, estrone, vitamin E, L-phenylalanine, and fructose (**57**–**64**). Under standard conditions, fructose-derived aryl iodide coupled with dehydrocholic acid-derived alkyl iodide and ^{13}CO to yield the carbon isotope-labeled ketone **65** in 55%, while aryl iodides derived from synthetic drugs and their fragments also worked equally well, leading to the formation of ketones **66**–**68**. The overall success in ^{13}C isotope labeling of biologically relevant molecules underlines the pharmaceutical potential of this mild method.[81,82] In all cases, the exclusive formation of ^{13}C-labeled ketones demonstrated that the CO gas, rather than DMF, serves as the carbonylative reagent, albeit DMF is known to act as carbonylative reagent under electrochemical conditions.[83]

To gain mechanistic insights into this carbonylative electrochemical XEC approach, a series of control experiments

https://doi.org/10.1021/jacsau.5c00031
JACS Au 2025, 5, 1413−1420

were performed. When 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) was subjected to the standard conditions, the model reaction was completely inhibited with the formation of cyclohexyl/TEMPO adduct **69** in 90% yield (Figure 4A). In a radical clock experiment using cyclopropanemethyl bromide, the ring-opening ketone **70** was isolated in moderate yield, without cyclopropyl-containing product **71** being detected (Figure 4B). These observations indicated the radical nature of this electrochemical three-component coupling and the involvement of alkyl radicals.[84,85]

To further probe the roles of Ni and Co, an aryl acyl−Ni^{II} complex **72** was prepared upon the oxidative addition of benzoyl bromide to a Ni^0 species (Figure 4C). In a stoichiometric experiment, 1 equiv of complex **72** was subjected to standard conditions and reacted with **2** in the presence of catalytic amounts of $Co(acac)_3$, affording the coupled product **4** in 61% yield, which is comparable to the yield obtained in the three-component XEC coupling of iodobenzene, **2** and CO. Moreover, an aryl-Ni^{II} complex as an intermediate en route to the formation of aryl acyl−Ni^{II} complex prior to CO insertion was also synthesized. The stoichiometric reaction of this complex with iodocyclohexane and CO in the presence of a Co catalyst also gave the desired ketone in 59% yield. These results indicated that the acyl−Ni^{II} intermediate forms and operates within the catalytic cycle.[31,58] In a parallel experiment, the addition of TEMPO to the stoichiometric reaction inhibited the desired coupling, resulting in the formation of radical adduct **69** in 41% yield. Furthermore, an increase in the reduction peak current of alkyl iodide was observed upon adding $Co(acac)_3$ in cyclic voltammetry studies (see Supporting Information, Figure S6).[86,87] These observations suggested that Co might play a role in the formation of alkyl radicals.[88−93]

Both Ni and Co alone can also promote carbonylation, albeit with significantly lower yields (Figure 1D, entries 3 and 4), and the possibility of single-metal catalysis cannot be entirely ruled out. Nevertheless, in combination with our preliminary mechanistic investigations and the literature precedents,[94,95] we tentatively propose a concerted pathway, in which Ni accounts for the activation of aryl electrophile and the subsequent capture of CO to form acyl−Ni^{II} complex, while Co may activate the alkyl electrophile to generate alkyl radical. These two metals work synergistically to secure a high-yielding performance of the three-component carbonylative XEC reaction.

In the Ni catalytic cycle, a Ni^0 species **I** forms by the electroreduction of Ni^{II} precursor, followed by CO coordination to **I**, forming complex **II** (Figure 4D).[57] The Ni^0 species **II** then undergoes two-electron oxidative addition with aryl iodide to form Ni^{II} intermediate **III**. Subsequently, CO inserts into intermediate **III**, giving rise to key acyl−Ni^{II} complex **IV**. Simultaneously, in the Co cycle, the electroreduction of the Co^{III} precatalyst affords a reductive Co^{I} species **VII**. A single electron transfer from **VII** to alkyl iodide generates an alkyl radical and Co^{II} species **VIII**. This alkyl radical is then captured by **IV**, leading to the formation of Ni^{III} intermediate **V**, upon which reductive elimination delivers the desired aryl−alkyl ketone and Ni^{I} complex **VI**. The Ni^{I} species **VI** and Co^{II} species **IX** are reduced on the cathode to regenerate active species **I** and **VII**, respectively.

CONCLUSIONS

In conclusion, we have developed an efficient, concerted dual Ni/Co-catalyzed cross-electrophile coupling of unactivated alkyl halides and aryl halides with CO under standard atmospheric pressure. This method exhibits excellent functional group tolerance and avoids the use of organometallic reagents. As a result, a broad range of readily accessible aryl and alkyl electrophiles can efficiently participate in the carbonylative coupling process, enabling unsymmetric ketone synthesis. Control experiments and cyclic voltammetry studies revealed the radical nature of this methodology and the synergistic roles of nickel and cobalt catalysts. Moreover, ^{13}CO was also successfully employed as a carbonylative reagent, particularly in ^{13}CO-labeled ketone formation starting from biologically relevant compounds, highlighting the potential application of our methods in the area of drug discovery.

METHODS

General Procedure for the Synthesis of Aryl−Alkyl Ketones

Electrochemical carbonylative reactions were carried out in undivided cells using predried Schlenk tube with a stainless steel sheet (0.3 mm × 10.0 mm × 15.0 mm) and graphite felt (2.0 mm × 10.0 mm × 15.0 mm). The predried Schlenk tube equipped with a stir bar was evacuated and backfilled with N_2 (3 times). After that, the tube was opened and charged with $NiCl_2$·dme (0.0125 mmol), $Co(acac)_3$ (0.050 mmol), 2,2′-bpy (0.075 mmol), $TBAPF_6$ (0.30 mmol), corresponding alkyl iodides (0.50 mmol, 2.00 equiv), and corresponding aryl iodides (0.25 mmol, 1.00 equiv). Then, the tube was evacuated and backfilled with 1 atm CO (3 times), followed by the addition of DMF (3 mL). The tube was sealed and heated at 80 °C with a constant current at 15 mA for 20 h. The electrodes were removed and washed with DCM (3 × 5 mL)·H_2O (20 mL) was added to the combined reaction mixture, and the resulting mixture was extracted with DCM (2 × 20 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by preparative thin-layer chromatography to furnish the desired product.

General Procedure for the Synthesis of ^{13}C-Labeled Aryl−Alkyl Ketones

Carbon-13 isotope labeling reactions were carried out in undivided cells using a predried Schlenk tube with a stainless steel sheet (0.3 mm × 10.0 mm × 15.0 mm) and graphite felt (2.0 mm × 10.0 mm × 15.0 mm). The predried Schlenk tube equipped with a stir bar is evacuated and backfilled with N_2 (3 times). After that, the tube was opened and charged with $NiCl_2$·dme (0.0125 mmol), $Co(acac)_3$ (0.050 mmol), 2,2′-bpy (0.075 mmol), $TBAPF_6$ (0.30 mmol), corresponding aryl iodides (0.25 mmol, 1.00 equiv), and corresponding alkyl iodides (0.50 mmol, 2.00 equiv). Subsequently, the tube was connected to a three-way stopcock system, one port was linked to a vacuum, and the other port was connected to a ^{13}CO gas bag. Then, the tube was evacuated and backfilled with 1 atm of ^{13}CO (3 times), followed by the addition of DMF (3 mL). The tube was sealed and heated at 80 °C with a constant current at 15 mA for 20 h. The electrodes were removed and washed with DCM (3 × 5 mL)·H_2O (20 mL) was added to the combined reaction mixture, and the resulting mixture was extracted with DCM (2 × 20 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by preparative thin-layer chromatography to furnish the desired product.

https://doi.org/10.1021/jacsau.5c00031
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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacsau.5c00031.

Additional experimental details, materials, and methods, and spectroscopic data for complete reproducibility of all experimental findings (PDF)

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Author Contributions

S.T. initiated and conducted the primary experiments, analyzed data, and contributed to the drafting of the manuscript; Y.Y. and L.C. did some experiments and characterization of products; J.X., H.F., H.C., W.J., and R.L. contributed to the discussion on the study. W.X. and X.Z. supervised the research and provided critical revisions to the manuscript. All authors contributed to this research project through in-depth discussions, data analysis, and result interpretation.

Funding

This work was supported by Sichuan Science and Technology Program (2024ZYD0099), and the Fundamental Research Funds for the Central Universities (1082204112I96).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank Chunchun Zhang from the Center of Analysis & Testing, as well as Jing Li and Dongyan Deng from the Comprehensive Training Platform of the Specialized Laboratory, College of Chemistry, Sichuan University, for their assistance with NMR and HRMS measurements.

■ REFERENCES

(1) Lin, M. T.; Sperling, L. J.; Frericks Schmidt, H. L.; Tang, M.; Samoilova, R. I.; Kumasaka, T.; Iwasaki, T.; Dikanov, S. A.; Rienstra, C. M.; Gennis, R. B. A rapid and robust method for selective isotope labeling of proteins. *Methods* **2011**, *55*, 370−378.

(2) Johnson, K.; Le, H.; Khojasteh, S. C. *Identification and Quantification of Drugs, Metabolites, Drug Metabolizing Enzymes, and Transporters*, 2nd ed.; Ma, S.; Chowdhury, S. K., Eds.; Elsevier: Amsterdam, 2020; pp 439−460.

(3) Bsharat, O.; Doyle, M. G. J.; Munch, M.; Mair, B. A.; Cooze, C. J. C.; Derdau, V.; Bauer, A.; Kong, D.; Rotstein, B. H.; Lundgren, R. J. Aldehyde-catalysed carboxylate exchange in α-amino acids with isotopically labelled CO_2. *Nat. Chem.* **2022**, *14*, 1367−1374.

(4) Mägerlein, W.; Indolese, A. F.; Beller, M. Development of new palladium catalysts for the alkoxycarbonylation of aryl chlorides. *J. Organomet. Chem.* **2002**, *641*, 30−40.

(5) Ton, S. J.; Neumann, K. T.; Nørby, P.; Skrydstrup, T. Nickel-Mediated Alkoxycarbonylation for Complete Carbon Isotope Replacement. *J. Am. Chem. Soc.* **2021**, *143*, 17816−17824.

(6) Ai, H.-J.; Leidecker, B. N.; Dam, P.; Kubis, C.; Rabeah, J.; Wu, X.-F. Iron-Catalyzed Alkoxycarbonylation of Alkyl Bromides via a Two-Electron Transfer Process. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202211939.

(7) Liu, N.; Wu, X.; Wang, C.; Qu, J.; Chen, Y. Nickel-catalyzed alkoxycarbonylation of aryl iodides with 1 atm CO. *Chem. Commun.* **2022**, *58*, 4643−4646.

(8) Liu, J.; Zhang, R.; Wang, S.; Sun, W.; Xia, C. A General and Efficient Copper Catalyst for the Double Carbonylation Reaction. *Org. Lett.* **2009**, *11*, 1321−1324.

(9) Cheung, C. W.; Leendert Ploeger, M.; Hu, X. Amide synthesis via nickel-catalysed reductive aminocarbonylation of aryl halides with nitroarenes. *Chem. Sci.* **2018**, *9*, 655−659.

(10) Wang, L.-C.; Chen, B.; Wu, X.-F. Cobalt-Catalyzed Direct Aminocarbonylation of Ethers: Efficient Access to α-Amide Substituted Ether Derivatives. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202203797.

(11) Liang, Y.-F.; Steinbock, R.; Münch, A.; Stalke, D.; Ackermann, L. Manganese-Catalyzed Carbonylative Annulations for Redox-Neutral Late-Stage Diversification. *Angew. Chem., Int. Ed.* **2018**, *57*, 5384−5388.

(12) Cheng, L.-J.; Mankad, N. P. Cu-Catalyzed Carbonylative Silylation of Alkyl Halides: Efficient Access to Acylsilanes. *J. Am. Chem. Soc.* **2020**, *142*, 80−84.

(13) Tung, P.; Mankad, N. P. Light-Mediated Synthesis of Aliphatic Anhydrides by Cu-Catalyzed Carbonylation of Alkyl Halides. *J. Am. Chem. Soc.* **2023**, *145*, 9423−9427.

(14) Tung, P.; Mankad, N. P. Photochemical Synthesis of Acyl Fluorides Using Copper-Catalyzed Fluorocarbonylation of Alkyl Iodides. *Org. Lett.* **2024**, *26*, 3299−3303.

(15) Wotal, A. C.; Weix, D. J. Synthesis of Functionalized Dialkyl Ketones from Carboxylic Acid Derivatives and Alkyl Halides. *Org. Lett.* **2012**, *14*, 1476−1479.
(16) Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. Catalytic Asymmetric Reductive Acyl Cross-Coupling: Synthesis of Enantioenriched Acyclic α,α-Disubstituted Ketones. *J. Am. Chem. Soc.* **2013**, *135*, 7442−7445.
(17) Zhao, C.; Jia, X.; Wang, X.; Gong, H. Ni-Catalyzed Reductive Coupling of Alkyl Acids with Unactivated Tertiary Alkyl and Glycosyl Halides. *J. Am. Chem. Soc.* **2014**, *136*, 17645−17651.
(18) Moragas, T.; Correa, A.; Martin, R. Metal-Catalyzed Reductive Coupling Reactions of Organic Halides with Carbonyl-Type Compounds. *Chem. - Eur. J.* **2014**, *20*, 8242−8258.
(19) Cheng, L.-J.; Mankad, N. P. Cu-Catalyzed Hydrocarbonylative C−C Coupling of Terminal Alkynes with Alkyl Iodides. *J. Am. Chem. Soc.* **2017**, *139*, 10200−10203.
(20) Wu, X.-F.; Neumann, H.; Beller, M. Palladium-catalyzed carbonylative coupling reactions between Ar−X and carbon nucleophiles. *Chem. Soc. Rev.* **2011**, *40*, 4986−5009.
(21) Wu, X.-F.; Neumann, H.; Beller, M. Palladium-catalyzed carbonylative coupling reactions between Ar−X and carbon nucleophiles. *Chem. Catal.* **2022**, *2*, 477−498.
(22) Yang, M.; Liu, Y.; Qi, X.; Zhao, Y.; Wu, X.-F. Carbonylative transformation of aryl halides and strong bonds via cheap metal catalysts and sustainable technologies. *Green Synth. Catal.* **2024**, *5*, 211−269.
(23) Ishiyama, T.; Miyaura, N.; Suzuki, A. Palladium-catalyzed carbonylative cross-coupling reaction of 1-halo-1-alkenes with 9-alkyl-9-BBN derivatives. A direct synthesis of α,β-unsaturated ketones. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1999−2001.
(24) Ishiyama, T.; Miyaura, N.; Suzuki, A. Palladium-catalyzed carbonylative cross-coupling reaction of iodoalkanes with 9-alkyl-9-BBN derivatives. A direct and selective synthesis of ketones. *Tetrahedron Lett.* **1991**, *32*, 6923−6926.
(25) Ishiyama, T.; Murata, M.; Suzuki, A.; Miyaura, N. Synthesis of ketones from iodoalkenes, carbon monoxide and 9-alkyl-9-borabicyclo[3.3.1]nonane derivatives via a radical cyclization and palladium-catalysed carbonylative cross-coupling sequence. *J. Chem. Soc., Chem. Commun.* **1995**, 295−296.
(26) Potuzak, J. S.; Tan, D. S. Synthesis of C1-alkyl- and acylglycals from glycals using a B-alkyl Suzuki−Miyaura cross coupling approach. *Tetrahedron Lett.* **2004**, *45*, 1797−1801.
(27) Pye, D. R.; Cheng, L.-J.; Mankad, N. P. Cu/Mn bimetallic catalysis enables carbonylative Suzuki−Miyaura coupling with unactivated alkyl electrophiles. *Chem. Sci.* **2017**, *8*, 4750−4755.
(28) Yin, H.; Kumke, J. J.; Domino, K.; Skrydstrup, T. Palladium Catalyzed Carbonylative Coupling of Alkyl Boron Reagents with Bromodifluoroacetamides. *ACS Catal.* **2018**, *8*, 3853−3858.
(29) Zhao, H.-Y.; Gao, X.; Zhang, S.; Zhang, X. Nickel-Catalyzed Carbonylation of Difluoroalkyl Bromides with Arylboronic Acids. *Org. Lett.* **2019**, *21*, 1031−1036.
(30) Cheng, R.; Zhao, H.-Y.; Zhang, S.; Zhang, X. Nickel-Catalyzed Carbonylation of Secondary Trifluoromethylated, Difluoromethylated, and Nonfluorinated Aliphatic Electrophiles with Arylboronic Acids under 1 atm of CO. *ACS Catal.* **2020**, *10*, 36−42.
(31) Zhou, M.; Zhao, H.-Y.; Zhang, S.; Zhang, Y.; Zhang, X. Nickel-Catalyzed Four-Component Carbocarbonylation of Alkenes under 1 atm of CO. *J. Am. Chem. Soc.* **2020**, *142*, 18191−18199.
(32) Mühlfenzl, K. S.; Enemærke, V. J.; Gahlawat, S.; Golbækdal, P. I.; Munksgaard-Ottosen, N.; Neumann, K. T.; Hopmann, K. H.; Norrby, P.-O.; Elmore, C. S.; Skrydstrup, T. Nickel Catalyzed Carbonylative Cross Coupling for Direct Access to Isotopically Labeled Alkyl Aryl Ketones. *Angew. Chem., Int. Ed.* **2024**, *63*, No. e202412247.
(33) Tanaka, M. Unsymmetrical ketone synthesis from organic halides, carbon monoxide, and organotin compounds catalyzed by a palladium complex. *Tetrahedron Lett.* **1979**, *20*, 2601−2602.
(34) Echavarren, A. M.; Stille, J. K. Palladium-catalyzed carbonylative coupling of aryl triflates with organostannanes. *J. Am. Chem. Soc.* **1988**, *110*, 1557−1565.
(35) Dai, Y.; Feng, X.; Liu, H.; Jiang, H.; Bao, M. Synthesis of 2-naphthols via carbonylative Stille coupling reaction of 2-bromobenzyl bromides with tributylallylstannane followed by the Heck reaction. *J. Org. Chem.* **2011**, *76*, 10068−10077.
(36) Wang, Q.; Chen, C. Nickel-catalyzed carbonylative Negishi cross-coupling reactions. *Tetrahedron Lett.* **2008**, *49*, 2916−2921.
(37) Custar, D. W.; Le, H.; Morken, J. P. Pd-catalyzed carbonylative conjugate addition of dialkylzinc reagents to unsaturated carbonyls. *Org. Lett.* **2010**, *12*, 3760−3763.
(38) Wu, X.-F.; Schranck, J.; Neumann, H.; Beller, M. Palladium-catalyzed carbonylative Negishi-type coupling of aryl iodides with benzyl chlorides. *Chem. - Asian J.* **2012**, *7*, 40−44.
(39) Andersen, T. L.; Donslund, A. S.; Neumann, K. T.; Skrydstrup, T. Carbonylative coupling of alkyl zinc reagents with benzyl bromides catalyzed by a nickel/NN_2 pincer ligand complex. *Angew. Chem., Int. Ed.* **2018**, *57*, 800−804.
(40) Peng, J.-B.; Chen, B.; Qi, X.; Ying, J.; Wu, X.-F. Palladium-catalyzed carbonylative coupling of aryl iodides with alkyl bromides: Efficient synthesis of alkyl aryl ketones. *Adv. Synth. Catal.* **2018**, *360*, 4153−4160.
(41) Esteves, H. A.; Darbem, M. P.; Pimenta, D. C.; Stefani, H. A. Carbonylative Negishi-type coupling of 2-iodoglycals with alkyl and aryl halides. *Eur. J. Org. Chem.* **2019**, *2019*, 7384−7388.
(42) Weng, Y.; Zhang, C.; Tang, Z.; Shrestha, M.; Huang, W.; Qu, J.; Chen, Y. Nickel-catalyzed allylic carbonylative coupling of alkyl zinc reagents with tert-butyl isocyanide. *Nat. Commun.* **2020**, *11*, No. 392.
(43) Zhang, Y.; Cao, Q.; Xi, Y.; Wu, X.; Qu, J.; Chen, Y. Nickel-Catalyzed Carbonylative Negishi Cross-Coupling of Unactivated Secondary Alkyl Electrophiles with 1 atm CO Gas. *J. Am. Chem. Soc.* **2024**, *146*, 7971−7978.
(44) Harada, S.; Taguchi, T.; Tabuchi, N.; Narita, K.; Hanzawa, Y. Acylzirconocene chloride as an "unmasked" acyl anion. *Angew. Chem., Int. Ed.* **1998**, *37*, 1696−1698.
(45) Kakuuchi, A.; Taguchi, T.; Hanzawa, Y. Formation of α-amino ketones: addition of acylzirconocene chlorides to imines catalyzed by $Yb(OTf)_3$/TmsOTf and brønsted acids and three-component reactions of acylzirconocene chlorides, aldehydes, and amines. *Eur. J. Org. Chem.* **2003**, *2003*, 116−122.
(46) Zhao, Y.; Jin, L.; Li, P.; Lei, A. Palladium-catalyzed oxidative carbonylation of alkyl and aryl indium reagents with CO under mild conditions. *J. Am. Chem. Soc.* **2008**, *130*, 9429−9433.
(47) Chen, B.; Wu, X.-F. Palladium-catalyzed synthesis of 1,2-diketones from aryl halides and organoaluminum reagents using *tert*-butyl isocyanide as the CO source. *Org. Lett.* **2020**, *22*, 636−641.
(48) Everson, D. A.; Shrestha, R.; Weix, D. J. Nickel-catalyzed reductive cross-coupling of aryl halides with alkyl halides. *J. Am. Chem. Soc.* **2010**, *132*, 920−921.
(49) Yu, X.; Yang, T.; Wang, S.; Xu, H.; Gong, H. Nickel-catalyzed reductive cross-coupling of unactivated alkyl halides. *Org. Lett.* **2011**, *13*, 2138−2141.
(50) Knappke, C. E. I.; Grupe, S.; Gärtner, D.; Corpet, M.; Gosmini, C.; Jacobi von Wangelin, A. Reductive Cross-Coupling Reactions between Two Electrophiles. *Chem. - Eur. J.* **2014**, *20*, 6828−6842.
(51) Weix, D. J. Methods and mechanisms for cross-electrophile coupling of Csp^2 halides with alkyl electrophiles. *Acc. Chem. Res.* **2015**, *48*, 1767−1775.
(52) Gu, J.; Wang, X.; Xue, W.; Gong, H. Nickel-catalyzed reductive coupling of alkyl halides with other electrophiles: Concept and mechanistic considerations. *Org. Chem. Front.* **2015**, *2*, 1411−1421.
(53) Hamby, T. B.; LaLama, M. J.; Sevov, C. S. Controlling Ni redox states by dynamic ligand exchange for electroreductive Csp^3−Csp^2 coupling. *Science* **2022**, *376*, 410−416.
(54) Duan, J.; Wang, K.; Xu, G.-L.; Kang, S.; Qi, L.; Liu, X.-Y.; Shu, X.-Z. Cross-Electrophile $C(sp^2)$−Si Coupling of Vinyl Chlorosilanes. *Angew. Chem., Int. Ed.* **2020**, *59*, 23083−23088.

https://doi.org/10.1021/jacsau.5c00031
JACS Au 2025, 5, 1413−1420

(55) Su, P.-F.; Wang, K.; Peng, X.; Pang, X.; Guo, P.; Shu, X.-Z. Nickel-Catalyzed Reductive C−Ge Coupling of Aryl/Alkenyl Electrophiles with Chlorogermanes. *Angew. Chem., Int. Ed.* **2021**, *60*, 26571−26576.
(56) Zhang, L.; Oestreich, M. Nickel-catalyzed, reductive C(sp^3)−Si cross-coupling of α-cyano alkyl electrophiles and chlorosilanes. *Angew. Chem., Int. Ed.* **2021**, *60*, 18587−18590.
(57) Dolhem, E.; Barhdadi, R.; Folest, J. C.; Nédelec, J. Y.; Troupel, M. Nickel catalysed electrosynthesis of ketones from organic halides and iron pentacarbonyl. Part 2: Unsymmetrical ketones. *Tetrahedron* **2001**, *57*, 525−529.
(58) Wotal, A. C.; Ribson, R. D.; Weix, D. J. Stoichiometric reactions of acylnickel(II) complexes with electrophiles and the catalytic synthesis of ketones. *Organometallics* **2014**, *33*, 5874−5881.
(59) Rérat, A.; Michon, C.; Agbossou-Niedercorn, F.; Gosmini, C. Synthesis of symmetrical diaryl ketones by cobalt-catalyzed reaction of arylzinc reagents with ethyl chloroformate. *Eur. J. Org. Chem.* **2016**, *2016*, 4554−4560.
(60) Shi, R.; Hu, X. From alkyl halides to ketones: Nickel-catalyzed reductive carbonylation utilizing ethyl chloroformate as the carbonyl source. *Angew. Chem., Int. Ed.* **2019**, *58*, 7454−7458.
(61) Chen, H.; Yue, H.; Zhu, C.; Rueping, M. Reactivity in nickel-catalyzed multi-component sequential reductive cross-coupling reactions. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202204144.
(62) Jiang, Y.; Yang, K.; Wei, Y.; Wang, Q.; Li, S.-J.; Lan, Y.; Koh, M. J. Catalytic Multicomponent Synthesis of C-Acyl Glycosides by Consecutive Cross-Electrophile Couplings. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202211043.
(63) Wang, J.; Yin, Y.; He, X.; Duan, Q.-L.; Bai, R.; Shi, H.-W.; Shi, R. Nickel-Catalyzed Highly Selective Reductive Carbonylation Using Oxalyl Chloride as the Carbonyl Source. *ACS Catal.* **2023**, *13*, 8161−8168.
(64) Xie, S.; Yin, Y.; Wang, Y.; Wang, J.; He, X.; Bai, R.; Shi, R. Current-controlled nickel-catalyzed multi-electrophile electroreductive cross-coupling. *Green Chem.* **2023**, *25*, 1522−1529.
(65) Xie, S.; Lu, M.; Wang, P.; Shi, R. Current-Regulated Selective Nickel-Catalyzed Electroreductive Cross-Electrophile Carbonylation to β/γ-Hydroxy Ketones. *Angew. Chem., Int. Ed.* **2025**, *64*, No. e202418147.
(66) Geng, H.-Q.; Wang, W.; Wu, X.-F. Nickel-catalyzed carbonylative synthesis of dihydrobenzofurans. *Catal. Commun.* **2021**, *148*, No. 106170.
(67) Huo, Y.-W.; Bao, Z.-P.; Wang, L.-C.; Schmoll, A.; Wu, X.-F. Nickel-catalyzed reductive carbonylative coupling of vinyl triflates with alkyl bromides toward enones with oxalyl chloride as the carbonyl source. *J. Catal.* **2025**, *442*, No. 115890.
(68) Yan, X.-B.; Wang, N.; Zhou, J.; Ge, H.; Wang, Z.; Lin, Y.; Shui, H. Nickel/Photoredox-Catalyzed Carbonylative Cross-Electrophile Coupling of Organohalides and Carboxylic Acid Esters with Phenyl Formate. *Org. Lett.* **2024**, *26*, 6518−6522.
(69) Francke, R.; Little, R. D. Redox catalysis in organic electrosynthesis: Basic principles and recent developments. *Chem. Soc. Rev.* **2014**, *43*, 2492−2521.
(70) 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.
(71) Sauermann, N.; Meyer, T. H.; Qiu, Y.; Ackermann, L. Electrocatalytic C−H activation. *ACS Catal.* **2018**, *8*, 7086−7103.
(72) Xiong, P.; Xu, H.-C. Chemistry with electrochemically generated N-Centered radicals. *Acc. Chem. Res.* **2019**, *52*, 3339−3350.
(73) Yuan, Y.; Lei, A. Electrochemical oxidative cross-coupling with hydrogen evolution reactions. *Acc. Chem. Res.* **2019**, *52*, 3309−3324.
(74) 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.
(75) Röckl, J. L.; Pollok, D.; Franke, R.; Waldvogel, S. R. A decade of electrochemical dehydrogenative C,C-coupling of aryls. *Acc. Chem. Res.* **2020**, *53*, 45−61.
(76) 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.
(77) Shen, T.; Lambert, T. H. Electrophotocatalytic diamination of vicinal C−H bonds. *Science* **2021**, *371*, 620−626.
(78) Liu, Y.; Li, P.; Wang, Y.; Qiu, Y. Electroreductive cross-electrophile coupling (eXEC) reactions. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202306679.
(79) Hu, L.; Liu, X.; Liao, X. Nickel-catalyzed methylation of aryl halides with deuterated methyl iodide. *Angew. Chem., Int. Ed.* **2016**, *55*, 9743−9747.
(80) Xue, W.; Jia, X.; Wang, X.; Tao, X.; Yin, Z.; Gong, H. Nickel-catalyzed formation of quaternary carbon centers using tertiary alkyl electrophiles. *Chem. Soc. Rev.* **2021**, *50*, 4162−4184.
(81) Hong, B.; Luo, T.; Lei, X. Late-stage diversification of natural products. *ACS Cent. Sci.* **2020**, *6*, 622−635.
(82) Huo, T.; Zhao, X.; Cheng, Z.; Wei, J.; Zhu, M.; Dou, X.; Jiao, N. Late-stage modification of bioactive compounds: Improving druggability through efficient molecular editing. *Acta Pharm. Sin. B* **2024**, *14*, 1030−1076.
(83) Zhang, W.; Lin, S. Electroreductive carbofunctionalization of alkenes with alkyl bromides via a radical-polar crossover mechanism. *J. Am, Chem. Soc.* **2020**, *142*, 20661−20670.
(84) 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 α-chloroesters and aryl bromides. *Nat. Commun.* **2022**, *13*, No. 7318.
(85) Zhu, C.; Chen, H.; Yue, H.; Rueping, M. Electrochemical chemo- and regioselective arylalkylation, dialkylation and hydro-(deutero)alkylation of 1,3-enynes. *Nat. Synth.* **2023**, *2*, 1068−1081.
(86) Zheng, Y.-T.; Song, J.; Xu, H.-C. Electrocatalytic dehydrogenative cyclization of 2-vinylanilides for the synthesis of indoles. *J. Org. Chem.* **2021**, *86*, 16001−16007.
(87) Li, P.; Zhu, Z.; Guo, C.; Kou, G.; Wang, S.; Xie, P.; Ma, D.; Feng, T.; Wang, Y.; Qiu, Y. Nickel-electrocatalysed C(sp^3)−C(sp^3) cross-coupling of unactivated alkyl halides. *Nat. Catal.* **2024**, *7*, 412−421.
(88) Ohmiya, H.; Tsuji, T.; Yorimitsu, H.; Oshima, K. Cobalt-catalyzed cross-coupling reactions of alkyl halides with allylic and benzylic grignard reagents and their application to tandem radical cyclization/cross-coupling reactions. *Chem. - Eur. J.* **2004**, *10*, 5640−5648.
(89) Amatore, M.; Gosmini, C. Direct method for carbon−carbon bond formation: the functional group tolerant cobalt-catalyzed alkylation of aryl halides. *Chem. - Eur. J.* **2010**, *16*, 5848−5852.
(90) Ackerman, L. K. G.; Anka-Lufford, L. L.; Naodovic, M.; Weix, D. J. Cobalt co-catalysis for cross-electrophile coupling: Diarylmethanes from benzyl mesylates and aryl halides. *Chem. Sci.* **2015**, *6*, 1115−1119.
(91) Hofstra, J. L.; Cherney, A. H.; Ordner, C. M.; Reisman, S. E. Synthesis of enantioenriched allylic silanes via nickel-catalyzed reductive cross-coupling. *J. Am. Chem. Soc.* **2018**, *140*, 139−142.
(92) Komeyama, K.; Michiyuki, T.; Osaka, I. Nickel/cobalt-catalyzed C(sp^3)−C(sp^3) cross-coupling of alkyl halides with alkyl tosylates. *ACS Catal.* **2019**, *9*, 9285−9291.
(93) Lutter, F. H.; Grokenberger, L.; Benz, M.; Knochel, P. Cobalt-catalyzed Csp^3−Csp^3 cross-coupling of functionalized alkylzinc reagents with alkyl iodides. *Org. Lett.* **2020**, *22*, 3028−3032.
(94) Diccianni, J. B.; Diao, T. Mechanisms of nickel-catalyzed cross-coupling reactions. *Trends Chem.* **2019**, *1*, 830−844.
(95) Lin, Q.; Spielvogel, E. H.; Diao, T. Carbon-centered radical capture at nickel(II) complexes: Spectroscopic evidence, rates, and selectivity. *Chem* **2023**, *9*, 1295−1308.

https://doi.org/10.1021/jacsau.5c00031
JACS Au 2025, 5, 1413−1420