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Low-valent cobalt catalyzed direct dehydroxylative cross-coupling of benzyl alcohols with aryl-chlorides

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The direct functionalization of alcohols *via* C–O bond cleavage is a synthetically valuable but challenging transformation. In this work, we report a reductive C(sp^3)–C(sp^2) cross-coupling reaction between benzyl alcohols and a broad range of aryl chlorides. The success of this transformation is attributed to the development of low-coordinate cobalt/bipyridine complexes, which enable the selective conversion of benzyl alcohols into the corresponding diarylmethanes, while minimizing undesired homocoupling of either the benzyl alcohol or aryl chlorides.

Alcohols are among the most abundant and widely distributed functional groups in natural products and bioactive molecules and they also serve as important industrial feedstock chemicals.[1–3] One of the most common functional group interconversions in synthetic chemistry involves the conversion of alcohols to halides and pseudohalides. However, these reactions often require significant time and resources for synthesis, purification and waste management, creating a bottleneck in the efficient production of pharmaceutical compound libraries derived from alcohols.[4–6] Therefore, developing a general and mild approach to functionalize alcohols has received attention[7–24] and their conversion to alkyl halides,[25] sulfonate esters,[26–31] alkyl acetates,[32–35] pivalates,[36,37] methyl ethers,[38] chloroformates,[39] redox-activated intermediates,[40,41] and other derivatives[42–45] has become a crucial strategy to achieve alkylative cross-coupling reactions.

The generation of alkyl radicals through dehydroxylation of alcohols under mild conditions is strategically appealing as alcohols can be directly used as alkylating reagents without the pre-conversion to more activated derivatives.[46–57] However, the strong C–O bond dissociation energy (BDE $\approx$ 95 kcal mol^{-1}) and the high redox potentials of unactivated alcohols make the radical cleavage of the hydroxyl group challenging, often requiring harsh reaction conditions and posing significant difficulties.[58–60] Thus far, Barton-deoxygenation for alkyl C–O bond fragmentation represents the most widely used protocol that effectively generates alkyl radicals by homolytic scission of C(sp^3)–O bonds under photo- or radical-initiator-induced conditions.[61,62]

More recently, alkyl oxalates have been developed as an alternative to the Barton deoxygenation.[63–66] Building on these pioneering studies, several methods have been developed for the deoxygenative activation of alcohols using oxalate esters, enabling the generation of open-shell species for various C–C bond-forming reactions.[67–70]

Shu[67,71–74] and Gong's[75–78] research group independently reported the functionalization of oxalate esters, which were prepared either separately or *in situ* using dialkyl oxalates and stoichiometric amounts of zinc or manganese powder as reducing agents. More recently, this transformation has been accomplished with highly reactive organo-magnesium, lithium, or zinc reagents. However, the use of pyrophoric metal sources in stoichiometric amounts and the need for well-defined dialkylzinc reagents can constitute drawbacks of these methods.[79–82] Consequently, there is growing interest in developing alternative strategies that employ more stable and readily available coupling partners. Such approaches offer an attractive pathway for generating benzyl radicals directly from benzyl alcohol, a more accessible and benign precursor.[83–85] In this context, metal-catalyzed deoxygenative coupling of alcohols with organohalides or pseudohalides has emerged as a direct and efficient method for synthesizing deoxygenative coupling products, such as diarylmethanes, structural motifs that are prevalent in a wide range of bioactive compounds, pharmaceuticals, and functional organic materials.[86–90]

In the current study, we envisioned *in situ* electrochemically generated methyl-oxalate as an activating group, which was pioneered by Utley and co-workers.[91–94] Consistent with their findings, it was observed that methyl oxalate effectively facilitates C–O bond activation.[95] Over the past decade, synthetic electrochemistry has emerged as a powerful and sustainable platform for redox reactions, transforming a broad array of classical transformations into greener and more efficient

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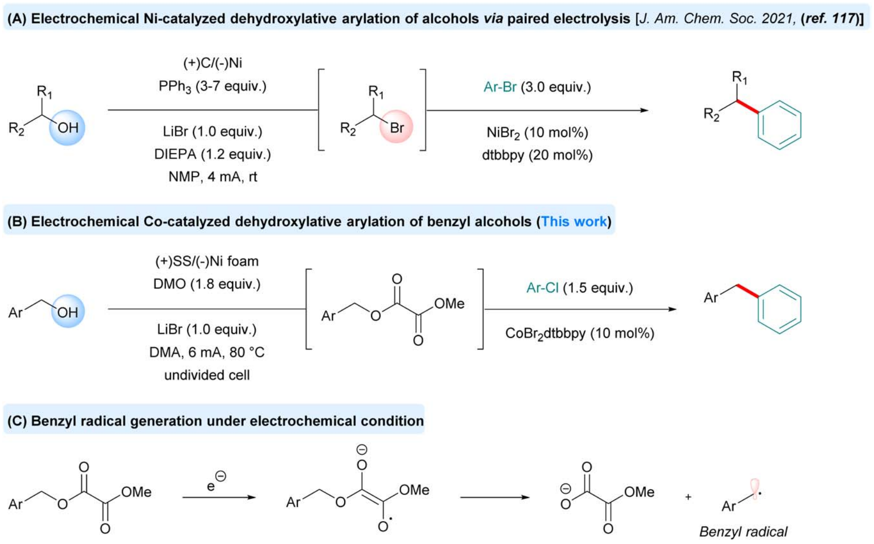


Scheme 1 Electrochemical approaches for dehydroxylative arylation of alcohols.

processes.[96–116] A notable example is the recent work by Li and co-workers, who developed a paired electrolysis protocol that merges the anodic Appel reaction with a nickel-catalyzed cathodic cross-electrophile coupling in an undivided electrochemical cell. This method enables the direct arylation of readily available alcohols with aryl bromides, providing a streamlined and environmentally friendly approach to C–C bond formation (Scheme 1). In addition to its broad substrate scope and excellent functional group compatibility, this method offers a significant advantage by avoiding the use of stoichiometric and hazardous halogenating agents such as CBr_4 or Br_2, commonly employed in the Appel reaction. However, the protocol still requires the use of 3–7 equivalents of triphenylphosphine (PPh_3), which not only increases material cost but also leads to the formation of byproducts and may complicate purification, reducing overall efficiency.[117]

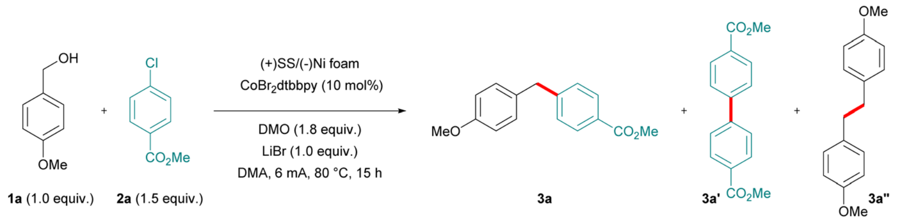
We sought to develop a complementary approach that enables efficient catalysis for $C(sp^2)$–$C(sp^3)$ bond formation under electrochemical conditions. However, the implementation of our proposed electrolysis strategy presented two key challenges. First, it was essential to match the intrinsic redox properties of the paired reaction partners to ensure selective and efficient electron transfer. Second, successful reaction execution required careful adjustment of the rates of the anodic oxidation, cathodic reduction, and the metal-catalyzed cross-coupling cycle. These interdependent processes had to be finely balanced to avoid unproductive pathways and achieve high overall efficiency.

To initiate our study, we began by evaluating earth-abundant transition metal catalysts, such nickel and cobalt with 4-methoxy benzyl alcohol (**1a**) and methyl 4-chlorobenzoate (**2a**) as the standard coupling partners (Table 1).

The reaction was carried out in an undivided electrochemical cell equipped with a stainless-steel anode and a nickel foam cathode, affording the desired product **3a** in 40–45% yield, along with minor side products **3a′** and **3a″**. Subsequent efforts focused on optimizing the reaction parameters to improve efficiency and selectivity. Key variables investigated included the nature of the electrodes (both anodes and cathodes), electrolyte composition, current density, solvent system, and the choice of metal complexes for promoting the deoxygenative reductive cross-coupling reaction[118,119] (see the SI for details, S3–S5). After extensive efforts, the desired product was obtained in 90% isolated yield by using 10 mol% $CoBr_2$(dtbbpy) as the catalyst, 1.8 equiv. of dimethyl oxalate (DMO) as the activator, LiBr as the electrolyte, in DMA solvent (entry 1, Table 1). The use of a nickel catalyst slightly diminished the yield of the diaryl methane product with the formation of a homodimerized side product (entry 2, Table 1). Using different cobalt catalysts led to lower product yields along with some side reactions [**3a′** & **3a″**] (entries 3 and 4, Table 1). Altering the anode or cathode resulted in decreased yields (entries 5 and 6). The use of a non-sacrificial anode along with a sacrificial donor such as Et_3N and TMEDA yielded no product (entries 7 and 8). The reaction was less efficient in solvents such as ACN, DMF and NMP (entries 9–11). Finally, the control experiments demonstrated that all reaction parameters, including the cobalt catalyst, DMO, and electricity are essential for accomplishing this transformation (entries 12–15).

Following the successful optimization, we evaluated the scope and generality of the developed protocol. As shown in Fig. 1 and 2, a series of electronically and sterically diverse benzyl alcohols and aryl chlorides participated in this newly developed cobalta-electrocatalyzed protocol, and the corresponding diaryl methane products were isolated in good to excellent yields. Notably, aryl chlorides as reaction partners provided better yields as compared to aryl bromides and aryl triflates due to homocoupling of both reaction partners (**3a** Fig. 1). Reaction with primary alcohols bearing biphenyl, naphthyl, phenanthrene and fluorene substituents proceeds with good efficiency (**3c–3f**). Benzyl alcohols with methylthio (**3g**), *m*-methoxy (**3h**), di- and trimethoxy (**3i–3j**) reacted equally

Table 1 Optimization of direct deoxygenative cross coupling of benzyl alcohol with aryl chlorides under electrochemical conditions



Entry	Variation from standard conditions[a,b]	**3a** (%)	**3a′** (%)	**3a″** (%)
1	Standard conditions	90[c]	Trace	Trace
2	$NiBr_2$dtbbpy (10 mol%)	78[c]	18	Trace
3	$CoBr_2$bpy (10 mol%)	84[c]	10	Trace
4	$CoCl_2(PPh_3)_2$ (10 mol%)	76	Trace	18
5	(+)Fe/(−)Ni foam	70	21	09
6	(+)Zn/(−)Ni foam	77	10	12
7	(+)RVC/(−)Ni foam, Et_3N (3.0 equiv.)	ND	ND	24
8	(+)RVC/(−)Ni foam, TMEDA (3.0 equiv.)	ND	ND	15
9	ACN as solvent	46	21	24
10	DMF as solvent	77[c]	20	15
11	NMP as solvent	72	15	ND
12	w/o $CoBr_2$dtbbpy	ND	ND	45[c]
13	w/o DMO	ND	70	10
14	w/o electricity	ND	ND	ND
15	Reaction at rt	ND	78[c]	10

[a] Standard conditions: **1a** (0.4 mmol), **2a** (0.6 mmol), $CoBr_2$dtbbpy (10 mol%), DMO (1.8 equiv.), LiBr (1.0 equiv.), DMA, (4.0 mL), constant current i = 6 mA, 80 °C, 15 h. [b] GC-FID yield using dodecane as the internal standard. [c] Isolated yield. ND = not detected.

well under the reaction conditions. Importantly, free phenolic hydroxyl groups at various positions as well as the dimethylamino group were also well tolerated. The chemoselectivity of the transformation was found to be good as illustrated by the tolerance of functional groups including fluoro (**3p**, **3r**), trifluoromethyl (**3q**), trifluoromethoxyl (**3s**) and cyano (**3u**) moieties. Furthermore, reactive functional groups such as fluoro or chloro substituents or boronic esters were tolerated, providing opportunities for further late-stage functionalization (**3r**, **3s**, **3t**, and **3v**). In addition, the reaction also proceeds with good efficiency using heterocyclic benzyl alcohol substrates containing furan, thiophene, pyridinyl, benzofuran, and indole motifs (**3w–3ab**). Notably, cinnamyl alcohol as a substrate also provided 1,1′-(1-propene-1,3-diyl)dibenzene (**3ac**) in 72% yield. 1,4-benzenedimethanol also underwent the reaction, affording the desired product in moderate yield (**3ad**).

We next turned our attention to evaluate the scope of aryl chlorides (**2**), using 4-methoxy benzyl alcohol (**1a**) as a model substrate (Fig. 2). As anticipated a variety of aryl chlorides having various steric and electronic substituents at different positions of the aryl ring were well tolerated under the standard reaction conditions. Substituents such as deuterium (**3ae**), methyl (**3af**), ^{t}Bu (**3ag**), biphenyl (**3ah**), naphthyl (**3ai** and **3aj**), and methoxy (**3ak**) afforded diarylmethanes in good to excellent yields. Halo-substituted aryl halides such as fluoro (**3al**) and trifluoromethyl (**3m**) derivatives, resulted in 81% and 87% yields respectively. Of note, the method also allowed the formation of monosubstituted chloro-diaryl methane (**3an**) from a 1,4-dichloroarene substrate which can be used as a handle for further functionalization.

Furthermore, substituents such as cyano (**3ao**), esters (**3ap–3as**), aldehyde (**3at**), alkene (**3au**), and aliphatic and aromatic ketones (**3av** and **3aw**), also proved efficient. In addition, heteroaromatic chlorides with groups such as thiophene (**3ax**), pyridine (**3ay** and **3az**), dibenzofuran (**3aaa**), carbazole (**3aab**) provided the corresponding products in good to moderate yields. Notably, the current methodology is suitable for late-stage functionalization as chloro compounds derived from L-menthol, clofibrate, fenofibrate and furegrelates reacted smoothly, affording the corresponding products (**3aac–3aag**) in good to moderate yields.

To gain insights into the reaction mechanism, a series of control experiments were conducted (Fig. 3). First, the formation of the oxalate ester intermediate was confirmed under the optimized reaction conditions. The conversion of 4-methoxybenzyl alcohol (**1a**) to oxalate ester (**4**) was sluggish at room temperature but proceeded efficiently at 80 °C. In the presence of the cobalt catalyst, the reaction afforded oxalate ester (**4**) in 36% yield and the deoxygenative homocoupled product (**3a″**) in 42% yield. In contrast, in the absence of cobalt, the oxalate ester (**4**) was obtained in 27% yield and **3a″** in 34% yield (Fig. 3, equation (A)). The enhanced formation of the oxalate ester in the presence of cobalt suggests that the cobalt catalyst facilitates transesterification. In another experiment the use of separately prepared oxalate ester (**4**) under standard reaction conditions led to the exclusive formation of deoxygenative homocoupled product (**3a″**) (Fig. 3, equation (B)). The reductive cross coupling reaction of the oxalate ester with aryl chlorides under standard reaction conditions afforded the cross-coupled diaryl methane compound (**3a**) in 77% yield (Fig. 3, equation (C)). Upon adding an excess amount of the radical scavenger TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxy), only a trace

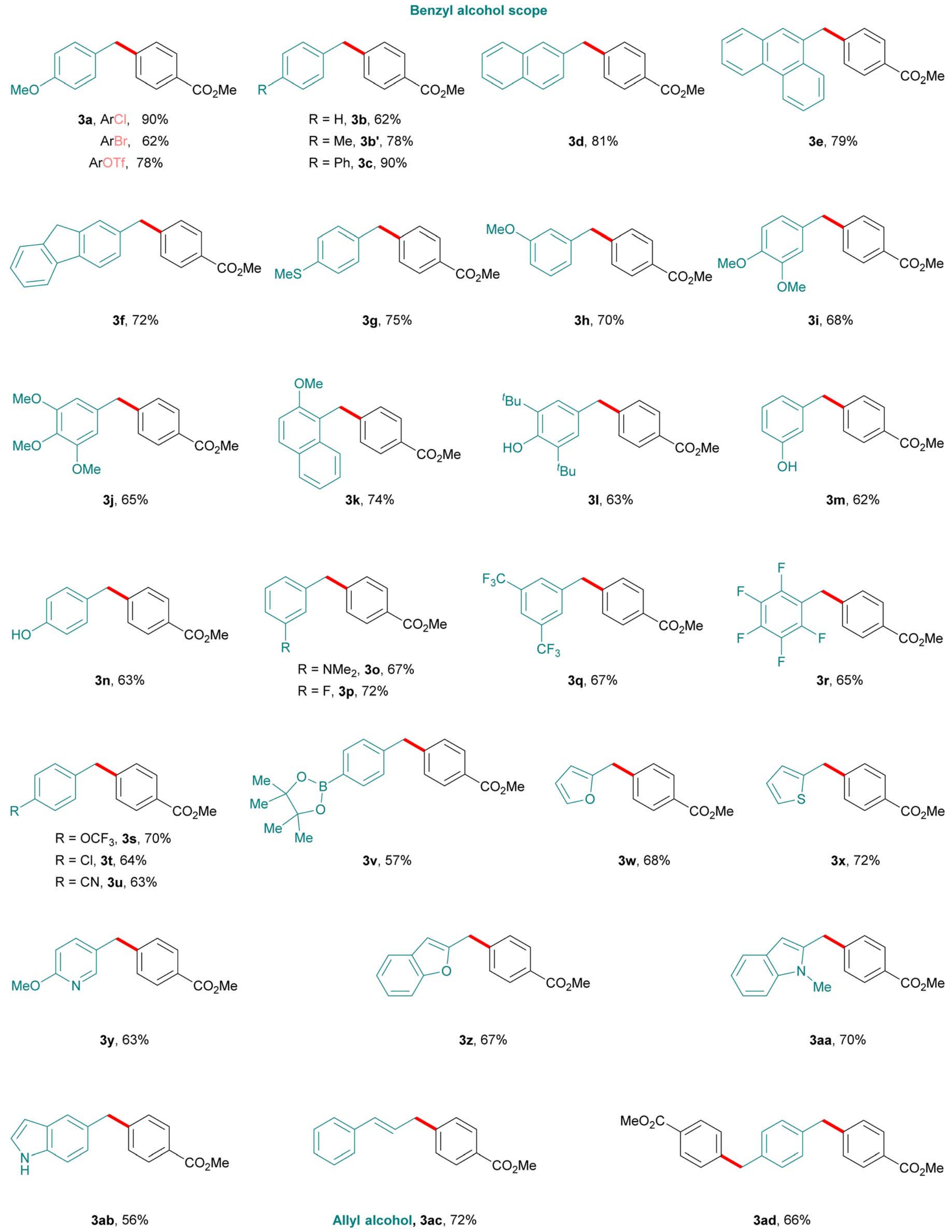


Fig. 1 Benzyl alcohol scope. Reaction was performed with **1a** (0.4 mmol), **2a** (0.6 mmol), $CoBr_2$dtbbpy (10 mol%), DMO (1.8 equiv.), LiBr (1.0 equiv.), DMA, (4.0 mL), constant current $i = 6$ mA, 80 °C, 15 h.

amount of product (**3a**) was detected (Fig. 3, equation (D)). Finally, the reaction with 1,1-diphenylethylene afforded the benzyl radical addition product (**6**) in 27% isolated yield (Fig. 3, equation (E)). These experiments indicate that a benzyl radical intermediate is involved in the reaction pathway, and the benzyl alcohol serves as the radical precursor *via* oxalate ester formation for the cross-coupling reaction. Notably, when 4-methoxybenzyl chloride was employed instead of 4-methoxybenzyl

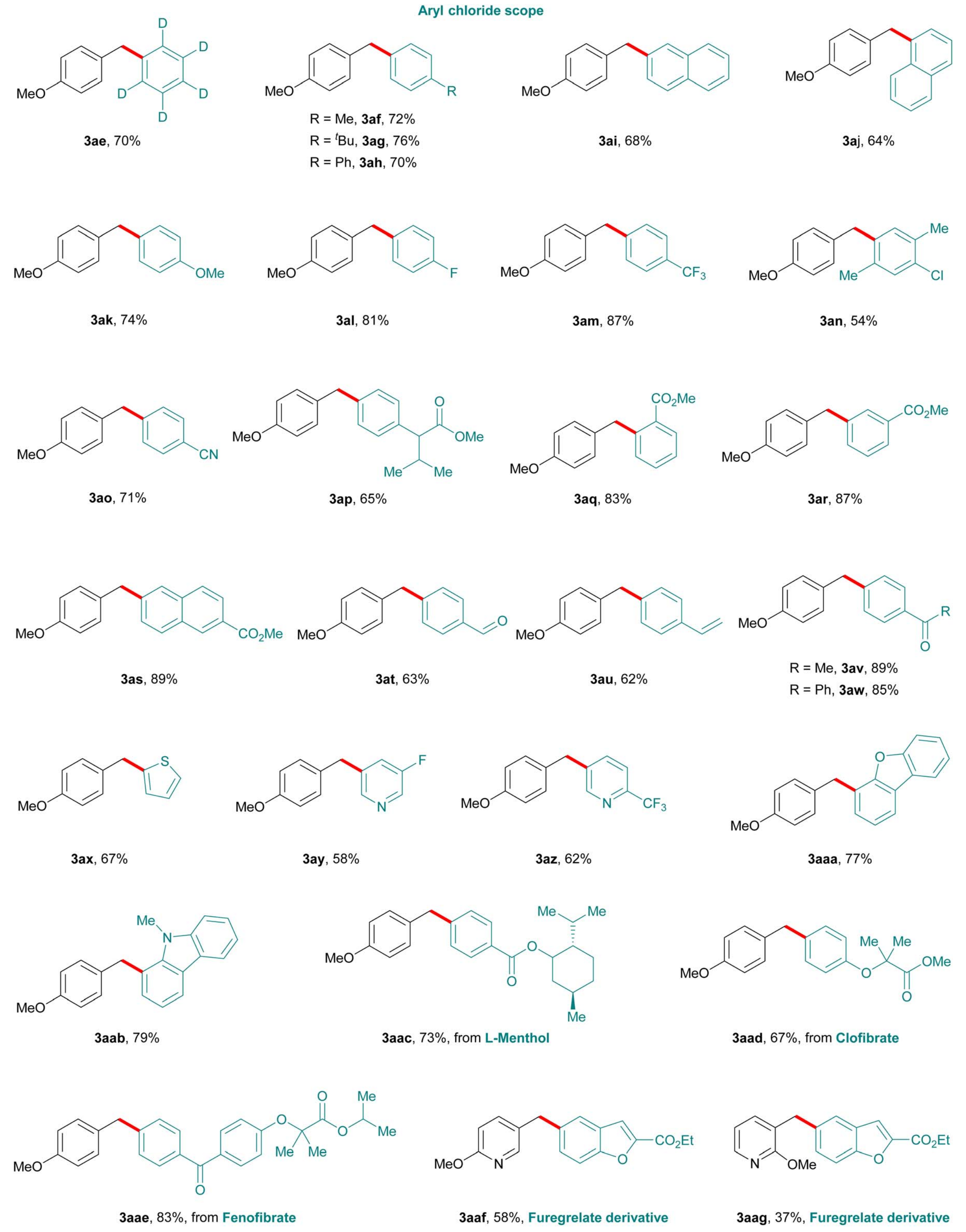


Fig. 2 Aryl chloride scope. Reaction was performed with **1a** (0.4 mmol), **2a** (0.6 mmol), $CoBr_2$dtbbpy (10 mol%), DMO (1.8 equiv.), LiBr (1.0 equiv.), DMA, (4.0 mL), constant current $i = 6$ mA, 80 °C, 15 h.

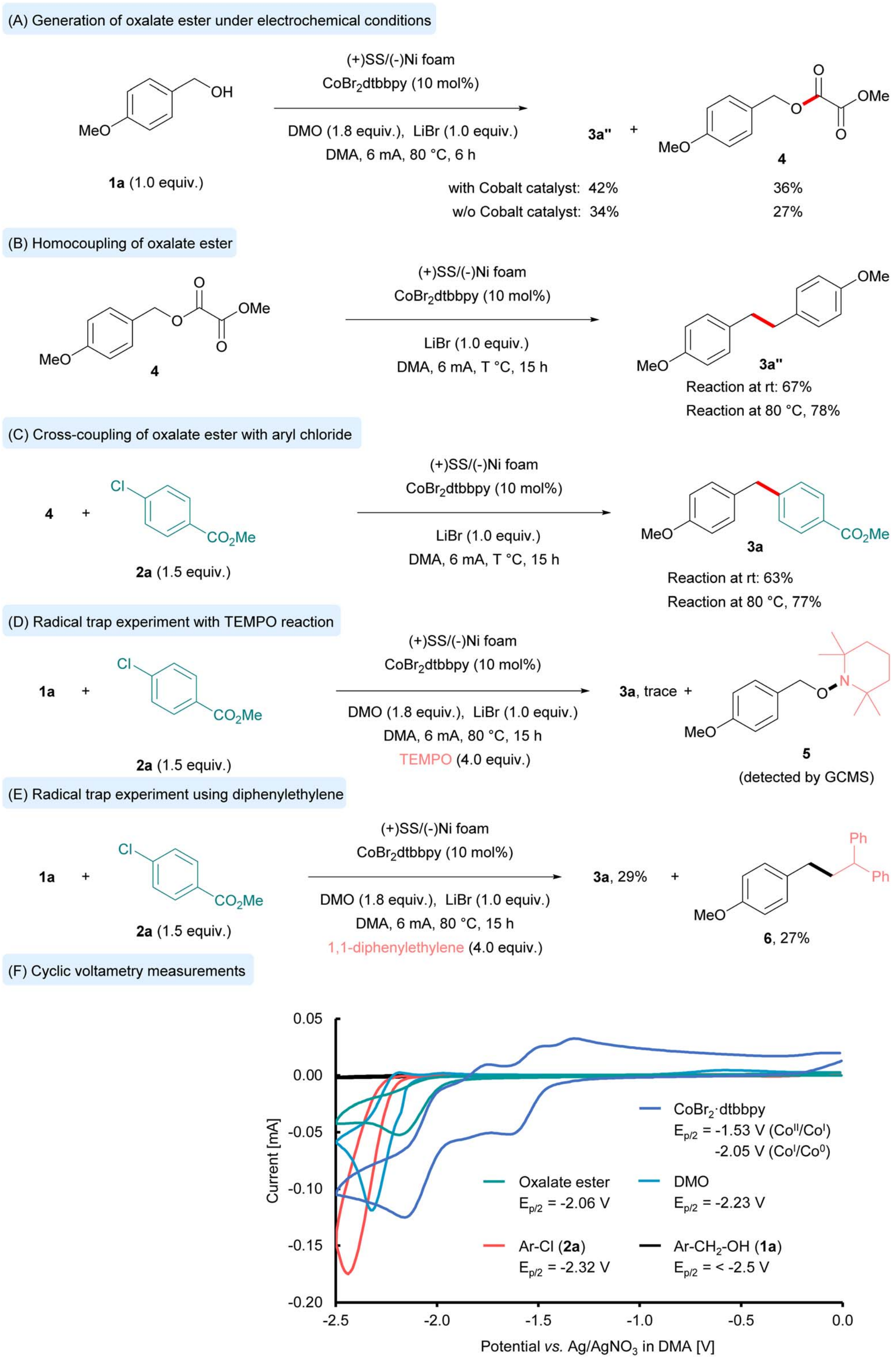


Fig. 3 Mechanistic studies.

alcohol (**1a**) with methyl 4-chlorobenzoate (**2a**), only a trace amount of the cross-coupled product was obtained (see detailed control experiments in the SI, S-7). We subsequently conducted cyclic voltammetry (CV) measurements in DMA, as illustrated in Fig. 3 (equation (F)). The reduction potential of 4-methoxybenzyl alcohol (**1a**) was ascertained to be below −2.5 V *vs.* Ag/AgNO$_3$, rendering its reduction unfeasible under the present protocol. Conversely, the reduction potentials of methyl 4-chlorobenzoate (**2a**), DMO, and oxalate ester were −2.32 V, −2.23 V, and −2.06 V *vs.* Ag/AgNO$_3$, respectively. These findings

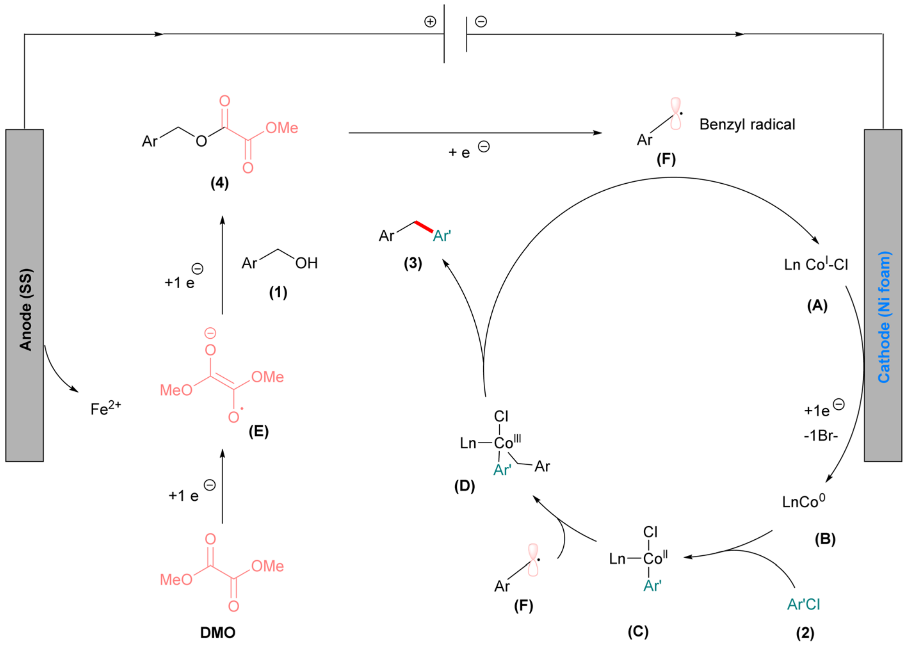


Fig. 4 Plausible reaction mechanism of the cobalt catalyzed C–C bond forming reaction.

suggest that DMO is initially reduced at the cathode, leading to the *in situ* formation of the oxalate ester. This oxalate ester can subsequently undergo further reduction at the cathode, yielding the benzylic radical. We also determined the reduction potential of the cobalt catalyst ($CoBr_2 \cdot dtbbpy$), observing two reduction peaks. These peaks correspond to the Co^{II}/Co^{I} reduction (−1.53 V *vs.* $Ag/AgNO_3$) and the Co^{I}/Co^{0} reduction (−2.05 V *vs.* $Ag/AgNO_3$). Given that the reduction of Co^{I} to Co^{0} is more facile than that of DMO and aryl chloride (**2a**), we postulate that Co^{0} is produced during the electrochemical reaction. This suggests that aryl chloride more readily undergoes oxidative addition with Co^{0} than direct reduction.

Based on the gathered experimental evidence and literature reports[72,75,93,120–122] we proposed a reaction mechanism that accounts for the formation of the observed product (Fig. 4). Initially, the pre-catalyst $CoBr_2$dtbbpy undergoes cathodic reduction to form the catalytically competent low valent Co^{0} species (**B**) *via* two electron transfer processes. The low valent cobalt species then undergoes oxidative addition with aryl chloride (**2**) that leads to formation of a Co^{II} intermediate (**C**). In parallel, under electrochemical conditions, DMO undergoes single electron reduction to afford the radical anion intermediate (**E**). The subsequent proton exchange process yields the alcohol anion and the *trans*-esterification with benzyl alcohol (**1**) leads to the formation of the oxalate ester (**4**) intermediate. The oxalate ester (**4**) immediately undergoes one electron reduction, generating the reactive benzyl radical (**F**). The generated benzyl radical (**F**) now participates in the catalytic cycle, resulting in the formation of the Co^{III} intermediate (**D**). Finally intermediate (**D**) undergoes reductive elimination to afford the diarylmethane (**3**) along with Co^{I} species that again enters the next catalytic cycle. The alternative pathway of benzyl radical addition to the Co^{0} complex (**B**) to afford the Co^{I} intermediate followed by oxidative addition of aryl chloride to generate the Co^{III} intermediate (**C**) cannot be completely ruled out.

In conclusion, we present the first example of *in situ* generated *O*-benzyl oxalate ester pronucleophiles derived from abundant benzyl alcohols in $C(sp^3)$–$C(sp^2)$ cross-coupling reactions by the strategic merger of electrochemistry with cobalt catalysis. The method relies on the electrochemical generation of benzyl radicals *via* selective cleavage of the oxalate ester, employing dimethyl oxalate, a low-molecular-weight, inexpensive, and commercially available reagent as an effective activator under mild electrochemical conditions. A key feature of this protocol is its ability to selectively suppress competing radical dimerization pathways, leveraging the inherent chemoselectivity of the electrocatalytic cobalt catalyst. Notably, the method circumvents the use of stoichiometric metal reductants such as Zn or Mn, or costly reagents like hydrosilanes, which are often employed in reductive cross-coupling reactions. By utilizing alcohols as unconventional radical precursors, this approach opens a new avenue for C (sp^3)–C (sp^2) bond-forming chemistry, expanding the synthetic utility of readily available alcohols beyond their traditional use in sustainable and modular C–C bond construction.

Author contributions

P. S. S., V. S. S., and M. R. conceived and designed the experiments. P. S. S. and V. S. S. conducted the experiments, analyzed the data and wrote the manuscript, while M. R. supervised the project and manuscript preparation.

Conflicts of interest

The authors declare no competing financial interests.

Data availability

Experimental procedures and characterization of the new compounds are available in the supplementary information (SI). Supplementary information is available. See DOI: **https://doi.org/10.1039/d5sc05919d**.

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Notes and references

1 P. Ertl and T. Schuhmann, A Systematic Cheminformatics Analysis of Functional Groups Occurring in Natural Products, *J. Nat. Prod.*, 2019, **82**, 1258–1263.

2 P. Ertl, E. Altmann and J. M. McKenna, The most common functional groups in bioactive molecules and how their popularity has evolved over time, *J. Med. Chem.*, 2020, **63**, 8408–8418.

3 T. Henkel, R. M. Brunne, H. Müller and F. Reichel, Statistical investigation into the structural complementarity of natural products and synthetic compounds, *Angew. Chem., Int. Ed.*, 1999, **38**, 643–647.

4 J. S. Carey, D. Laffan, C. Thomson and M. T. Williams, Analysis of the reactions used for the preparation of drug candidate molecules, *Org. Biomol. Chem.*, 2006, **4**, 2337–2347.

5 S. D. Roughley and A. M. Jordan, The medicinal chemist's toolbox: an analysis of reactions used in the pursuit of drug candidates, *J. Med. Chem.*, 2011, **54**, 3451–3479.

6 N. Schneider, D. M. Lowe, R. A. Sayle, M. A. Tarselli and G. A. Landrum, Big data from pharmaceutical patents: a computational analysis of medicinal chemists' bread and butter, *J. Med. Chem.*, 2016, **59**, 4385–4402.

7 S.-Y. Zhang, F.-M. Zhang and Y.-Q. Tu, Direct Sp^3 α-C–H activation and functionalization of alcohol and ether, *Chem. Soc. Rev.*, 2011, **40**, 1937–1949.

8 J. M. Ketcham, I. Shin, T. P. Montgomery and M. J. Krische, Catalytic Enantioselective C-H Functionalization of Alcohols by Redox-Triggered Carbonyl Addition: Borrowing Hydrogen, Returning Carbon, *Angew. Chem., Int. Ed.*, 2014, **53**, 9142–9150.

9 E. J. Tollefson, L. E. Hanna and E. R. Jarvo, Stereospecific nickel-catalyzed cross-coupling reactions of benzylic ethers and esters, *Acc. Chem. Res.*, 2015, **48**, 2344–2353.

10 E. Bisz and M. Szostak, Iron-Catalyzed C− O Bond Activation: Opportunity for Sustainable Catalysis, *ChemSusChem*, 2017, **10**, 3964–3981.

11 I. Borthakur, A. Sau and S. Kundu, Cobalt-catalyzed dehydrogenative functionalization of alcohols: Progress and future prospect, *Coord. Chem. Rev.*, 2022, **451**, 214257.

12 R. Kuwano and Y. Kondo, Palladium-catalyzed benzylation of active methine compounds without additional base: Remarkable effect of 1, 5-cyclooctadiene, *Org. Lett.*, 2004, **6**, 3545–3547.

13 B. Su, Z.-C. Cao and Z.-J. Shi, Exploration of earth-abundant transition metals (Fe, Co, and Ni) as catalysts in unreactive chemical bond activations, *Acc. Chem. Res.*, 2015, **48**, 886–896.

14 B.-T. Guan, S.-K. Xiang, B.-Q. Wang, Z.-P. Sun, Y. Wang, K.-Q. Zhao and Z.-J. Shi, Direct benzylic alkylation via Ni-catalyzed selective benzylic sp^3 C− O activation, *J. Am. Chem. Soc.*, 2008, **130**, 3268–3269.

15 L. Niu, J. Liu, X.-A. Liang, S. Wang and A. Lei, Visible light-induced direct α C–H functionalization of alcohols, *Nat. Commun.*, 2019, **10**, 467.

16 B. L. Taylor, E. C. Swift, J. D. Waetzig and E. R. Jarvo, Stereospecific nickel-catalyzed cross-coupling reactions of alkyl ethers: Enantioselective synthesis of diarylethanes, *J. Am. Chem. Soc.*, 2011, **133**, 389–391.

17 D.-G. Yu, X. Wang, R.-Y. Zhu, S. Luo, X.-B. Zhang, B.-Q. Wang, L. Wang and Z.-J. Shi, Direct arylation/alkylation/magnesiation of benzyl alcohols in the presence of Grignard reagents via Ni-, Fe-, or Co-catalyzed sp^3 C–O bond activation, *J. Am. Chem. Soc.*, 2012, **134**, 14638–14641.

18 A. J. Oelke, J. Sun and G. C. Fu, Nickel-catalyzed enantioselective cross-couplings of racemic secondary electrophiles that bear an oxygen leaving group, *J. Am. Chem. Soc.*, 2012, **134**, 2966–2969.

19 L. R. Jefferies and S. P. Cook, Iron-catalyzed arene alkylation reactions with unactivated secondary alcohols, *Org. Lett.*, 2014, **16**, 2026–2029.

20 H.-B. Wu, X.-T. Ma and S.-K. Tian, Palladium-catalyzed stereospecific cross-coupling of enantioenriched allylic alcohols with boronic acids, *Chem. Commun.*, 2014, **50**, 219–221.

21 Z.-C. Cao, D.-G. Yu, R.-Y. Zhu, J.-B. Wei and Z.-J. Shi, Direct cross-coupling of benzyl alcohols to construct diarylmethanes via palladium catalysis, *Chem. Commun.*, 2015, **51**, 2683–2686.

22 R. Martin-Montero, T. Krolikowski, C. Zarate, R. Manzano and R. Martin, Stereospecific nickel-catalyzed borylation of secondary benzyl pivalates, *Synlett*, 2017, **28**, 2604–2608.

23 S. Akkarasamiyo, J. Margalef and J. S. Samec, Nickel-Catalyzed Suzuki-Miyaura Cross-Coupling Reaction of Naphthyl and Quinolyl Alcohols with Boronic Acids, *Org. Lett.*, 2019, **21**, 4782–4787.

24 P. T. Marcyk, L. R. Jefferies, D. I. AbuSalim, M. Pink, M. H. Baik and S. P. Cook, Stereoinversion of unactivated alcohols by tethered sulfonamides, *Angew. Chem., Int. Ed.*, 2019, **58**, 1727–1731.

25 Q. Lin, G. Ma and H. Gong, Ni-catalyzed formal cross-electrophile coupling of alcohols with aryl halides, *ACS Catal.*, 2021, **11**, 14102–14109.

26 G. A. Molander, K. M. Traister and B. T. O'Neill, Engaging nonaromatic, heterocyclic tosylates in reductive cross-coupling with aryl and heteroaryl bromides, *J. Org. Chem.*, 2015, **80**, 2907–2911.

27 L. K. Ackerman, L. L. Anka-Lufford, M. Naodovic and D. J. Weix, Cobalt co-catalysis for cross-electrophile coupling: diarylmethanes from benzyl mesylates and aryl halides, *Chem. Sci.*, 2015, **6**, 1115–1119.

28 W. Liu, X. Yang, Y. Gao and C.-J. Li, Simple and efficient generation of aryl radicals from aryl triflates: synthesis of aryl boronates and aryl iodides at room temperature, *J. Am. Chem. Soc.*, 2017, **139**, 8621–8627.

29 J. Wang, J. Zhao and H. Gong, Nickel-catalyzed methylation of aryl halides/tosylates with methyl tosylate, *Chem. Commun.*, 2017, **53**, 10180–10183.

30 B. A. Vara, N. R. Patel and G. A. Molander, O-benzyl xanthate esters under Ni/photoredox dual catalysis: selective radical generation and Csp^3–Csp^2 cross-coupling, *ACS Catal.*, 2017, **7**, 3955–3959.

31 M. Y. Ibrahim, G. R. Cumming, R. Gonzalez de Vega, P. Garcia-Losada, O. de Frutos, C. O. Kappe and D. Cantillo, Electrochemical nickel-catalyzed C (sp^3)–C (sp^3) cross-coupling of alkyl halides with alkyl tosylates, *J. Am. Chem. Soc.*, 2023, **145**, 17023–17028.

32 L. L. Anka-Lufford, M. R. Prinsell and D. J. Weix, Selective cross-coupling of organic halides with allylic acetates, *J. Org. Chem.*, 2012, **77**, 9989–10000.

33 X. Cui, S. Wang, Y. Zhang, W. Deng, Q. Qian and H. Gong, Nickel-catalyzed reductive allylation of aryl bromides with allylic acetates, *Org. Biomol. Chem.*, 2013, **11**, 3094–3097.

34 H. Chen and M. Rueping, Facile, general allylation of unactivated alkyl halides via electrochemically enabled radical-polar crossover, *Chem. Sci.*, 2025, **16**, 6317–6324.

35 H. Chen, C. Zhai, C. Zhu and M. Rueping, Allylgermane synthesis *via* facile and general nickela-electrocatalyzed electrophile coupling, *Chem Catal.*, 2025, **5**, 101257.

36 M. O. Konev, L. E. Hanna and E. R. Jarvo, Intra- and Intermolecular Nickel-Catalyzed Reductive Cross-Electrophile Coupling Reactions of Benzylic Esters with Aryl Halides, *Angew. Chem., Int. Ed.*, 2016, **55**, 6730–6733.

37 X. Tao, Y. Chen, J. Guo, X. Wang and H. Gong, Preparation of α-amino acids *via* Ni-catalyzed reductive vinylation and arylation of α-pivaloyloxy glycine, *Chem. Sci.*, 2021, **12**, 220–226.

38 K. M. Arendt and A. G. Doyle, Dialkyl Ether Formation by Nickel-Catalyzed Cross-Coupling of Acetals and Aryl Iodides, *Angew. Chem., Int. Ed.*, 2015, **54**, 9876–9880.

39 Y. Pan, Y. Gong, Y. Song, W. Tong and H. Gong, Deoxygenative cross-electrophile coupling of benzyl chloroformates with aryl iodides, *Org. Biomol. Chem.*, 2019, **17**, 4230–4233.

40 Y. Wei, B. Ben-Zvi and T. Diao, Diastereoselective Synthesis of Aryl C-Glycosides from Glycosyl Esters via C-O Bond Homolysis, *Angew. Chem., Int. Ed.*, 2021, **60**, 9433–9438.

41 J. Xu, Y. Liu, Q. Wang, X. Tao, S. Ni, W. Zhang, L. Yu, Y. Pan and Y. Wang, Electrochemical deoxygenative amination of stabilized alkyl radicals from activated alcohols, *Nat. Commun.*, 2024, **15**, 6116.

42 L.-L. Zhang, Y.-Z. Gao, S.-H. Cai, H. Yu, S.-J. Shen, Q. Ping and Z.-P. Yang, Ni-catalyzed enantioconvergent deoxygenative reductive cross-coupling of unactivated alkyl alcohols and aryl bromides, *Nat. Commun.*, 2024, **15**, 2733.

43 W. L. Lyon and D. W. MacMillan, Expedient access to underexplored chemical space: deoxygenative $C(sp^3)$–$C(sp^3)$ cross-coupling, *J. Am. Chem. Soc.*, 2023, **145**, 7736–7742.

44 Q. Cai, I. M. McWhinnie, N. W. Dow, A. Y. Chan and D. W. MacMillan, Engaging alkenes in metallaphotoredox: a triple catalytic, radical sorting approach to olefin-alcohol cross-coupling, *J. Am. Chem. Soc.*, 2024, **146**, 12300–12309.

45 Z. Li, L. Wang, T. Zeng, Z. Huang, S. Song, X. Qi and J. Zhu, Cross-Double Deoxygenative Carbon–Carbon Bond Formation between Benzyl Benzoates and Allylic Alcohols, *ACS Catal.*, 2024, **14**, 9496–9504.

46 D.-H. Lee, K.-H. Kwon and C. S. Yi, Selective catalytic C–H alkylation of alkenes with alcohols, *Science*, 2011, **333**, 1613–1616.

47 J. Cornella, C. Zarate and R. Martin, Metal-catalyzed activation of ethers via C–O bond cleavage: a new strategy for molecular diversity, *Chem. Soc. Rev.*, 2014, **43**, 8081–8097.

48 J. Jin and D. W. MacMillan, Alcohols as alkylating agents in heteroarene C–H functionalization, *Nature*, 2015, **525**, 87–90.

49 T. Suga and Y. Ukaji, Nickel-catalyzed cross-electrophile coupling between benzyl alcohols and aryl halides assisted by titanium co-reductant, *Org. Lett.*, 2018, **20**, 7846–7850.

50 Y. Gao, Z. Wu, L. Yu, Y. Wang and Y. Pan, Alkyl Carbazates for Electrochemical Deoxygenative Functionalization of Heteroarenes, *Angew. Chem., Int. Ed.*, 2020, **59**, 10859–10863.

51 X. Pang and X.-Z. Shu, Titanium: a unique metal for radical dehydroxylative functionalization of alcohols, *Synlett*, 2021, **32**, 1269–1274.

52 A. Cai, W. Yan and W. Liu, Aryl radical activation of C–O bonds: copper-catalyzed deoxygenative difluoromethylation of alcohols, *J. Am. Chem. Soc.*, 2021, **143**, 9952–9960.

53 H.-M. Guo and X. Wu, Selective deoxygenative alkylation of alcohols via photocatalytic domino radical fragmentations, *Nat. Commun.*, 2021, **12**, 5365.

54 B. K. Chi, J. K. Widness, M. M. Gilbert, D. C. Salgueiro, K. J. Garcia and D. J. Weix, In-situ bromination enables formal cross-electrophile coupling of alcohols with aryl and alkenyl halides, *ACS Catal.*, 2021, **12**, 580–586.

55 W. Guan, Y. Chang and S. Lin, Electrochemically driven deoxygenative borylation of alcohols and carbonyl compounds, *J. Am. Chem. Soc.*, 2023, **145**, 16966–16972.

56 A. Cook, P. St. Onge and S. G. Newman, Deoxygenative Suzuki–Miyaura arylation of tertiary alcohols through silyl ethers, *Nat. Synth.*, 2023, **2**, 663–669.

57 T. Mandal, S. Mallick, M. Islam and S. De Sarkar, Alcohols as Alkyl Synthons Enabled by Photoredox-Catalyzed Deoxygenative Activation, *ACS Catal.*, 2024, **14**, 13451–13496.

58 J. B. Pedley, *Thermochemical data of organic compounds*, Springer Science & Business Media, 2012.

59 V. B. Oyeyemi, J. A. Keith and E. A. Carter, Trends in bond dissociation energies of alcohols and aldehydes computed with multireference averaged coupled-pair functional theory, *J. Phys. Chem. A*, 2014, **118**, 3039–3050.

60 H. G. Roth, N. A. Romero and D. A. Nicewicz, Experimental and calculated electrochemical potentials of common organic molecules for applications to single-electron redox chemistry, *Synlett*, 2016, **27**, 714–723.

61 S. W. McCombie, W. B. Motherwell and M. J. Tozer, in *Organic Reactions*, ed. S. E. Denmark, Wiley, Hoboken, New Jersey, 2012, vol. 77, pp. 161–591.

62 J. M. Herrmann and B. König, Reductive deoxygenation of alcohols: catalytic methods beyond Barton–McCombie deoxygenation, *Eur. J. Org Chem.*, 2013, **2013**, 7017–7027.

63 G. L. Lackner, K. W. Quasdorf and L. E. Overman, Direct construction of quaternary carbons from tertiary alcohols via photoredox-catalyzed fragmentation of *tert*-alkyl N-phthalimidoyl oxalates, *J. Am. Chem. Soc.*, 2013, **135**, 15342–15345.

64 C. C. Nawrat, C. R. Jamison, Y. Slutskyy, D. W. MacMillan and L. E. Overman, Oxalates as activating groups for alcohols in visible light photoredox catalysis: formation of quaternary centers by redox-neutral fragment coupling, *J. Am. Chem. Soc.*, 2015, **137**, 11270–11273.

65 C. R. Jamison and L. E. Overman, Fragment coupling with tertiary radicals generated by visible-light photocatalysis, *Acc. Chem. Res.*, 2016, **49**, 1578–1586.

66 X. Zhang and D. W. MacMillan, Alcohols as latent coupling fragments for metallaphotoredox catalysis: sp^3–sp^2 cross-coupling of oxalates with aryl halides, *J. Am. Chem. Soc.*, 2016, **138**, 13862–13865.

67 X.-B. Yan, C.-L. Li, W.-J. Jin, P. Guo and X.-Z. Shu, Reductive coupling of benzyl oxalates with highly functionalized alkyl bromides by nickel catalysis, *Chem. Sci.*, 2018, **9**, 4529–4534.

68 F. W. Friese and A. Studer, Deoxygenative borylation of secondary and tertiary alcohols, *Angew. Chem., Int. Ed.*, 2019, **58**, 9561–9564.

69 S. G. E. Amos, D. Cavalli, F. Le Vaillant and J. Waser, Direct Photoexcitation of Ethynylbenziodoxolones: An Alternative to Photocatalysis for Alkynylation Reactions, *Angew. Chem., Int. Ed.*, 2021, **60**, 23827–23834.

70 Y. Chen, F. Wang, B.-X. Liu, W.-D. Rao and S.-Y. Wang, A Ni (ii)-catalyzed reductive cross-coupling reaction of oxalates and thiosulfonates/selenosulfonates, *Org. Chem. Front.*, 2022, **9**, 731–736.

71 P. Guo, K. Wang, W.-J. Jin, H. Xie, L. Qi, X.-Y. Liu and X.-Z. Shu, Dynamic kinetic cross-electrophile arylation of benzyl alcohols by nickel catalysis, *J. Am. Chem. Soc.*, 2020, **143**, 513–523.

72 W.-Y. Ma, G.-Y. Han, S. Kang, X. Pang, X.-Y. Liu and X.-Z. Shu, Cobalt-catalyzed enantiospecific dynamic kinetic cross-electrophile vinylation of allylic alcohols with vinyl triflates, *J. Am. Chem. Soc.*, 2021, **143**, 15930–15935.

73 M.-X. You, P.-F. Su, Z.-H. She and X.-Z. Shu, Nickel-catalyzed cross-electrophile C-Ge coupling of benzyl pivalates and chlorogermanes, *Sci. China:Chem.*, 2023, **66**, 3562–3566.

74 X. Peng, J. Huang, G.-Y. Han and X.-Z. Shu, Nickel-catalyzed dynamic kinetic cross-electrophile coupling of benzylic alcohols and alkenyl triflates, *Org. Chem. Front.*, 2024, **11**, 94–99.

75 Y. Ye, H. Chen, J. L. Sessler and H. Gong, Zn-mediated fragmentation of tertiary alkyl oxalates enabling formation of alkylated and arylated quaternary carbon centers, *J. Am. Chem. Soc.*, 2018, **141**, 820–824.

76 M. Gao, D. Sun and H. Gong, Ni-catalyzed reductive C–O bond arylation of oxalates derived from α-hydroxy esters with aryl halides, *Org. Lett.*, 2019, **21**, 1645–1648.

77 H. Chen, Y. Ye, W. Tong, J. Fang and H. Gong, Formation of allylated quaternary carbon centers via C–O/C–O bond fragmentation of oxalates and allyl carbonates, *Chem. Commun.*, 2020, **56**, 454–457.

78 Y. Ye, H. Chen, K. Yao and H. Gong, Iron-catalyzed reductive vinylation of tertiary alkyl oxalates with activated vinyl halides, *Org. Lett.*, 2020, **22**, 2070–2075.

79 M. Amatore and C. Gosmini, Synthesis of functionalised diarylmethanes via a cobalt-catalysed cross-coupling of arylzinc species with benzyl chlorides, *Chem. Commun.*, 2008, 5019–5021.

80 A. D. Benischke, I. Knoll, A. Rérat, C. Gosmini and P. Knochel, A practical cobalt-catalyzed cross-coupling of benzylic zinc reagents with aryl and heteroaryl bromides or chlorides, *Chem. Commun.*, 2016, **52**, 3171–3174.

81 X. Shao, Y. Zheng, V. Ramadoss, L. Tian and Y. Wang, Recent advances in P III-assisted deoxygenative reactions under photochemical or electrochemical conditions, *Org. Biomol. Chem.*, 2020, **18**, 5994–6005.

82 Y. Wang, J. Xu, Y. Pan and Y. Wang, Recent advances in electrochemical deoxygenation reactions of organic compounds, *Org. Biomol. Chem.*, 2023, **21**, 1121–1133.

83 A. Flaherty, A. Trunkfield and W. Barton, Palladium-catalyzed cross-coupling of B-benzyl-9-borabicyclo [3.3. 1] nonane to furnish methylene-linked biaryls, *Org. Lett.*, 2005, **7**, 4975–4978.

84 L. S. Chupak, J. P. Wolkowski and Y. A. Chantigny, Palladium-catalyzed cross-coupling reactions of benzyl indium reagents with aryl iodides, *J. Org. Chem.*, 2009, **74**, 1388–1390.

85 J. C. Tellis, D. N. Primer and G. A. Molander, Single-electron transmetalation in organoboron cross-coupling by photoredox/nickel dual catalysis, *Science*, 2014, **345**, 433–436.

86 Y.-Q. Long, X.-H. Jiang, R. Dayam, T. Sanchez, R. Shoemaker, S. Sei and N. Neamati, Rational design and synthesis of novel dimeric diketoacid-containing inhibitors of HIV-1 integrase: implication for binding to two metal ions on the active site of integrase, *J. Med. Chem.*, 2004, **47**, 2561–2573.

87 S. Messaoudi, A. Hamze, O. Provot, B. Tréguier, J. Rodrigo De Losada, J. Bignon, J. M. Liu, J. Wdzieczak-Bakala, S. Thoret and J. Dubois, Discovery of isoerianin analogues

as promising anticancer agents, *ChemMedChem*, 2011, **6**, 488–497.

88 D. Ameen and T. J. Snape, Chiral 1, 1-diaryl compounds as important pharmacophores, *MedChemComm*, 2013, **4**, 893–907.

89 S. Mondal and G. Panda, Synthetic methodologies of achiral diarylmethanols, diaryl and triarylmethanes (TRAMs) and medicinal properties of diaryl and triarylmethanes-an overview, *RSC Adv.*, 2014, **4**, 28317–28358.

90 T. Jia, P. Cao and J. Liao, Enantioselective synthesis of gem-diarylalkanes by transition metal-catalyzed asymmetric arylations (TMCAAr), *Chem. Sci.*, 2018, **9**, 546–559.

91 J. H. Utley and S. Ramesh, Electroorganic reactions. Part 58. Revisiting the cleavage of oxalate ester radical-anions, *Arkivoc*, 2003, **12**, 18–26.

92 D. W. Sopher and J. H. Utley, Alkene formation in the cathodic reduction of oxalates, *J. Chem. Soc. Chem. Commun.*, 1981, 134–136.

93 N.-u. Islam, D. W. Sopher and J. H. Utley, Electro-organic reactions: Part 27. The mechanism of cathodic cleavage of activated esters; oxalates, squarates and oxamates, *Tetrahedron*, 1987, **43**, 959–970.

94 D. W. Sopher and J. H. Utley, Electro-organic reactions. part 28. preparative applications of the oxalate cathodic cleavage reaction including one-pot conversions of aldehydes and ketones, *Tetrahedron*, 1987, **43**, 2741–2748.

95 P. Villo, A. Shatskiy, M. D. Kärkäs and H. Lundberg, Electrosynthetic C– O bond activation in alcohols and alcohol derivatives, *Angew. Chem., Int. Ed.*, 2023, **62**, e202211952.

96 E. J. Horn, B. R. Rosen and P. S. Baran, Synthetic organic electrochemistry: an enabling and innately sustainable method, *ACS Cent. Sci.*, 2016, **2**, 302–308.

97 H. Wang, X. Gao, Z. Lv, T. Abdelilah and A. Lei, Recent advances in oxidative R1-H/R2-H cross-coupling with hydrogen evolution via photo-/electrochemistry: focus review, *Chem. Rev.*, 2019, **119**, 6769–6787.

98 D. Pollok and S. R. Waldvogel, Electro-organic synthesis–a 21 st century technique, *Chem. Sci.*, 2020, **11**, 12386–12400.

99 R. D. Little, A perspective on organic electrochemistry, *J. Org. Chem.*, 2020, **85**, 13375–13390.

100 Y. Kawamata and P. S. Baran, Electrosynthesis: Sustainability is not enough, *Joule*, 2020, **4**, 701–704.

101 T. H. Meyer, I. Choi, C. Tian and L. Ackermann, Powering the future: how can electrochemistry make a difference in organic synthesis?, *Chem*, 2020, **6**, 2484–2496.

102 P. Gandeepan, L. H. Finger, T. H. Meyer and L. Ackermann, 3d metallaelectrocatalysis for resource economical syntheses, *Chem. Soc. Rev.*, 2020, **49**, 4254–4272.

103 C. Zhu, N. W. Ang, T. H. Meyer, Y. Qiu and L. Ackermann, Organic electrochemistry: molecular syntheses with potential, *ACS Cent. Sci.*, 2021, **7**, 415–431.

104 C. A. Malapit, M. B. Prater, J. R. Cabrera-Pardo, M. Li, T. D. Pham, T. P. McFadden, S. Blank and S. D. Minteer, Advances on the merger of electrochemistry and transition metal catalysis for organic synthesis, *Chem. Rev.*, 2021, **122**, 3180–3218.

105 N. Li, R. Sitdikov, A. P. Kale, J. Steverlynck, B. Li and M. Rueping, A review of recent advances in electrochemical and photoelectrochemical late-stage functionalization classified by anodic oxidation, cathodic reduction, and paired electrolysis, *Beilstein J. Org. Chem.*, 2024, **20**, 2500–2566.

106 H. Chen, C. Zhai, H. Zhang, C. Zhu and M. Rueping, Switchable electrochemical pathways for the selective C(sp^3)-Ge bond formation, *Nat. Commun.*, 2025, **16**, 7247.

107 H. Chen and M. Rueping, Alkynyl-Germanium Architectures Through Electrochemical Low-Valent Iron-Catalyzed Conjunctive Coupling, *Angew. Chem., Int. Ed.*, 2025, e202516109.

108 M. Ghosh, V. S. Shinde and M. Rueping, A review of asymmetric synthetic organic electrochemistry and electrocatalysis: concepts, applications, recent developments and future directions, *Beilstein J. Org. Chem.*, 2019, **15**, 2710–2746.

109 G. S. Kumar, A. Peshkov, A. Brzozowska, P. Nikolaienko, C. Zhu and M. Rueping, Nickel-Catalyzed Chain-Walking Cross-Electrophile Coupling of Alkyl and Aryl Halides and Olefin Hydroarylation Enabled by Electrochemical Reduction, *Angew. Chem., Int. Ed.*, 2020, **59**, 6513–6519.

110 C. Zhu, A. P. Kale, H. Yue and M. Rueping, Redox-neutral cross-coupling amination with weak N-nucleophiles: arylation of anilines, sulfonamides, sulfoximines, carbamates, and imines via nickelaelectrocatalysis, *JACS Au*, 2021, **1**, 1057–1065.

111 C. Zhu, H. Yue and M. Rueping, Nickel catalyzed multicomponent stereodivergent synthesis of olefins enabled by electrochemistry, photocatalysis and photo-electrochemistry, *Nat. Commun.*, 2022, **13**, 3240.

112 H. Chen, C. Zhu, H. Yue and M. Rueping, Carbon–Germanium Bond Formation via Low-Valent Cobalt-Catalyzed Cross-Electrophile Coupling, *ACS Catal.*, 2023, **13**, 6773–6780.

113 H. Chen, C. Zhu, H. Yue and M. Rueping, Group 14 Elements Hetero-Difunctionalizations via Nickel-Catalyzed Electroreductive Cross-Coupling, *Angew. Chem., Int. Ed.*, 2023, **62**, e202306498.

114 G. S. Kumar, C. Zhu, R. Kancherla, P. S. Shinde and M. Rueping, Metal Cations from Sacrificial Anodes Act as a Lewis Acid Co-Catalyst in Electrochemical Cross-Coupling of Aryl Bromides and Aziridines, *ACS Catal.*, 2023, **13**, 8813–8820.

115 C. Zhu, H. Chen, H. Yue and M. Rueping, Electrochemical chemo-and regioselective arylalkylation, dialkylation and hydro (deutero) alkylation of 1, 3-enynes, *Nat. Synth.*, 2023, **2**, 1068–1081.

116 P. S. Shinde, V. S. Shinde and M. Rueping, Electrochemical low valent cobalt-catalyzed addition of aryl and vinyl chlorides to α-ketoamides via C–Cl bond activation, *Chem. Commun.*, 2024, **60**, 3826–3829.

117 Z. Li, W. Sun, X. Wang, L. Li, Y. Zhang and C. Li, Electrochemically enabled, nickel-catalyzed

dehydroxylative cross-coupling of alcohols with aryl halides, *J. Am. Chem. Soc.*, 2021, **143**, 3536–3543.

118 X. Pang, P.-F. Su and X.-Z. Shu, Reductive cross-coupling of unreactive electrophiles, *Acc. Chem. Res.*, 2022, **55**, 2491–2509.

119 Y. Liu, P. Li, Y. Wang and Y. Qiu, Electroreductive cross-electrophile coupling (eXEC) reactions, *Angew. Chem., Int. Ed.*, 2023, **135**, e202306679.

120 P. S. Shinde, V. S. Shinde, C. Zhu and M. Rueping, Electrochemical Cobalt-Catalyzed Cross-Electrophile Coupling of Alcohols and Trifluoroalkenes via Simultaneous C–F and C–O Bond Cleavage, *ACS Catal.*, 2025, **15**, 17198–17205.

121 Y. Yan, W. Xiong, S. Li, Z. Wang, T. Kang, G. Li, G. Song, J. Dong and D. Xue, Nickel-Catalyzed O-Alkylisourea-Enabled Electrochemical Radical C(sp^3)– C(sp^2) Cross-Coupling, *Angew. Chem., Int. Ed.*, 2025, e202516173.

122 C. Dorval, M. Tricoire, J.-M. Begouin, V. Gandon and C. Gosmini, Cobalt-catalyzed C(sp^2)–CN bond activation: cross-electrophile coupling for biaryl formation and mechanistic insight, *ACS Catal.*, 2020, **10**, 12819–12827.