Electrocatalytic Oxidative Hydrofunctionalization Reactions of

Alkenes via Co(II/III/IV) Cycle

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**Abstract** 

Here we disclose a general and versatile Co(II/III/IV) electrocatalytic platform for alkene

functionalization. Driven by electricity, a set of the oxidative hydrofunctionalization reactions initiated

by hydrogen atom transfer were demonstrated without the need for stochiometric chemical oxidants. The

scope of the reactions encompasses hydroalkoxylation, hydroacyloxylation, hydroarylation, semi-

pinacol rearrangement, and deallylation. Mechanistic studies and stereochemical evidence support an

ECEC process involving an electrochemically-generated organocobalt(IV) intermediate. This work

presents an example of reactivity space expansion in electrocatalysis of VB<sub>12</sub>-systems by going beyond

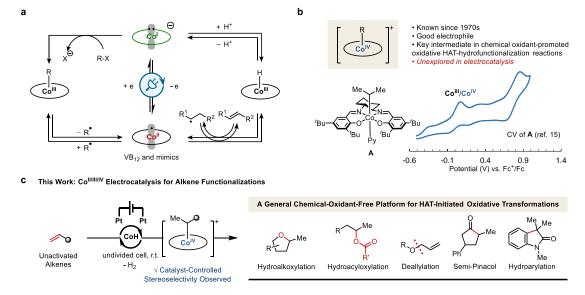
the common oxidation states of Co(I/II/III).

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Using electric current as a traceless reagent in transition metal catalysis has opened up a new avenue for the development of sustainable transformations.<sup>[1]</sup> Transition metal complexes can serve as electron transfer mediators to reduce overpotentials, and meanwhile bring in rich and tunable reactivities for electrosynthesis.<sup>[2]</sup> Cobalt complexes were among the first explored metal-based redox catalysts in electrosynthesis due to their multiple accessible oxidation states.<sup>[3]</sup> In particular, vitamin B<sub>12</sub> and its mimics (cobaloxime, CoSalen, etc.) have received considerable attention for their good redox cyclability and distinct reactivities at Co<sup>1</sup>, Co<sup>II</sup>, and Co<sup>III</sup> oxidation states, respectively (Figure 1a).<sup>[4]</sup> For example, the square planar four-coordinate Co<sup>1</sup> "supernucleophile" has been employed for electroreductive dehalogenation,<sup>[5]</sup> Giese reaction<sup>[6]</sup> and carboxylation<sup>[7]</sup> since 1980s, and more recently in Co–H-catalyzed olefin isomerization<sup>[8]</sup> and related reactions<sup>[9]</sup> via hydrogen-atom-transfer (HAT). The combination of electrochemical HAT reaction and copper-mediated radical functionalization has resulted in an elegant solution for enantioselective hydrocyanation of conjugated alkenes.<sup>[10]</sup>

Electrochemically going beyond the common oxidation states ( $Co^{III/III}$ ) may allow one to explore new reactivity space. An inspiring example is Ackermann's discovery of a formal  $Co^{IV}$  intermediate in electrocatalytic C–H functionalization reactions.<sup>[11]</sup> In VB<sub>12</sub>-related systems, cationic organocobalt(IV) complexes have been known since 1970s (Figure 1b).<sup>[12]</sup> Their organometallic radical cation nature makes them susceptible to nucleophilic displacement at the alkyl ligand.<sup>[13]</sup> This was recently leveraged in a series of HAT-initiated oxidative hydrofunctionalization reactions using stoichiometric chemical oxidants such as *N*-fluoropyridiniums, hypervalent iodine reagents and persulfates.<sup>[14]</sup> In our previous work, a well-defined organocobalt(III) complex was electrochemically characterized, where the  $Co^{III/IV}$  oxidation proved accessible at quite low potential ( $E_{p/2}$  vs  $Fc^+/Fc$   $\sim -0.01 \text{ V}$ ).<sup>[15]</sup> However, to the best of our knowledge, such a  $Co^{IV}$  state in  $VB_{12}$ -related catalysts has not been explored in electrosynthesis.

Here we report a general electrocatalytic platform enabling a set of HAT-initiated oxidative transformations in undivided cells via electrochemically generated Co<sup>IV</sup> intermediates (Figure 1c). Replacing stoichiometric oxidants leads to a more cost-effective and/or safer protocol that generates less waste stream. The scope of the reactions encompasses hydroalkoxylation, hydroacyloxylation, hydroarylation, semi-pinacol rearrangement, and deallylation without the need for tedious optimizations. The relevance of Co<sup>IV</sup> intermediates was supported by the observed catalyst-controlled stereoselectivity.

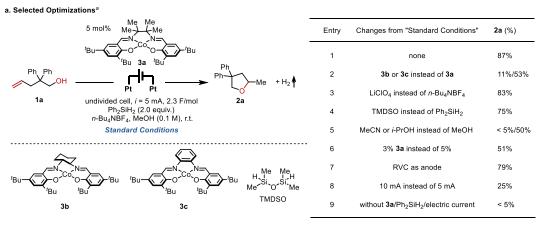


**Figure 1.** a) Established electrosynthesis catalyzed by VB<sub>12</sub> and analogues typically involves oxidation states I, II, and III. b) Related organocobalt(IV) complex remains unexplored in electrocatalysis. c) This work: a general platform for electrocatalytic oxidative functionalization of olefins via Co<sup>IV</sup>.

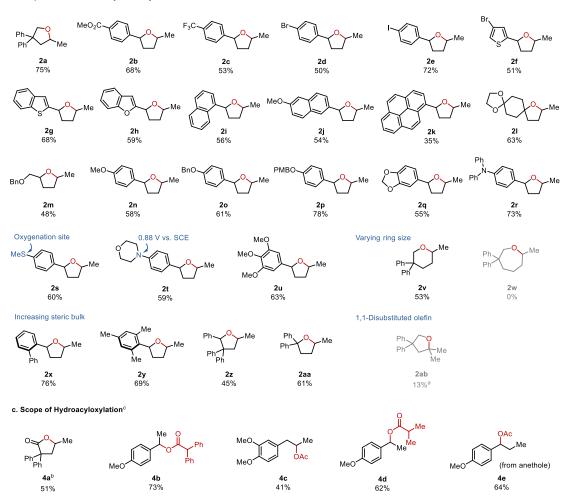
We commenced our investigation by studying the electrocatalytic intramolecular hydroalkoxylation of 2,2-diphenylpent-4-en-1-ol (1a) as the model reaction (Figure 2a). A set of optimal conditions was identified as shown in entry 1. In methanol at ambient temperature, constant current (5 mA) electrolysis using platinum mesh electrodes was performed in the presence of a catalytic amount of CoSalen complex 3a and diphenylsilane as a hydride source. The cyclization product 2a was obtained in 87% yield after 3.75-hour electrolysis (2.3 F/mol, corresponding to 87% faradaic efficiency). CoSalen complex 3b, bearing a less sterically hindered backbone, furnished substantially lower conversion and yield, which could be attributable to the instability of the ligand backbone during electrolysis (entry 2). The reaction proved relatively insensitive to the choice of the electrolyte or the silane (entry 3-4), while was significantly affected by the solvent and catalyst loading (entry 5-6). Changing the anode from platinum mesh to reticulated vitreous carbon (RVC) provided a comparable yield (entry 7). Doubling the current led to catalyst decomposition and thus low conversion (entry 8). Control experiments established the essential roles of the catalysts, silane, and electricity, respectively (entry 9).

With the optimized protocol in hand, the scope and limitation of the intramolecular hydroalkoxylation was first investigated (Figure 2b). Various  $\gamma$ -hydroxy alkenes were examined bearing a range of functional groups including esters (2b), aryl halides (2d-e), heterocycles (2f-h), fused aromatics (2i-k), and acid-sensitive protecting groups (2l), which afforded cyclization products in good yields. We were particularly interested in substrates that are

incompatible with strong chemical oxidants such as *N*-fluoropyridiniums or I<sup>III</sup> reagents. To this, the electrocatalytic system demonstrated excellent compatibility with electrophores such as sulfide (2s), tertiary amines (2t), [16] or electron-rich aryls (2u), which is consistent with the low potential of Co<sup>III/IV</sup> transition. Ring closure to afford a 6-membered-ring proceeded smoothly (2v), while medium-ring formation was rather difficult (2w). On the nucleophile side, more hindered secondary alcohols as well as tertiary alcohols can be employed (2x-2aa). The addition of carboxylic acid was also demonstrated in both intra- and intermolecular fashion (Figure 2c). Notably, potential byproducts derived from anodic decarboxylation were not observed. Regarding the alkene substitutions, unactivated monosubstituted alkenes and styrenes proved viable, while 1,1-disubstituted alkenes afforded mostly isomerization (2ab). This corroborates with previous observations in chemical oxidant-mediated reactions, which could be attributable to the disfavored formation of corresponding organocobalt(IV) species. Internal olefins except for aryl substituted ones (4e) generally displayed low reactivity, which was anticipated for Co–H HAT-initiated reactions.



#### b. Scope of Intramolecular Hydroalkoxylation<sup>b</sup>



**Figure 2.** Selected optimizations and scope of the electrocatalytic hydroalkoxylation and hydroacyloxylation reactions. <sup>a</sup>Yields were determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. <sup>b</sup>Isolated yields under standard conditions (d.r. ranged from 1.1:1 to 1.9:1 in the cases where diastereomers were produced, see SI). <sup>c</sup>Isolated yields under modified standard conditions where MeCN and TMDSO were used in place of MeOH and Ph<sub>2</sub>SiH<sub>2</sub>. For **4b-e**, 3.0 equiv. carboxylic acid was used.

Under the electrocatalytic conditions, methanol was found to add across a vinyl ether (5) in Markovnikov-selective fashion (Figure 3a). Inspired by recent reports on HAT-initiated alkene isomerization under chemical oxidation or electroreduction conditions<sup>[8, 17]</sup> as well as results from our own lab, we envisioned a tandem isomerization/hydromethoxylation reaction that leads to trapping at the more cation-stabilizing site (Figure 3b). The *in situ* hydrolysis of the resulting acetal would provide a cheap and chemoselective means for allyl deprotection, which is alternative to strong base-mediated<sup>[18]</sup> or precious metal-catalyzed methods.<sup>[19]</sup> Indeed, we were able to show efficient deallylation to reveal 1°, 2°, 3° alcohols, carboxylic acids, and anilines (Figure 3c).

#### a. Reaction with Vinyl Ethers

#### b. Proposed Tandem Sequence

#### c. Scope of One-Pot Deallylation<sup>a</sup>

**Figure 3.** Selective deallylation via tandem isomerization/hydromethoxylation sequence. <sup>a</sup>Isolated yields. Conditions: substrate (0.30 mmol, 1 equiv.), **3a** (5 mol%), TMDSO (2.0 equiv.), n-Bu<sub>4</sub>NBF<sub>4</sub> (2.0 equiv.) in MeOH (3.0 mL), Pt mesh electrode, undivided cell, constant current i = 5 mA, 2.3 F/mol, 25 °C. <sup>b</sup>Yield was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

To demonstrate the generality of this electrocatalytic protocol, C–C bond forming rearrangement and cyclization reactions were carried out (Figure 4). For example, semi-pinacol rearrangement of a cyclobutane-containing allylic alcohol 9 was achieved, furnishing the ring-expansion product 10 in good yield. An intramolecular hydroarylation reaction was demonstrated (12). Cyclization at the  $\alpha$ -position of an amide likely proceeded via a radical rather than a cationic intermediate, which is in line with Vanderwal's proposal on HAT-initiated oxidative polyene cyclization. [20]

Compared to chemical oxidant-based systems, the electrocatalytic method displayed similar efficiency at lower expense and less organic waste production, which could be important for scaling up applications.

## Semi-Pinacol-Type Rearrangement

**Figure 4.** Electrocatalytic C–C bond forming hydrofunctionalizations. <sup>a</sup> Determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

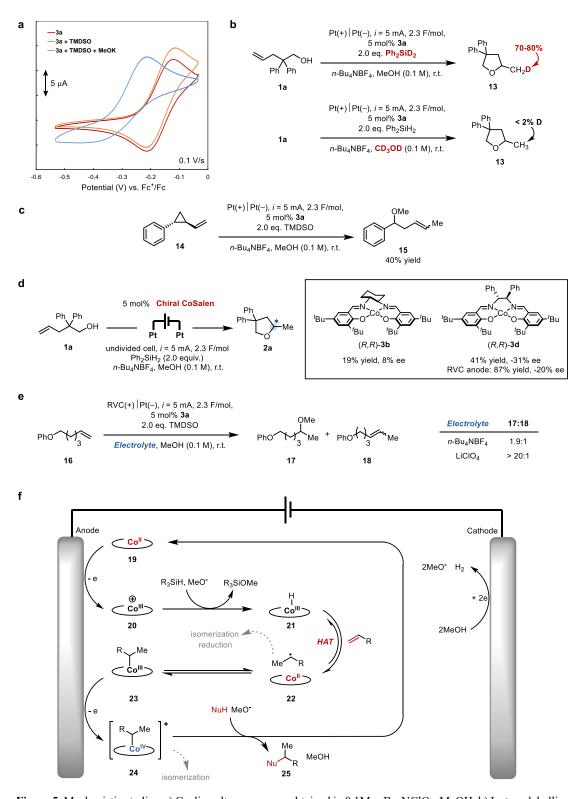
A series of experiments were performed in order to probe the mechanism of the electrocatalytic hydrofunctionalization reactions (Figure 5). First, cyclic voltammetry of Co complex **3a** displayed a reversible oxidation event at E<sub>1/2</sub> = -0.17 V vs. Fc<sup>+</sup>/Fc in methanol, which was not affected by the addition of silane (Figure 5a). Interestingly, the reduction wave disappeared upon adding potassium methoxide. It indicates that methoxide, which could be cathodically generated, might serve as a necessary catalyst for silane activation and thus effect the formation of Co–H from Co<sup>III</sup>. This also corroborates with the solvent effect observed during optimization (Figure 2a, entry 5). Next, hydride transfer from the silane was confirmed by a deuterium-labeling experiment, whereas running the reaction in CD<sub>3</sub>OD provided nearly no D incorporation (Figure 5b). Interestingly, the D% incorporation was substantially lower than expected in the first case, which is most likely due to H/D scrambling by reversible HAT (rather than Co–D/H<sup>+</sup> exchange or oxidation of methanol). Further, the HAT process was evaluated by a radical clock substrate, where the ring-opening trapping product was predominantly observed, suggesting the radical nature of the intermediate generated by HAT (Figure 5c).

A key mechanistic evidence for the involvement of a Co<sup>IV</sup> intermediate was provided by the attempted asymmetric synthesis using a chiral CoSalen catalyst (Figure 5d). Despite the low enantiomeric excess, this observed catalyst controlled stereoselectivity strongly supports the Co<sup>IV</sup> hypothesis.<sup>[14b, 14d, 14f]</sup> Nonetheless, we observed an interesting correlation between the anode material and the selectivity. Tentatively, this might be attributable to the more facile

oxidation of free radicals on RVC compared to platinum.<sup>[21]</sup> Unfortunately, substantial optimizations did not provide satisfying ee's.

The putative Co<sup>IV</sup> species generated at the electrode could be intercepted either before or after diffusing into the bulk solution. An electrolyte effect could be used to probe this step. Moeller has shown that for a radical cation mediated reaction carried out in methanol, the effective methanol concentration near the anode could be lowered by an electrolyte that forms a more hydrophobic electric double layer (EDL).<sup>[22]</sup> Indeed, we noticed that for the hydromethoxylation reaction shown in Figure 5e, the selectivity for methanol trapping over isomerization was substantially lower with the more hydrophobic NBu<sub>4</sub>BF<sub>4</sub> than with LiClO<sub>4</sub>. Therefore, it seems that the Co<sup>IV</sup> species is mostly trapped near the electrode rather than in the bulk solution, which is consistent with the irreversible oxidation wave assigned to Co<sup>III/IV</sup> in Figure 1b.

Based on these observations, a plausible catalytic cycle involving an ECEC sequence is depicted in Figure 5f. Anodic oxidation of the Co<sup>II</sup> complex and cathode reduction of methanol would afford Co<sup>III</sup> and methoxide anion, respectively. Hydride exchange between the silane and Co<sup>III</sup> could be facilitated by methoxide. The resulting Co–H species 21 would undergo HAT with an alkene to afford an alkyl radical 22, followed by Co<sup>II</sup> trapping to give an alkylcobalt(III) complex 23. A second anodic oxidation then takes place to convert 23 to a highly electrophilic Co<sup>IV</sup> complex 24, which would be rapidly intercepted by a nucleophile next to the anode to form the hydrofunctionalization product 25 and regenerate the Co<sup>II</sup> complex. The major side pathways include reduction (hydrogenation) and isomerization. The latter could be a result of either back-HAT from the alkyl radical to Co<sup>II</sup> and/or the deprotonation of Co<sup>IV</sup> complex 24.



**Figure 5.** Mechanistic studies. a) Cyclic voltammograms obtained in 0.1M *n*-Bu<sub>4</sub>NClO<sub>4</sub>, MeOH. b) Isotope labelling experiment. c) Radical clock test. d) Observation of catalyst-controlled stereoselectivity was consistent with the involvement of Co<sup>IV</sup>. e) Electrolyte effect in hydromethoxylation reaction. f) Current mechanistic hypothesis.

In conclusion, we disclose a general electricity-driven method for the Co-catalyzed oxidative hydrofunctionalization reactions of alkenes via a Co<sup>II/III/IV</sup> cycle. Being free of stoichiometric chemical oxidants, this method applies to the formal Markovnikov-selective addition of alcohols and carboxylic acids to unactivated alkenes with excellent functional group compatibility, as well as two types of C–C bond forming reactions. A tandem isomerization/hydromethoxylation sequence was also developed for selective allyl deprotection. Mechanistic studies provided evidence for an ECEC mechanism involving Co<sup>IV</sup> intermediates, where moderate enantioselectivity was achieved to preliminarily demonstrate the potential of catalyst control. We anticipate that the results reported here will facilitate future investigations on chemo- and stereoselective electrocatalysis involving high valent cobalt organometallics.

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## Data availability

The authors declare that all other data supporting the findings of this study are available within the article and Supplementary Information files, and also are available from the corresponding author upon reasonable request.

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# **Author contributions**

R. Z. conceived the idea, guided the project and wrote the manuscript, with feedbacks from the other authors. F. Y.,

Y.-C. N. and H.-Y. L. performed the experiments. F. Y., Y.-C. N., L. Z., F. M. and R. Z. analyzed the results.