

Title

The Interface is a Tunable Dimension in Electricity-Driven Organic Synthesis

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Abstract

Predictive control over the selectivity outcome of an organic synthetic method is an essential hallmark of reaction success. Electricity-driven synthesis offers a reemerging approach to facilitate the design of reaction sequences towards increased molecular complexity. In addition to the desirable sustainability features of electroorganic processes, the inherent interfacial nature of electrochemical systems present unique opportunities to tune reaction selectivity. To illustrate this feature, we outline examples of mechanism-guided interfacial control over CO₂ electroreduction selectivity, a well-studied and instructive electrochemical process with multiple reduction products that are thermodynamically accessible. These studies reveal how controlled proton delivery to the electrode surface and substrate electroadsorption with the electrode dictate reaction selectivity. We describe and compare simple, yet salient, examples from the electroorganic literature, where we postulate that similar effects predominate the observed reactivity. This perspective highlights how the interface serves as a tunable dimension in electrochemical processes, delineating unique tools to study, manipulate, and achieve reaction selectivity in electricity-driven organic synthesis.

Introduction

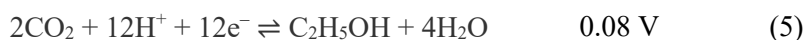
The discovery of organic synthetic methods enables the production of agrochemicals, pharmaceuticals, and soft materials that underpin modern living. The inquiry of the reaction mechanisms that underlie the reported transformations facilitates further creative manipulations of chemical reactivity, thereby contributing to the ever-increasing catalog of versatile approaches to access new chemical space. As synthetic efforts become increasingly automated and environmental impact considered, protocols that are simultaneously sustainable become valuable additions to this growing lexicon.^{1–3} Electrifying synthetic methods presents an opportunity to both drive reactivity via renewable sources of electricity and facilitate automated scale-up in flow.^{4–9} The growing literature^{10,11} shows that electroorganic reactivity can be tuned and optimized by modifications to the electrode^{12–15} and electrolyte^{16,17}; however, beyond these studies, the detailed mechanistic role of the electrified interface remains largely tacit in modern reaction design, and thereby product selectivity. The electrified surface is primarily viewed as one that provides a source or sink of electrons. In this view, the electrode enables the formation of high-energy intermediates or active forms of fine-tuned molecular catalysts via outer-sphere electron transfer,^{18–21} thereby serving to replace (super)stoichiometric oxidants or reductants. In the limit where the electrode enables direct access to reactive intermediates, a key differentiating aspect of electrosynthesis from other radical-based organic transformations is that electrochemical processes are *inherently* heterogeneous; redox equivalents are delivered at a phase boundary, i.e. at the interface of electrified solid electrodes and solution-dissolved reagents.²² This unique feature can offer complementary tools to direct reaction selectivity in electrosynthetic sequences.²³

Integrating interfacial manipulation into reaction design requires a molecular-level understanding of the electrified interface. Its mechanistic role remains the subject of intense study in the field of energy conversion and storage for over 70 years. Subtle changes in the interfacial structure have large effects on the efficiencies of electricity or fuels generation, a dominant factor in assessing the viability of emerging alternative energy technologies.²⁴ Thus, uncovering the mechanistic origin of interfacial control over enhanced efficiency enables the construction of new molecular-level roadmaps detailing how to manipulate this key parameter. While the efficient use of renewable electricity, as has previously been noted,^{10,25} is not the primary goal when developing synthetic schemes, progress made in elucidating the underlying chemical processes gating the *selectivity* of electrocatalytic fuel formation at electrified interfaces can translate across the two fields of electroorganic synthesis and energy conversion. In particular, two strategies – controlled proton delivery to the electrode surface and substrate (electro)adsorption with the electrode – have shown to significantly redirect the product selectivity in various energy conversion catalysis schemes, ranging from oxygen reduction^{26,27} to the CO₂ reduction reaction (CO₂RR)^{28–30}. With this backdrop, the following questions begin to emerge. Can these interfacial tuning strategies, unique to electrified interfaces, also be utilized to envision new electrosynthetic reaction design? How can these effects be studied, manipulated, and improved? Here, we explore these questions by offering the perspective that an interdisciplinary approach targeting a molecular-level understanding of the interfacial structure, its manipulation, and its effects on electroorganic reactivity will enable additional dimensionality to advance and develop the science of selective electricity-driven organic synthesis.

Scope of this Perspective

To address these questions, we discuss examples from the electrocatalytic CO₂RR literature that highlight the roles that controlled proton delivery and substrate electroadsorption play in enabling selective CO₂ activation. CO₂RR presents an instructive system to analyze because there are several products, in addition

to the competing reduction of protons to hydrogen, that are thermodynamically accessible within a narrow potential range^{31,32} (potentials listed below are referenced versus the Reversible Hydrogen Electrode at pH 7):



Therefore, selective CO₂RR requires control over the relative rates of these competing processes, and an analysis of the strategies to control product selectivity offer opportunities to study and direct the outcome of electrosynthetic processes. Following, we delineate simple, yet salient, examples from the electroorganic literature, where we postulate that similar effects predominate the observed reactivity.

As the reactions discussed in this perspective are inherently heterogeneous, detailed investigation of the interfacial structure requires a complementary set of in-situ and ex-situ surface-sensitive characterization techniques in conjunction with standard physical electrochemical methods. We highlight the tools typically utilized in the inorganic energy conversion community,^{33,34} e.g. surface-enhanced infrared absorption spectroscopy,^{35–38} surface-enhanced Raman spectroscopy,³⁹ atomic force microscopy,⁴⁰ thermal programmed desorption,⁴¹ electrokinetic analyses⁴² and voltametric analyses^{43,44}, that, together, reveal information on the surface structure, substrate binding, and dynamics as a function of common electrosynthetic parameters. In addition, incorporating in-line product detection methods, such as differential electrochemical mass spectroscopy⁴⁵ or gas chromatography, enables detailed insight into how these spectroscopic or voltametric observables translate to the observed reactivity in real time. We also discuss examples of how interfacial structure, both through electrolyte, additive, and electrode tuning can be manipulated. Together, these tools enable a bottom-up approach, uncovering the physical organic and inorganic principles that underpin observed electrochemical reactivity, allowing for further predictive mechanism-driven manipulations of the interface to redirect synthetic outcomes.

This perspective adds to the growing literature of electroorganic synthesis. For detailed highlights of past and recent work on the scope of electroorganic synthetic methods advanced and discovered, we direct the reader to several reviews in the field.^{4–7,18–21,23,46–48} It is well-established how physical electrochemical tools that delineate current-voltage relationships can be utilized to uncover mechanistic insights into electroorganic processes; however, these reviews primarily focus on the homogeneous chemistry of electrochemical systems.^{22,49–51} We note that the electrode materials' impact on electrosynthetic processes has been extensively documented,¹¹ and this perspective is not intended to address practical concerns associated with choosing suitable electrode materials, e.g. suppressing materials corrosion or deposition of insulating organic layers, a topic that has been recently covered¹⁰. For a comprehensive review on design strategies utilized to manipulate electrode interfaces to increase CO₂ electroreduction efficiency and selectivity, we direct the interested reader towards recent reviews.^{52–54} In this perspective, we aim to delineate two bridging molecular-level concepts between recent examples from CO₂ electroreduction and electroorganic synthesis in directing product selectivity – controlled proton delivery and substrate electroadsorption – that transcend the topical nature of either field and revealed new opportunities to utilize this molecular level understanding in designing electroorganic processes.

Controlling Electrosynthetic Reaction Selectivity via Controlled Proton Delivery

Several electrochemical processes, including CO₂ electroreduction, Equation 1 and Equations 3-6, hydrogen evolution, Equation 2, and organic functional group manipulations, are proton-coupled electron transfer (PCET) reactions. While the addition and removal of protons and electrons define the overall PCET stoichiometry and thermodynamic potential of the reactions (e.g. Equations 1-6), the kinetics of the process are dictated by the barriers associated with the elementary steps that delineate the concertedness of electron and proton motion.⁵⁵⁻⁵⁸ To highlight the role of the electrified interface in tuning PCET product selectivity, we choose to describe CO₂RR systems in which the electrode material is catalytically active, i.e. an electrocatalyst, to magnify the interfacial effects. As all the reductive electrochemical half reactions, Equations 1-6, are PCET processes, H⁺ are consumed local to the electroactive surface, leading to a dynamic proton coordinate that is unique to interfacial systems, **Figure 1a**. This interfacial gradient is enhanced when reactions are occurring at diffusion-limited currents, i.e. approximately greater than 1 mAcm⁻², on high surface area electrode materials. These conditions are met for electroorganic processes because lower currents would lead to intractable reaction times to form products (e.g. to react 1 mmol of substrate consuming 1e⁻mol⁻¹ with 0.1 mA requires 11 days). Thus, the necessary use of high surface area electrodes for electroorganic syntheses requires the identification of the effects of mass transfer on the outcome of the transformation via a systematic investigation in electrode materials synthesis; electrochemically accessible surface area, and modeling of the resulting concentration gradients. Below, we discuss how the mechanistic investigation of the concurring electrochemical PCET half reactions informs how to further augment and manipulate the interfacial proton donor coordinate to enhance the selectivity for electrocatalytic CO₂RR (**Figure 1b**). Following, we discuss an example from ketone reduction that demonstrates how this knowledge can be applied in tuning electroorganic reaction selectivity (**Figure 1c**). These considerations uncover design principles to systematically and predictively fully capitalize this interfacial dimension intrinsically present in electroorganic systems.

The possible elementary PCET steps can be graphically represented by classical square schemes. As an example, we delineate the scheme associated with PCET activation of CO₂, **Figure 2a**. CO₂ electroreduction can proceed via a sequential electron transfer- proton transfer (ET-PT, across then down via intermediate **1**, **Figure 2a**) mechanism, a concerted proton electron transfer (CPET, diagonal in **Figure 2a**) mechanism or a sequential proton transfer-electron transfer (PT-ET) mechanism. The latter is ruled out because direct protonation of CO₂ is thermodynamically unfavorable under the neutral reaction conditions.⁵⁹ Within the theory of PCET, it is well-established⁶⁰ that an enabling feature of a CPET pathway is that it lowers the energy barrier associated with this elementary process if either the PT or ET step exhibits a large energy penalty, i.e. the free energy change for PT (pK_a) or ET (potential) are prohibitively high. Recent work also demonstrated how PCET can be exploited in photoredox processes, where ET is enabled by a photoreductant, permitting light-driven reactivity otherwise inaccessible by the redox potentials of using commonly available photoredox catalysts.⁶¹ In addition to increasing reaction efficiency via CPET pathways, PCET processes can also enable opportunities for tuning selectivity if there are several competing reactions that are proton-coupled but mechanistically distinguishable, i.e. stepwise vs. CPET, by exploiting the different requirements for proton transfer. For example, in contrast to CO₂ electroactivation, where both stepwise and concerted pathways are possible to form the intermediate **2**, direct H⁺ electroactivation occurs via a compulsory concerted pathway, **Figure 2a**, to form intermediate **3**. Indeed, literature reports have shown that controlling proton delivery to the electroactive surface enables the activation of CO₂ versus H⁺, suppressing undesired H₂ evolution. Utilizing Au electrode surfaces known to competitively produce CO and H₂,^{32,62} reported electrokinetic data are consistent with a stepwise ET-PT activation^{28,63,64} of CO₂ and

CPET activation²⁸ of H⁺. These conclusions are established by employing rotating electrodes^{65–67} coupled with in-line gas chromatography, **Figure 2b**. These tools enable the elucidation of the activation-controlled, and not mass-transfer controlled, partial current density for a given product. As this activation-controlled current is proportional to the reaction rate,²⁴ this observable can be tracked as a function of various experimental conditions to derive rate laws consistent with the data. These studies reveal that undesirable H₂ evolution proceeded, as expected, via CPET and was strongly sensitive to the proton donor environment⁶⁷ while CO₂RR proceeded through rate-limiting ET to CO₂ and was largely insensitive to the proton donor environment, **Figure 2c**.^{28,63,64} These insights suggest that as both half reactions consume protons local to the electroactive interface, leading to mathematically modelled^{64,68} and spectroscopically observed⁶⁹ proton concentration gradients, attenuating proton transfer to the interface would decrease the rate of HER while maintaining a robust rate for CO₂RR, leading to more selective catalysis. These studies exemplify how the heterogeneous nature of electrochemical reactions can be exploited to manipulate the dynamic proton coordinate, thereby facilitating selective reactions.

The studies outlined above enable us to draw on these concepts to affect product selectivity for electroorganic transformations. For comparison, the selectivity of a simple, but nevertheless instructive, electrochemical reduction of ketones is examined, which has also been recently utilized as a model PCET reaction to describe the efficacy of new homogeneous PCET mediator-based strategies.⁷⁰ The pH-dependent pinacol versus alcohol product selectivity observed in the reduction of phenyl ketones, **4**, is a well-documented phenomenon and extensive mechanistic studies have been conducted over several decades ago.^{48,71–73} While the pH-dependent product bifurcation has been shown to be dependent on the structure of the ketone,⁷² general consensus of the mechanism has been established (**Figure 2e** and **Figure 2f**).^{48,71–73} At pH values less than the pK_a for the one-electron reduced radical anion intermediate, **5**, (for acetophenone, pK_a = 9.9^{74,75}), a PCET voltametric wave is observed, corresponding to the horizontal step in **Figure 2e** that scales in a Nernstian fashion (60 mV pH⁻¹, **Figure 2f**, blue) to form **6**. Constant potential electrolyses under these conditions gives rise to the exclusive formation of pinacol following a 1F mol⁻¹ process, consistent with the mechanistic scheme of PCET reduction followed by dimerization, **Figure 2g**. At more negative potentials, an additional wave is observed, however, the wave is pH-independent. Thus, this result suggests that the second wave corresponds to the pH-independent reduction of **6** to form **7**, **Figure 2e** and **Figure 2f**, black solid line. As the pH becomes more basic (pH ≈ pK_a of **5**), the two voltametric waves are replaced by a single two-electron voltametric wave that scales 30 mV pH⁻¹, **Figure 2f**, red. This observation is consistent with the coalescence of the first pH-dependent voltametric wave to form **6** with the pH-independent reduction of **6** to form **7**. Under these more basic conditions, constant potential electrolyses affords the formation of alcohol as the primary product following a 2F mol⁻¹ process, consistent with the mechanistic scheme of CPET reduction followed by ET and rapid protonation, **Figure 2g**, or via a disproportionation chemical reaction.⁷⁶ As the pH is further increased such that pH >> pK_a of **5**, **5** is directly accessed following a pH-independent reduction, **Figure 2e** and **Figure 2f**, black dotted line. Constant potential electrolysis under these extremely basic conditions afford the pinacol as the principle product following the passage of 1 F mol⁻¹. These observations are consistent with dimerization afforded by reaction of the **5** with the neutral product **6** formed in minor equilibrium, which are, in some cases, more difficult to reduce than the starting material⁷⁷. Together these studies highlight how the PCET reactivity of a simple functional group reduction can be tuned to affect the product distribution.

The above studies into PCET mechanisms enable the development of synthetic strategies to control and direct product selectivity by manipulating and further augmenting the dynamic proton donor coordinate, **Figure 3a**. Electrode materials design can be manipulated to exploit and magnify the interfacial proton coordinate to enable more selective processes. CO₂RR Au electrocatalysts with a tunable array of interconnected pores have been shown to systematically control the selectivity and efficiency of fuel

production from CO₂, **Figure 3b**.⁷⁸ Modeling of the diffusional profiles on related Ag electrocatalysts support these findings⁷⁹. Understanding of the interfacial proton coordinate enables not only manipulation by the solid electrode materials design, but also by molecular additives that further augment the local proton donor environment. Utilization of organic modifiers, such as N-substituted pyridinium additives,^{80,81} **Figure 3c**, drop-casted organic modifiers,⁸² **Figure 3d**, trimethylammonium surfactants,^{83–85} **Figure 3e**, have resulted in enhanced CO₂RR selectivity. For CO₂RR conducted in the presence of trimethylammonium surfactants, it was shown that the data are consistent with reduced surface concentration of H₂O at the electroactive interface, suggesting that the enhanced selectivity can be attributed to an interfacial diminishment of viable proton donors, such as H₂O.⁸⁶ For CO₂RR conducted in the presence of drop-casted organic modifiers,⁸² **Figure 3d**, studies showed that similarly the hydrophobicity of the surface can be manipulated via the use of organic modifiers, which could similarly alter the concentration of viable proton donors at the interface. Finally, for CO₂RR conducted in the presence of N-substituted pyridinium additives,^{80,81} the formation of organic films from pyridinium-based molecules significantly enhanced the selectivity for CO₂RR. Later *in-situ* spectroscopic studies revealed that the enhanced selectivity is consistent with a model where an interfacial proton gradient is magnified, leading to large local pH swing and more selective catalysis, **Figure 3c**.⁸⁷ Together, these studies reveal how molecular tuning of the electroactive interface can augment the local proton coordinate, manipulating the selectivity for the desired transformation in heterogeneous electrochemical environments.

The PCET reactivity of simple functional group manipulations suggest that interfacial designs that tune and augment the proton coordinate can also alter the product selectivity for electroorganic transformations. The presence of trimethylammonium surfactants has been shown to affect the product distribution for pinacol versus alcohol formation from electrochemical reduction of acetophenone.⁸⁸ In its absence, indiscriminate selectivity for alcohol versus pinacol was observed (33% current efficiency towards alcohol; 30% towards pinacol), and in its presence, alcohol formation was significantly favored (67% current efficiency towards alcohol; 4% towards pinacol).⁸⁸ While this result has been attributed to a stabilization effect *via* ion-pairing of the ammonium with the radical anion of the reduced substrate, the results could also be explained by an increase in the buildup of an alkaline region as a result of the decreased concentration of viable proton donors near the electroactive surface, **Figure 3f**. This alkaline region would favor alcohol relative to dimer formation around the pK_a value for acetophenone as described above. It is noted that, under electrochemical conditions, recent findings have shown that quaternary ammonium salts were also found to suppress HER and Pb cathode corrosion, both which are exacerbated by presence of H⁺ in the reduction of menthone oxime⁸⁹ and amide deoxygenation⁹⁰. However, in the study concerning acetophenone reduction in the presence of trimethylammonium surfactants, HER suppression cannot be the origin of selectivity enhancement as the total current efficiencies remain the same in its presence and absence.⁸⁸

Together, these studies reveal how the PCET reactivity of both fuel-forming half reactions and electroorganic reactivity can be studied and subsequently manipulated to enable more selective electrosynthetic reactions *via* controlled proton donor delivery. By combining mechanistic insight gleaned from electroanalytical and spectroscopic methods with interfacial manipulation strategies, including electrode materials design and organic/inorganic hybrid materials, the dynamic proton coordinates inherent to electrochemical processes involving PCET can be utilized as an opportunity to manipulate and control electrosynthetic reaction selectivity via controlled proton delivery.

Controlling Electrosynthetic Reaction Selectivity via Substrate Electroadsorption

Another key factor inherent to the heterogeneous nature of electrochemical processes is the interaction of neutral organic substrates with polarized electrode surfaces, known as electroadsorption.⁹¹ These electroadsorptive processes are sensitive to the interfacial field, leading to varying concentrations of the organic molecule on the electrode surface as a function of the applied potential, **Figure 4a**. The potential-dependence is a result of a competition between the interaction of charged electrolyte constituents (we list anions denoted as E^- in **Figure 4a**, the transposition to cations being straightforward), solvent (Sol in **Figure 4a**), or substrate (Sub in **Figure 4a**). For example, the potential-dependence of neutral organics, such as benzene, in aqueous electrolytes is gated by a solvent exchange process, whereby water dipoles align as a function of the interfacial field and displace the adsorbed organic molecule.^{92–100} In this mechanistic framework, the solvent exchange process occurs most favorably at the potential of zero free charge (PZFC), a property that describes where the interfacial field is weakest, is intrinsic to the electrode material, and directly proportional to the materials' work function. At potential values more positive and negative of the PZFC, water molecules reorient and align as the interfacial field increases.^{92–98,101} In addition to the interaction of solvents with the electrode surface, the intrinsic enthalpy of adsorption of the organic molecule, i.e. binding energy of the organic molecule to the surface, contributes to the overall surface population. These binding events can be described by the strength of the molecule-material interactions¹⁰² – between the extended bands of the metal and molecular orbitals of the neutral substrate – that can outcompete the native solvent and electrolyte interactions with the surface. Together, these potential-dependent interactions define the substrate surface population, and thus, reactivity under given electrochemical conditions. These electroadsorption events become particularly important if direct, outer-sphere electron transfer activation occurs at extremely high reduction or oxidation potentials, which, for energy conversion processes limits efficiencies, and for electroorganic processes, limits the substrate scope. In the case of CO₂ electroreduction, the outersphere direct reduction potential for CO₂ is –1.48 V vs RHE (pH 7);³¹ this high value imparts too great an energy penalty to drive efficient CO₂RR. Thus, adsorption events dramatically stabilize the reduction process and enable electrocatalysis, although it is estimated that catalysis may still be operative at an overpotential with respect to the thermodynamic potential for forming the adsorbed reduced CO₂ species.¹⁰³ Furthermore, substrate electroadsorption has also been invoked as a key distinguishing factor to explain why certain metal electrode surfaces selectively form CO and others produce higher order products beyond CO from CO₂, **Figure 4b**. Below, we discuss how the metal electrode material is invoked as a critical component that dictates the selectivity in CO₂ and CO electroreduction processes and its relation to the surface adsorption isotherm of the substrate. Following, we discuss an example from alkyl halide reductions that demonstrates how this knowledge can also be applied in tuning electroorganic reaction selectivity (**Figure 4c**).

Cu electrode surfaces have been identified as a unique material that enables reductive C-C bond coupling reactivity from CO₂ or CO.^{32,104–108} The selectivity for these processes, however, is poor. As such, numerous studies have postulated why Cu-based materials enable this desired multi-electron reactivity and others do not.^{32,109–111} The consensus hypothesis in the literature suggests that stronger metal-CO (M-CO) bonds enable higher surface coverage of M-CO,^{109,112} and thus, upon the application of a suitable reductive potential, these M-CO can be coupled, **Figure 5a**. In contrast, on electrode surfaces that do not form higher order products, such as Au, the weaker binding strength of CO leads to a lower surface coverage, and thus facile liberation of CO over its accumulation, **Figure 5b**.²⁸ Indeed, in-situ spectroscopic studies revealed that a high surface coverage of labile M-CO can be maintained on copper at reductive potentials,^{113,114} most likely the result of a displacement reaction with solution-dissolved (bi)carbonate,¹¹⁵ while negligible coverage of kinetically competent CO is observed on Au.²⁸ These insights can be made using surface-enhanced infrared absorption spectroscopy (SEIRAS) in attenuated total reflectance mode, **Figure 5c**. The SEIRAS technique utilizes nanostructured electrode surfaces that amplify the incident IR absorption via

adsorbed species with transition dipole moments perpendicular to the surface.^{35–38} This technique is well-suited to visualize the electrode surface structure because SEIRAS provides: (a) linear response in adsorbate coverage and signal intensity¹¹⁶; (b) unrestricted mass transport to the catalyst surface; and (c) surface sensitivity within ~10 nm of the electrode surface.³⁵ In this way, the spectroscopic signatures of characteristic molecular vibrations of molecules bound to the surface and electrolyte constituents can be tracked as a function of various experimental parameters (electrolyte, potential, additive). While the surface is heterogeneous in nature, it is the aggregate ensemble of electrochemically accessible surface-active sites that govern the relevant interfacial structure; thus, these spectroscopic tools provide a way of visualizing the aggregate, steady state surface population of key intermediates and substrates. For CO reduction, thus, it is hypothesized that adsorption enables high surface population of CO, and the surface exerts a catalytic effect in enabling charge transfer process between these two fragments. Together, these studies exemplify how an understanding of the surface adsorption processes can be achieved, and therefore suggest that they can be manipulated to further augment surface electroadsorption, thereby facilitating selective reactions.

The critical role of tuning CO adsorption strengths onto catalyst surfaces has also led to understanding of the electrode materials' properties necessary to enable more selective catalysis. It has been shown that introducing defects, known as grain boundaries, is correlated to the increase in binding energy of CO on Cu.^{41,117} The adsorption energies determined for CO bound to these defects are in line with the values that were determined from defects on crystalline Cu(100) surfaces via isotherm studies,¹¹⁸ and are consistent with the view that defect sites lead to higher binding energies of CO. These defect-rich surface structures have interestingly shown higher activity for CO and CO₂ reduction. Manipulation of the underlying defects, including grain boundaries, altered CO reduction activity and selectivity.^{41,117,119} Increased CO binding enthalpy to Cu surfaces was shown for more defect-rich Cu surfaces, and correlated with higher selectivity for C-C coupled products, **Figure 5d**.⁴¹ These conclusions were drawn from thermal programmed desorption studies in the absence of electrolyte or potential. SEIRAS measurements show that the potential for CO adsorption and CO electroreduction are distinct,^{113,114} i.e. CO pre-equilibrium adsorption precedes activation; therefore, these insights are consistent with the TPD results and hypothesis that higher CO bond strengths enable higher pre-equilibrium CO surface coverage. Together, these studies reveal how the materials tuning of the electroactive interface can augment the substrate interactions with the active surface, manipulating the selectivity for desired transformations in these heterogeneous electrochemical environments.

The studies outlined on electrosorption in the context of electrocatalytic fuel formation offer opportunities to compare and draw on these concepts to affect the product selectivity for electroorganic transformations. For electroorganic processes, substrate specific-interactions with the surface facilitates selective reactivity. Alkyl halides, a commercially available electrophilic feedstock, interact and adsorb on both unpolarized and polarized transition metal surfaces.¹²⁰ Additionally, under ultra-high vacuum, alkyl halides were found to adsorb onto transition metal surfaces at as low as liquid N₂ temperature.¹²¹ Under electrochemical conditions, *in-situ* Raman spectroscopic studies suggest that benzyl halide substrates can adsorb onto transition metal electrode surfaces, such as Ag.^{122,123} These results suggest that in contrast to direct outer-sphere SET that is commonly employed for radical-based chemistries, electroadsorptive properties could enable inner-sphere SET to electroadsorbed substrates. Indeed, it has been documented that electroadsorptive properties alter product selectivity for simple alkyl halide reduction processes. For the reduction of 1-iododecane in DMF on glassy carbon surfaces, the reaction proceeds at –2.17 V SCE (aqueous saturated calomel electrode), and the primary product of the reaction was the dehalogenated product.¹²⁴ This selectivity is consistent with electroanalytical results revealing a two-electron wave at potential values at 0.87-0.75 V more negative than the thermodynamic potential for primary radical reduction to the carbanion, **Figure 5e**.^{124–126} It is postulated that the two-electron wave arises due to the

extra excursion away from the thermodynamic potential, which renders the second reduction kinetically facile.¹²⁶ Thus, the data are consistent with the formation of a carbanion, **8**, via outer-sphere electron transfer (OSET) in solution, which is protonated by solvent or trace water. In contrast, on silver electrode surfaces, the potential for reduction is -1.06 V vs SCE, around 1.11 V more positive than that on glassy carbon.^{124,127} These electrocatalytic properties of Ag towards organic halides is well-documented,^{128,129} and the alkyl halide example is chosen as bulk electrolysis data for both Ag and carbon electrodes are available. The primary product for 1-iodohexane reduction on silver electrode surfaces was the dimer, rather than the dehalogenated product. It is hypothesized that the adsorption of iodide provides additional thermodynamic advantage to effect robust electrocatalysis.¹²⁹ The intermediacy of a radical, **9**, instead of a carbanion was supported by the single-electron, in contrast to the two-electron, stoichiometry. In terms of product selectivity, this result bears resemblance to the redox-leveling effect observed for solution-dissolved organic or inorganic redox mediators.^{130,131} In the absence of the redox mediator, the two-electron protodehalogenated product was selectively obtained, however, in its presence, the SET radical reactivity was instead observed.^{130,132} The rationale for the leveling effect, however, is different for the two systems. In the solution-dissolved case, the effect is due to taking a two-dimensional scaffold and rendering it in a three-dimensional one.⁴³ In the transition-metal electrode catalyzed process, there are two possible explanations for the leveling effect observed. First, the lowered potential energy profile by the interaction with the surface results in a less negative potential which disfavors the formal radical-polar crossover event to form the carbanion, **8**. Second, the reactivity may proceed via an elementary step akin to reductive elimination. Thus, these results highlight that the changes in product distribution observed when altering electrode materials could be the result of electrosorptive mechanisms of the substrate with the material followed by inner-sphere electron transfer, **Figure 5e** versus **Figure 5f**. Thus, these studies motivate further manipulations of electrode materials design to augment electrosorption events, thereby tuning electroorganic reaction selectivity.

Together, these studies highlight how substrate electroadsorption of both small molecule substrates relevant to the solar fuels paradigm and those utilized in synthetic organic methodology can be studied and subsequently manipulated to enable more selective electrosynthetic reactions. By combining mechanistic insight obtained from electroanalytical methods and *in-situ* spectroelectrochemistries with ex-situ surface analysis and electrode materials design, the unique added electrosorptive properties inherent to electrochemical systems can be utilized as an opportunity to manipulate and control electrosynthetic reaction selectivity. The studies highlighted in this perspective lie in contrast to the view that adsorption should be avoided because it leads to competing deleterious electrocatalytic reactivity. While this strategy is important when targeting formal outersphere electron transfer to substrates,¹⁰ emerging opportunities exist in manipulating innersphere electron transfer for electrosynthetic applications.

Outlook

While discovered over 150 years ago, electroorganic chemistry, the facilitation of organic reactivity driven by electricity, is relevant today because it enables a pathway to achieve sustainable synthesis goals. This revival has provided chemists with the opportunity to add additional ways to access high energy and reactive intermediates under mild conditions. In addition, the revival also provides the opportunity to revisit the physical inorganic and organic electrochemistry of these processes to delineate the underlying principles gating chemical reactivity at electrified interfaces. Organic chemists have explored the mechanistic aspects of reactivity to inspire new ones, and we similarly envision that understanding the underlying complexity of interfaces will afford more creative manipulations of electricity-driven synthesis. A key ingredient to achieve this vision is the appreciation that electrochemistry is an interdisciplinary study concerning the electrode materials design and the manipulation of the solid/liquid phase boundary, which are both dynamic

and change as a function of the electrode potential. In this perspective, we have delineated two concepts – tuning proton transfer events via interfacial microenvironments and facilitation of key inner-sphere electron transfer events via electrosorption – that translate across the field of CO₂ electroreduction, where interfacial physical principles have been extensively studied, and electroorganic chemistry, where these principles have been less explored. Together, this perspective highlights how lessons learned from the energy conversion and catalysis field translates into mechanism-guided electrosynthetic strategies that increase product selectivity via interfacial tuning and contextualizes them as an opportunity to build a richer science that embraces the complexity of interfacial structure in reaction design.

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Figures

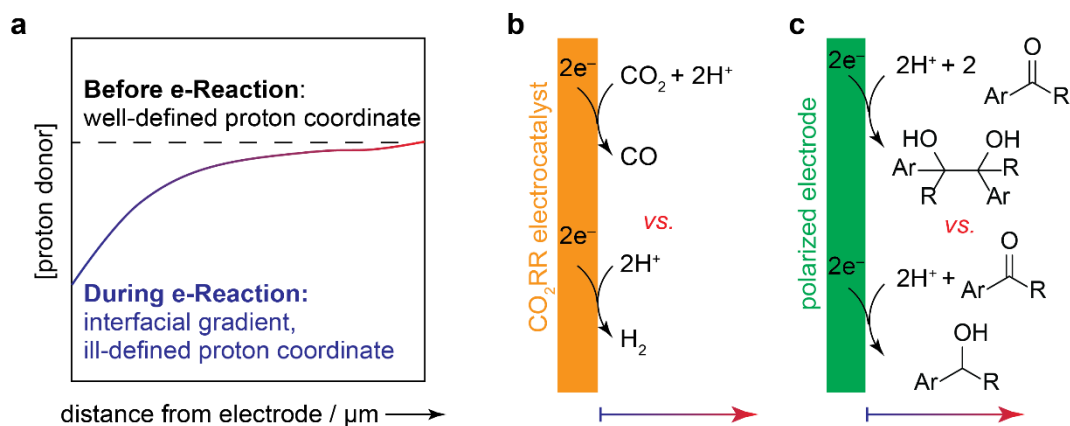


Figure 1: (a) Schematic depiction of the dynamic proton-coordinate manipulated during reductive electrochemical PCET processes that consume proton donors, such as CO_2RR and reduction of aromatic carbonyl compounds. (b) Depiction of the selectivity challenges in enabling selective PCET activation of CO_2 versus H^+ at an electrified CO_2RR electrocatalyst. (c) Depiction of the selectivity challenges in enabling selective PCET reduction of an aromatic carbonyl compound to favor alcohol versus pinacol formation. Gradient arrow represents the buildup of interfacial pH gradient during the electrochemical processes in (b) and (c) to mirror the schematic in (a).

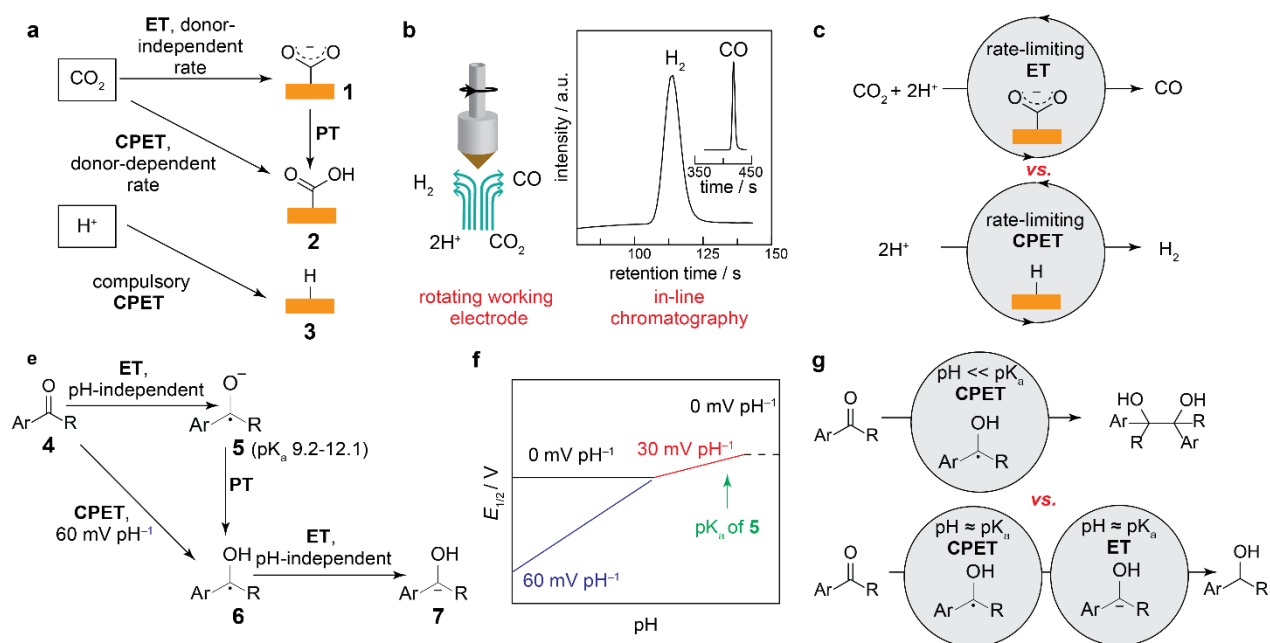


Figure 2: Inquiry of the PCET mechanism informs how to further augment and manipulate the interfacial proton donor coordinate. Possible PCET pathways for CO_2 initial activation and compulsory CPET activation with an electrified surface (**a**). Example experimental setup to investigate proton-donor dependence of electrocatalytic CO and H_2 formation under well-defined mass transport, i.e. activation-controlled conditions (**b**). Divergent proton donor requirements for CO_2 vs H^+ electroactivation (modified from reference²⁸). (**c**) Possible PCET pathways for activation of **4** to investigate proton-donor dependence of pinacol versus alcohol formation. (**d**) Schematic depiction of cyclic voltammograms analyses to investigate proton-donor dependence of electrochemical pinacol versus alcohol formation. (**e**) Divergent proton donor requirements for pinacol versus alcohol formation. (**f** and **g**) (modified from references^{48,71-73}).

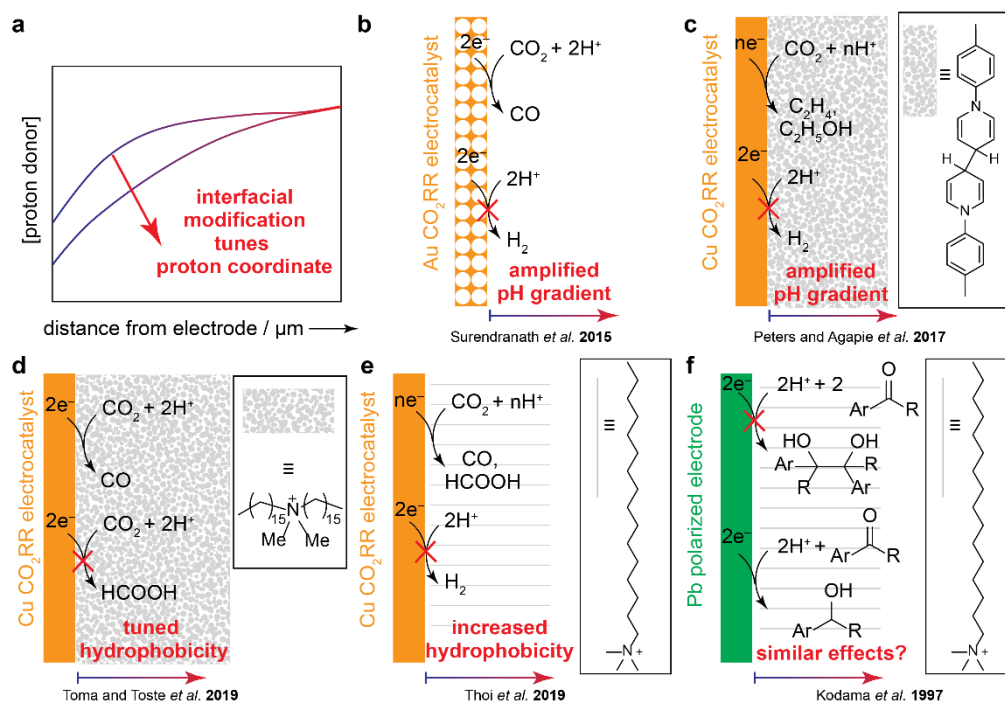


Figure 3: (a) Schematic depiction of how interfacial modification augments the dynamic proton coordinate. Examples follow: (b) Porous electrocatalysts enhance CO_2RR selectivity over HER via amplified pH gradients (modified from reference⁷⁸). (c) Electrodeposited films enhance CO_2RR selectivity over H_2 evolution via amplified pH gradients (modified from reference⁸⁰). (d) Drop-cast organic modifiers enhance CO_2RR selectivity via tuned hydrophobicity at the interface (modified from reference⁸²). (e) CO_2RR performed in the presence of surfactants enable enhance CO_2RR selectivity over HER (modified from reference⁸³). (f) Acetophenone (Ar = phenyl, R = methyl) reduction selectivity enhanced in the presence of surfactants (modified from reference⁸⁸).

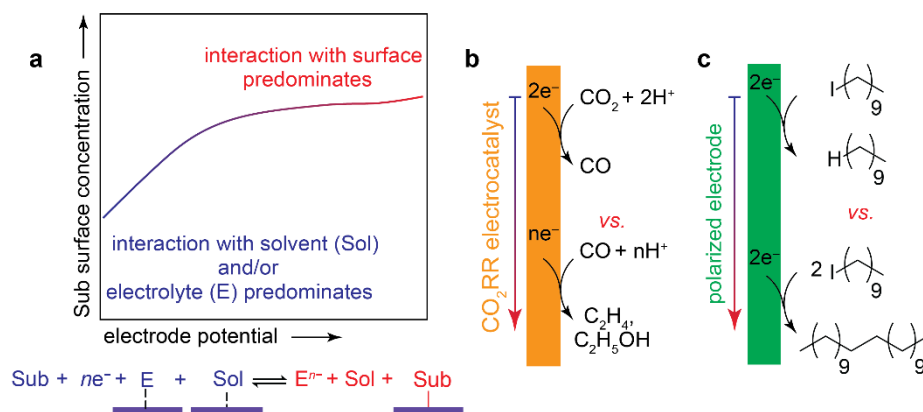


Figure 4: (a) Schematic depiction of the potential-dependence of neutral organic substrate surface concentration manipulated via interactions with surface, solvent, and/or interaction with electrolyte constituents. (b) Depiction of selectivity challenges in enabling selective CO formation from CO₂ versus further reduction to form higher order products. (c) Depiction of selectivity challenges in enabling selective C-C bond formation versus protodehalogenation. Gradient arrow represents the changes in the substrate interaction with the surface leading to differing product selectivity in (b) and (c) to mirror the schematic in (a).

References

1. Bryan MC, Dunn PJ, Entwistle D, et al. Key Green Chemistry research areas from a pharmaceutical manufacturers' perspective revisited. *Green Chem.* 2018;20(22):5082-5103. doi:10.1039/c8gc01276h
2. Ferlin F, Lanari D, Vaccaro L. Sustainable flow approaches to active pharmaceutical ingredients. *Green Chem.* 2020;22(18):5937-5955. doi:10.1039/d0gc02404j
3. Vaccaro L. Green Shades in Organic Synthesis. *European J Org Chem.* 2020;2020(28):4273-4283. doi:10.1002/ejoc.202000131
4. Yan M, Kawamata Y, Baran PS. Synthetic Organic Electrochemical Methods since 2000: On the Verge of a Renaissance. *Chem Rev.* 2017;117(21):13230-13319. doi:10.1021/acs.chemrev.7b00397
5. Fuchigami T, Inagi S, Atobe M. *Fundamentals and Applications of Organic Electrochemistry: Synthesis, Materials, Devices.* Wiley-VCH; 2014. doi:10.1002/9781118670750
6. Wiebe A, Gieshoff T, Möhle S, Rodrigo E, Zirbes M, Waldvogel SR. Electrifying Organic Synthesis. *Angew Chem Int Ed.* 2018;57(20):5594-5619. doi:10.1002/anie.201711060
7. Cembellin S, Batanero B. Organic Electrosynthesis Towards Sustainability: Fundamentals and Greener Methodologies. *Chem Rec.* 2021;21:tcr.202100128. doi:10.1002/tcr.202100128
8. Zhu C, Ang NWJ, Meyer TH, Qiu Y, Ackermann L. Organic Electrochemistry: Molecular Syntheses with Potential. *ACS Cent Sci.* 2021;7(3):415-431. doi:10.1021/acscentsci.0c01532
9. Schiffer ZJ, Manthiram K. Electrification and Decarbonization of the Chemical Industry. *Joule.* 2017;1(1):10-14. doi:10.1016/j.joule.2017.07.008
10. Heard DM, Lennox AJJ. Electrode Materials in Modern Organic Electrochemistry. *Angew Chem Int Ed.* 2020;59(43):18866-18884. doi:10.1002/anie.202005745
11. Couper AM, Pletcher D, Walsh FC. Electrode Materials for Electrosynthesis. *Chem Rev.* 1990;90(5):837-865. doi:10.1021/cr00103a010
12. Delano TJ, Reisman SE. Enantioselective Electroreductive Coupling of Alkenyl and Benzyl Halides via Nickel Catalysis. *ACS Catal.* 2019;9(8):6751-6754. doi:10.1021/acscatal.9b01785
13. Hu P, Peters BK, Malapit CA, et al. Electroreductive Olefin-Ketone Coupling. *J Am Chem Soc.* 2020;142(50):20979-20986. doi:10.1021/jacs.0c11214
14. Yin Z, Pang H, Guo X, et al. CuPd Nanoparticles as a Robust Catalyst for Electrochemical Allylic Alkylation. *Angew Chem Int Ed.* 2020;59(37):15933-15936. doi:10.1002/anie.202006293
15. Little RD, Schwaebel MK. Reductive cyclizations at the cathode. In: Springer, Berlin, Heidelberg; 1997:1-48. doi:10.1007/3-540-61454-0_69
16. Shono T, Mitani M. Electroorganic chemistry-XI. The stereochemistry of electroreduction of cyclic ketones. *Tetrahedron.* 1972;28(18):4747-4750. doi:10.1016/0040-4020(72)88082-7
17. Peters BK, Rodriguez KX, Reisberg SH, et al. Scalable and safe synthetic organic electroreduction inspired by Li-ion battery chemistry. *Science.* 2019;363(6429):838-845. doi:10.1126/science.aav5606
18. Siu JC, Fu N, Lin S. Catalyzing Electrosynthesis: A Homogeneous Electrocatalytic Approach to

- Reaction Discovery. *Acc Chem Res.* 2020;53(3):547-560. doi:10.1021/acs.accounts.9b00529
19. Novaes LFT, Liu J, Shen Y, Lu L, Meinhardt JM, Lin S. Electrocatalysis as an enabling technology for organic synthesis. *Chem Soc Rev.* Published online 2021. doi:10.1039/D1CS00223F
 20. Wang F, Stahl SS. Electrochemical Oxidation of Organic Molecules at Lower Overpotential: Accessing Broader Functional Group Compatibility with Electron-Proton Transfer Mediators. *Acc Chem Res.* 2020;53(3):561-574. doi:10.1021/acs.accounts.9b00544
 21. Francke R, Little RD, Itogawa S-J, et al. Redox catalysis in organic electrosynthesis: basic principles and recent developments. *Chem Soc Rev.* 2014;43:2492. doi:10.1039/c3cs60464k
 22. Costentin C, Savéant JM. Concepts and tools for mechanism and selectivity analysis in synthetic organic electrochemistry. *Proc Natl Acad Sci U S A.* 2019;166(23):11147-11152. doi:10.1073/pnas.1904439116
 23. Jing Q, Moeller KD. From Molecules to Molecular Surfaces. Exploiting the Interplay between Organic Synthesis and Electrochemistry. *Acc Chem Res.* 2020;53(1):135-143. doi:10.1021/acs.accounts.9b00578
 24. Gileadi E. *Physical Electrochemistry, Fundamentals, Techniques, and Applications.* Wiley-VCH; 2011.
 25. Kawamata Y, Baran PS. Electrosynthesis: Sustainability Is Not Enough. *Joule.* 2020;4(4):701-704. doi:10.1016/j.joule.2020.02.002
 26. Tse ECM, Barile CJ, Kirchschrager NA, et al. Proton transfer dynamics control the mechanism of O₂ reduction by a non-precious metal electrocatalyst. *Nat Mater.* 2016;15(7):754-759. doi:10.1038/nmat4636
 27. Kulkarni A, Siahrostami S, Patel A, Nørskov JK. Understanding Catalytic Activity Trends in the Oxygen Reduction Reaction. *Chem Rev.* 2018;118(5):2302-2312. doi:10.1021/acs.chemrev.7b00488
 28. Wuttig A, Yaguchi M, Motobayashi K, Osawa M, Surendranath Y. Inhibited proton transfer enhances Au-catalyzed CO₂-to-fuels selectivity. *Proc Natl Acad Sci.* 2016;113(32):E4585-E4593. doi:10.1073/pnas.1602984113
 29. Hansen HA, Varley JB, Peterson AA, Nørskov JK. Understanding Trends in the Electrocatalytic Activity of Metals and Enzymes for CO₂ Reduction to CO. *J Phys Chem Lett.* 2013;4(3):388-392. doi:10.1021/jz3021155
 30. Liu X, Xiao J, Peng H, Hong X, Chan K, Nørskov JK. Understanding trends in electrochemical carbon dioxide reduction rates. *Nat Commun.* 2017;8(1):1-7. doi:10.1038/ncomms15438
 31. Rosenthal J. Progress Toward the Electrocatalytic Production of Liquid Fuels from Carbon Dioxide. In: Karlin KD, ed. *Progress in Inorganic Chemistry.* Progress in Inorganic Chemistry. John Wiley & Sons; 2014:299-338. doi:10.1002/9781118869994
 32. Hori Y. Electrochemical CO₂ Reduction on Metal Electrodes. In: Vayenas C, White R, Gamboa-Aldeco M, eds. *Modern Aspects of Electrochemistry.* Vol 42. Modern Aspects of Electrochemistry. Springer; 2008:89-189. doi:10.1007/978-0-387-49489-0_3
 33. Bockris JO, Khan SUM. Some Experimental Techniques. In: *Surface Electrochemistry.* Springer US; 1993:1-58. doi:10.1007/978-1-4615-3040-4_1

34. Bard AJ. Inner-sphere heterogeneous electrode reactions. Electrocatalysis and photocatalysis: The challenge. *J Am Chem Soc.* 2010;132(22):7559-7567. doi:10.1021/ja101578m
35. Osawa M. Dynamic Processes in Electrochemical Reactions Studied by Surface-Enhanced Infrared Absorption Spectroscopy(SEIRAS). *Bull Chem Soc Jpn.* 1997;70:2861-2880.
36. Osawa M. Surface enhanced infrared absorption spectroscopy. In: Chalmers JM, Griffiths PR, eds. *Handbook of Vibrational Spectroscopy*. Wiley-VCH; 2002:785-800.
37. Osawa M. In-situ Surface-enhanced Infrared Spectroscopy of the Electrode/Solution Interface. In: Alkire RC, Kolb DM, Lipkowski J, Ross PN, eds. *Diffraction and Spectroscopic Methods in Electrochemistry (Advances in Electrochemical Science and Engineering, Vol.9)*. Wiley-VCH; 2006:269-314.
38. Osawa M. Surface-Enhanced Infrared Absorption. In: Kawata S, ed. *Near-Field Optics and Surface Plasmon Polaritons. Topics in Applied Physics*. Vol 81. Springer; 2001:163-187.
39. Sarkar S, Maitra A, Lake WR, Warburton RE, Hammes-Schiffer S, Dawlaty JM. Mechanistic Insights about Electrochemical Proton-Coupled Electron Transfer Derived from a Vibrational Probe. *J Am Chem Soc.* 2021;143(22):8381-8390. doi:10.1021/jacs.1c01977
40. Simon GH, Kley CS, Roldan Cuenya B. Potential-Dependent Morphology of Copper Catalysts During CO₂ Electroreduction Revealed by In Situ Atomic Force Microscopy. *Angew Chem Int Ed.* 2021;60(5):2561-2568. doi:10.1002/anie.202010449
41. Verdaguer-Casadevall A, Li CW, Johansson TP, et al. Probing the active surface sites for CO reduction on oxide- derived copper electrocatalysts. *J Am Chem Soc.* 2015;137:9808-9811.
42. Surendranath Y, Nocera DG. Oxygen Evolution Reaction Chemistry of Oxide-Based Electrodes. In: *Progress in Inorganic Chemistry*. Vol 57. John Wiley and Sons Inc.; 2011:505-560. doi:10.1002/9781118148235.ch9
43. Savéant J-M, Costentin C. *Elements of Molecular and Biomolecular Electrochemistry: An Electrochemical Approach to Electron Transfer Chemistry*. 2nd ed. John Wiley & Sons; 2019.
44. Savéant JM. Molecular catalysis of electrochemical reactions. Mechanistic aspects. *Chem Rev.* 2008;108(7):2348-2378. doi:10.1021/cr068079z
45. Clark EL, Bell AT. Direct Observation of the Local Reaction Environment during the Electrochemical Reduction of CO₂. *J Am Chem Soc.* 2018;140(22):7012-7020. doi:10.1021/jacs.8b04058
46. Wu T, Moeller KD. Organic Electrochemistry: Expanding the Scope of Paired Reactions. *Angew Chem Int Ed.* 2021;60(23):12883-12890. doi:10.1002/anie.202100193
47. Hammerich O, Speiser B, eds. *Organic Electrochemistry*. CRC Press; 2015.
48. Grimshaw J. *Electrochemical Reactions and Mechanisms in Organic Chemistry*. Elsevier; 2000.
49. Sandford C, Edwards MA, Klunder KJ, et al. A synthetic chemist's guide to electroanalytical tools for studying reaction mechanisms. *Chem Sci.* 2019;10(26):6404-6422. doi:10.1039/c9sc01545k
50. Little RD. A Perspective on Organic Electrochemistry. *J Org Chem.* 2020;85(21):13375-13390. doi:10.1021/acs.joc.0c01408
51. Moeller KD. Using Physical Organic Chemistry to Shape the Course of Electrochemical Reactions. *Chem Rev.* 2018;118(9):4817-4833. doi:10.1021/acs.chemrev.7b00656

52. Wagner A, Sahm CD, Reisner E. Towards molecular understanding of local chemical environment effects in electro- and photocatalytic CO₂ reduction. *Nat Catal*. Published online 2020. doi:10.1038/s41929-020-00512-x
53. Nam DH, De Luna P, Rosas-Hernández A, et al. Molecular enhancement of heterogeneous CO₂ reduction. *Nat Mater*. Published online 2020. doi:10.1038/s41563-020-0610-2
54. Smith PT, Nichols EM, Cao Z, Chang CJ. Hybrid Catalysts for Artificial Photosynthesis: Merging Approaches from Molecular, Materials, and Biological Catalysis. *Acc Chem Res*. 2020;53(3):575-587. doi:10.1021/acs.accounts.9b00619
55. Darcy JW, Koronkiewicz B, Parada GA, Mayer JM. A Continuum of Proton-Coupled Electron Transfer Reactivity. *Acc Chem Res*. 2018;51(10):2391-2399. doi:10.1021/acs.accounts.8b00319
56. Koper MTM. Theory of the transition from sequential to concerted electrochemical proton-electron transfer. *Phys Chem Chem Phys*. 2013;15(5):1399-1407. doi:10.1039/c2cp42369c
57. Huynh MH V, Meyer TJ. Proton-coupled electron transfer. *Chem Rev*. 2007;107(11):5004-5064. doi:10.1021/cr0500030
58. Hammes-Schiffer S, Stuchebrukhov AA. Theory of coupled electron and proton transfer reactions. *Chem Rev*. 2010;110(12):6939-6960. doi:10.1021/cr1001436
59. Cummings S, Hratchian HP, Reed CA. The Strongest Acid: Protonation of Carbon Dioxide. *Angew Chem Int Ed*. 2016;55(4):1382-1386. doi:10.1002/anie.201509425
60. Warren JJ, Tronic TA, Mayer JM. Thermochemistry of proton-coupled electron transfer reagents and its implications. *Chem Rev*. 2010;110(12):6961-7001. doi:10.1021/cr100085k
61. Tarantino KT, Liu P, Knowles RR. Catalytic ketyl-olefin cyclizations enabled by proton-coupled electron transfer. *J Am Chem Soc*. 2013;135(27):10022-10025. doi:10.1021/ja404342j
62. Hori Y, Murata A 1985, Ira, Kikuchi K, Suzuki S. Electrochemical reduction of carbon dioxides to carbon monoxide at a gold electrode in aqueous potassium hydrogen carbonate. *J Chem Soc Chem Commun*. Published online 1987:728-729. doi:10.1039/C39870000728
63. Zhang BA, Ozel T, Elias JS, Costentin C, Nocera DG. Interplay of Homogeneous Reactions, Mass Transport, and Kinetics in Determining Selectivity of the Reduction of CO₂ on Gold Electrodes. *ACS Cent Sci*. 2019;5(6):1097-1105. doi:10.1021/acscentsci.9b00302
64. Wuttig A, Yoon Y, Ryu J, Surendranath Y. Bicarbonate Is Not a General Acid in Au-Catalyzed CO₂ Electroreduction. *J Am Chem Soc*. 2017;139(47):17109-17113. doi:10.1021/jacs.7b08345
65. Opekar F, Beran P. Rotating disk electrodes. *J Electroanal Chem Interfacial Electrochem*. 1976;69(1):1-105.
66. Kirowa-Eisner E. The Rotating Cone Electrode. *J Electrochem Soc*. 1976;123(1):22. doi:10.1149/1.2132756
67. Goyal A, Marcandalli G, Mints VA, Koper MTM. Competition between CO₂ Reduction and Hydrogen Evolution on a Gold Electrode under Well-Defined Mass Transport Conditions. *J Am Chem Soc*. 2020;142(9):4154-4161. doi:10.1021/jacs.9b10061
68. Gupta N, Gattrell M, MacDougall B. Calculation for the cathode surface concentrations in the electrochemical reduction of CO₂ in KHCO₃ solutions. *J Appl Electrochem*. 2005;36(2):161-172. doi:10.1007/s10800-005-9058-y

69. Yang K, Kas R, Smith WA. In Situ Infrared Spectroscopy Reveals Persistent Alkalinity near Electrode Surfaces during CO₂ Electroreduction. *J Am Chem Soc.* 2019;141(40):39. doi:10.1021/jacs.9b07000
70. Chalkley MJ, Garrido-Barros P, Peters JC. A molecular mediator for reductive concerted proton-electron transfers via electrocatalysis. *Science.* 2020;369(6505):850-854. doi:10.1126/SCIENCE.ABC1607
71. Elving PJ, Leone JT. Mechanism of the Electrochemical Reduction of Phenyl Ketones. *J Am Chem Soc.* 1958;80(5):1021-1029. doi:10.1021/ja01538a002
72. Coulson DM, Crowell WR. Polarography of Carbonyl Compounds. II. A Theoretical Relationship between the Polarographic Half-wave Potentials and Structures of Carbonyl Compounds. *J Am Chem Soc.* 1952;74(5):1294-1297. doi:10.1021/ja01125a045
73. Stradins JP. Studies on the electrochemical mechanism of reduction of carbonyl compounds. *Electrochim Acta.* 1964;9(6):711-720. doi:10.1016/0013-4686(64)80059-1
74. Hayon E, Ibata T, Lichtin NN, Simic M. Electron and hydrogen atom attachment to aromatic carbonyl compounds in aqueous solution. Absorption spectra and dissociation constants of ketyl radicals. *J Phys Chem.* 1972;76(15):2072-2078. doi:10.1021/j100659a003
75. Adams GE, Willson RL. Ketyl radicals in aqueous solution pulse radiolysis study. *J Chem Soc Faraday Trans 1 Phys Chem Condens Phases.* 1973;69(0):719-729. doi:10.1039/F19736900719
76. Nadjo L, Saveant JM. Dimerization, disproportionation and e.c.e. mechanisms in the reduction of aromatic carbonyl compounds in alkaline media. *J Electroanal Chem.* 1971;33(2):419-451. doi:10.1016/S0022-0728(71)80127-4
77. Andrieux CP, Grzeszczuk M, Savéant JM. Electrochemical Generation and Reduction of Organic Free Radicals. α -Hydroxybenzyl Radicals from the Reduction of Benzaldehyde. *J Am Chem Soc.* 1991;113(23):8811-8817. doi:10.1021/ja00023a032
78. Hall AS, Yoon Y, Wuttig A, Surendranath Y. Mesostructure-Induced Selectivity in CO₂ Reduction Catalysis. *J Am Chem Soc.* 2015;137(47):14834-14837. doi:10.1021/jacs.5b08259
79. Suter S, Haussener S. Optimizing mesostructured silver catalysts for selective carbon dioxide conversion into fuels. *Energy Environ Sci.* 2019;12(5):1668-1678. doi:10.1039/c9ee00656g
80. Han Z, Kortlever R, Chen HY, Peters JC, Agapie T. CO₂ Reduction Selective for C_{≥2} Products on Polycrystalline Copper with N-Substituted Pyridinium Additives. *ACS Cent Sci.* 2017;3(8):853-859. doi:10.1021/acscentsci.7b00180
81. Li F, Thevenon A, Rosas-Hernández A, et al. Molecular tuning of CO₂-to-ethylene conversion. *Nature.* 2020;577(7791):509-513. doi:10.1038/s41586-019-1782-2
82. Buckley AK, Lee M, Cheng T, et al. Electrocatalysis at organic-metal interfaces: Identification of structure-reactivity relationships for co₂ reduction at modified cu surfaces. *J Am Chem Soc.* 2019;141(18):7355-7364. doi:10.1021/jacs.8b13655
83. Banerjee S, Han X, Thoi VS. Modulating the Electrode-Electrolyte Interface with Cationic Surfactants in Carbon Dioxide Reduction. *ACS Catal.* 2019;9(6):5631-5637. doi:10.1021/acscatal.9b00449
84. Quan F, Xiong M, Jia F, Zhang L. Efficient electroreduction of CO₂ on bulk silver electrode in aqueous solution via the inhibition of hydrogen evolution. *Appl Surf Sci.* 2017;399:48-54.

doi:10.1016/j.apsusc.2016.12.069

85. Chen L, Li F, Zhang Y, et al. Electrochemical Reduction of Carbon Dioxide in a Monoethanolamine Capture Medium. *ChemSusChem*. 2017;10(20):4109-4118. doi:10.1002/cssc.201701075
86. Zhang ZQ, Banerjee S, Thoi VS, Shoji Hall A. Reorganization of Interfacial Water by an Amphiphilic Cationic Surfactant Promotes CO₂ Reduction. *J Phys Chem Lett*. 2020;11(14):5457-5463. doi:10.1021/acs.jpcelett.0c01334
87. Ovalle VJ, Waagele MM. Understanding the Impact of N-Arylpyridinium Ions on the Selectivity of CO₂ Reduction at the Cu/Electrolyte Interface. *J Phys Chem C*. 2019;123(40):48. doi:10.1021/acs.jpcc.9b08666
88. Kodama Y, Imoto M, Ohta N, Kitani A, Ito S. Control of product distribution by use of surfactants in cathodic reduction of acetophenone. *Chem Lett*. 1997;(4):337-338. doi:10.1246/cl.1997.337
89. Kulisch J, Nieger M, Stecker F, Fischer A, Waldvogel SR. Efficient and stereodivergent electrochemical synthesis of optically pure menthylamines. *Angew Chem Int Ed*. 2011;50(24):5564-5567. doi:10.1002/anie.201101330
90. Edinger C, Grimaudo V, Broekmann P, Waldvogel SR. Stabilizing Lead Cathodes with Diammonium Salt Additives in the Deoxygenation of Aromatic Amides. *ChemElectroChem*. 2014;1(6):1018-1022. doi:10.1002/celec.201402050
91. Köster K, Riemenschneider P, Wendt H. Influence of Electrosorption on Kinetics and Selectivity of Electroorganic Synthetic Reactions. *Isr J Chem*. 1979;18(1-2):141-151. doi:10.1002/ijch.197900018
92. Bockris JO, Devanathan MA V., Muller K. On the Structure of Charged Interfaces. *Proc R Soc A Math Phys Eng Sci*. 1963;274(1356):55-79. doi:10.1098/rspa.1963.0114
93. Gileadi E. The combined adsorption isotherm. *Electrochim Acta*. 1987;32(2):221-229. doi:10.1016/0013-4686(87)85028-4
94. Gileadi E. Electrosorption. In: *Physical Electrochemistry, Fundamentals, Techniques and Applications*. Wiley-VCH; 2011:175-194.
95. Bockris JO, Jeng KT. In-situ studies of adsorption of organic compounds on platinum electrodes. *J Electroanal Chem*. 1992;330(1-2):541-581. doi:10.1016/0022-0728(92)80330-7
96. Blomgren E, Bockris JOM, Jesch C. The adsorption of butyl, phenyl and naphthyl compounds at the interface mercury-aqueous acid solution. *J Phys Chem*. 1961;65(11):2000-2010. doi:10.1021/j100828a019
97. Bockris JO, Reddy A, Gambou-Aldeco ME. The Electrified Interface. In: *Modern Electrochemistry 2A Fundamentals of Electrodics*. 2nd ed. Kluwer Academic/Plenum Publishers; 2002:933-984.
98. Gileadi E. On the potential dependence of electrosorption of neutral organic molecules. *J Electroanal Chem*. 1971;30(1):123-128. doi:10.1016/0368-1874(71)85040-2
99. Heiland W, Gileadi E, Bockris JOM. Kinetic and thermodynamic aspects of the electrosorption of benzene on platinum electrodes. *J Phys Chem*. 1966;70(4):1207-1216. doi:10.1021/j100876a040
100. Gileadi E, Rubin BT, Bockris JOM. Electrosorption of ethylene on platinum as a function of potential, concentration, and temperature. *J Phys Chem*. 1965;69(10):3335-3345.

doi:10.1021/j100894a019

101. Ataka K, Yotsuyanagi T, Osawa M. Potential-Dependent Reorientation of Water Molecules at an Electrode/Electrolyte Interface Studied by Surface-Enhanced Infrared Absorption Spectroscopy. *J Phys Chem.* 1996;100:10664-10672.
102. Hoffmann R. A chemical and theoretical way to look at bonding on surfaces. *Rev Mod Phys.* 1988;60(3):601-628. doi:10.1103/RevModPhys.60.601
103. Zhang BA, Costentin C, Nocera DG. Driving force dependence of inner-sphere electron transfer for the reduction of CO₂ on a gold electrode. *J Chem Phys.* 2020;153(9):094701. doi:10.1063/5.0016298
104. Hori Y, Takahashi I, Koga O, Hoshi N. Selective Formation of C₂ Compounds from Electrochemical Reduction of CO₂ at a Series of Copper Single Crystal Electrodes. *J Phys Chem B.* 2001;106(1):15-17. doi:10.1021/jp013478d
105. Hori Y, Murata A, Takahashi R, Suzuki S. Enhanced formation of ethylene and alcohols at ambient temperature and pressure in electrochemical reduction of carbon dioxide at a copper electrode. *J Chem Soc Chem Commun.* 1988;(1):17. doi:10.1039/c39880000017
106. Hori Y, Kikuchi K, Suzuki S. Production of CO and CH₄ in electrochemical reduction of CO₂ at metal electrodes in aqueous hydrogencarbonate solution. *Chem Lett.* 1985;14:1695-1698. doi:10.1246/cl.1985.1695
107. Hori Y, Kikuchi K, Murata A, Suzuki S. Production of methane and ethylene in electrochemical reduction of carbon dioxide at copper electrode in aqueous hydrogencarbonate solution. *Chem Lett.* 1986;15(6):897-898. doi:10.1246/cl.1986.897
108. Murata A, Hori Y. Product selectivity affected by cationic species in electrochemical reduction of CO₂ and CO at a Cu electrode. *Bull Chem Soc Jpn.* 1991;64(1):123-127. doi:10.1246/bcsj.64.123
109. Kortlever R, Shen J, Schouten KJP, Calle-Vallejo F, Koper MTM. Catalysts and Reaction Pathways for the Electrochemical Reduction of Carbon Dioxide. *J Phys Chem Lett.* 2015;6(20):4073-4082. doi:10.1021/acs.jpcclett.5b01559
110. Peterson AA, Nørskov JK. Activity Descriptors for CO₂ Electroreduction to Methane on Transition-Metal Catalysts. *J Phys Chem Lett.* 2012;3(2):251-258. doi:10.1021/jz201461p
111. Gattrell M, Gupta N, Co A. A review of the aqueous electrochemical reduction of CO₂ to hydrocarbons at copper. *J Electroanal Chem.* 2006;594(1):1-19. doi:http://dx.doi.org/10.1016/j.jelechem.2006.05.013
112. Kuhl KP, Hatsukade T, Cave ER, Abram DN, Kibsgaard J, Jaramillo TF. Electrocatalytic conversion of carbon dioxide to methane and methanol on transition metal surfaces. *J Am Chem Soc.* 2014;136(40):14107-14113. doi:10.1021/ja505791r
113. Wuttig A, Liu C, Peng Q, et al. Tracking a Common Surface-Bound Intermediate during CO₂-to-Fuels Catalysis. *ACS Cent Sci.* 2016;2(8):522-528. doi:10.1021/acscentsci.6b00155
114. Hori Y, Koga O, Yamazaki H, Matsuo T. Infrared spectroscopy of adsorbed CO and intermediate species in electrochemical reduction of CO₂ to hydrocarbons on a Cu electrode. *Electrochim Acta.* 1995;40(16):2617-2622. doi:10.1016/0013-4686(95)00239-B
115. Hori Y, Wakebe H, Tsukamoto T, Koga O. Adsorption of CO accompanied with simultaneous charge transfer on copper single crystal electrodes related with electrochemical reduction of CO₂

- to hydrocarbons. *Surf Sci.* 1995;335(C):258-263. doi:10.1016/0039-6028(95)00441-6
116. Samjeské G, Komatsu K, Osawa M. Dynamics of CO Oxidation on a Polycrystalline Platinum Electrode: A Time-Resolved Infrared Study. *J Phys Chem C.* 2009;113:10222-10228.
 117. Feng X, Jiang K, Fan S, Kanan MW. A Direct Grain-Boundary-Activity Correlation for CO Electroreduction on Cu Nanoparticles. *ACS Cent Sci.* 2016;2(3):169-174. doi:10.1021/acscentsci.6b00022
 118. Truong CM, Rodriguez J, Goodman DW. CO adsorption isotherms on Cu(100) at elevated pressures and temperatures using infrared reflection absorption spectroscopy. *Surf Sci.* 1992;271(3):L385-L391. doi:10.1016/0039-6028(92)90896-E
 119. Li CW, Ciston J, Kanan MW. Electroreduction of carbon monoxide to liquid fuel on oxide-derived nanocrystalline copper. *Nature.* 2014;508(7497):504-507. doi:10.1038/nature13249
 120. Lou YY, Fontmorin JM, Amrane A, Fourcade F, Geneste F. Metallic nanoparticles for electrocatalytic reduction of halogenated organic compounds: A review. *Electrochim Acta.* 2021;377:138039. doi:10.1016/j.electacta.2021.138039
 121. Zaera F. Molecular approach to the study of the mechanisms of alkyl reactions on metal surfaces. *J Mol Catal.* 1994;86(1-3):221-242. doi:10.1016/0304-5102(93)E0149-B
 122. Huang YF, Wu DY, Wang A, et al. Bridging the gap between electrochemical and organometallic activation: Benzyl chloride reduction at silver cathodes. *J Am Chem Soc.* 2010;132(48):17199-17210. doi:10.1021/ja106049c
 123. Wang A, Huang YF, Sur UK, et al. In situ identification of intermediates of benzyl chloride reduction at a silver electrode by SERS coupled with DFT calculations. *J Am Chem Soc.* 2010;132(28):9534-9536. doi:10.1021/ja1024639
 124. Cleary JA, Mubarak MS, Vieira KL, Anderson MR, Peters DG. Electrochemical reduction of alkyl halides at vitreous carbon cathodes in dimethylformamide. *J Electroanal Chem.* 1986;198(1):107-124. doi:10.1016/0022-0728(86)90030-6
 125. Andrieux CP, Gallardo I, Savéant JM, Su KB. Dissociative Electron Transfer. Homogeneous and Heterogeneous Reductive Cleavage of the Carbon-Halogen Bond in Simple Aliphatic Halides. *J Am Chem Soc.* 1986;108(4):638-647. doi:10.1021/ja00264a013
 126. Andrieux CP, Savéant JM, Gallardo I. Outer-Sphere Electron-Transfer Reduction of Alkyl Halides. A Source of Alkyl Radicals or of Carbanions? Reduction of Alkyl Radicals. *J Am Chem Soc.* 1989;111(5):1620-1626. doi:10.1021/ja00187a014
 127. Strawsine LM, Sengupta A, Raghavachari K, Peters DG. Direct Reduction of Alkyl Monohalides at Silver in Dimethylformamide: Effects of Position and Identity of the Halogen. *ChemElectroChem.* 2015;2(5):726-736. doi:10.1002/celec.201402410
 128. Isse AA, Mussini PR, Gennaro A. New insights into electrocatalysis and dissociative electron transfer mechanisms: The case of aromatic bromides. *J Phys Chem C.* 2009;113(33):14983-14992. doi:10.1021/jp904797m
 129. Isse AA, Berzi G, Falcicola L, Rossi M, Mussini PR, Gennaro A. Electrocatalysis and electron transfer mechanisms in the reduction of organic halides at Ag. *J Appl Electrochem.* 2009;39(11):2217-2225. doi:10.1007/s10800-008-9768-z
 130. Wuttig A, Derrick JS, Loipersberger M, et al. Controlled Single-Electron Transfer via Metal–

- Ligand Cooperativity Drives Divergent Nickel-Electrocatalyzed Radical Pathways. *J Am Chem Soc.* 2021;143(18):6990-7001. doi:10.1021/jacs.1c01487
131. James H.P. Utley, Little RD, Nielsen MF. Reductive Coupling. In: Hammerich O, Speiser B, eds. *Organic Electrochemistry*. 5th ed. CRC Press; 2015:621-704.
132. Dahm CE, Peters DG. Catalytic Reduction of Iodoethane and 2-Iodopropane at Carbon Electrodes Coated with Anodically Polymerized Films of Nickel(II) Salen. *Anal Chem.* 1994;66(19):3117-3123. doi:10.1021/ac00091a020