ELECTROCATALYSIS

Understanding organic electrosynthesis

A deeper understanding of reaction mechanisms should lead to improvements in the selectivity of organic electrosynthesis methods. Now, this approach has been used to explain the role of magnesium diacetate in the Ag-electrocatalysed reductive coupling of sp[3] organic chlorides with aldehydes or ketones with increased selectivity towards the alcohol product.

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Organic electrosynthesis' long history dates back to the report by Faraday in 1834[1] of ethane production by electrochemically oxidising acetate in aqueous solutions — a Kolbe reaction.[2] C–C coupling remains one of its most common applications, which include other challenging reactions like functional-group interconversion, the installation of moieties containing heteroatoms and the formation of heteroatom–heteroatom linkages.[3] Organic electrosynthesis methods are also intrinsically green, as they avoid the use of strongly oxidising or reducing reagents. These characteristics have led to a renaissance of the field in the last two decades.[3–5] However, detailed studies aimed at understanding these interfacial processes using electrochemical methods,[6] let alone combining spectroscopic and electrochemical techniques *in situ*, are very scarce, despite being necessary for the rational improvement and further development of organic electrosynthesis methods, both at the lab scale and, where applicable, industrially.

Now, writing in *Nature Catalysis*, Wuttig and co-workers demonstrate the strengths of combining detailed electrochemical experiments with in-situ spectroscopy to reach an impressive level of description, at the molecular scale, of organic electrosynthesis reactions.[7] They focus on the Ag-electrocatalysed reductive coupling of sp[3] organic chlorides with aldehydes/ketones, which only in the presence of magnesium diacetate (Mg(OAc)$_2$) selectively results in C-C coupling of the alkyl residue of the organic chloride with the aldehyde/ketone to yield an alcohol. Their work reveals the relevance of the structure of the electrode-electrolyte interface in determining the reaction pathway, and the role of Mg(OAc)$_2$ suitably pre-organising the surface of the Ag electrode for the reaction.

The researchers focus their attention on the reductive coupling between *m*-cyanobenzyl chloride (*m*CNBzCl) and *p*-anisaldehyde (*p*AN) to yield 2-(3-cyanophenyl)-1-(4-metoxyphenyl)-ethanol, a reaction that involves the transfer of 1 proton and 2 electrons (Figure 1). They choose Ag as the electrode material because it has been shown previously to reduce (and therefore activate) sp[3] organic halides at potentials 500 mV less negative than carbon,[8] another very common electrode material in organic electrosynthesis. The reaction proceeds with high selectivity and yield (94%) only in the presence of Mg(OAc)$_2$, whereas in its absence and under otherwise identical conditions, other products like *m*-tolunitrile (3%) and the epoxide analogue of the desired alcohol product (25%) are obtained alongside the desired product (36%).

By analysing independently the reduction of *m*CNBzCl and *p*AN on glassy carbon and Ag electrodes using cyclic voltammetry in the presence and absence of Mg(OAc)$_2$, Wuttig and coworkers determine that Ag catalyses the 1-electron reduction of *m*CNBzCl, while the one-electron reduction of *p*AN is shown to be an outer-sphere electron transfer (OSET) and therefore insensitive to the electrode used. They conclude, based on this, that the catalytic effect of the Ag electrode on the 1-electron reduction of *m*CNBzCl is what enables the reductive C(sp[3])-C(sp[3]) coupling. When the solution only contains either *p*AN or *m*CNBzCl, the

addition of Mg(OAc)$_2$ barely affects the voltametric profiles and the product distribution at all. Conversely, the cyclic voltammogram of a Ag electrode in a solution containing both pAN and mCNBzCl, changes considerably when Mg(OAc)$_2$ is added. In the absence of Mg(OAc)$_2$, an additional 1-electron reduction process appears at -2.46 V vs. Fc$^+$/Fc, just positive of the voltammetric peak corresponding to the reduction of pAN. This is attributed to the formation of an open shell alkoxy radical following the reduction of mCNBzCl and the coupling of the product to pAN. This radical mediates the formation of both the target alcohol (36% yield) and the corresponding epoxide (25% yield). In the presence of Mg(OAc)$_2$, this separate voltametric wave merges with that corresponding to the reduction of mCNBzCl to result in a 2-electron reduction wave peaking just negative of -2.0 V vs. Fc$^+$/Fc. In other words, Mg(OAc)$_2$ enables the selective Ag-catalysed reductive coupling of pAN and mCNBzCl to yield the alcohol, which is confirmed by the near quantitative production of the alcohol product (94%) after passing 2 faradays per mol of mCNBzCl at -2.23 V vs. Fc$^+$/Fc. To highlight the relevance of combining the catalytic activity of Ag with the presence of the Mg(OAc)$_2$ additive, electrolysis at -2.23 V vs. Fc$^+$/Fc on glassy carbon in the presence of Mg(OAc)$_2$ results in the drop of the alcohol yield to 50%.

Despite the relevance of this detailed electrochemical study, what really sets apart the work of Wuttig and colleagues is the use, *in-situ*, of surface enhanced infrared absorption spectroscopy in the attenuated total reflection mode (ATR-SEIRAS) to unveil the role of Mg(OAc)$_2$ in determining the selectivity of the reaction. ATR-SEIRAS reveals that, in the absence of Mg(OAc)$_2$, both pAN and mCNBzCl interact with the surface. The absence of the C=O stretching mode of the aldehyde suggests that pAN adsorbs side-on with the C=O bond parallel to the surface, and spectra collected at -2.23 V vs. Fc$^+$/Fc suggest that Ag-catalysed reduction of mCNBzCl at $E < -2.0$ V activates the coupling between the two reactants. ATR-SEIRAS also reveals that when Mg(OAc)$_2$ is added, it accumulates at the interface. The addition of pAN results in a clear C=O stretching band at 1701 cm^{-1}, indicating that the aldehyde no longer adsorbs parallel to the electrode surface, because the aldehyde electrophile rather interacts with the Mg(OAc)$_2$ Lewis acid. Under these circumstances, the 1-electron reduction of mCNBzCl and subsequent coupling to pAN do not result in an alkoxy radical, but rather in a Mg alkoxide salt, which upon transfer of a proton and a second electron converts to the target alcohol product.

During the last four decades, the combination of electrochemical and spectroscopic methods has allowed us to reach deep levels of insight into the molecular details of electrocatalytic reactions relevant for energy conversion and storage and into the structure of the electrode-electrolyte interface in aqueous and non-aqueous electrolytes. Such an approach, however, has barely been applied, if at all, to unveiling the details of the interfacial electron transfer processes at the heart of organic electrosynthesis. Wuttig and coworkers have addressed this gap, offering, for example, an explanation to previous findings that sacrificial Mg anodes increase the yield of select aldehyde/ketone functionalisation reactions at non-catalytic cathodes.[9,10] They also show how this deeper knowledge can be applied to generalise and further develop the electrosynthetic method using an undivided electrochemical cell with a sacrificial Mg anode and an Ag cathode. They demonstrate its versatility by targeting 32 different alcohols which are obtained with yields between 32 and 90% by combining a variety of organic halides and aldehydes.

It would be desirable to see this multi-technique approach to organic electrosynthesis expanding and becoming the rule rather than the exception, and to see spectroscopic techniques other than the one used here applied to this endeavour. ATR-SEIRAS is very well suited for detection of adsorbed intermediates and, in general, stable species within the interface,[11–13] but it is less appropriate for detection of radicals and other short-lived intermediates, for which other methods like UV-vis potential-

modulated reflectance spectroscopy (PMRS) might be better suited.[14] The field would also benefit from the application and further development of online methods for the detection of reaction products in real time, rather than after prolonged electrolysis, as the latter might be affected by subsequent reactions. I would expect these developments to result in an exponential increase in the number of green organic electrosynthesis methods available both at the lab and industrial scale.

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Figure captions:

Fig. 1. Electrochemical reductive C(sp^3) – C(sp^3) coupling of organic chlorides with aldehydes/ketones.

M-cyanobenzyl chloride (blue) couples with *p*-anisaldehyde (red) to yield 2-(3-cyanophenyl)-1-(4-metoxyphenyl)-ethanol. The reaction involves the transfer of 2 electrons and one proton.

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Competing Interests:

The author declares no competing interests.