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Electrochemical Formation and Removal of Homogeneous Cu Catalysts

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Transition metal ions and their complexes play a crucial role in homogeneous catalysis. These catalysts are pivotal for the production of, for example, fine chemicals and pharmaceuticals. Nevertheless, because of the homogeneous nature of these catalysts, their extraction and removal from the crude reaction mixture is cumbersome. Here, we propose an alternative approach where metal-based homogeneous catalysts are generated electrochemically from a metallic anode (Cu), followed by their use without current, and finally again electrochemically deposited on the cathode. The generated Cu ions were used as catalysts in three different reactions of lauroyl peroxide: one ligand-free (coupling with dienes), one without ligand but with a heteroatom containing substrate (coupling with toluidine and styrene) and one in the presence of 1,10-phen as ligand (coupling with indazole). In the first two cases, performance of the electrochemically generated catalysts was similar to those reported in literature for classically prepared homogeneous catalysts, whereas in the last case a new reaction was observed. After reaction, the homogeneous copper catalyst could be efficiently removed electrochemically: 99% of the copper could be removed for the ligand-free reaction, 97% for the amine coupling, whereas 89% of copper could be removed for the reaction containing N-heterocycle and 1,10-phenanthroline.

1. Introduction

Homogeneous metal-based catalysts are essential for the production of functional organic molecules via (asymmetric) reactions such as carbon–carbon,[1] carbon–heteroatom bond formation reactions,[2] oxidation,[3] reduction,[4] and polymerization[5] reactions. Prime industrial examples are the hydrogenation,[6] hydroformylation reactions,[7] acetic acid production (Cativa process),[8] and alkene oxidation via the Wacker process.[9] Homogeneous catalysts are used in only 17%–30% of the total industrial catalytic conversions.[10] Heterogeneous catalysts are more ubiquitous, mainly because of their more facile separation from the reaction mixture. For separation of homogeneous catalysts after reaction, methods such as precipitation, extraction, and recrystallization are traditionally employed,[11] resulting in waste production and a high energy demand.

Recently, Su et. al. reported a new approach to recovery, that is, the electrochemical recovery of homogeneous platinum group metal catalysts from a reaction mixture.[12] "RedOx" metallopolymer-based electrosorbents were employed to capture and again release platinum group homogeneous catalysts with efficiencies of up to 99% for platinum or palladium catalyst solutions. This example indicates the potential of this approach, but its scope still needs to be demonstrated. For other commonly used nonnoble metal catalysts, a general method that would allow electrochemical separation of the homogeneous metal catalyst (or reagents) after reaction, especially at higher concentrations, is still lacking.

Here, we widen the scope of electrochemical homogeneous catalyst recycling by demonstrating catalyst generation (genesis), catalysis (application), and removal (capture). A new method for the generation and removal of homogeneous copper catalysts is presented using an electric potential. Using the electrochemically generated Cu catalyst not only allows to run numerous sequences of reactions using same electrode but also provides easier storage and lower toxicity of elementary metal compared to its salts (which are often used in homogeneous catalysis). This approach of catalyst generation and removal by an electrical current is inspired by the fields of electroplating, where decorative or protective surfaces on a substrate are created,[13] and wastewater treatment, where dissolved heavy metals and other contaminants are electrochemically removed.[14] Although these applications are mostly performed in aqueous solutions, but in the current study we extend this strategy to organic solutions and catalysis, which has not received much attention. Copper catalysis was chosen

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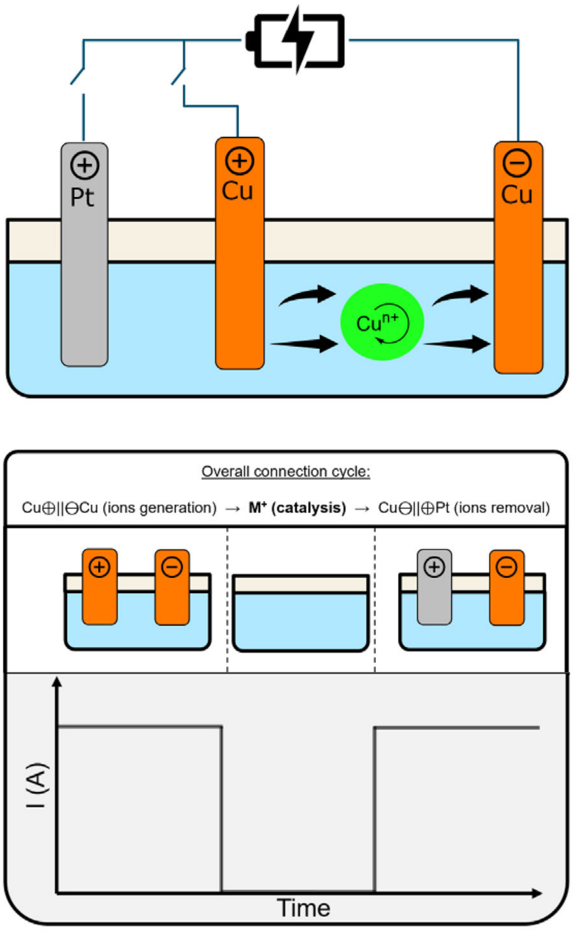


Figure 1. Schematic representation of reaction setup and methodological approach using different currents for ions generation, catalysis, and ions removal.

as model case as Cu is widely employed as catalyst in organic reactions like Ullmann and Goldberg couplings,[15] synthesis of various heterocyclic structures,[16] including well-known azide–alkyne cycloadditions.[17] For environmental and health reasons, removal of a homogeneous catalyst, extending beyond copper, from a reaction mixture is highly important. As homogeneous reactions are often (not always) performed in the presence of ligands, we investigated here the copper electrodeposition from the reaction mixtures in the presence of coordinators/ligands of different coordination strengths.

2. Experimental

Figure 1 shows a schematic presentation of the concept of catalyst genesis (ion generation), use (catalysis), and removal (ion removal). An undivided electrochemical cell was equipped with two Cu electrodes and one Pt electrode. A complete cycle consists of three steps: Cu dissolution, that is, ions generation from the anode, catalytic reaction in presence of dissolved Cu (without current), and removal, that is, Cu ions deposition on the cathode. To generate the Cu ions (catalyst), typically a current of 25 mA (5 mA/cm^2) was applied galvanostatically between the copper anode and the copper cathode (Figure 1, ions generation). Cu ion release from the anode is concurrent with an ion deposition on the cathode, but dissolution occurs at a higher rate. This resulted in the gradual increase of concentration of copper ions in the solution. When the desired concentration of Cu ions was reached, the current was stopped, electrodes were removed from the solution, and then reactants (and optionally other additives) were added to perform the reaction (Figure 1, catalysis). Upon completion of the reaction, the copper anode for an inert platinum cathode were inserted into the reaction mixture and Cu^{+}/Cu^{2+} catalyst was removed (Figure 1, ions removal) by applying a current of 25 mA (5 mA/cm^2) galvanostatically.

For the process to work efficiently, good solubility of the electrolyte, as well as conductivity and long-term stability of the catalyst in an organic solvent is required. Experiments were performed using acetonitrile/cosolvent mixtures (MeCN) as a solvent and triflate salts as the electrolyte, as commonly employed in conventional homogeneous catalysis.[18]

3. Results and Discussion

First, the dissolution/deposition of the metal was studied in absence of reactants to optimize the choice of solvent, electrolyte, and current. Finally, optimized conditions were applied for three different coupling reactions of lauroyl peroxide, a versatile substrate that can serve as showcase for transition metal-catalyzed radical reactions.[19] In this study, Cu-catalyzed coupling of diacyl peroxide with a diene (2,3-dimethyl-1,3-butadiene),[20] a three-component coupling with styrene and *p*-toluidine,[21] and coupling with an N-heterocycle (indazole, in presence of 1,10-phen as a ligand)[22] were investigated. These three cases were selected to study the influence of donor strength, of the ligands, and of ligating substrates on the electrochemical deposition. MeCN (solvent), *p*-toluidine, and indazole with 1,10-phenanthroline represent the ligating substrates with different strengths of donor effect. The strength of donor effect was evaluated by HEP (Huynh electronic parameter) values: weakest was 157.4 for MeCN and strongest was 161.4 for 1,10-phen.[23] Furthermore, the reactions are well-documented, allowing facile comparison of the new approach.

The choice of electrolyte proved to be important for catalyst stability. A first trial with 1 mmol NaOTf (0.05 M) in MeCN and a galvanostatic current of 15 mA (3 mA/cm^2) exhibited dissolution of the copper anode, but also the formation of a black precipitate. This indicated that dissolved copper (confirmed by ICP analysis) was not stable in solution under these conditions. Excessive copper precipitation was prevented by switching to ammonium triflate (NH_4OTf) instead of sodium triflate (NaOTf), though some cloudiness of the solution was still observed, which was not studied in more detail.

Variation of the solvent composition exhibited that addition of (increasing amounts of) THF and dioxane (solvents typically used in the homogeneously catalyzed coupling of fatty peroxides)[24] to MeCN resulted in (increasingly) more clear solutions during both dissolution and deposition phases. Between THF and dioxane, the latter one was the preferred solvent due to its higher boiling point, expanding the potential window of operation. Notably, for MeCN/dioxane (1:2), the solution remained clear during both dissolution and deposition phases, indicating that Cu precipitation in solution was prevented, that

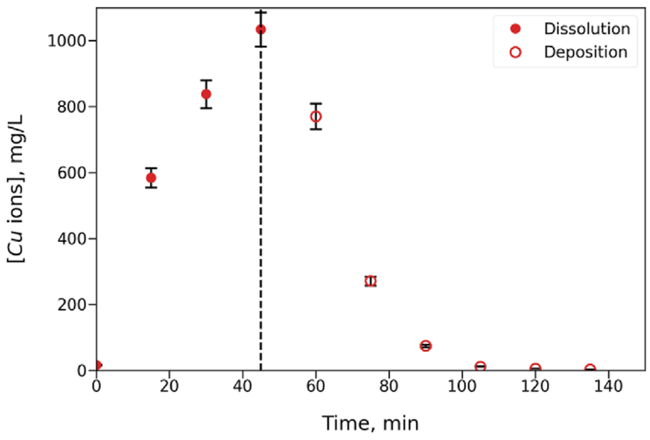


Figure 2. Copper concentration versus time during dissolution and deposition in the solution without reactants.

is, under these conditions, copper remained homogeneous in the reaction mixture.

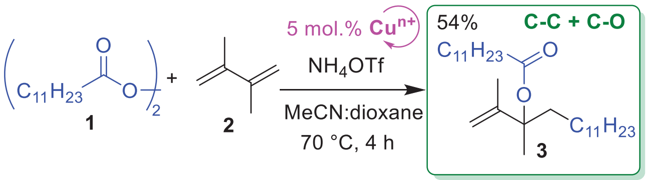
Finally, the influence of current was investigated using ammonium triflate (0.05 M) in MeCN/dioxane (1:2). Applying currents of 35 mA (7 mA/cm^2) and higher resulted in cloudy solutions, which was not observed at currents of 25 mA (5 mA/cm^2) and below. Therefore, a current of 25 mA was used in further studies.

The effectiveness of Cu dissolution and deposition was then quantified by ICP analysis. For this, aliquots were taken from the mixture for Cu content analysis by ICP during a dissolution phase (45 min. at 25 mA, Cu||Cu) followed by a removal phase (90 min. at 0.025 A, Cu||Pt).

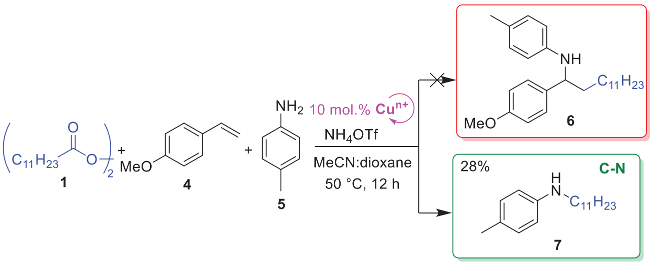
Figure 2 displays the Cu concentration in solution during the different phases (see Table S1 of the Supporting Information for more information on ICP data). During dissolution, the Cu concentration gradually increased, reaching a concentration of approximately 1000 mg/L after 45 min. Upon removal, the copper concentration decreased to 0.056 mg/L after 90 min., that is, more than 99% of the initially dissolved copper could again be electrochemically deposited on the cathode, resulting in a residual Cu content of 3.9 ppm in solution.

Having established that Cu ions could be electrochemically generated and redeposited, the performance of these ions in catalysis was investigated. To study the performance of the electrochemically generated catalysts in organic reactions, a Cu ion concentration of 1000 mg/L, which was reached within 45 min, was chosen as that was in the range reported for in literature for the conventional reactions. All the experimental details as well as the characterization of the resulting compounds are reported in the Supporting Information.

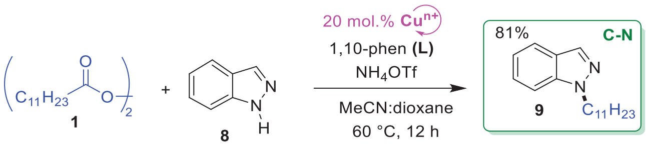
The first reaction investigated was the reaction between lauroyl peroxide **1** and diene **2** (Scheme 1). This transformation, originally reported by Li et. al., is typically run with 5 mol% of CuTC (copper(I) thiophene-2-carboxylate) in dioxane at 70 °C to yield 1,2-alkylesterified dienes as products.[20]



Scheme 1. Coupling of lauroyl peroxide with 2,3-dimethylbuta-1,3-diene catalyzed by electrochemically generated copper species.



Scheme 2. Coupling of lauroyl peroxide with *p*-toluidine and 4-methoxystyrene catalyzed by electrochemically generated copper species.



Scheme 3. Coupling of lauroyl peroxide with 1*H*-indazole catalyzed by electrochemically generated copper species.

By using the same copper/reactant ratio, that is, 5 mol% Cu (but with an absolute concentration of 1000 mg/L) and similar reaction conditions, that is, 70 °C and 4 h reaction time (Scheme 1) Product **3** was obtained with a yield of 54% (which is slightly lower, but in a similar range as that (77%) reported by Li et. al.).[20] Please note that yields are reported here to compare our results to those reported in literature.

To investigate the performance of the generated catalyst in the presence of a heteroatom containing substrate, the cocoupling of lauroyl peroxide **1** with 4-methoxystyrene 4 and *p*-toluidine **5** (Scheme 2) was investigated. Li et. al. demonstrated this reaction to be copper-catalyzed,[21] reporting a 43% yield of Product **6** when using 10 mol% Cu(OTf)$_2$ in MeCN at 50 °C.

Surprisingly, under similar reaction conditions (same Cu/reactant ratio, same temperature, and reaction time), but with the electrochemically generated Cu catalyst at a concentration of 1000 mg/L, we obtained the alkylated amine **7** in 28% yield, instead of the expected three-component coupling Product **6** (Scheme 2). During this experiment, we observed full conversion of peroxide **1**, only partial conversion of amine **5**, and no conversion of styrene **4**. As the reference reaction reported by Li et al. is part of an optimization campaign, it is not clear whether the same product was also in their work.

Finally, the effect of more strongly coordinating ligands on the process was studied in the reaction between lauroyl peroxide **1** and indazole **8** in the presence of 1,10-phenanthroline (Scheme 3). This reaction was originally reported by Tang et. al., who achieved N-alkylation of N-nucleophiles in the presence of 20 mol% of CuBr with 30 mol% 1,10-phen in dioxane at 70 °C.[22]

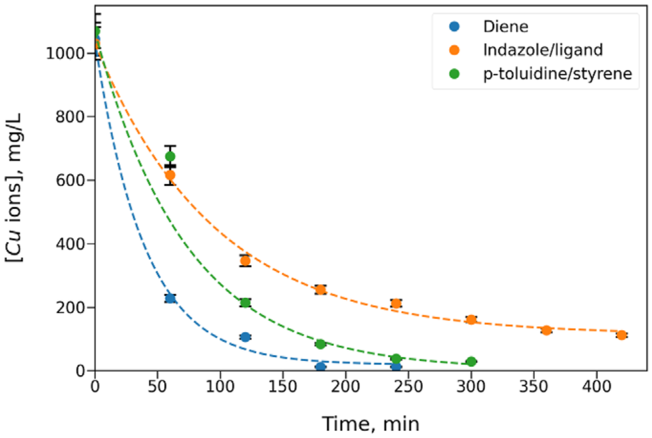


Figure 3. Copper concentration versus time during catalyst removal after reaction.

Table 1. Summary of results.

Reaction	Yield[a] (lit), %	Ligands	% of Cu removed	Residual Cu Concentration, ppm
Indazole	81(91)[22]	1,10-phen, indazole, alkylated indazole	89	112
p-toluidine[b]	28(43)[21]	*p*-toluidine, alkylated *p*-toluidine	97	29
Diene	54(77)[20]	–	99	12

[a] Isolated yield.
[b] Alkylated amine was obtained instead of the expected product.

Again, under the same reaction conditions (reaction time, temperature, copper molar percentage, ligand, and its molar percentage), but with electrochemically generated copper at 1000 mg/L, Product **9** was synthesized with 81% yield (Scheme 3), which compares well to the 91% reported by Tang et. al.[22]

Clearly, the electrochemically dissolved copper was active for the transformations of lauroyl peroxide, indicating the success of catalyst formation by the electrochemical method. In two cases, (coupling with diene, Scheme 1; and coupling with indazole, Scheme 3) the obtained products matched the expected ones and yields were similar to those reported for the traditional homogeneously catalyzed reactions. The difference in yields might be explained by the difference in solvent used that was needed to stabilize the Cu species in solution. In case of co-coupling with styrene and toluidine (Scheme 2), it was demonstrated that the electrochemically generated catalyst was still active in the transformation; the control experiment exhibited that the obtained product was not formed under the same conditions in the absence of Cu catalyst in the solution.

Next, catalyst removal was studied at 25 mA (5 mA/cm^2). Figure 3 illustrates that the concentration of copper in solution decreases as function of time during galvanostatic catalyst deposition in all cases, but also that extent of removal is system dependent (see Table S2 of the Supporting Information for more information on ICP data).

For the ligand- and amine-free reaction mixture (coupling with diene), 99% of the copper could be electrochemically removed from the reaction mixture after 240 min of electrodeposition, resulting in a final Cu concentration of 12 ppm.

Removal from the toluidine/styrene reaction mixture was slower; after 420 minutes of electrodeposition, copper concentration could be reduced by 97% to 29 ppm. This suggests that the substrate and product of this reaction act as ligands, stabilizing the copper species in solution and making it more difficult to remove them electrochemically.

For the indazole system, that is, in presence of the 1,10-phen ligand, 89% of the initially dissolved Cu ions could be electrochemically deposited after 420 min to give a 112 ppm Cu solution. During the electrolysis, the deposition rate significantly decreased over time from 9.1 mg/h during the first 60 min to 0.3 mg/h after 420 min of electrolysis. Similar to the case with amine described above, this might be explained by the fact that copper was forming a stable complex with 1,10-phenanthroline,[25] which did not allow complete metal deposition. An overview of the results is presented in Table 1.

4. Conclusion

Overall, it can be concluded that active homogeneous Cu catalysts can be removed from actual reaction mixtures by electrodeposition. The effectiveness of the deposition process appears to be correlated with the presence of (strong) metal coordinating groups, such as monodentate amines from the substrate or product or from the ligands necessary for reactivity. In the absence of strong ligands, 99% of dissolved copper was removed after reaction, which is similar in performance to the electrosorption method by Su et al.[12] In the presence of ligand and heteroatom containing substrate, 89% and 97% of copper was removed, respectively. These results indicate that the concept of electrodeposition of homogeneous transition metal catalyst is a feasible concept, allowing to recycle valuable metals and reach low levels of metal ions in the reaction mixture. Further studies on other transition metals, as well as the effect of coordination on electrodeposition are in progress.

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: Copper · Electrochemistry · Electrodeposition · Homogeneous catalysis · Metal removal

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