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Reductive Amination

Metallic Impurities in Electrolysis: Catalytic Effect of Pb Traces in Reductive Amination and Acetone Reduction

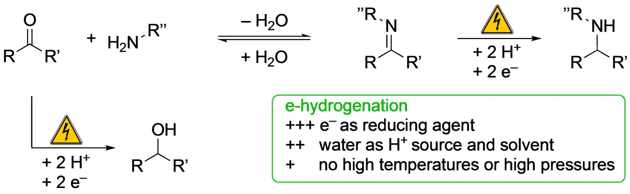
*Justus Kümper, Sonja D. Mürtz, Yani Guan, Simran Kumari, Peter J. C. Hausoul, Nils Kurig, Philippe Sautet, and Regina Palkovits**

Abstract: The electrochemical hydrogenation (e-hydrogenation) of unsaturated compounds like imines or carbonyls presents a benign reduction method. It enables direct use of electrons as reducing agent, water as proton source, while bypassing the need for elevated temperatures or pressures. In this contribution, we discuss the active species in electrocatalytic reductive amination with the transformation of acetone and methylamine as model reaction. Surprisingly, lead impurities in the ppm-range proved to possess a significant effect in e-hydrogenation. Accordingly, the influence of applied potential and cathode material in presence of 1 ppm Pb was investigated. Finally, we transferred the insights to the reduction of acetone manifesting comparable observations as for imine reduction. The results suggest that previous studies on electrochemical reduction in the presence of lead electrodes should be re-evaluated.

Introduction

Organic compounds are widely used in daily life, for example, as pharmaceuticals,[1] materials,[2] agrochemicals,[3] or as solvents.[4] The incorporation of heteroatoms such as oxygen or nitrogen into hydrocarbon-based molecules changes the properties significantly.[5] For example, many drugs contain *N*-functionalities, as this introduces a bioactive moiety into the backbone.[1,6] Among others, these types of molecules are synthesized from carbonyl compounds and amines via reductive amination, a transformation occurring in two steps (Scheme 1). Initially, condensation of a carbonyl compound with an amine proceeds forming the corresponding imine followed by imine reduction requiring transfer of two protons and two electrons.[7] As imine formation is an equilibrium reaction, the reduction of the carbonylic compound is also feasible, leading to the corresponding alcohol as competing by-product.[7–8]

In the past, molecular reducing agents like sodium borohydride ($NaBH_4$), sodium cyanoborohydride ($NaBH_3CN$), or sodium triacetoxyborohydride ($NaBH(OAc)_3$) were frequently used for the reduction of imines.[1a,6b,9] However, the use of e.g. $NaBH_4$ suffers from low atom efficiency and waste in stochiometric amounts.[10] The formation of waste can be circumvented by utilizing



Scheme 1. Reductive amination of carbonylic compounds by e-hydrogenation. In the first step, the carbonyl compound reacts with the primary amine in a condensation reaction yielding the imine. The reduction of the imine leads to the amine. A typical side reaction of the one-pot reaction presents the hydrogenation of the carbonyl compound to the respective alcohol.

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[*] J. Kümper, S. D. Mürtz, Dr. P. J. C. Hausoul, Dr. N. Kurig,
Prof. Dr. R. Palkovits
Chair of Heterogeneous Catalysis and Technical Chemistry
RWTH Aachen University
Worringerweg 2, 52074 Aachen (Germany)
E-mail: palkovits@itmc.rwth-aachen.de

Y. Guan, Dr. S. Kumari, Prof. Dr. P. Sautet
Department of Chemical and Biomolecular Engineering
University of California, Los Angeles
5531-J Boelter Hall, Los Angeles, CA 90095 (USA)

Dr. N. Kurig
Department of Chemistry
Scripps Research
La Jolla, CA 92037 (USA)

Prof. Dr. P. Sautet
Department of Chemistry and Biochemistry
University of California, Los Angeles
5531-J Boelter Hall, Los Angeles, CA 90095 (USA)

Prof. Dr. R. Palkovits
Institute for Sustainable Hydrogen Economy (INW-2)
Forschungszentrum Jülich
Marie-Curie-Str. 5, 52428 Jülich (Germany)
E-mail: r.palkovits@fz-juelich.de

Prof. Dr. R. Palkovits
Max-Planck-Institute for Chemical Energy Conversion
Stiftstr. 34–36
45470 Mülheim an der Ruhr (Germany)

molecular hydrogen as reducing agent. The activation of hydrogen can be achieved via homogeneous (Rh,[11] Ru[12]) or heterogeneous (Pd,[13] Rh,[14] Pt,[15] Ru,[14a,16] Ni,[17] Co[18]) catalysts.[8] Nevertheless, this approach often requires elevated hydrogen pressures and temperatures.[14b,16–19] In addition, hydrogen is still majorly derived from fossil fuels, e.g. by methane steam reforming, leading to a high CO_2 footprint.[20]

A sustainable alternative is the e-hydrogenation. In this case, electrons serve as benign reducing agents.[10,21] Furthermore, water is applicable as proton source and solvent at the same time. Therefore, the process is atom efficient, circumvents costly reducing agents and the related waste formation, as well as the need for producing and storing hydrogen.[6b,8,10] Accordingly, e-hydrogenation presents a promising technology for the reduction of organic compounds.[21] Especially for producing smaller quantities of organic compounds, such as pharmaceuticals, electrochemistry can be beneficial allowing a decentralized manufacturing.[5a]

The one-pot e-hydrogenation of imines in alkaline aqueous solutions ($pH > 10$) competes with both carbonyl reduction and hydrogen formation. In general, the reduction of imines is favored over the reduction of carbonyls.[7,22] In order to achieve high Faraday efficiencies in imine reduction, hydrogen evolution reaction (HER) needs to be suppressed, e.g. by using cathode materials possessing a high overpotential for HER.[7–8,9c,22–23] Pb or Hg were initially used as cathode materials,[22–23,24] but later, greener alternatives were found, e.g. Ag and Cu.[8,9c]

The development and understanding of the electrochemical reduction of imines was initially started by Zuman[24] in 1950, reporting the formation of propan-2-amine from acetone and ammonia after electrolysis. Between 1950 and 1992, the substrate scope was extended to different linear and cyclic aldehydes or ketones and primary amines.[22–23] Until then, a systematic investigation of e-hydrogenation starting from primary aliphatic amines and carbonyls had not been discussed in the literature. This changed in 1992, when Smirnov and Tomilov investigated the impact of amine/ketone ratio, cathode material, structure of the ketones and amines, pH, and current density on the yield of the resulting secondary amine and alcohol.[23b] As a result, imine formation was identified as decisive step for high amine yields ranging between 60 % and 70 %. In general, higher yields are observed for less sterically demanding carbonyls (e.g.: acetone + methylamine: 62 %; 3-pentanone + methylamine: 18 %) or amines (e.g.: acetone + methylamine: 62 %; acetone + ethylamine: 55 %), as this facilitates imine formation. In addition, the equilibrium of the condensation reaction shifts towards imine formation with higher pH and initial amine to ketone ratio. Current density affects the amine yield as well. Increasing the current density from $19\,mA\,cm^{-2}$ to $159\,mA\,cm^{-2}$ decreased the amine yield by 50 %, so the probability for electrochemical side reactions, e.g. carbonyl reduction, increases with higher current densities.[23b]

Smirnov and Tomilov's[23b] study was extended and supported by Mürtz et al.[8] in 2021, emphasizing that substrate concentrations of 2.4 M acetone and 2.9 M methylamine are required for an efficient reductive amination in aqueous alkaline medium (pH 12). This study also highlighted Cu and Ag as promising cathodes in e-hydrogenation of imines instead of Pb, facilitating similar yields and superior selectivity.[8]

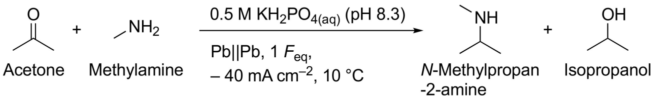
Also e-hydrogenation of carbonyl compounds has industrial relevance. In 1899, *Merck* patented the electrochemical reduction of acetone at a Pb cathode to isopropanol and pinacol.[25] In the following decades, several further patents were published, displaying the early interest in e-hydrogenation.[26]

The e-hydrogenation presents a promising alternative to the usual reduction methods, which is why we took a closer look at it. As a result of the investigations, it became clear that small Pb impurities have a decisive impact in this reaction. The reductive amination of acetone with methylamine as well as acetone reduction serve as model reactions to elucidate the contribution of Pb species and the role of different electrode materials. The results suggest that previous studies on electrochemical reduction in the presence of lead electrodes should be re-evaluated.

Results and Discussion

The optimum conditions for the reductive amination of acetone with methylamine reported by Mürtz et al.[8] were used as starting point (Scheme 2). To describe the utilized cell assembly, the following nomenclature is used: Cathode||Anode, where || is a Nafion-324 (N-324) or Nafion-424 (N-424) membrane. As the highest yield was obtained with Pb as cathode and anode,[8] this was tested first, resulting in an amine yield of 62 % (±3 %) (Figure 1), determined by proton nuclear magnetic resonance (^1H-NMR) measurements (Figure S1). Compared to Mürtz et al.,[8] the yield was 9 % lower due to a decrease in the carbon balance (C.B.) from 93 %[8] (±3 %) to 78 % (±4 %) in the reproduction experiments. Since acetone and methylamine are very volatile molecules, small changes in temperature possess a strong impact on the evaporation of the substrates potentially causing the observed decrease in C.B. and thus, affecting yield.

The electrochemical reductive amination is not limited to Pb as cathode material. Mürtz et al.[8] and Roylance and Choi[9c] described Ag as alternative cathode material. Additionally, the adsorption of an imine on a Ag electrode was observed in situ by attenuated total reflectance surface-



Scheme 2. Conditions of the first experiment with 2.4 M acetone and 2.9 M methylamine. The pH of the resulting substrate solution was 12.9 at 10 °C. Cathode and anode compartment were separated from each other by a N-324 membrane. The anode compartment contained a 25 % H_3PO_4 solution. The conditions were taken from Mürtz et al.[8]

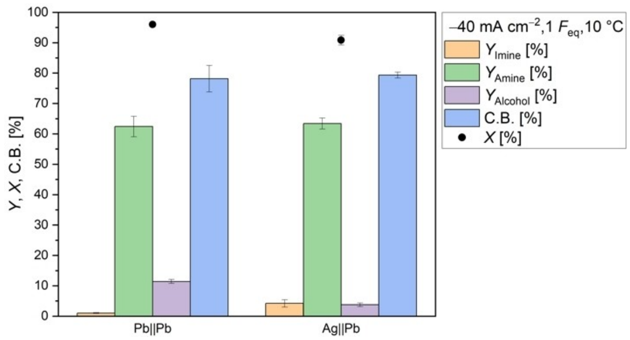


Figure 1. Comparison of Pb as cathode with a mirror-like Ag electrode in the reductive amination of acetone with methylamine. The yields of *N*-methylpropan-2-imine (Y_{Imine}), *N*-methylpropan-2-amine (Y_{Amine}) and isopropanol (Y_{Alcohol}) are shown. Furthermore, the conversion of acetone (X) and the carbon balance (C.B.) are visualized. Conditions: $j=-40$ mA cm^{-2}; $F_{\mathrm{eq}}=1$; solvent: 0.5 M KH_2PO_4 (pH 8.3); substrates: acetone: 2.4 M, methylamine: 2.9 M; $T=10$ °C; pH at 10 °C: 12.9; anolyte: 25 % H_3PO_4; and a N-324 membrane (used at least 3 times before with Pb as anode).

enhanced infrared absorption spectroscopy (ATR-SEIRAS) at reductive potentials.[27] Therefore, a mirror-like Ag cathode was utilized and an amine yield of 63 % (±2 %) was obtained. The Ag electrode enabled a similar yield (+1 %) compared to Pb as cathode as well as higher selectivity for the amine due to a suppressed alcohol formation (11.4 % (±0.6 %) for Pb *vs* 3.8 % (±0.6 %) for Ag).

High reproducibility of the amine yield using Ag as cathode is indicated by an error margin of ±2 %. This was achieved by using a N-324 membrane with Pb as anode at least three times beforehand (Figure 2). Interestingly, usage of a fresh membrane resulted in an amine yield of only 29 % (±10 %). However, the yield increased continuously the more often the same membrane was used with Pb as anode, reaching a value of 63.8 % (±1.9 %) in the fourth use. In addition to increasing yield, reproducibility also improved as shown by the continuously decreasing error margin. After using the membrane more than three times, steady product formation was possible. As such an induction period was not observed with Pb||Pb as electrode pair (Figure S2), the Pb concentration in the cathode compartment for Ag||Pb as electrode pair (Figure 2) was determined by elemental analysis. Small amounts of Pb (0.9 ppm (±0.2 ppm)–3.8 ppm (±1.1 ppm)) were measured after electrolysis in the product solutions, indicating a crossover of Pb through the membrane from the anode to the cathode compartment. These findings indicate that Pb plays a central role in e-hydrogenation.

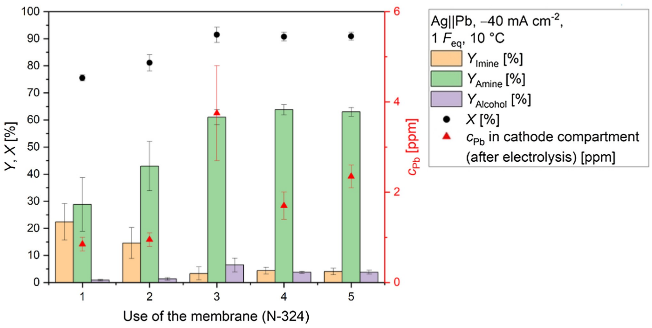


Figure 2. Correlation between the use of the N-324 membrane with Pb as anode and the resulting yields of *N*-methylpropan-2-imine (Y_{Imine}), *N*-methylpropan-2-amine (Y_{Amine}) and isopropanol (Y_{Alcohol}). Furthermore, the conversion of acetone (X) and the Pb concentration (c_{Pb}) in the cathode compartment after electrolysis are shown. Carbon balance (C.B.): 76 %–80 %. Conditions: Ag||Pb; $j=-40$ mA cm^{-2}; $F_{\mathrm{eq}}=1$; solvent: 0.5 M KH_2PO_4 (pH 8.3); substrates: acetone: 2.4 M, methylamine: 2.9 M; $T=10$ °C; pH at 10 °C: 12.9; anolyte: 25 % H_3PO_4.

Identification of Pb's Role as Mediator or Catalyst

To better understand the role of Pb, product formation without Pb in the system was investigated. By using a Pb free cell, a new N-324 membrane and platinum as anode (Ag||Pt), amine yields of less than 3 % were generated (Figure S3). Moreover, no increase in yield was observed with repeated use of the new N-324 membrane in the Pb free system, indicating an essential functionality of Pb in e-hydrogenation. To verify this assumption, a concentration series of Pb was performed (Figure 3), whereby it was added in form of an aqueous $Pb(NO_3)_2$ solution to the substrate solution, followed by galvanostatic electrolysis.

With 0.25 ppm of Pb in the system, similar results were achieved in e-hydrogenation of the imine as with the Pb free system (0 ppm) (+1.6 %). Doubling the Pb concentration to 0.5 ppm increased the amine yield by more than tenfold to 37 % with an error margin of ±10 %. A constant amine formation was reached when 1 ppm of Pb was present, facilitating a yield of 62.9 % (±1.6 %). A further doubling of

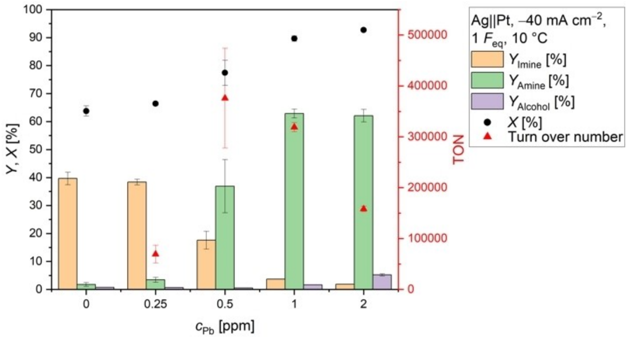


Figure 3. Addition of different Pb amounts to the substrate solution and their impact on e-hydrogenation with acetone and methylamine as model compounds. The yields of *N*-methylpropan-2-imine (Y_{Imine}), *N*-methylpropan-2-amine (Y_{Amine}) and isopropanol (Y_{Alcohol}) are displayed. Furthermore, the conversion of acetone (X) and the turn over number (TON) are visualized. Pb was added in form of Pb^{2+}, using an aqueous $Pb(NO_3)_2$ solution. The x-axis displays the final Pb concentration in the substrate solution before electrolysis. Carbon balance (C.B.): 75 %–78 %. Conditions: Ag||Pt; $j=-40$ mA cm^{-2}; $F_{\mathrm{eq}}=1$; solvent: 0.5 M KH_2PO_4 (pH 8.3); substrates: acetone: 2.4 M, methylamine: 2.9 M; $T=10$ °C; pH at 10 °C: 12.9; anolyte: 25 % H_3PO_4; a N-324 membrane; and a Pb free cell.

Pb concentration to 2 ppm just increased the yield of the undesired side product isopropanol (from 1.7 % (±0 %) to 5.2 % (±0.4 %)), indicating that higher Pb concentrations than 1 ppm are not required for e-hydrogenation of the imine. Since electrolysis without Pb resulted in a yield of 1.8 % (±0.7 %), but the presence of 1 ppm Pb enabled a yield of around 63 %, Pb is suggested to act as catalyst or mediator. Assuming that each Pb atom participates in the reduction of the imine, enables the calculation of a turnover number (TON). For 1 ppm Pb a TON of 319068 (±9088) is obtained, displaying its efficiency.

Although highest efficiency was achieved with 0.5 ppm Pb, this was accompanied by a high error margin of ±26 % (TON: 375948 (±97937)). The system appears to be stable as soon as 1 ppm Pb is present, as the error is then ±3 %. Since the yield remained the same when using 2 ppm compared to 1 ppm of Pb, TON decreases from 319098 (± 9088) to 158218 (±5420). Based on these findings, applying 1 ppm Pb for e-hydrogenation showed the best trade-off between efficiency and amine yield, so this concentration was utilized for the next steps. In general, the results confirm the importance of ppm-amounts of Pb for e-hydrogenation of *N*-methylpropan-2-imine.

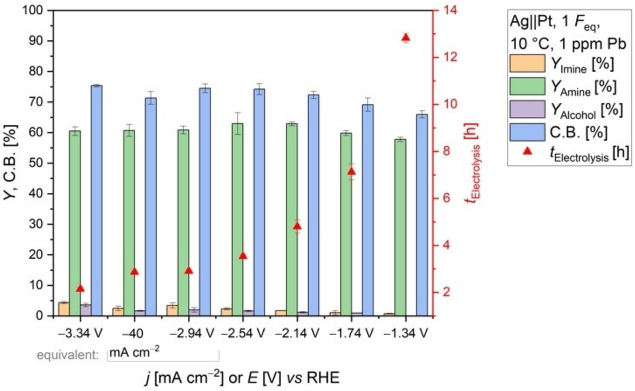


Figure 4. Transition from galvanostatic to potentiostatic conditions and studying the impact of applied potential on e-hydrogenation of *N*-methylpropan-2-imine. The yields of *N*-methylpropan-2-imine (Y_{Imine}), *N*-methylpropan-2-amine (Y_{Amine}) and isopropanol ($Y_{Alcohol}$) are displayed. Furthermore, the carbon balance (C.B.) and the duration of electrolysis ($t_{Electrolysis}$) are visualized. Conversion (X): 87 %–91 %. Conditions: Ag | | Pt; $F_{eq}=1$; solvent: 0.5 M KH_2PO_4 (pH 8.3); substrates: acetone: 2.4 M, methylamine: 2.9 M; $T=10$ °C; pH at 10 °C: 12.9; anolyte: 25 % H_3PO_4; a N-424 membrane; and 1 ppm Pb in the final substrate solution (added in form of an aqueous $Pb(NO_3)_2$ solution).

Potential-Dependent Activity of 1 ppm Pb

The major contribution of Pb was first identified in experiments based on galvanostatic electrolysis. This type of electrolysis is characterized by the fact that the global reaction rate is controlled and the applied potential is changed.[28] The potential describes the energy required to move electrons in the circuit.[28] Depending on how high this is, the electrons are moved at different rates. Conversely, the amount of energy must also be sufficient for the reaction to take place at all. Some reactions require a higher energy input than other reactions, so that specific reactions can be addressed with potentiostatic electrolysis.[21,28–29] Since Pb has been identified as a catalyst or mediator, it is now interesting to find out to what extent its activity in e-hydrogenation depends on the applied potential.

The averaged potential that was applied during galvanostatic electrolysis using a current density of −40 mA cm^{-2} was −2.94 V *vs* reversible hydrogen electrode (RHE) (Figure S4). Applying −2.94 V *vs* RHE and 1 Faraday equivalent (F_{eq}) resulted in the same amine yield (60.8 % (± 1.2 %)) as obtained by galvanostatic electrolysis (60.7 % (± 1.9 %)) within the same reaction time of 2.9 h (Figure 4). This illustrates successful transition from galvanostatic to potentiostatic conditions. Starting from −2.94 V *vs* RHE, the potential was changed in 0.4 V steps between −3.34 V and −1.34 V *vs* RHE. Changing the applied potential from −3.34 V to −2.54 V or −2.14 V *vs* RHE increased the amine yield by roundabout 2.5 %. However, the application of more positive potentials than −2.14 V *vs* RHE led to a decrease in yield (−1.74 V: 59.8 % (±0.8 %); −1.34 V: 57.8 % (±0.7 %)), explainable by a strong increase in reaction time. With increasing reaction time, the C.B. can decrease as evaporation of the substrates becomes more likely. If less substrate is available, the yield decreases. When −1.34 V *vs* RHE was utilized, the duration of electrolysis was 12.8 h (±0.2 h), 9 h longer than using −2.54 V *vs* RHE. As a result of the prolonged reaction time, the C.B. decreased by 8 % (Figure 4). Accordingly, slightly lower yields were caused by a decreased C.B. due to the potential-induced increase in reaction time. Nevertheless, the narrow yield range of 5 % for *N*-methylpropan-2-amine ($Y_{Amine}=58$ %–63 %) indicated the flexible applicability of 1 ppm Pb between −3.34 V and −1.34 V *vs* RHE for one-pot e-hydrogenation of *N*-methylpropan-2-imine.

For the formation of the side product isopropanol, a clear trend with respect to the applied potential was observable: the more negative the applied potential was, the higher the yield of isopropanol, reaching a maximum of 4 %.

Since −2.94 V *vs* RHE showed a good trade-off between productivity, selectivity, and yield for e-hydrogenation of the imine, this potential was defined as standard potential for the next experiments. The fact that the reaction performance stayed constant over a wide range of potentials supports that Pb is acting as catalyst or mediator. Therefore, selection of the cathode material does not depend on reducibility of the imine, but on reducibility of the Pb species on the electrode. Thus, the impact of the cathode material on e-hydrogenation in presence of 1 ppm Pb was investigated to gain insights into the reaction.

Activity of Cathode Materials in Presence of 1 ppm Pb

According to Mürtz et al.[8] and Roylance and Choi,[9c] electrode materials with a high HER overpotential, like Ag or Cu, facilitate high yields in e-hydrogenation, while cathode materials with a low HER overpotential, like Pt or

Ni, possess low performance.[8,9c] Mürtz et al. already investigated different cathode materials for e-hydrogenation of a reaction mixture containing acetone and methylamine, but under galvanostatic conditions and with Pb as anode.[8] Using potentiostatic conditions in presence of 1 ppm Pb was not tested yet for different cathode materials that differ in their HER overpotential.

Cathode materials known to be active in HER are Pt or Ni.[30] With these materials amine yields of 3 % were obtained, although 1 ppm Pb was present (Figure 5). After applying 1 F_{eq}, the yield of the imine, the thermally produced intermediate, was higher than 30 %, while less than 2 % alcohol was formed. HER is suggested as dominant reaction when Pt or Ni were used (cf. Figure 3). Applying Cu as cathode resulted as well in a low amine yield. This was unexpected, since Mürtz et al. reported comparable amine yields for Cu and Ag.[8] An explanation why a similar yield for e-hydrogenation of the imine was not observed under potentiostatic conditions could be the reduced stability of Cu in presence of methylamine (Figure S6; Figure S7).[31,43] Before electrolysis was started, the temperature of the reaction solution was adjusted to 10 °C using an 18 min cooling period. During this time, the reaction solution was in contact with the electrode, but no potential was applied. Such a cooling procedure was not used in the experiments discussed in literature,[8,9c] which could explain the different observations regarding the performance of Cu.

The scope of cathode materials was extended to carbon based materials, i.e. glassy carbon (GC) and boron-doped diamond (BDD), both known for high overpotential in HER.[30b] In presence of 1 ppm Pb, these materials are good alternatives to Ag enabling similar amine yields (Y_{Amine}= Ag: 60.8 % (±1.2 %); GC: 62.2 % (±1.3 %); BDD: 62.2 % (±1.9 %)) (Figure 5). Reference experiments confirmed that the good performance of these electrodes could only be reached when the substrate solution contained 1 ppm Pb (Figure S8). In general, the successful e-hydrogenation of the imine requires the presence of 1 ppm Pb and cathode materials characterized by a high HER overpotential.

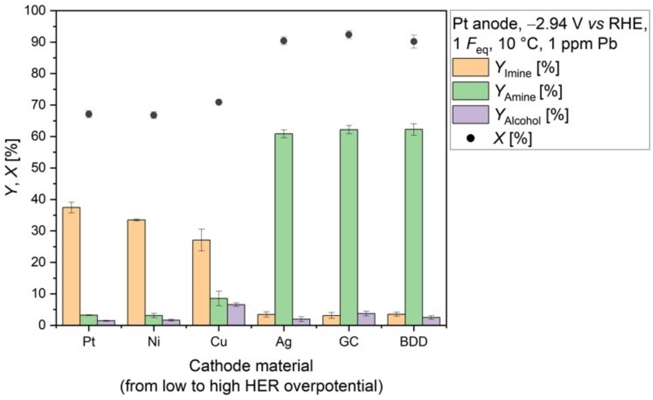


Figure 5. Impact of cathode material on e-hydrogenation of *N*-methylpropan-2-imine. The yields of *N*-methylpropan-2-imine (Y_{Imine}), *N*-methylpropan-2-amine (Y_{Amine}) and isopropanol ($Y_{Alcohol}$) are displayed. Furthermore, the conversion of acetone (X) is visualized. Carbon balance (C.B.): 70 %–77 %. Conditions: Pt anode; $E=-2.94$ V *vs* RHE; $F_{eq}=1$; solvent: 0.5 M KH_2PO_4 (pH 8.3); substrates: acetone: 2.4 M, methylamine: 2.9 M; $T=10$ °C; pH at 10 °C: 12.9; anolyte: 25 % H_3PO_4; a N-424 membrane; and 1 ppm Pb in the final substrate solution (added as aqueous $Pb(NO_3)_2$ solution).

So far, it has not been investigated whether the added Pb^{2+} is deposited irreversible onto the electrode during electrolysis or remains in the bulk solution. This question was addressed by using a Ag electrode, as this can be mechanically polished and allows an easier handling compared to GC or BDD.

Before Ag was used in the 1st experiment, it was freshly polished with a 1 µm alumina suspension (Figure 6).

Using the freshly polished Ag electrode in presence of 1 ppm Pb led to an amine yield of 60.8 % (±1.2 %) while 3.4 % (±0.9 %) of the imine remained (Figure 7). After reaction, the electrode was rinsed with water and dried with compressed air. No mechanical polishing of the electrode was carried out. The same electrode was applied in the 2nd experiment, but no Pb was added to the substrate solution. Without external Pb addition, the amine yield dropped to 1.1 % (±0.2 %), while an imine yield of 35.7 % (±0.7 %)

Figure 6. Experimental procedure to investigate if Pb deposits irreversibly onto the electrode during electrolysis and thus activates it.

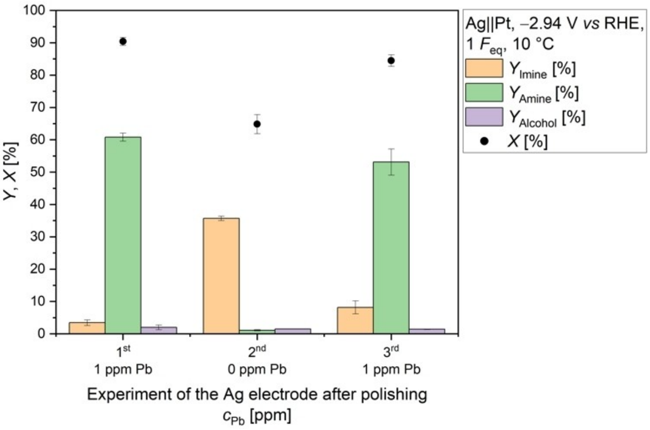
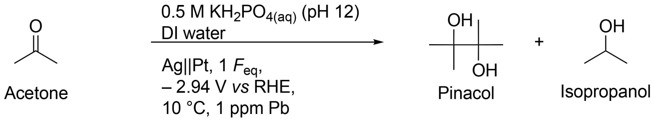


Figure 7. Switching from a Pb contaminated to a Pb free system and back to study whether Pb is irreversibly deposited onto the electrode and thereby activates it for e-hydrogenation of *N*-methylpropan-2-imine. The electrode was not polished between the experiments. The yields of *N*-methylpropan-2-imine (Y_{Imine}), *N*-methylpropan-2-amine (Y_{Amine}) and isopropanol ($Y_{Alcohol}$) are displayed. Furthermore, the conversion of acetone (X) is visualized. Carbon balance (C.B.): 73 %–76 %. Conditions: Ag||Pt; $E=-2.94$ V *vs* RHE; $F_{eq}=1$; solvent: 0.5 M KH_2PO_4 (pH 8.3); substrates: acetone: 2.4 M, methylamine: 2.9 M; $T=10$ °C; pH at 10 °C: 12.9; anolyte: 25 % H_3PO_4; a N-424 membrane; and 1 ppm Pb in the final substrate solutions of the 1st and 3rd experiment (added in form of an aqueous $Pb(NO_3)_2$ solution).

was measured after electrolysis. After the 2nd experiment, the electrode was rinsed with water and dried with compressed air. In order to verify that the electrode was not completely deactivated beforehand, Pb was added to the substrate solution of the 3rd experiment. In this experiment an amine yield of 53 % (±4 %) was generated, while the imine yield decreased to 8 % (±2 %) suggesting that the added Pb^{2+} did not irreversibly activate the electrode in the 1st experiment through e.g. deposition or doping. It is more likely that the active species remains in solution. This is supported by Lucas et al.[32] who studied the electrochemical reduction of levulinic acid to 4-hydroxyvaleric acid at a Pb cathode.[32] By using attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy, they observed in situ a signal indicating the formation of PbH_2 and proposed a “possible participation” of the hydride in substrate reduction.[32] The formation of PbH_2 was suggested to take place at the cathode, while levulinic acid was reduced by PbH_2 in solution.[32–33] This study provides a first hint, what the active species in e-hydrogenation of the imine could be. A possible mechanism for the imine reduction based on PbH_2 is discussed in the Supporting Information (Scheme S1). Nevertheless, in order to gain a better understanding of the role of Pb in electrochemical reduction, further experiments and computational studies are required. Therein, experimental studies are significantly challenged by the low Pb concentrations.



Scheme 3. Adapted reaction conditions for the electrochemical reduction of acetone (2.4 M), based on the findings of the imine reduction. The pH of the resulting substrate solution was 12.8 at 10 °C. Cathode and anode compartment were separated from each other by a N-424 membrane. The anode compartment contained a 25 % H_3PO_4 solution.

E-Hydrogenation of Acetone

In the final step, e-hydrogenation of acetone was investigated to test the transferability of Pb assisted reduction to alternative substrates. Acetone was chosen as model compound, because its electrochemical reducibility is already known since 1899,[25] yielding in isopropanol and pinacol.[25,26c,34]

Transferring the reaction conditions of imine reduction to acetone reduction required an adjustment of the substrate solution. Since no alkaline methylamine was added, the pH of the electrolyte was increased to 12 to guarantee a pH of 12.8 at 10 °C and methylamine was replaced by DI water. The further reaction conditions were taken from imine reduction (Scheme 3).

Electrolysis of an alkaline acetone solution at a freshly polished Ag cathode and in presence of 1 ppm Pb was successful. Isopropanol (47.4 % (±0.1 %)) was produced as main product and pinacol (12.4 % (±0.4 %)) as side product (Table 1), measured by ^{1}H-NMR (Figure S10). In order to investigate whether 1 ppm Pb is also required for e-hydrogenation of acetone, the same experimental procedure was applied as for imine reduction (Figure 6). In the 2nd experiment, the yield of isopropanol decreased to 8.9 % (±0.6 %), while no pinacol was formed. Adding Pb to the substrate solution and using the same Ag electrode in a 3rd experiment, increased the isopropanol yield to 28 % (±5 %). Besides, pinacol was formed in a yield of 7.2 % (±1.8 %). Overall, the electrochemical reduction of acetone can be significantly improved by the addition of 1 ppm Pb. Without Pb in the system, no pinacol formation was observed. As in the imine study, no doping of the cathode or deposition of Pb on the electrode was observed in this series of experiments.

In general, pinacol is postulated to be formed from acetone via single electron transfer (SET) and subsequent dimerization.[7,35] If Pb would solely act as a hydride transfer agent, isopropanol would be the only product. Therefore, it is plausible that Pb might have two functionalities: 1. hydride transfer agent and 2. single electron transfer agent (Scheme S1). However, further studies are required to verify this.

Table 1: Switching from a Pb contaminated to a Pb free system and back to study whether Pb is irreversibly deposited onto the electrode and thereby activates it for the e-hydrogenation of acetone. The electrode was not polished between the experiment. The yields of pinacol ($Y_{Pinacol}$) and isopropanol ($Y_{Alcohol}$) as well as the conversion of acetone (X) are displayed. Carbon balance (C.B.): 74 %–82 %.[a]

Experiment after polishing the Ag electrode c_{Pb} [ppm]	$Y_{Pinacol}$ [%]	$Y_{Alcohol}$ [%]	X [%]
1st 1 ppm Pb	12.4 % (±0.4 %)	47.4 % (±0.1 %)	77.7 % (±0.6 %)
2nd 0 ppm Pb	0 %	8.9 % (±0.6 %)	35.8 % (±0.3 %)
3rd 1 ppm Pb	7.2 % (±1.8 %)	28 % (±5 %)	58 % (±5 %)

[a] Conditions: Ag||Pt; $E = -2.94$ V *vs* RHE; $F_{eq} = 1$; solvent: 0.5 M KH_2PO_4 (pH 12) + DI water; substrate: acetone: 2.4 M; $T = 10$ °C; pH at 10 °C: 12.8; anolyte: 25 % H_3PO_4; a N-424 membrane; and 1 ppm Pb in the final substrate solutions of the 1st and 3rd experiment (added in form of an aqueous $Pb(NO_3)_2$ solution).

Conclusion

Studying the reductive amination by using acetone and methylamine as model compounds revealed that ppm-amounts of Pb were required to produce high yields of the amine. Based on the results, Pb appears to act as catalyst or mediator in e-hydrogenation. 1 ppm Pb in the system offered the best balance between efficiency (TON: 319068 (±9088)) and amine yield (62.9 % (±1.6 %)) in galvanostatic experiments. Moreover, the transition from galvanostatic to potentiostatic experiments was successful. Potentiostatic electrolysis with 1 ppm Pb resulted in amine yields between 58 % and 63 %, indicating the flexible applicability of 1 ppm Pb in a 2 V potential window between −1.34 V and −3.34 V *vs* RHE. Various cathode materials were tested in presence of 1 ppm Pb, emphasizing that materials with high HER overpotential allow good performance in e-hydrogenation of *N*-methylpropan-2-imine with e.g. glassy carbon ($Y_{\mathrm{Amine}}=62.2\,\%$ (±1.3 %)) or boron-doped diamond ($Y_{\mathrm{Amine}}=62.2\,\%$ (±1.9 %)) as alternatives to Ag ($Y_{\mathrm{Amine}}=60.8\,\%$ (±1.2 %)).

The addition of Pb to the substrate solution did not irreversibly change the cathode surface during electrolysis confirming the important role of dissolved Pb for e-hydrogenation.

In the last step, the findings on Pb catalyzed imine reduction were transferred to e-hydrogenation of acetone. The electrolysis was successful in presence of 1 ppm Pb and yielded 47.4 % (±0.1 %) isopropanol and 12.4 % (±0.4 %) pinacol. Without Pb, the yield of isopropanol decreased to 8.9 %, while no pinacol was formed.

Overall, an important role of trace amounts of Pb in e-hydrogenation could be verified opening the quest to revisit various prior literature studies with Pb electrode materials.

Supporting Information

Supporting Information is available in the Wiley Online Library.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available via Zenodo: DOI: 10.5281/zenodo.13375716

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