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Electrocatalytic upgrading of itaconic acid to methylsuccinic acid using fermentation broth as a substrate solution†

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Biomass presents a promising renewable feedstock allowing access to valuable platform chemicals. In particular, biotechnological processes enable a highly selective product formation but are carried out in aqueous electrolyte-containing solutions. Consequently, the separation of usually polar products poses severe challenges on product separation associated with a high energy demand of product purification. A direct further catalytic transformation within fermentation broth reduces the number of unit operations and the need for an energy intensive separation. We herein study the potential of a chemo- and electrochemical reduction of itaconic acid (IA) to methylsuccinic acid (MS) using acidic media or crude fermentation broth as a case study. Despite an efficient chemo-catalytic hydrogenation of neat IA over Ru/C or RANEY® nickel, the presence of various salts as well as glucose prohibits a direct chemo-catalytic valorisation in fermentation broth. In contrast, the electrochemical hydrogenation enabled very benign conditions. The selection of the electrode material proved to be decisive and had, together with the voltage, a strong influence on the conversion and faradaic efficiency of electrolysis facilitating 99% faradaic efficiency. The conversion of IA only slightly declined for an IA fermentation broth instead of neat IA in a diluted sulfuric acid environment reaching 60 *versus* 64%. Moreover, a full conversion and yield could also be achieved by simple optimizations of the reaction period and the substrate concentration. The electrocatalytic valorisation of a crude biotechnological product stream reduces not only energy demand and unit operations but presents a promising approach to introduce renewable electrical energy in biomass utilization.

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Introduction

Since the beginning of the 21st century, the societal need for eco-friendly and renewable energy sources has become increasingly imperative. In this regard, biomass resources have attracted plenty of attention over the last decade as a renewable carbon source for the production of potentially CO₂-neutral chemicals and fuels.^{1–4} Besides building blocks such as levulinic acid and 5-hydroxymethylfurfural, the US Department of Energy (DOE) named itaconic acid (IA) as one of the 12 future

major platform molecules derived from biomass feedstocks.⁵ Since the 1960s the production of IA is in general accomplished by the fermentation of *Aspergillus terreus* on sugar containing media.^{6,7} Unsaturated di-carboxylic acid is typically used as a starting material in the manufacturing of polymers,^{6,7} but it is also considered to be a promising substrate for tailor made fuels, such as 3-methyltetrahydrofuran.^{8–11} In particular the use of IA as an alternative monomer for the production of poly (methyl methacrylate) is of recent interest and will likely promote the production of IA further.^{12,13} In addition, studies on the economic potential of IA estimate the projected market for IA to nearly 410 000 MT with a value of 570 million USD in 2020.¹⁴ This also shows the strong increase of the market size of IA since the year 2001.⁶ Methylsuccinic acid (MS) can be obtained from IA *via* hydrogenation of the double bond.¹⁵ The saturated product of IA can *e.g.* find applications as a substrate for polymerization reactions and as an additive in coating agents.¹⁶ The diethylester of methylsuccinic acid on the other hand is considered as a suitable solvent in cosmetics.¹⁷ Recently, the Wong Chang group showed that methylsuccinic

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monoesters have great properties as a substrate for the electrochemical coupling reaction called “Kolbe electrolysis”. The obtained product 2,5-dimethyladipic acid after release of the ester groups might possess very promising characteristics in the polymer industry.¹⁸

One of the key steps in the production of biofuels or value-added chemicals from biomass presents a suitable connection between the highly selective biotechnological transformation of biomass, *e.g.* cellulose, into platform chemicals such as ethanol and lactic acid or IA with subsequent processing.^{2,19,20} Indeed, fermentation processes delivering high-boiling and polar products in aqueous electrolyte-solutions often cause highly demanding and energy intensive separation processes.^{21–24} These challenges make a close integration with further transformation attractive avoiding intermediate product separation.²⁵ However, despite promising progress in the design of efficient catalysts for a valorisation of biomass-derived platform chemicals, few examples demonstrate a direct catalytic transformation of crude fermentation broth.

Beside conventional chemo-catalysis, electrocatalysis poses an efficient methodology for the production of bio-derived chemicals.^{26–35} In this regard, in particular the hydrogenation (or reduction) of levulinic acid into valeric acid and γ -valerolactone reported by Nilges, Xin, Qiu and Dos Santos *et al.* revealed that electrochemistry represents a feasible tool for the effective and sustainable production of promising chemicals.^{26,28,31,33} The mentioned reaction was carried out in aqueous acidic solutions and at room temperature, using Pb electrodes for high valeric acid selectivities and glassy carbon electrodes for high γ -valerolactone selectivities.²⁸ Among these electrochemical approaches also the mild electrosynthesis of 2,5-furandicarboxylic acid from HMF has received attention, as it does not require high temperatures and oxygen pressure.^{29,36} The mild process conditions fulfil the major criteria of green chemistry and open a window of opportunity to integrate renewable electrical energy into biomass valorization.

In the recent past, literature studies described the electrochemical hydrogenation (ECH) of muconic acid to different diacid monomers³⁴ and the reduction of 5-hydroxymethylfurfural to 2,5-bis(hydroxymethyl)furan.³² A recent contribution by Matthiesen *et al.* also highlights the potential of an electrochemical transformation of biologically produced muconic acid.³⁵ Regarding the electrocatalytic transformation of IA, only a few examples exist. In 1989 Smigielski *et al.* reported an electrocatalytic conversion of IA (83%) to methylsuccinic acid (MS) at 60 °C under strongly basic conditions using a high excess of RANEY® Ni as a catalyst and an electrode (molar ratio of Ni/IA = 1.4, Fig. 1).³⁷ The second study

describes water soluble manganese complexes such as manganese porphyrin as efficient electrocatalysts for the oxidation of different unsaturated dicarboxylic acids. However, these complexes are very pH-dependent and therefore difficult to implement for the often very acidic environments in electrochemical reactions.³⁸

Herein, we present the successful direct transformation of biotechnologically produced IA in an electrochemical process running at ambient pressure and temperature over an inexpensive full metal electrode. Prior to the electrocatalytic conversion of crude biotechnological IA solution the electrode material, which provided the highest MS yield and best faradaic efficiency, was optimized by varying the applied negative potential. This provided valuable insights into achieving high selectivity of the ECH over the competitive hydrogen evolution reaction. With the goal of assessing the impact of ECH, we have also examined the ability of Ru/C and RANEY® nickel catalysts in a conventional hydrogenation reaction (applying H₂ pressure and heat) for comparison.

Experimental

Fermentation

Cultivation of *Aspergillus terreus* DSM 23081 was performed in a minimal medium according to Kuenz *et al.*³⁹ and Hevekerl *et al.*⁴⁰ The medium contained 180 g L^{−1} glucose, 0.8 g L^{−1} KH₂PO₄, 3 g L^{−1} NH₄NO₃, 1 g L^{−1} MgSO₄·7H₂O, 5 g L^{−1} CaCl₂·2H₂O, 0.00167 g L^{−1} FeCl₃·6H₂O, 0.008 g L^{−1} ZnSO₄·7H₂O and 0.015 g L^{−1} CuSO₄·5H₂O. The main substrate glucose was obtained from Carl Roth GmbH & Co. KG (Karlsruhe, Germany) as a monohydrate with a purity of ≥99.5%. The medium was completed from stock solutions, which, except for the CaCl₂ and FeCl₃ solutions, were adjusted to pH 3.1 with 1 M H₂SO₄ and were autoclaved separately. Experiments were conducted at 33 °C in unbaffled 250 mL shake flasks with a filling volume of 20 mL and an initial spore concentration of 5 × 10⁶ spores per mL. The flasks were shaken at 300 min^{−1} with a shaking diameter of 50 mm. After 130 hours of cultivation without interruption of shaking, the culture broth was harvested and fungal biomass was removed *via* filtration.

Electrocatalysis

All electrochemical reactions were conducted in a custom designed single compartment three-electrode cell under potentiostatic or galvanostatic control using a potentiostat/galvanostat (Autolab PGSTAT 302N). The electrode reactions were undertaken using a three-electrode arrangement. In this regard, *E*_{WE} stands for potential applied *vs.* reference electrode, for which Ag/AgCl saturated KCl electrodes (ProSense, 0.195 V *vs.* standard hydrogen electrode (SHE)) were used throughout the study. All electrode potentials in this study are reported *vs.* Ag/AgCl sat. KCl, but normalized to SHE for energetic calculations and for better comparability.

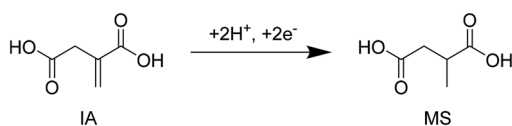
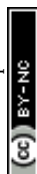


Fig. 1 The proposed ECH of IA to MS.



D device. The samples were directly injected without any additional treatment.

Results and discussion

Chemocatalytic batch reactions

The electrochemical production of MS was up to now only investigated by one group.³⁷ Moreover, since previous studies required additional heating the conditions need further optimization. These findings motivated us to investigate the ECH reaction of IA to MS over different electrodes in more detail. In this regard, the metals Cu, Ni, Fe, Pb and Cu-Pb (plastic bronze) have been investigated for electrochemical activity using a fixed voltage (Fig. 2).

The ECH of IA was studied in an aqueous acidic solution ($0.5 \text{ mol L}^{-1} \text{ H}_2\text{SO}_4$). For all experiments, a potential of -1.06 V vs. SHE has been applied for a 1 h reaction period. Cu and Cu-Pb electrodes showed only a very low electrochemical performance for the hydrogenation reaction at this voltage, whereas for Pb the voltage was not high enough to achieve a current flow. The highest catalytic activity as well as faradaic efficiency was observed for Ni, while Fe still revealed a notable yield and conversion. Interestingly, when switching the applied potential from -1.06 V to -1.41 V vs. SHE Pb electrodes meet the required overpotential for hydrogenation and start to clearly stand out over the other tested electrodes in terms of substrate conversion (96%), yield of MS (96%) and faradaic efficiency (16%, calculation described in the ESI†). The obtained current value at -1.41 V is comparable to the values observed when using other electrodes at lower potentials (see cyclic voltammograms in the ESI†). As it was already stated by dos Santos *et al.*,²⁸ the higher performance of Pb for ECH reactions can be often explained by the higher overpotential of water electrolysis.⁴¹ Hydrogen evolution at Cu-, Fe- and Ni-cathodes start already before -1.0 V vs. SHE in acidic media.^{41,42}

¹H NMR spectra were recorded at 25 °C on a Bruker Avance 400 MHz spectrometer. The samples were in the case of low concentrations of IA (0.1 mol L⁻¹) dried at 60 °C under vacuum, reconstituted in deuterium oxide (Deutero), and subsequently analysed. In the case of high concentrations of IA and when using fermentation broth, 0.2 mL of the product mixture was diluted in deuterium oxide. Ethanol was in each case used as an internal standard during the quantitative measurements. The spectra of the reactant and product are depicted in the ESI.†

Inductively coupled plasma atomic emission spectroscopy (ICP-AES)

For the determination of the metal amount in the aqueous solutions, the samples were analysed on a spectro-flame

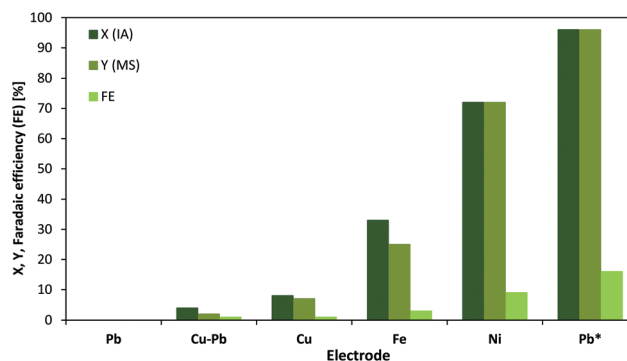


Fig. 2 Screening of various metal electrodes in the ECH of IA to MS. Conditions: r.t., 1 h, counter electrode: glassy carbon, $E = -1.06$ V vs. standard-hydrogen-electrode (SHE), water (16 mL), H_2SO_4 (0.5 mol L^{-1}), IA (0.1 mol L^{-1} , 1.6 mmol, 0.208 g). * $E = -1.41$ V vs. SHE (X denotes conversion, Y means yield).

In summary, MS can be obtained from IA using acidic aqueous solutions and Pb-cathodes with excellent selectivity and yields, while the faradaic efficiency needs to be optimized. However, the faradaic efficiency is very dependent on the initial substrate concentration and therefore, can be increased using higher substrate concentrations.

Kinetic potential dependent experiments with Pb-cathodes

Considering the results from the section before, another set of experiments was conducted in order to reveal the impact of different applied potentials on conversion, and the change of the faradaic efficiency over a 1 h reaction time in comparison with the studied electrode potentials (Fig. 3).

Since Pb-cathodes showed the highest reaction rates and best faradaic efficiencies, they were utilised for further experiments. The effect of the voltage ranging from -1.31 to -1.51 V *vs.* SHE shows that the time for reduction decreases for higher voltages. However, when reaching -1.41 V *vs.* SHE the effect becomes negligible, which can likely be attributed to mass transfer limitations during the process. As mentioned in the literature applying a potential to a certain electrode, it is found that, upon increasing the applied voltage the current value at first increases until it reaches a saturation level, called a current plateau. It then requires clearly higher potentials to achieve higher current growth again. When this limiting is encountered, it is in most cases caused by the slowness of

transport of charged or uncharged species through the solution.⁴³ Using a stirrer or a rotational disk electrode can shift the limitation to a higher value emphasising the high impact of reactor design in such a transformation. Another important factor relates to an electrode material with a higher specific surface area; however, also there mass transfer limitations will be encountered at a certain potential.⁴³ According to the obtained results, the highest faradaic efficiency of 62% is achieved after 10 min when applying lower potentials. The difference in higher potentials rises when it comes to longer reaction periods; however, this behaviour is probably intensified due to low IA amounts in solution after 50% conversion. This suggestion implies a better faradaic efficiency for all potentials when using higher substrate solutions and that low efficiencies are also connected to lower concentrations of IA in solution. On this account, it is expected that the faradaic efficiency can be clearly increased when using higher initial substrate concentrations or when performing the ECH of IA in a continuous setup. Nevertheless, a very mild process for the production of MS from IA has been elaborated, which does not require the addition of thermal heat as it was necessary in a previous study of Smigielski *et al.*³⁷ For this reason, and especially with regard to the rules of green chemistry, the ECH of IA when using Pb-cathodes and an acidic aqueous solution presents a very sustainable system and promising setup for continuing investigations.

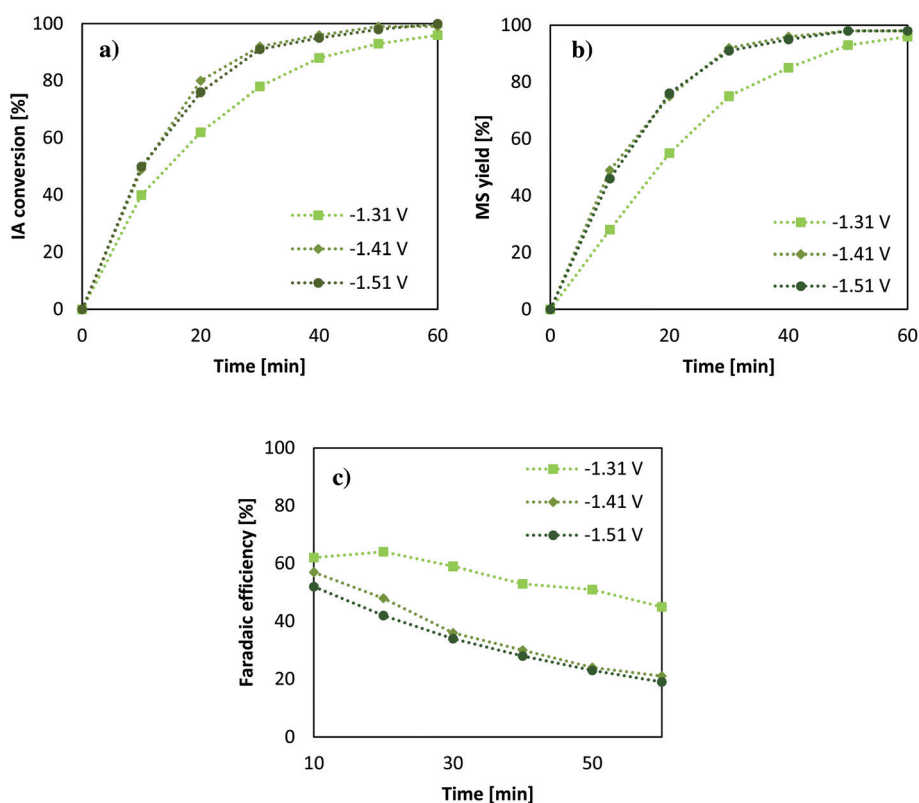


Fig. 3 The effect of the applied potential on the conversion, yield and faradaic efficiency: (a) IA conversion, (b) yield of MS, and (c) faradaic efficiency. Conditions: r.t., working electrode: Pb, counter electrode: glassy carbon, water (16 mL), H_2SO_4 (0.5 mol L^{-1}), IA (0.1 mol L^{-1} , 1.6 mmol, 0.208 g). The dashed lines are added as guide to the eye.



Although, the applied potential has to be increased (approximately -1.4 to -4.4 V *vs.* SHE) as the resistance of the mixture is higher when using fermentation broth, this problem is easily solved when mixing the broth with a diluted sulfuric acid solution (0.5 mol L $^{-1}$). According to the obtained faradaic efficiencies for both substrate mixtures, there is a

In order to determine the Ru/C stability in pure IA solution and fermentation broth recycling tests were conducted (Fig. 5). Between the cycles the catalyst was washed with distilled water and methanol and dried at 60 °C under vacuum. Ru/C shows excellent recyclability with only slight loss of yield and conversion under these conditions and using neat substrate solution. However, only 3% conversion and 1% yield were achieved after the first experiment when applying this catalyst to fermentation broth. These findings imply that because of high amounts of glucose, which might plug the Ru/C pores, the catalyst deactivates fast. In addition, the various salts could inhibit the performance. In order to ensure that the low activity was not only related to the properties of the Ru/C catalyst, additional tests were conducted with a conventional hydrogenation catalyst.⁴⁵ RANEY® nickel (4 wt% of the substrate amount) showed

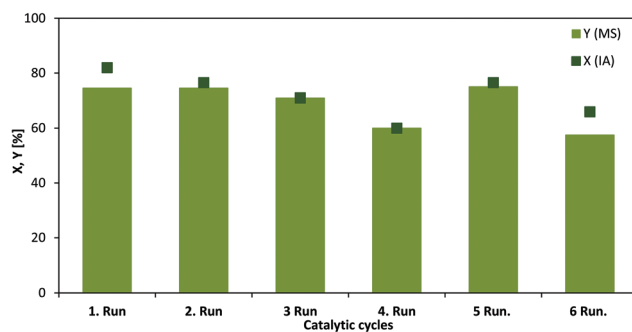


Fig. 5 Chemo-catalytic batch hydrogenation of IA over a Ru/C catalyst including recycling: 100 mg Ru/C in pure IA solution (0.61 mol L⁻¹, 9.1 mmol, 1.187 g). Reaction conditions: 1 h, 70 °C, 10 bar of H₂, 15 mL water, 500 rpm stirring speed.

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