Process for the Preparation of Fatty Aldehydes from Renewable Resources

Jens Johannsen*, Francesca Meyer, Georg Fieg, and Thomas Waluga

Common methods for the chemical production of fatty aldehydes, widely applied as artificial flavors and fragrances, use fossil starting materials, harsh reaction conditions, and hazardous chemicals. This contribution introduces a novel, environmentally friendly process for the preparation of fatty aldehydes from the natural, renewable resource plant oil. It has successfully been shown that bringing a fatty acid into contact with zerovalent iron leads to the reduction of the fatty acid to the corresponding fatty aldehyde. In this paper, the three-step process is presented and discussed, exemplary for the preparation of dodecylaldehyd from dodecanoate.

1 Introduction

Scarcity of fossil raw materials is an omnipresent topic of our time. Nonetheless, fossil starting materials are presently described in literature as a common origin of commercially available flavoring agents or fragrances consisting of fatty aldehydes. In the processes for these fatty aldehydes, harsh reaction conditions are necessary, causing pollution due to a high demand of energy and to the use of hazardous chemicals. The methods for the synthesis of fatty aldehydes can be described through two main categories: dehydration and hydroformylation. The first method consists of the dehydration of fatty alcohols, a typical process for the production of long-chain aldehydes [1–4]. The second method is the hydroformylation of alkenes, mostly obtained on the basis of crude oil, and is typically applied to produce short-chain aldehydes [2, 5, 6]. In both methods, fossil starting materials are used, and high temperatures up to 500 °C as well as very high pressures up to 600 bar are applied [2]. While alternative methods are described in literature that avoid using fossil starting materials, such as extraction from natural products, the resulting yields of fatty aldehydes for these methods are very low [7, 8].

Considering the importance of achieving independence from fossil starting materials, it is desirable to develop a process for the production of fatty aldehydes that allows for the use of renewable resources. In view of the self-evident effort to reduce energy consumption in industry, further desired criteria for such a process are mild reaction conditions in form of rather low temperatures and/or pressures, the renounce of hazardous chemicals, and a high selectivity. This paper introduces a novel process for the preparation of fatty aldehydes, using renewable starting materials and rather mild reaction conditions, showing exemplarily the preparation of dodecylaldehyd from dodecanoate [9].

Dodecanoate is a component found in high concentrations in plants such as *Laurus nobilis* (Laurel), while dodecylaldehyd is a flavoring agent and fragrance used in industrial products such as perfumes – a prominent example being Chanel No.5 [10, 11]. The introduced process consists of three main steps that are shown in Fig. 1. In the first step, dodecanoate is hydrolyzed by a lipase in the presence of water. Enzymatic reactions like these allow for very mild reaction conditions and are well described in literature [12–15]. In the following step, the corresponding fatty acid (dodecanoic acid) is separated from the reaction mixture. Dodecanoic acid is brought into contact with zerovalent iron particles and, in the last step, heated to reduce the fatty acid to dodecylaldehyd. In the following the novel preparation process is described and experimental data is presented and discussed. It goes without saying that the reduction – the crucial step within this process – can be started directly from fatty acids. This contribution, however, focuses on a holistically sustainable process; therefore, it deliberately starts with the hydrolysis of esters, which occur in high amounts in plants.

2 Analysis and Chemicals

All measurements were performed in triplets. The organic compounds were measured in a PerkinElmer Clarus 500 gas chromatograph with ionization detector, using a capil-

Jens Johannsen, Francesca Meyer, Prof. Dr.-Ing. Georg Fieg, Dr.-Ing. Thomas Waluga
jens.johannsen@tuhh.de
Hamburg University of Technology, Institute of Process and Plant Engineering, Am Schwarzenberg-Campus 4(C), 21073 Hamburg, Germany.
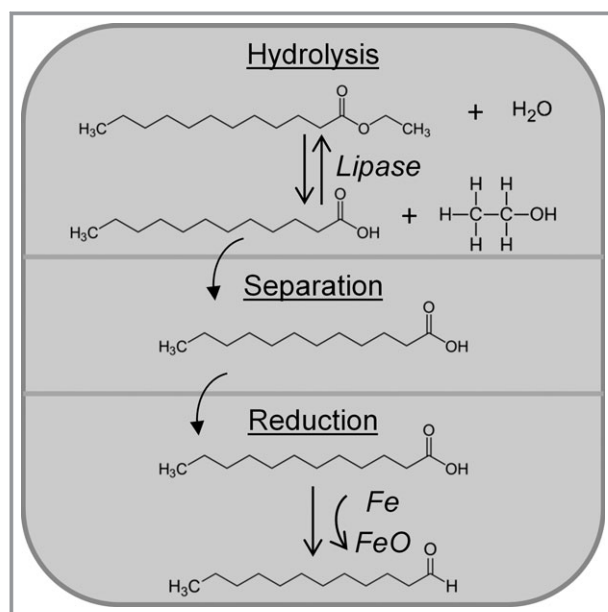
Wiley Online Library

Figure 1. The three steps of the novel process for the preparation of fatty aldehydes consisting of hydrolysis, separation, and reduction, exemplarily for the preparation of dodecylaldehyd.

lary column type SUPELCO SLB-5ms and nitrogen as mobile phase, at 200 °C oven temperature for 7 min. The water concentrations were measured using Karl-Fischer titration in a Mettler Toledo C30-all-round coulometer. The chemicals used in this study are listed in Tab. 1.

Table 1. Chemicals used in this study.

Component	Supplier	Specification
Dodecanoate	Sigma-Aldrich	≥ 98 %
Dodecanoic acid	Merck	≥ 99 %
Dodecylaldehyd	Sigma-Aldrich	≥ 95 %
Ethanol	Carl Roth	≥ 99.8 %
Iron particles	Laborladen.de	90 µm
Lipase	Novozymes	Novozym® 435
Triton X-100	Carl Roth	≥ 97 %

3   Process Description

The presented process for the preparation of fatty aldehydes consists of three main steps, including the two reaction steps hydrolysis and reduction intermitted by a separation step. In this section, the applied methods are described, experimental data is presented, and the results are discussed.

3.1 Hydrolysis

In the first step, dodecanoate is hydrolyzed in the presence of water, catalyzed by the commercially available immobilized lipase Novozym® 435, which is active in the organic phase, resulting in the products ethanol and dodecanoic acid. To characterize this reaction, 10 mg of enzyme particles packed in a bag were added to 4 mL of a tempered dodecanoate-water system and shaken at 1400 rpm for 15 min. The lipase supplier Novozymes provides a range of 30–60 °C for optimal enzyme activity [16]. Furthermore, it is reported that a significant deactivation of enzyme activity occurs at temperatures above 60 °C, while up to 60 °C enzyme deactivation is negligible [15, 17, 18]. Besides the temperature, a crucial factor is water saturation in the organic phase. Fig. 2 shows the temperature dependency of the water saturation concentration in dodecanoate.
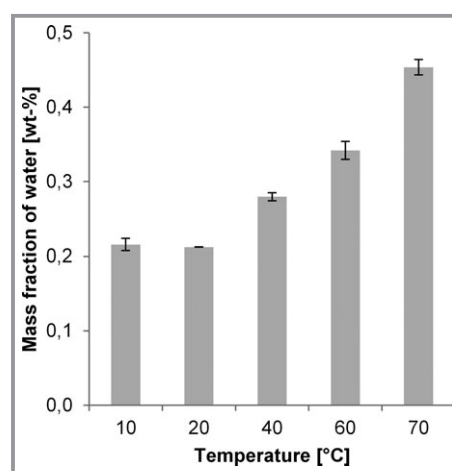

Figure 2. Mass fraction of water in dodecanoate in dependency of the temperature.

As expected, Fig. 2 indicates that a higher temperature allows for higher water concentrations in the organic phase. A temperature increase from 60 °C to 70 °C causes an increase in water concentration, which would strongly enhance the accessibility of both educts for the enzyme. Due to enzyme deactivation at high temperatures and based on the given temperature range by the enzyme supplier, however, a temperature of 60 °C is chosen for the hydrolysis step of this process [15–18]. For the determined conditions, the reaction rate of the enzyme and the conversion of water were measured, considering the saturation concentration of 0.35 wt % at 60 °C as the maximal water concentration available for the reaction. Fig. 3 shows the reaction rate of the lipase in dependency of the water concentration.

As indicated in Fig. 3, the saturation concentration of water in dodecanoate at around 0.35 wt % limits the reaction rate of the lipase at to a maximum of approx. 0.09 g min^{-1}g$_{\text{Enzyme}}^{-1}$. Up to the saturation concentration, a typical increase of the reaction rate can be observed, as
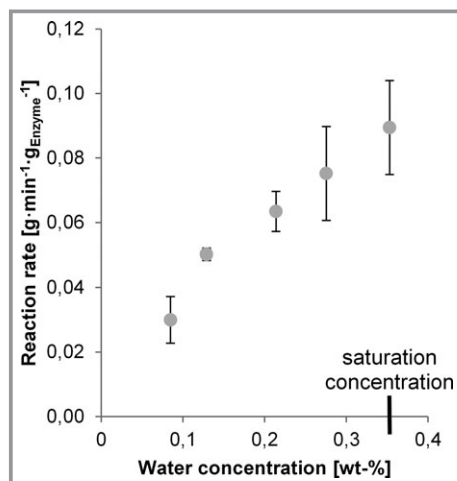
Figure 3. Reaction rate of Novozyme 435 at 60 °C in dependency of the water concentration.

described in literature [12, 18]. The conversion of water in the hydrolysis reaches values of 75.63 ± 0.03 %. These results fall are line with literature data for lipase reactions, which are in the range of 30–92 % conversion for the same enzymes and both same and similar reaction systems [12, 13, 18]. The catalytic efficiency of the hydrolysis was evaluated by calculating the Thiele modulus and determining the diffusion coefficient for leached Novozym® 435 particles [19, 20]. Leaching was performed with Triton X-100 [21]. The diffusion coefficient was calculated by non-linear regression of experimental data points of water diffusion into the leached pores in spherical particles [22]. A catalytic efficiency of 60 % was determined.

Due to the low solubility of water, two principles are considered for the further development of this process: firstly, the hydrolysis is carried out in an oversaturated two-phase system of water and dodecanoate, thereby ensuring constant water saturation of the organic phase and an increase in the yield of dodecanoic acid. Secondly, due to the relatively high temperature, the produced ethanol partially evaporates in situ from the system, resulting in a higher dodecanoic acid yield according to the principle of Le Chatelier and Braun. Taking these results into consideration, the hydrolysis was performed in a 1000-mL stirred tank reactor, using 500 mL dodecanoate, 200 mL water, and 10 g Novozym® 435. Aliquots of 80 mL of the organic phase were sampled after 12 h for further processing in the following steps.

3.2 Separation (Removal of Oxidizing Components)

The product mixture of step 1 (hydrolysis) consists of dodecanoate saturated with 0.35 wt % water as not consumed educts, and of dodecanoic acid and traces of ethanol as products. Prior to the final reduction step, a purification of the mixture is necessary in order to prevent unwanted

side reactions. Due to the application of zerovalent iron particles, the potentially oxidizing components water and ethanol are to be removed from the target intermediate dodecanoic acid. Additionally, the separation of water avoids a possible oxidation of the obtained fatty aldehyde in the reduction step. Thermal separation has proven to be a suitable unit operation for this step, as indicated by the pure component boiling points of the components (see Tab. 2).

Table 2. Pure component boiling points of the intermediates at 100 mbar and 1000 mbar.

Component	Boiling point [°C] at	
	1000 mbar	100 mbar
Water	100	46
Ethanol	78	29.5
Ethyl dodecanoat	275	194.5[a]
Dodecanoic acid	298.7	219.4[a]
Ethanol-water azeotrop	78	29

a) own experimental data.

As shown in Tab. 2, a thermal separation of the low-boiling components water and ethanol is applicable at temperatures below 50 °C at a pressure of 100 mbar. Such low temperature prevents side reactions of the fatty acids during distillation. 80 mL of the sample from the first step were transferred to a 100-mL flask with an attached distillation bridge. The flask was exposed to 70 °C and 100 mbar to ensure the separation of all potentially oxidizing components. The known homogeneous azeotrope of ethanol/water at around 95 wt % ethanol does not affect such separation, since both components are to be removed. Heterogeneous azeotropes of water/acid and water/ester were expected [13]. After thermal separation, the components water and ethanol were not traceable in the mixture anymore. Thus, the aforementioned possible azeotropes do not negatively affect the process.

3.3 Reduction

After the first two steps, samples of 9.2 mmol dodecanoic acid dissolved in dodecanoate were obtained. The reduction reaction was carried out in a 100-mL stirred tank reactor. The mixture of dodecanoate and dodecanoic acid was brought into contact with zerovalent iron particles and heated to 220 °C at a pressure of 200 mbar for 30 min. During the reaction, the fatty acid was reduced to the corresponding fatty aldehyde, while the iron was oxidized to iron oxide. Due to strong turbidity in the reaction medium it was impossible to analyze the samples directly via gas chromatography. Therefore, the mixture was heated in a

distillation unit to obtain a clear distillate, which was then analyzed. The reduction resulted in the production of 1.1 μmol dodecylaldehyd. The total surface area of the iron particles, and consequently the mole number of iron atoms available for the reaction, was calculated. A yield of dodecylaldehyd of 71 % in relation to the available iron atoms was achieved, resulting in the successful production of the fatty aldehyde. 71 % conversion rate falls in line with literature data that describe the reduction of fatty acids to fatty aldehydes with similar carbon chain length (45–95 % conversion) [23–25]. Due to a high excess of dodecanoic acid relative to the available iron atoms, the conversion of acid is consequently rather low. However, these results only take into consideration the product measured in the distillate. Any produced dodecylaldehyd remaining in the bottom part of the distillation unit at the end of the process could not be measured because of the aforementioned turbidity and would lead to a further increase in the conversion rate.

4 Conclusions and Outlook

The fatty aldehyde dodecylaldehyd was successfully produced from a natural resource, thereby introducing a novel, environmentally friendly process as an alternative for the currently used reaction pathways [9]. The process consists of three steps, where the first steps hydrolysis and separation are based on state-of-the-art knowledge. The conversion of dodecanoate to dodecylaldehyd was presented exemplary for this process. 75 % conversion of water was achieved in the hydrolysis step. In the separation step, a complete separation of the remaining water and the produced ethanol was possible in the range of measurement accuracy. The reduction of the intermediate fatty acid to fatty aldehyde with zerovalent iron was successful, achieving 71 % conversion in relation to the available iron atoms. This result aligns with literature data. It is worth mentioning, however, that the research described in the literature makes use of environmentally hazardous chemicals such as tetrahydrofuran, toluene, or hydrochloric acid, and requires mostly much higher temperatures and pressures [23–25]. This contradicts the effort to achieve more environmentally friendly processes.

The present work, by contrast, shows the possibility to achieve high yields of fatty aldehydes exclusively using zerovalent iron particles. First consecutive experiments prove the applicability of the process to different target compounds such as hexanal and alternative zerovalent metals such as copper. Additionally, iron particles of different sizes have been applied and successfully tested. For very small particle sizes, and therefore very large surface areas, the reduction of the fatty acid seems to result in the (co-)production of fatty alcohol. This is also described in [9].

Further encompassing work will now systematically characterize the reduction reaction for different systems and different zerovalent metals, including the influence of their respective particle size distribution on the yields of fatty aldehyde and the corresponding fatty alcohol. Additionally, the regeneration of the oxidized iron is to be investigated to allow for a smaller iron input. A practical way of reducing the iron oxide would be to bring it into contact with the alcohol produced in the hydrolysis. The consequential next step will be the use of triglycerides obtained from plant oils, from which glycerol can be used for the reduction of iron oxide.

References

[1] T. F. De Graaf, H. J. Delahaye, *Patent EP0037149*, **1981**.

[2] C. Chapuis, D. Jacoby, *Appl. Catal., A* **2001**, *221 (1–2)*, 93–117. DOI: https://doi.org/10.1016/S0926-860X(01)00798-0

[3] G. Bjornson, *Patent US4304943*, **1981**.

[4] M. L. Kalja et al., *Patent SU789491*, **1980**.

[5] M. Beller et al., *J. Mol. Catal. A: Chm.* **1995**, *104 (1)*, 17–85. DOI: https://doi.org/10.1016/1381-1169(95)00130-1

[6] J. E. Bludworth, *Patent US2128908*, **1938**.

[7] M. Palma, L. T. Taylor, *J. Agric. Food Chem.* **1999**, *47 (12)*, 5044–5048. DOI: https://doi.org/10.1021/jf990019p

[8] D. Chouchi, D. Barth, *J. Agric. Food Chem.* **1996**, *44 (4)*, 1100–1104. DOI: https://doi.org/10.1021/jf950469r

[9] J. Johannsen et al., Process for the preparation of a fatty aldehyde, *Patent application LU101281*, **2019**.

[10] S. H. Beis, N. T. Dunford, *J. Am. Oil Chem. Soc.* **2006**, *83 (11)*, 963–957. DOI: https://doi.org/10.1007/s11746-006-5052-8

[11] K. Truong et al., *ChemPhysChem* **2017**, *18 (19)*, 2631–2636. DOI: https://doi.org/10.1002/cphc.201700341

[12] P. Krause, *Modellierung und kombinierte experiment- und simulationsbasierte Analyse eines zweiphasig durchströmten enzymatischen Festbettreaktors*, Ph.D. Thesis, Hamburg University of Technology **2013**.

[13] P. Zitzewitz, *Systematik zur modellgestützten Analyse enzymkatalysierter LLS-Synthesen auf Basis mehrkriterieller Optimierung*, Ph.D. Thesis, Hamburg University of Technology **2019**.

[14]: M. Rucka et al., *Bioprocess Eng.* **1991**, *7 (3)*, 133–135. DOI: https://doi.org/10.1007/BF00369424

[15] T. Egger, G. Fieg, *AIChE J.* **2017**, *63 (6)*, 2198–2211. DOI: https://doi.org/10.1002/aic.15598

[16] *Immobilized lipases for biocatalysis*, Novozymes A/S, Bagsvaerd **2016**.

[17] M. Leipold, *Ganzheitliche Analyse enzymkatalytischer Syntheseprozesse im Festbettreaktor*, Ph.D. Thesis, Hamburg University of Technology **2014**.

[18] S. D. Gawas et al., *Appl. Biochem. Biotechnol.* **2016**, *180 (7)*, 1428–1445. DOI: https://doi.org/10.1007/s12010-016-2177-6

[19] T. Waluga, S. Scholl, *Chem. Eng. Technol.* **2015**, *38 (10)*, 1817–1826. DOI: https://doi.org/10.1002/ceat.201500166

[20] S. Enfors, L. Häggström, *Bioprocess technology fundamentals and application*, Stockholm Royal Inst. of Technology, Stockholm **2000**.

[21] Z. Cabrera et al., *J. Mol. Catal. B: Enzym.* **2009**, *57 (1–4)*, 171–176. DOI: https://doi.org/10.1016/j.molcatb.2008.08.012

[22] T. Waluga, S. Scholl, *Chem. Eng. Technol.* **2013**, *36 (4)*, 681–686. DOI: https://doi.org/10.1002/ceat.201200522

[23] L. C. M. Castro et al., *Chem. Commun.* **2012**, *48*, 10514–10516. DOI: https://doi.org/10.1039/c2cc35727e

[24] D. S. Mérel et al., *Coord. Chem. Rev.* **2015**, *288*, 50–68. DOI: https://doi.org/10.1016/j.ccr.2015.01.008

[25] K. Miyamoto et al., *Chem. Lett.* **2012**, *41 (3)*, 229–231. DOI: https://doi.org/10.1246/cl.2012.229