

# Selective Degradation of Lignosulfonate and Lignin with Periodate to 5-Iodovanillin

Jana Klein, Kristian Alt, and Siegfried R. Waldvogel\*

This work represents a new method that uses electrochemically generated periodate to oxidize side-stream lignins. Using periodate, a lignin-derived product other than vanillin becomes accessible. The development of an eco-friendly method for generating 5-iodovanillin from lignin is reported and is of significant interest for the wood-based industry. Wider utilization of lignin can substitute fossil-based chemicals and fuels, reduce the emission of greenhouse gases, and facilitate the dependence on fossil energy. The reaction conditions are easy to conduct, the lignin is modified, and no specific setup is required. This one-pot cost-efficient method does not use toxic or harmful metals and yields more than 15 wt% 5-iodovanillin. 5-Iodovanillin represents an advanced building block for the synthesis of complex molecules, such as active pharmaceutical ingredients.

## 1. Introduction

Cellulose is the most abundant building block on earth, with a content of about 55%<sup>[1]</sup> in wood.<sup>[2]</sup> Also, hemicellulose is included followed by lignin.<sup>[3]</sup> Lignin is the third-largest biopolymer feedstock.<sup>[4]</sup> Lignin can be exploited as a renewable resource of aromatic building blocks.<sup>[1,5]</sup> It is generated as a side-stream of pulping factories and offers tremendous potential as a source of bio-based fine chemicals (such as vanillin, acetovanillone),<sup>[4]</sup> surfactants,<sup>[6]</sup> polymers,<sup>[3]</sup> and biomaterials.<sup>[1]</sup> Due to large amounts of lignin available, it is of great interest from an economic and environmental point of view to find value-added products<sup>[4]</sup> and cost-effective processing.<sup>[7]</sup> The utilization of lignin as renewable feedstock would rival petroleum refining.<sup>[6]</sup>

Lignins have a polyphenolic backbone and consists of three monomer units: *p*-coumaryl (H-unit), coniferyl (G-unit), and sinapyl alcohol (S-unit).<sup>[8–10]</sup> The composition depends on many factors such as the plant species, harvesting time and growing areas.<sup>[10]</sup> Depending on the pulping process, lignin shows different functionalization and backbones.<sup>[10]</sup> There exist two types of

linkages: condensed and ether linkages.<sup>[11]</sup> Compared to Kraft lignin and organosolv lignin, lignosulfonate contains additional sulfonate groups, which strongly increase the solubility in water.<sup>[12]</sup> Due to the complexity and stability of their structure, selective degradation for the formation of value-added compounds is challenging.<sup>[3,6,9,13,14]</sup>

Several studies have been conducted during the past decades for the degradation of lignin into its aromatic intermediates. For example, enzymes are used for the depolymerization of lignin to achieve phthalates and benzoic acids, but the efficiency was low.<sup>[15]</sup> Other studies worked in a flow reactor using catalysts, which were often deactivated due to interactions of sulfur and active sites.<sup>[16]</sup>

Low yields, raising costs for operation, elevated temperatures, and pressure represent limiting factors. Also, some electrochemical degradation pathways were designed, selectively yielding flavor chemicals like vanillin in interesting yields.<sup>[4,14,17]</sup>

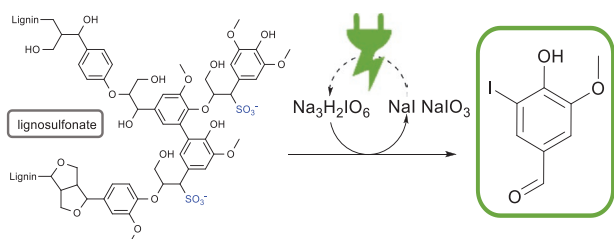
Over the last few decades, electro-organic synthesis experienced a renaissance in both, laboratory and technical synthesis.<sup>[18]</sup> The advantages of this powerful method are working reagent-free, cost-reduced, inherently safe, economically, and environmentally friendly.<sup>[19]</sup> Periodate could be generated electrochemically and is often used as a high performance oxidizing agent in organic synthesis.<sup>[20]</sup> When direct electrolysis is not successful, an ex-cell approach is an alternative option.<sup>[21]</sup> A disadvantage of the conventional synthesis of periodate is the costly production and subsequent purification, which results from the use of lead dioxide anodes.<sup>[22]</sup> Using a durable and nontoxic boron-doped diamond anode (BDD)<sup>[23]</sup> opens a new path for a direct and cost-efficient electrochemical method to generate periodate directly from iodide.<sup>[20,24]</sup> In this study, a new and simple method for the successful degradation of different types of lignin with electro-generated periodate is presented (**Scheme 1**). Using this protocol 5-iodovanillin is formed selectively. Iodovanillin is utilized as a central building block for example in annulation and cross-coupling reactions.<sup>[25,26]</sup> More than 10 reports use iodovanillin as the starting material for example for the synthesis of antiviral inhibitors.<sup>[26,27]</sup> 5-Iodovanillin represents a quite costly and advanced building block. A direct synthesis without petroleum-based chemicals, nor use of iodine and vanillin, is a highly attractive target.<sup>[28]</sup> The degradation with periodate does not need a separation step between the oxidation and the thermal treatment. Therefore, lignin is used directly as a sustainable source to achieve iodovanillin as the target product. Further, this process does not use toxic reagents, such as in the nitrobenzene oxidation, which is often considered as a benchmark to determine the highest achievable vanillin content.<sup>[29]</sup>

J. Klein, K. Alt, S. R. Waldvogel  
Department of Chemistry  
Johannes Gutenberg University  
Duesbergweg 10-14, 55128 Mainz, Germany  
E-mail: waldvogel@uni-mainz.de

 The ORCID identification number(s) for the author(s) of this article can be found under <https://doi.org/10.1002/adsu.202100391>.

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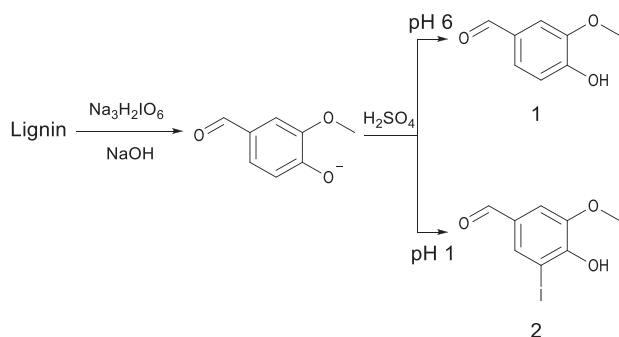
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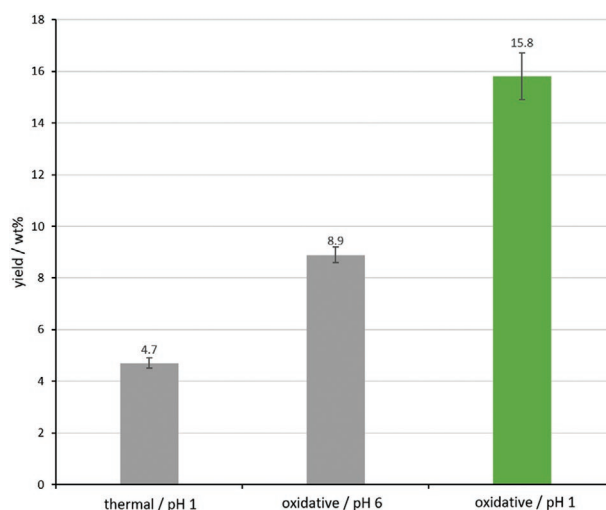
**Scheme 1.** Selective one-pot degradation of liginosulfonate to 5-iodovanillin by electrochemically generated periodate as the oxidizing and iodination agent. Other organic products were not observed.

## 2. Results and Discussion

An innovative, sustainable method for the preparation of vanillin (1) or 5-iodovanillin (2) directly from different types of lignin has been developed. Control of selectivity over the product is achieved by the workup. The reaction is carried out in a simple autoclave (Figure S3, Supporting Information), which allows working in aqueous media at temperatures above 100 °C and up to 5 bar. By using this simple setup, iodovanillin (2) can be produced from several types of lignin in high selectivity. Liginosulfonate was chosen as model compound for screening of suitable conditions. Liginosulfonate is degraded oxidatively by periodate and simultaneously heated up to 160 °C in 2 M caustic soda. After the thermal and oxidative degradation, 5-iodovanillin (2) was detected as the dominant low molecular weight product. In comparison to the thermal degradation under alkaline conditions and subsequent addition of periodate, vanillin was the only observed product. For this reason, it was assumable, that the formation of 5-iodovanillin (2) occurs during workup. Indeed, in a comparative study it has been shown, that the treated lignin undergoes a selective formation of vanillin when brought to neutral/ weak acidic pH and the formation of 2 is observed when crude reaction mixture is acidified to pH 1 (Scheme 2). Nevertheless, when periodate was used for the degradation of liginosulfonate a twofold increase on vanillin (1) yield was observed, which shows the significant positive impact of periodate on the oxidative degradation (Figure 1). For all experiments the same electrochemically generated periodate was used. The production of periodate has already been published.<sup>[20]</sup> Changing parameters in the electrochemical treatment would decrease the periodate yield, but will



**Scheme 2.** pH dependent lignin degradation to achieve either vanillin (1) or iodovanillin (2). pH decreases by acidifying with conc. H<sub>2</sub>SO<sub>4</sub>



**Figure 1.** Comparison between the thermal degradation of liginosulfonate and the addition of periodate treated at different pH/conditions.

not affect its structure or the selective degradation of lignin. To determine the vanillin content, the nitrobenzene oxidation was performed on three different types of lignin (Table 1).

A vanillin yield of 83% was achieved when compared to the nitrobenzene oxidation.

Liginosulfonate showed the highest yield. Due to this fact, the process was optimized using liginosulfonate.

Optimization was carried out using a Design of Experiments approach.<sup>[30]</sup> An investigation of five different parameters was conducted, namely: the degradation temperature, reaction time, concentration of caustic soda, mass concentration of lignin, and mass equivalents of periodate. Previous studies have shown that the temperature plays a crucial role in lignin depolymerization. Increasing the temperature from 120 to 190 °C resulted in a higher iodovanillin yield. Nevertheless, 170 °C was the limit for a suitable process. Beyond 170 °C the yield decreased, because of undefined side reactions. The reaction time between 6 and 18 h had a huge influence onto the yield. Increasing the reaction time from 18 to 24 h could improve the iodovanillin yield slightly. High caustic soda concentration decreased the iodovanillin yield. Nevertheless, the impact of 0.5–2 M was low and the optimum was 2 M caustic soda. After the second round of optimization, the lignin concentration did not influence the yield. High periodate equivalents resulted in low iodovanillin yield. Decreasing the periodate equivalents prevent the building of precipitation in the workup. The best conditions were found with a degradation temperature of 160 °C, 24 h reaction time in a 2 M caustic soda with 250 mg liginosulfonate and the

**Table 1.** Yield of vanillin after the nitrobenzene oxidation.

Type of lignin	Vanillin (1) <sup>a)</sup>
Liginosulfonate	10.7 wt%
Kraft lignin	9.2 wt%
Organosolv lignin	4.9 wt%

<sup>a)</sup>The yield of 1 is related to the amount of starting material and was determined by GC with *n*-dodecylbenzene as internal standard.

**Table 2.** Optimized reaction conditions carried out of a Design of Experiments.

Degradation temperature <sup>a)</sup>	Reaction time	Caustic soda concentration	Mass concentration of lignin	Mass periodate
160 °C	24 h	2 M	250 mg	250 mg

<sup>a)</sup>The established reaction conditions for the periodate treatment of lignosulfonate were applied to different types of lignin (Table 3) and compared to nitrobenzene oxidation (see the supporting Information for further details).

same amount of periodate resulting in 15.8 wt% iodovanillin (Table 2).

The degradation enabled a good yield of iodovanillin for all different types of lignin. The highest amount of iodovanillin (**2**) was observed for the lignosulfonate with 15.8 wt%. The yield was determined by GC using an internal standard. No other by-products were observed (Figure 2). Therefore, only 5-iodovanillin is the target product out of the periodate oxidation.

Upon purification via column chromatography, a yield of 14.7 wt% 5-iodovanillin (**2**) was achieved from lignosulfonate. Considering the pH dependency of the described method the maximum yield of vanillin out of the nitrobenzene oxidation was compared with the iodovanillin yield. The established yield corresponds to 75% of the nitrobenzene oxidation.

To monitor structural changes during the periodate oxidation, the lignosulfonate was investigated via Fourier transform infrared spectroscopy (FT-IR) before and after oxidation (see the Supporting Information for more details). The results are depicted for the lignosulfonate. The IR spectrum of the lignosulfonate (Figure 3) does not exhibit the characteristic bands of syringyl units (1326, 1117, and 843 cm<sup>-1</sup>) but the bands of guaiacyl units (1506, 1269, and 1140 cm<sup>-1</sup>).<sup>[15]</sup> In the oxidized lignosulfonate (black), the bands at 1506, 1456, and 1416 cm<sup>-1</sup> (aromatic ring of lignin) significantly decrease.<sup>[31]</sup> The characteristic band for the SO<sub>3</sub>H group at 1032 cm<sup>-1</sup> disappears after the oxidation with periodate.<sup>[32]</sup> This indicates an effective degradation of lignosulfonate, which was also found in the quantitative studies shown in Table 3.

To determine the iodine content, inductively coupled plasma optical emission spectroscopy (ICP-OES) measurements were performed on the remaining lignosulfonate upon oxidation (see the Supporting Information for more details). The iodine

**Table 3.** Yield of 5-iodovanillin after the periodate oxidation on different lignins with the optimized conditions shown in Table 2.

Type of lignin	5-Iodovanillin ( <b>2</b> ) <sup>a)</sup>
Lignosulfonate	15.8 wt%
Kraft lignin	9.5 wt%
Organosolv lignin	3.1 wt%

<sup>a)</sup>The yield of **2** is related to the amount of starting material and was determined by GC with *n*-hexadecane as internal standard.

of used periodate (0.85 mmol) is included in iodovanillin (**2**, 17%, 0.14 mmol) and in the remaining lignosulfonate (2%, 0.02 mmol). The remaining iodine species (81%, 0.69 mmol) are not included in the product and lignosulfonate remain as inorganic iodine species (I<sup>-</sup>, IO<sub>3</sub><sup>-</sup>, I<sub>2</sub>).

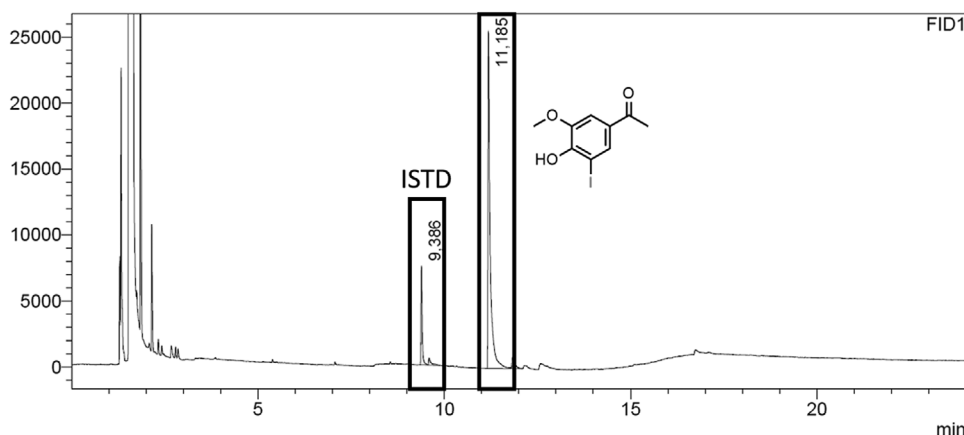
The iodine content in the remaining lignosulfonate is 2.5 wt%.

### 3. Conclusion

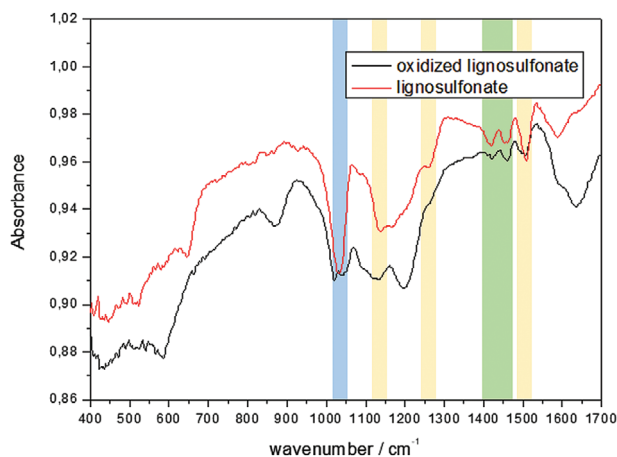
We successfully implemented the periodate oxidation at elevated temperatures for technical lignins. 5-Iodovanillin was obtained with high selectivity, yield of up to 15.8 wt%. FT-IR studies emphasized the effective periodate degradation of the respective lignosulfonate as a significant decrease in sulfonate and G-units substructures changes. Also, the remaining lignin shows a new iodinated substitution determined by ICP-OES measurements. Remaining lignosulfonate has more than 2 wt% iodine. This structural change in the oxidized lignosulfonate opens up new applications.

### 4. Experimental Section

**Oxidation Process:** 250 mg lignosulfonate was dissolved in aqueous caustic soda (1–3 M, 50 mL) under vigorous stirring. Periodate (1–4 mass equivalents of lignosulfonate) was added. The solution was transferred into the autoclave (see the Supporting Information for more details); the cell was sealed and stirred at different temperatures (100–190 °C) for 5–24 h. The reactor was not pressurized externally. After the reaction was stopped, the reaction mixture was allowed to cool



**Figure 2.** Gas chromatogram of crude mixture after the periodate oxidation of lignosulfonate. ISTD: *n*-hexadecane.



**Figure 3.** Spectra of lignosulfonate before and after treatment with periodate characterized via FT-IR. Characteristic bands for guaiacyl units are assigned in yellow, aromatic rings of lignin green, and the  $\text{SO}_3\text{H}$  group blue.

(room temperature), and the pH of the reaction mixture was adjusted to pH 1 by addition of  $\text{H}_2\text{SO}_4$ . The aqueous layer was extracted with ethyl acetate ( $3 \times 150$  mL). The combined organic fractions were washed with saturated brine (30 mL) and dried over anhydrous magnesium sulfate followed by solvent removal under reduced pressure. The organic residue was dissolved in 8 mL ethyl acetate, 2  $\mu\text{L}$  of the internal standard *n*-hexadecane were added, and the sample was analyzed via GC/GC-MS.

**ICP-OES:** To determine the amount of iodine in the remaining lignosulfonate dialysis a ICP-OES measurement was performed. For the dialysis, the sample was put into a prewetted RC tubing dialysis Membrane (MWCO: 2 kD,  $\varnothing$  29 mm). After 1 week the sample was freeze-dried to remove the water. A precisely defined amount was weighed into a volumetric flask and solved in 100 mL of Milli-Q water. For the calibration a precisely defined amount of potassium iodide was weighed into a volumetric flask and solved in 100 mL of Milli-Q water, then a serial dilution was performed (see the Supporting Information for more information).

## Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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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 in the supplementary material of this article.

## Keywords

5-iodovanillin, lignin, oxidation, periodate, sustainable chemistry

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- [1] C. Chio, M. Sain, W. Qin, *Renewable Sustainable Energy Rev.* **2019**, *107*, 232.
- [2] D. Klemm, B. Heublein, H.-P. Fink, A. Bohn, *Angew. Chem.* **2005**, *44*, 3422; *Angew. Chem., Int. Ed.* **2005**, *44*, 3358.
- [3] R. Rinaldi, R. Jastrzebski, M. T. Clough, J. Ralph, M. Kennema, P. C. A. Bruijninx, B. M. Weckhuysen, *Angew. Chem.* **2016**, *128*, 8296; *Angew. Chem., Int. Ed.* **2016**, *55*, 8164.
- [4] M. Zirbes, L. L. Quadri, M. Breiner, A. Stenglein, A. Bomm, W. Schade, S. R. Waldvogel, *ACS Sustainable Chem. Eng.* **2020**, *8*, 7300.
- [5] R. L. Howard, E. Abotsi, R. E. L. van Jansen, S. Howard, *Afr. J. Biotechnol.* **2003**, *2*, 602.
- [6] M. D. Kärkäs, B. S. Matsuura, T. M. Monos, G. Magallanes, C. R. J. Stephenson, *Org. Biomol. Chem.* **2016**, *14*, 1853.
- [7] B. E. Dale, *J. Chem. Technol. Biotechnol.* **2003**, *78*, 1093.
- [8] F. G. Calvo-Flores, J. A. Dobado, *ChemSusChem* **2010**, *3*, 1227.
- [9] Z. Sun, B. Fridrich, A. de Santi, S. Elangovan, K. Barta, *Chem. Rev.* **2018**, *118*, 614.
- [10] C. Crestini, H. Lange, M. Sette, D. S. Argyropoulos, *Green Chem.* **2017**, *19*, 4104.
- [11] N. Mahmood, Z. Yuan, J. Schmidt, C. C. Xu, *Bioresour. Technol.* **2013**, *139*, 13.
- [12] T. Aro, P. Fatehi, *ChemSusChem* **2017**, *10*, 1861.
- [13] a) S. Constant, H. L. J. Wienk, A. E. Frissen, P. d. Peinder, R. Boelens, D. S. van Es, R. J. H. Grisel, B. M. Weckhuysen, W. J. J. Huijgen, R. J. A. Gosselink, P. C. A. Bruijninx, *Green Chem.* **2016**, *18*, 2651; b) C. Li, X. Zhao, A. Wang, G. W. Huber, T. Zhang, *Chem. Rev.* **2015**, *115*, 11559; c) C. Yang, S. Maldonado, C. R. J. Stephenson, *ACS Catal.* **2021**, *1*, 10104.
- [14] M. Zirbes, S. R. Waldvogel, *Curr. Opin. Green Sustainable Chem.* **2018**, *14*, 19.
- [15] a) F. A. Riyadi, A. A. Tahir, N. Yusof, N. S. A. Sabri, M. J. M. M. Noor, F. N. M. D. Akhir, N.'a. Othman, Z. Zakaria, H. Hara, *Sci. Rep.* **2020**, *10*, 7813; b) M. Ahmad, J. N. Roberts, E. M. Hardiman, R. Singh, L. D. Eltis, T. D. H. Bugg, *Biochemistry* **2011**, *50*, 5096; c) P. D. Sainsbury, Y. Mineyeva, Z. Mycroft, T. D. H. Bugg, *Bioorg. Chem.* **2015**, *60*, 102.
- [16] a) Q. Song, F. Wang, J. Xu, *Chem. Commun.* **2012**, *48*, 7019; b) K. Chen, M. Cao, C. Ding, X. Zheng, *RSC Adv.* **2018**, *8*, 26782.
- [17] a) M. Breiner, M. Zirbes, S. R. Waldvogel, *Green Chem.* **2021**, *23*, 6449; b) M. Zirbes, D. Schmitt, N. Beiser, D. Pitton, T. Hoffmann, S. R. Waldvogel, *ChemElectroChem* **2019**, *6*, 155; c) D. Schmitt, C. Regenbrecht, M. Schubert, D. Schollmeyer, S. R. Waldvogel, *Holzforchung* **2017**, *71*, 35; d) D. Schmitt, C. Regenbrecht, M. Hartmer, F. Stecker, S. R. Waldvogel, *Beilstein J. Org. Chem.* **2015**, *11*, 473; e) S. Waldvogel, M. Zirbes, R. Neuber, T. Matthée, WO 2020099350 A1 20200522, **2020**.
- [18] a) J. Seidler, J. Strugatchi, T. Gärtner, S. R. Waldvogel, *MRS Energy Sustainability* **2020**, *7*, E42; b) S. B. Beil, D. Pollok, S. R. Waldvogel, *Angew. Chem.* **2021**, *60*, 14750; *Angew. Chem. Int. Ed.* **2021**, *60*, 14750; c) S. R. Waldvogel, B. Janza, *Angew. Chem.* **2014**, *126*, 7248; *Angew. Chem., Int. Ed.* **2014**, *53*, 7122; d) D. Pollok, S. R. Waldvogel, *Chem. Sci.* **2020**, *11*, 12386.
- [19] a) A. Wiebe, T. Gieshoff, S. Möhle, E. Rodrigo, M. Zirbes, S. R. Waldvogel, *Angew. Chem.* **2018**, *130*, 5694; *Angew. Chem., Int.*

- Ed. **2018**, 130, 5594; b) S. Möhle, M. Zirbes, E. Rodrigo, T. Gieshoff, A. Wiebe, S. R. Waldvogel, *Angew. Chem.* **2018**, 57, 6124; *Angew. Chem., Int. Ed.* **2018**, 57, 6018; c) M. Yan, Y. Kawamata, P. S. Baran, *Chem. Rev.* **2017**, 117, 13230; d) K. D. Moeller, *Chem. Rev.* **2018**, 118, 4817; e) S. R. Waldvogel, S. Lips, M. Selt, B. Riehl, C. J. Kampf, *Chem. Rev.* **2018**, 118, 6706; f) J. L. Röckl, D. Pollok, R. Franke, S. R. Waldvogel, *Acc. Chem. Res.* **2020**, 53, 45; g) A. Wiebe, T. Gieshoff, S. Möhle, E. Rodrigo, M. Zirbes, S. R. Waldvogel, *Angew. Chem.* **2018**, 130, 5694; *Angew. Chem., Int. Ed.* **2018**, 57, 5594; h) R. Francke, *Curr. Opin. Electrochem.* **2019**, 15, 83.
- [20] S. Arndt, D. Weis, K. Donsbach, S. R. Waldvogel, *Angew. Chem.* **2020**, 132, 8112; *Angew. Chem., Int. Ed.* **2020**, 59, 8036.
- [21] a) J. D. Herszman, M. Berger, S. R. Waldvogel, *Org. Lett.* **2019**, 21, 7893; b) J. D. Haupt, M. Berger, S. R. Waldvogel, *Org. Lett.* **2019**, 21, 242.
- [22] D. R. Abernethy, A. J. Destefano, T. L. Cecil, K. Zaidi, R. L. Williams, *Pharm. Res.* **2010**, 27, 750.
- [23] S. Lips, S. R. Waldvogel, *ChemElectroChem* **2019**, 6, 1649.
- [24] S. Arndt, B. Grill, H. Schwab, G. Steinkellner, U. Pogorečnik, D. Weis, A. M. Nauth, K. Gruber, T. Opatz, K. Donsbach, S. R. Waldvogel, *Green Chem.* **2021**, 23, 388.
- [25] a) R. C. Larock, *J. Organomet. Chem.* **1999**, 576, 111; b) E. Awuah, A. Capretta, *Org. Lett.* **2009**, 11, 3210; c) G. Bringmann, R. Walter, R. Weirich, *Angew. Chem.* **1990**, 102, 1006; *Angew. Chem., Int. Ed.* **1990**, 29, 977; d) M. A. Rizzacasa, M. V. Sargent, *Aust. J. Chem.* **1988**, 41, 1087; e) F. Coelho, W. P. Almeida, D. Veronese, C. R. Mateus, E. C. Silva Lopes, R. C. Rossi, G. P. C. Silveira, C. H. Pavam, *Tetrahedron* **2002**, 58, 7437.
- [26] G. E. Schneiders, R. Stevenson, *J. Org. Chem.* **1981**, 46, 2969.
- [27] a) C. Nitsche, C. Steuer, C. D. Klein, *Bioorg. Med. Chem.* **2011**, 19, 7318; b) F. Zouhiri, J. F. Mouscadet, K. Mekouar, D. Desmaële, D. Savouré, H. Leh, F. Subra, M. L. e Bret, C. Auclair, J. d'Angelo, *J. Med. Chem.* **2000**, 43, 1533; c) M. J. Hearn, M. H. Cynamon, M. F. Chen, R. Coppins, J. Davis, H. Joo-On Kang, A. Noble, B. Tu-Sekine, M. S. Terrot, D. Trombino, M. Thai, E. Webster, R. Wilson, *Eur. J. Med. Chem.* **2009**, 44, 4169; d) E. K. Ryu, Y. S. Choe, K.-H. Lee, Y. Choi, B.-T. Kim, *J. Med. Chem.* **2006**, 49, 6111.
- [28] a) G. Varró, L. Hegedűs, A. Simon, I. Kádás, *Tetrahedron Lett.* **2016**, 57, 1544; b) C. G. Yeh, G. J. Dow, R. W. Lathrop, M. S. Chorghade, A. V. R. Rao, US2003/8914 A1, **2003**.
- [29] a) J. Luo, P. Melissa, W. Zhao, Z. Wang, Y. Zhu, *ChemistrySelect* **2016**, 1, 4596; b) R. Sun, J. M. Lawther, W. B. Banks, *Ind. Crops Prod.* **1995**, 4, 241; c) Y. Wang, S. Sun, F. Li, X. Cao, R. Sun, *Ind. Crops Prod.* **2018**, 116, 116.
- [30] M. Dörr, M. M. Hielscher, J. Proppe, S. R. Waldvogel, *ChemElectroChem* **2021**, 8, 2621.
- [31] a) C. G. Boeriu, D. Bravo, R. J. A. Gosselink, J. E. G. van Dam, *Ind. Crops Prod.* **2004**, 20, 205; b) I. A. Palamarchuk, O. S. Brovko, K. G. Bogolitsyn, T. A. Boitsova, A. V. Ladesov, A. D. Ivakhnov, *Russ. J. Appl. Chem.* **2015**, 88, 103.
- [32] D. Lee, *Molecules* **2013**, 18, 8168.