doi.org/10.1002/hlca.202500068

RESEARCH ARTICLE

HELVETICA chimica acta

A Simplified Approach for Electrochemical Allylic Oxidation of Olefins

Kamil Hofman,[a] Johannes Schneider,[a] Roman Goy,[b] Jan Schütz,[b] Werner Bonrath,[b]
and Siegfried R. Waldvogel*[c, d]

[a] Department of Chemistry, Johannes Gutenberg University (JGU), Duesbergweg 10-14, Mainz 55128, Germany
[b] dsm-firmenich AG, Wurmisweg 576, Kaiseraugst CH-4303, Switzerland
[c] Institute of Biological and Chemical Systems – Functional Molecular Systems (IBCS–FMS), Karlsruhe Institute of Technology (KIT), Kaiserstraße 12, Karlsruhe 76131, Germany, e-mail: siegfried.waldvogel@cec.mpg.de
[d] Max-Planck-Institute for Chemical Energy Conversion (MPI CEC), Stiftstraße 34-36, Mülheim an der Ruhr 45470, Germany

---

A simple method for the electrochemical allylic oxidation of olefins to enones based on peroxide-mediated C–H activation is presented. *t*-Butyl hydroperoxide serves a dual role as mediator and oxygen source, avoiding the utilization of expensive transition metal catalysts, potentially explosive supporting electrolytes such as perchlorates, or additional environmentally harmful mediators. This elegant methodology allows for an operationally simple and sustainable late-stage transformation of delicate natural compounds such as terpenes or steroids into highly value-added building blocks. Such an approach provides a greener alternative to conventional oxidation methods used for industrial applications. In total, 25 examples are demonstrated with isolated yields up to 80%. The robust scalability of the method was also demonstrated, and chromatography could be avoided in scale-up simply by using recrystallization, which decreases the cost of downstream processing.

Keywords: allylic oxidation, electrolysis, enones, natural products, sustainability

---

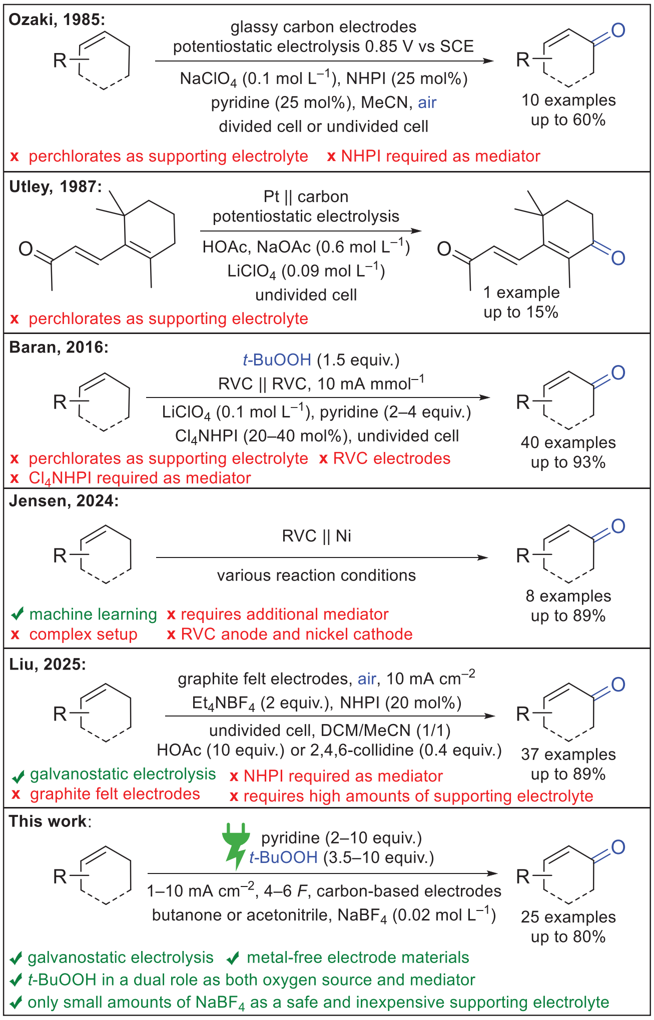
1. Introduction

The direct allylic oxidation of olefins by C–H activation is a principal method to access value-added α,β-unsaturated ketone motifs in fine chemicals,[1] highly interesting building blocks (e.g., 7-ketocholesterol),[2] flavor compounds and fragrances,[3] as well as pharmaceuticals.[4–5] The conventional methods[6–7] feature the use of toxic or expensive transition metals,[8–16] excess oxidizers,[17–18] (photo-)catalysts,[19–21] or enzymes.[22–25] However, these approaches are often less attractive for industrial applications because of complicated reaction setups, unfavorable atom economy, and overall low efficiency. Organic electrosynthesis provides a more sustainable methodology to achieve these transformations.[26] One of the many advantages of electrochemistry is the direct use of electricity as a comparably inexpensive and universal redox agent – which can originate from renewable energy sources – avoiding additional oxidizers, and minimizing costs, CO_2 footprint, and reagent waste.[27–28]

Despite the fact that electro-organic synthesis is currently experiencing an ongoing renaissance,[34–41] electrochemical approaches for allylic oxidations to provide α,β-unsaturated ketones have been rarely described in the literature until recently (Scheme 1). The first method was reported in 1985 by Ozaki et al. using *N*-hydroxyphthalimide (NHPI) as mediator in the presence of molecular oxygen and $NaClO_4$ as supporting electrolyte in a potentiostatic electrolysis setup.[29] In this

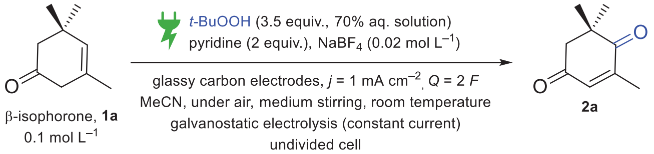
---

Supporting information for this article is available on the WWW under https://doi.org/10.1002/hlca.202500068



Scheme 1. Overview of electrochemical allylic oxidation reactions.[29–33]

work, only a limited number of 10 substrates were tested with isolated yields up to 60%. Another method was subsequently established by Utley et al. for the allylic oxidation of β-ionone.[30] By using platinum anodes and water as a nucleophile, the corresponding 4-oxo-β-ionone was obtained in 15% yield. In addition to their limited scope and rather sophisticated setups, these methods utilize various perchlorates as potentially explosive supporting electrolytes, and brittle or expensive electrode materials, making them unsuitable for larger technical applications. Based on this groundwork, Baran et al. reported an improved method in 2016.[31] Despite the usefulness of their work, it requires brittle reticulated vitreous carbon (RVC) electrodes,[42] tetrachloro-*N*-hydroxylphthalimide (Cl_4NHPI) as a rather unusual and environmentally critical mediator,[43–44] and $NaClO_4$ as a potentially explosive supporting electrolyte as well.[45]



Scheme 2. The standard reaction conditions of the test reaction used for optimization. Note that no care must be taken to exclude moisture because *t*-BuOOH is added as an aqueous solution anyways. More information about the experimental setup can be found in the Supporting Information.

Also recently, an interesting approach was published in 2024 by Jensen et al., which uses machine learning to optimize the reaction conditions already published in the literature.[32] Another method was recently developed in 2025 by Liu et al.,[33] which further develops the approach by the group of Ozaki, utilizing air as an inexpensive oxidizer. While this protocol is interesting, and it does not rely on perchlorates, it requires many equivalents of supporting electrolyte and NHPI as a mediator as well.

Here, we present a simplified method for electrochemical allylic oxidation using *t*-BuOOH in a dual role as mediator and oxygen source.[46] Acetonitrile or butanone can be chosen as the solvent, and pyridine is used as an (electro)chemically stable base. Glassy carbon, boron-doped diamond (BDD), or graphite can be employed as metal-free electrode materials. $NaBF_4$ is used as a safe, inexpensive, and inert supporting electrolyte, which is required in only very small concentrations. This approach simplifies downstream processing and provides a more attractive and greener protocol compared with the previously mentioned ones. Moreover, the method established here also features the valorization of biogenic substrates such as terpenes and biologically active steroid derivatives to the desired enones, which makes this approach particularly attractive for industrial and interdisciplinary applications.

2. Results and Discussion

For reaction optimization, β-isophorone **1a** was chosen as test substrate due to its established role in the synthesis of 4-oxoisophorone **2a**, which serves as a building block in the production of tocopherols and carotenoids like astaxanthin.[47–48] The reactions were performed in small Teflon cells,[49–52] which have proven to be very successful in our group (see Supporting Information).[53–56] The standard reaction conditions are depicted in Scheme 2. The yield and selec-

Table 1. Optimization of the test reaction.

#	Deviation from Standard Reaction Conditions[a]	Yield% (Selectivity%)[b]
1	None	35 (55)
2	NEt_4BF_4 instead of $NaBF_4$	39 (60)
3	NBu_4PF_6 instead of $NaBF_4$	33 (50)
4	NBu_4HSO_4 instead of $NaBF_4$	29 (62)
5	ethyl acetate instead of MeCN[c]	44 (58)
6	ethanol instead of MeCN	20 (30)
7	acetone instead of MeCN (1.8 *F*)[d]	37 (50)
8	butanone instead of MeCN	39 (59)
9	5 equiv pyridine, 10 equiv *t*-BuOOH, 10 mA cm^{-2}, 4 *F*	36 (51)
10	5 equiv pyridine, 10 equiv *t*-BuOOH, 10 mA cm^{-2}, 4 *F*, $c(1a) = 0.2$ mol L^{-1}	51 (70)
11	10 equiv pyridine, 10 equiv *t*-BuOOH, 10 mA cm^{-2}, 4 *F*, $c(1a) = 0.2$ mol L^{-1}	62 (84)
12	10 equiv pyridine, 10 equiv *t*-BuOOH, 10 mA cm^{-2}, 4 *F*, $c(1a) = 0.2$ mol L^{-1}, BDD electrodes	45 (62)
13	10 equiv pyridine, 10 equiv *t*-BuOOH, 10 mA cm^{-2}, 4 *F*, $c(1a) = 0.2$ mol $L^{-1,}$ butanone instead of MeCN	62 (90)
14	10 equiv pyridine, 10 equiv *t*-BuOOH, 10 mA cm^{-2}, 4 *F*, $c(1a) = 0.3$ mol L^{-1}, butanone instead of MeCN	56 (81)
15	10 equiv pyridine, 10 equiv *t*-BuOOH, 10 mA cm^{-2}, 4 *F*, $c(1a) = 0.2$ mol L^{-1}, butanone instead of MeCN, BDD electrodes	44 (58)
16	10 equiv pyridine, 10 equiv *t*-BuOOH, 10 mA cm^{-2}, 4 *F*, $c(1a) = 0.2$ mol L^{-1}, butanone instead of MeCN, graphite electrodes	49 (71)
17	no electricity	0 (–)

[a] The standard reaction conditions are depicted in Scheme 2.
[b] The yield and selectivity (= yield / conversion) were determined using ^1H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.
[c] The upper terminal voltage limit of the power supply was reached during electrolysis, but the desired amount of charge could be fully applied.
[d] The upper terminal voltage limit of the power supply was reached during electrolysis, and only the specified amount of charge could be applied.

tivity (= yield / conversion) was determined using ^1H NMR spectroscopy with 1,3,5-trimethoxybenzene as the internal standard.[57] The standard reaction conditions (Scheme 2 and Table 1, entry 1) gave **2a** in 35% yield and 55% selectivity. To our delight, all subsequent optimization reactions could be carried out with such a small concentration of supporting electrolyte (only 0.02 mol L^{-1}), which simplifies downstream processing.

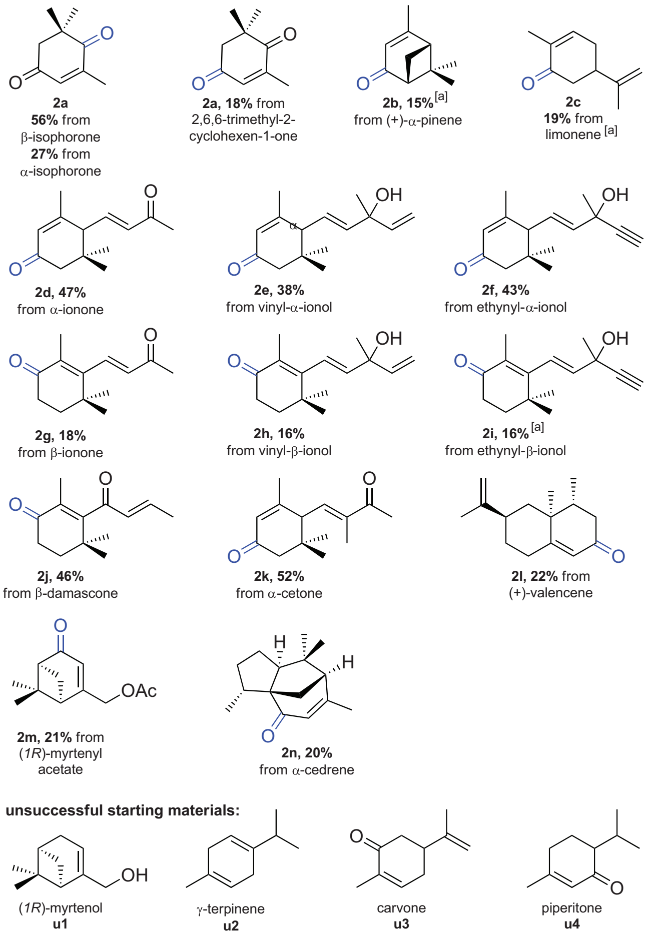
Testing other supporting electrolytes such as NEt_4BF_4, NBu_4PF_6, or NBu_4HSO_4 (Table 1, entries 2–4) gave no noteworthy increase in yield or selectivity. To simplify downstream processing, and to decrease cost, subsequent optimization reactions were continued using $NaBF_4$. Next, different solvents were tested. For ethyl acetate, ethanol, and acetone, yields of 44%, 20%, and 37% were obtained, respectively (entries 5–7). For ethyl acetate and acetone however, the upper terminal voltage limit was reached during electrolysis. In the case of ethyl acetate, the full 2 *F* could be applied, while the electrolysis came to an end after 1.8 *F* when acetone was used as the solvent. In general, high cell voltages cause high power consumption, meaning ethyl acetate and acetone were not further tested in optimization reactions. Since the yield was low as well when using ethanol as solvent, it was not tested further either. Butanone was also tested and gave 39% yield (entry 8). The objective of the optimization was not only to improve the yield and to investigate the selectivity, but also to increase the productivity by increasing the current density, which shortens the electrolysis time. Therefore, a current density of 10 mA cm^{-2} was tested in combination with an increase of equivalents of pyridine and *t*-BuOOH and an increase of applied charge to 4 *F*, which did not result in a significant increase in yield or selectivity (entry 9). Using the same reaction conditions as entry 9 but increasing the concentration of the starting material to 0.2 mol L^{-1} gave an increase in yield to 51% with a selectivity of 70% (entry 10). Repeating the experiment from entry 10 with more pyridine (entry 11) gave 62% yield with a selectivity of 84%. While these reaction conditions require more equivalents of pyridine and *t*-BuOOH and more applied charge, they allow for an increased productivity by using a higher current density and a higher concentration of starting material. The reaction conditions of entry 11 were used again with boron-doped diamond electrodes instead of glassy carbon,[58] which gave 45% yield (entry 12). Next, optimization was refined using butanone as solvent, because the scope of our work also includes steroids, for which butanone is a better solvent than MeCN. The use of butanone instead of acetonitrile does not complicate downstream processing, because both solvents can easily be removed by distillation after electrolysis. Using 10 equivalents of pyridine and *t*-BuOOH, 4 *F*, and 10 mA cm^{-2}, the product was obtained in 62% yield with 90% selectivity (entry 13). Using these reaction conditions from entry 13 but increasing the current density to 10 mA cm^{-2} and increasing the concentration of the starting material to 0.3 mol L^{-1} resulted in a yield of 56% with 81% selectivity (entry 14).

Based on these results, two optimization experiments using BDD electrodes (entry 15) and graphite electrodes (entry 16) were carried out, which gave 44% and 49% yield, respectively. This demonstrates that boron-doped diamond or graphite can be employed as an alternative to glassy carbon electrodes. Since all electrode materials which were tested are metal-free, this method is interesting for applications in medicinal chemistry, which is very reluctant about traces of transition metals.[59] Without electricity, no product could be found (entry 17).

2.1. Scope

Several substrates have been tested, as depicted in the following Scheme 3. The allylic oxidation product 4-oxoisophorone **2a** can be obtained from different starting materials, as will be later explained in the mechanism section. The numbering of starting materials and products is explained in the Supporting Information. In all schemes, the newly installed oxo functions are indicated in blue. Using β-isophorone or α-isophorone, product **2a** is obtained in 56% and 27%, respectively. With 2,6,6-trimethyl-2-cyclohexen-1-one as starting material, **2a** is isolated in 18% yield. Using (+)-α-pinene as starting material, product **2b** could be isolated in 15% yield, and for limonene, **2c** was obtained in 19% yield. One reason for the low yield of **2c** could be oxidation reactions at the exocyclic double bond. The Starting materials α-ionone, vinyl-α-ionol, and ethynyl-α-ionol gave products **2d**, **2e**, and **2f** in 47%, 38%, and 43% isolated yield, respectively. For β-ionone **2g**, vinyl-β-ionol **2h**, and ethynyl-β-ionol **2i**, overall lower yields of only 18%, 16%, and 16% were obtained. Higher yields than those were obtained for β-damascone and α-cetone, which gave the corresponding allylic oxidation products **2j** and **2k** in 46% and 52%. Using (+)-valencene, a yield of 22% was found for nootkatone **2l**. Myrtenyl acetate gave **2m** in 21% yield. From α-cedrene, **2n** was obtained in 20% yield. The low yield of product **2b**, **2m**, and **2n** could be due to the steric hindrance of the bridging CH_2 group, or its influence on the stability of the allylic radical intermediate.

The allylic oxidation of some substrates was unsuccessful. For example, while myrtenyl acetate could undergo allylic oxidation to product **2m** successfully, the corresponding unprotected starting material myrtenol **u1** could not be oxidized, as no reaction product could be found. When using gamma-terpinene **u2**, no conversion was observed, and the starting material was partially recovered upon workup.

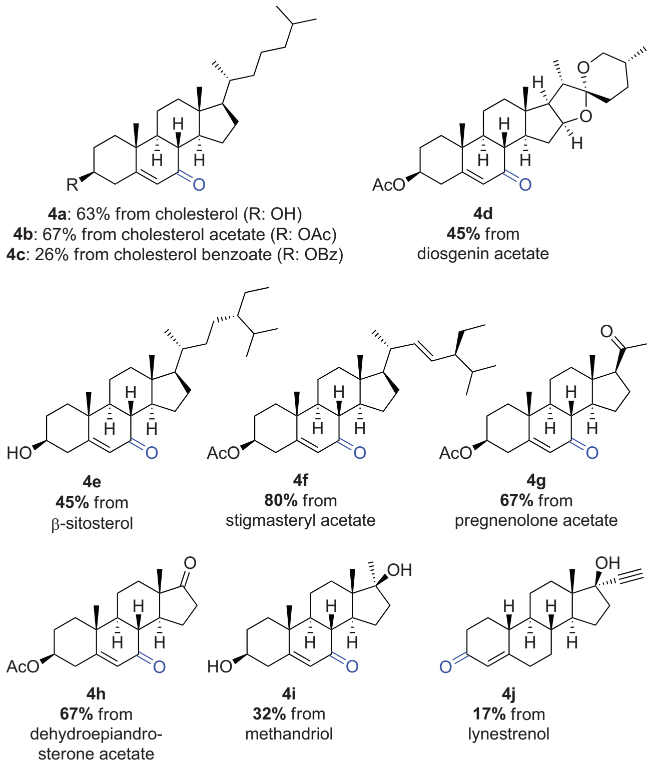


Scheme 3. Scope of transformation. Reaction conditions: starting material (0.5 mmol, 0.1 mol L^{-1}), butanone (5.0 mL), $NaBF_4$ (0.02 mol L^{-1}), amount of applied charge $Q = 4\,F$ (= 193 C for 0.5 mmol starting material), current density $j = 1$ mA cm^{-2}, *t*-BuOOH (3.5 equiv, 70% in aqueous solution), pyridine (5 equiv), glassy carbon electrodes, room temperature, undivided cell, under air, galvanostatic electrolysis (constant current). Note that no care must be taken to exclude moisture because *t*-BuOOH is an aqueous solution anyways. More details about the experimental setup can be found in the Supporting Information. [a] Using the aforementioned reaction conditions gave no product but using the following deviations from the reaction conditions was successful: MeCN instead of butanone, 2 equiv pyridine.

Using carvone **u3**, which is the product of the allylic oxidation of limonene, no further allylic oxidation could be observed either. Similarly, for piperitone **u4**, which is also already an enone, no conversion was found.

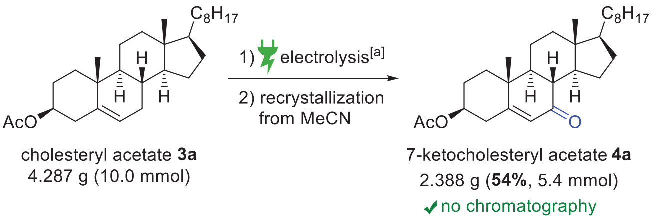
2.2. Steroids

Several steroids were also employed as substrates, as depicted in Scheme 4. From cholesterol,



Scheme 4. Scope of steroids. Reaction conditions: starting material (0.5 mmol, 0.1 mol L^{-1}), butanone (5.0 mL), NaBF$_4$ (0.02 mol L^{-1}), amount of applied charge $Q = 6\ F$ ($=$ 289 C for 0.5 mmol starting material), current density $j = 10$ mA cm^{-2}, *t*-BuOOH (10 equiv, 70% in aqueous solution), pyridine (10 equiv), glassy carbon electrodes, room temperature, undivided cell, under air, medium stirring, galvanostatic electrolysis (constant current). Note that no care must be taken to exclude moisture because *t*-BuOOH is an aqueous solution anyways. More details about the experimental setup can be found in the Supporting Information.

cholesteryl acetate, and cholesteryl benzoate, allylic oxidation products **4a**, **4b**, and **4c** were obtained in 63%, 67%, and 26%, respectively. For diosgenin acetate and *β*-sitosterol, the corresponding enones **4d** and **4e** were both obtained in 45% yield. Stigmasteryl acetate gave the highest yield of all substrates, as **4f** was obtained in 80% isolated yield. To compare this with methods reported in the literature: **4f** can be prepared by oxidation of stigmasteryl acetate with an excess of highly carcinogenic pyridinium chlorochromate (PCC) in 71% isolated yield.[60] From pregnenolone acetate, product **4g** was obtained in 67% yield, and from dehydroepiandrosterone acetate (DHEA acetate), **4h** was obtained in 67% as well. Methandriol (methylandrostenediol) and lynestrenol gave products **4i** and **4j** in lower yields of only 32% and 17%, respectively.



Scheme 5. Scale-up reaction of cholesteryl acetate (20-fold scale-up from 0.5 mmol to 10.0 mmol). [a] Electrolysis reaction conditions: *c*(starting material) $= 0.1$ mol L^{-1}, *t*-BuOOH (10 equiv), pyridine (10 equiv), NaBF$_4$ (0.02 mol L^{-1}), $j = 10$ mA cm^{-2}, $Q = 6\ F$, glassy carbon electrodes, butanone (100 mL), room temperature, undivided cell, galvanostatic electrolysis. More details about the experimental setup can be found in the Supporting Information.

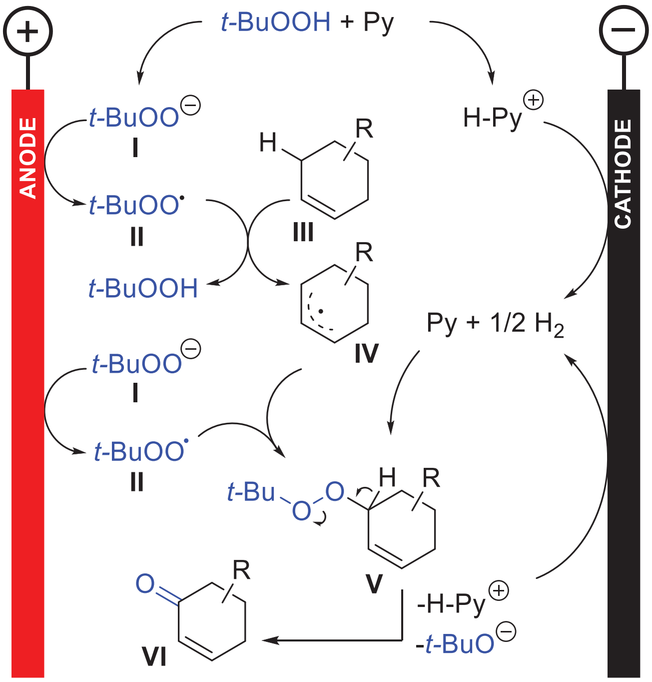
2.3. Scale-up

Demonstrating the robust scalability of an electrosynthetic method is important, because this paves the way for an application on technical scale.[61–62] Furthermore, scale-up reactions must avoid expensive and sophisticated purification techniques such as chromatography in order to be operationally simple and economically feasible. This is important because cost-efficient work-up is usually the key for the translation of electrosynthetic conversions.[63–64] Therefore, a gram-scale electrolysis of cholesteryl acetate was carried out as depicted in Scheme 5. The product 7-ketocholesteryl acetate **4a** was obtained in 54% yield. According to the ^{1}H NMR spectrum, it is 92% pure and contains 8% of the starting material cholesteryl acetate. After recrystallization, the rest of the remaining starting material stays dissolved in acetonitrile.

2.4. Reaction Mechanism

The proposed reaction mechanism is depicted in Scheme 6. Deprotonation of *t*-BuOOH by pyridine gives intermediate **I**, and its subsequent anodic oxidation results in the formation of radical **II**. This radical species undergoes hydrogen atom abstraction with olefin **III**, which results in the formation of a stabilized allylic radical **IV**. Another radical of type **II** recombines with **IV** to form intermediate **V**. Deprotonation of **V** by pyridine induces the elimination of *t*-BuO$^-$, forming the allylic oxidation product **VI**. At the cathode, hydrogen evolution is the counter reaction.[65] Pyridine proved to be essential for the success of this reaction.

In the presence of pyridine, the reduction potential of the starting material increases dramatically, and the reduction potential of *t*-BuOOH decreases, making **I** more susceptible to oxidation and decreasing the chance



Scheme 6. The proposed reaction mechanism. Py is pyridine.

of a possible direct oxidation of olefin **III** (see CV measurements in Supporting Information). In addition to that, the direct oxidation of either β-isophorone or α-isophorone via a carbocation species would lead to different isomers, proving that *t*-BuOOH serves both as a mediator and the oxygen source in the reaction. The formation of 4-oxoisophorone **2a** starting from either β-isophorone, α-isophorone, or 2,6,6-trimethyl-2-cyclohexen-1-one indicates an allylic intermediate **IV**.

3. Conclusion

A simplified method for the mediated electrochemical allylic oxidation of olefins to their corresponding enones was established. *t*-BuOOH serves a dual role as mediator and source of oxygen, which avoids the use of additional mediators such as NHPI or transition metals. Acetonitrile or butanone can be chosen as the solvent with pyridine as a base. Only very low concentrations of $NaBF_4$ are required as a safe and inexpensive supporting electrolyte, which strongly simplifies downstream processing. Glassy carbon, boron-doped diamond or graphite can be used as mechanically robust and metal-free electrode materials, making this approach predestined for applications in medicinal chemistry. The scalability of the electrolysis was demonstrated in a scale-up reaction of cholesteryl acetate, which utilized a simple recrystallization to avoid chromatography, and gave 7-ketocholesteryl acetate in 54% yield. In total, 25 examples are demonstrated with up to 80% isolated yield. This method valorizes delicate terpenes and biologically active steroidal derivatives to obtain highly value-added synthetic intermediates.

4. Experimental Section

The starting material (0.5 mmol, 0.1 mol L^{-1}) and the supporting electrolyte $NaBF_4$ (109.79 g mol^{-1}, 11 mg, 0.01 mmol, 0.02 mol L^{-1}) are dissolved in acetonitrile or butanone (5.0 mL) at room temperature in a small Teflon cell under medium stirring (500 rpm). The electrodes (1.0 cm x 7.0 cm x 0.3 cm) are assembled and put into the cell so that both electrodes have an immersion depth of 2.0 cm into the reaction solution. To prevent solvent evaporation, the assembled electrolysis cell is sealed with some stretch film (Parafilm). Pyridine (2.0 equiv, 1.0 mmol, 0.08 mL, 79.10 g mol^{-1}) and *t*-BuOOH (70% aqueous solution, 3.5 equiv, 1.75 mmol, 0.24 mL, 90.12 g mol^{-1}) are added through the top of the electrode holder using a syringe. Under continued medium stirring at room temperature, the electrolysis is started (current density $j = 1.0$ mA cm^{-2}, amount of applied charge $Q = 4\ F$). To determine NMR yield, 1,3,5-trimethoxybenzene (168.19 g mol^{-1}, 1.0 mL of a stock solution of 2.1001 g in 250.0 mL MeCN, 8.4 mg, 0.05 mmol) is added after electrolysis. The reaction solution is transferred into a round bottom flask, and the solvents are removed by distillation at reduced pressure using a rotary evaporator (40 °C water bath, 50 mbar, 10 min). The residue is dissolved in $CDCl_3$ (0.5 mL), and a ^1H NMR spectrum is measured. To isolate the product, the reaction solution is transferred into a round bottom flask, and the solvents are removed using a rotary evaporator under reduced pressure (40 °C water bath, 50 mbar, 10 min). The residue is transferred into a separatory funnel using a saturated aqueous solution of $NaHCO_3$ (30 mL). The round bottom flask is rinsed once with ethyl acetate (30 mL), which is also added to the separatory funnel. After mixing and separation of the ethyl acetate layer, the aqueous layer is extracted with ethyl acetate twice more (2 × 30 mL). The combined ethyl acetate fractions are dried over $MgSO_4$ (10 g), and the solution is filtered. The solvent was removed from the filtrate by distillation using a rotary evaporator at reduced pressure (40 °C water bath, 50 mbar, 10 min). The crude residue is dissolved in ethyl acetate again (5 mL) and adsorbed on Celite 545 (10 g). Depending on the substrate, either cyclohexane with ethyl acetate (normal phase) or water and acetonitrile (reversed phase) (linear gradient: 100:0 → 95:5 in 10 column volumes) is used for flash column chromatography.

Supporting Information

The authors have cited additional references within the Supporting Information.[66–81]

Acknowledgements

The authors gratefully acknowledge the financial support by dsm-firmenich AG. Benjamin R. Strücker is acknowledged for reaction optimization. Kamil Hofman would like to thank J. Nikl and L. G. Gombos for helpful discussions. The authors thank the MPG for the open access opportunity within the frame of DEAL agreement.

Open access funding enabled and organized by Projekt DEAL.

Conflict of Interests

The authors declare no conflict of interest.

Author Contributions

K.H. and J. Schneider contributed equally to this work. S. R. Waldvogel, R. Goy, J. Schütz, and W. Bonrath devised and supervised the project. K. Hofman and J. Schneider carried out optimization reactions, scope reactions, cyclic voltammetry studies, and data analysis. J. Schneider performed the scale-up reaction. All authors contributed to the discussion of results, writing of the manuscript, and writing of the Supporting Information.

Data Availability Statement

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

[1] R. A. Sheldon, H. van Bekkum, *Fine Chemicals through Heterogeneous Catalysis*, Wiley-VCH, Weinheim, New York **2001**, p. 519.

[2] Z. Yao, X. Hu, J. Mao, H. Li, 'An Environmentally Benign Catalytic Oxidation of Cholesteryl Acetate With Molecular Oxygen by Using N-hydroxyphthalimide', *Green Chem.* **2009**, *11*, 2013–2017.

[3] S. Schulz, M. Girhard, S. K. Gaßmeyer, V. D. Jäger, D. Schwarze, A. Vogel, V. B. Urlacher, 'Selective Enzymatic Synthesis of the Grapefruit Flavor (+)-Nootkatone', *ChemCatChem* **2015**, *7*, 601–604.

[4] G. J. Schroepfer Jr., 'Oxysterols: Modulators of Cholesterol Metabolism and Other Processes', *Physiol. Rev.* **2000**, *80*, 361–554.

[5] Y. Sato, Y. Sonoda, M. Morisaki, N. Ikekawa, 'Oxygenated Sterols as Inhibitors of Enzymatic Conversion of Dihydrolanosterol into Cholesterol', *Chem. Pharm. Bull.* **1984**, *32*, 3305–3308.

[6] A. Nakamura, M. Nakada, 'Allylic Oxidations in Natural Product Synthesis', *Synthesis* **2013**, *45*, 1421–1451.

[7] V. Weidmann, W. Maison, 'Allylic Oxidations of Olefins to Enones', *Synthesis* **2013**, *45*, 2201–2221.

[8] H. Choi, M. P. Doyle, 'Optimal TBHP Allylic Oxidation of Δ5-Steroids Catalyzed by Dirhodium Caprolactamate', *Org. Lett.* **2007**, *9*, 5349–5352.

[9] T. Akihisa, T. Matsumoto, H. Sakamaki, M. Take, Y. Ichinohe, 'Platinum-Catalyzed Oxidation of Cholesterol', *Bull. Chem. Soc. Jpn.* **1986**, *59*, 680–682.

[10] D. Kishore, A. E. Rodrigues, 'Liquid Phase Catalytic Oxidation of Isophorone With tert-butylhydroperoxide Over Cu/Co/Fe–MgAl Ternary Hydrotalcites', *Appl. Catal., A* **2008**, *345*, 104–111.

[11] T. Hirao, S. Mikami, M. Mori, Y. Ohshiro, 'Novel Allylic Oxidation of Conjugate Ketones With VO(OR)Cl2', *Tetrahedron Lett.* **1991**, *32*, 1741–1744.

[12] J. Liu, R. Huang, H. Zhu, 'An Improved and Efficient Synthesis for IPL576,092 and its Analogues', *Monatsh. Chem.* **2013**, *144*, 1081–1085.

[13] J. A. R. Salvador, J. H. Clark, 'The Allylic Oxidation of Unsaturated Steroids by Tert-butyl Hydroperoxide Using Surface Functionalised Silica Supported Metal Catalysts', *Green Chem.* **2002**, *4*, 352–356.

[14] C. N. de Melo, A. Moreira Meireles, V. S. Da Silva, P. Robles-Azocar, G. DeFreitas-Silva, 'Manganese Complex Catalyst for Valencene Oxidation: The First Use of Metalloporphyrins for the Selective Production of Nootkatone', *Inorg. Chim. Acta* **2021**, *515*, 120031.

[15] C. Nunes de Melo, Y. B. Rodrigues, P. A. Robles-Azocar, 'Pd-Catalyzed Aerobic Oxidation of the Sesquiterpene Isolongifolene: A Green and Heterogeneous Process', *Inorg. Chim. Acta* **2021**, *517*, 120192.

[16] J. Liu, S. Ma, 'Iron-Catalyzed Aerobic Oxidation of Allylic Alcohols: The Issue of C=C Bond Isomerization', *Org. Lett.* **2013**, *15*, 5150–5153.

[17] P. Marwah, A. Marwah, H. A. Lardy, 'An Economical and Green Approach for the Oxidation of Olefins to Enones', *Green Chem.* **2004**, *6*, 570–577.

[18] S. M. Silvestre, J. A. Salvador, 'Allylic and Benzylic Oxidation Reactions with Sodium Chlorite', *Tetrahedron* **2007**, *63*, 2439–2445.

[19] P. Zhang, Y. Wang, J. Yao, C. Wang, C. Yan, M. Antonietti, H. Li, 'Visible-Light-Induced Metal-Free Allylic Oxidation Utilizing a Coupled Photocatalytic System of g-C3N4 and N-Hydroxy Compounds', *Adv. Synth. Catal.* **2011**, *353*, 1447–1451.

[20] P. Zhang, H. Li, Y. Wang, 'Post-Functionalization Of Graphitic Carbon Nitrides by Grafting Organic Molecules: Toward C–H Bond Oxidation Using Atmospheric Oxygen', *Chem. Commun.* **2014**, *50*, 6312–6315.

[21] C. Liu, H. Liu, X. Zheng, S. Chen, Q. Lai, C. Zheng, M. Huang, K. Cai, Z. Cai, S. Cai, 'Visible-Light-Enabled Allylic C–H Oxidation: Metal-free Photocatalytic Generation of Enones', *ACS Catal.* **2022**, *12*, 1375–1381.

[22] V. Weidmann, M. Schaffrath, H. Zorn, J. Rehbein, W. Maison, 'Elucidation of the Regio- And Chemoselectivity of Enzymatic Allylic Oxidations With Pleurotus Sapidus – Conversion of Selected Spirocyclic Terpenoids and Computational Analysis', *Beilstein J. Org. Chem.* **2013**, *9*, 2233–2241.

[23] C. Aranda, M. Municoy, V. Guallar, J. Kiebist, K. Scheibner, R. Ullrich, J. C. del Río, M. Hofrichter, A. T. Martínez, A. Gutiérrez, 'Selective Synthesis Of 4-Hydroxyisophorone and 4-Ketoisophorone by Fungal Peroxygenases', *Catal. Sci. Technol.* **2019**, *9*, 1398–1405.

[24] P. C. Peart, K. P. McCook, F. A. Russell, W. F. Reynolds, P. B. Reese, 'Hydroxylation of Steroids by Fusarium Oxysporum, Exophiala Jeanselmei and Ceratocystis Paradoxa', *Steroids* **2011**, *76*, 1317–1330.

[25] J. Solé, J. Brummund, G. Caminal, M. Schürman, G. Álvaro, M. Guillén, 'Ketoisophorone Synthesis With An Immobilized Alcohol Dehydrogenase', *ChemCatChem* **2019**, *11*, 4862–4870.

[26] S. R. Waldvogel, M. Selt, 'Electrochemical Allylic Oxidation of Olefins: Sustainable and Safe', *Angew. Chem., Int. Ed.* **2016**, *55*, 12578–12580.

[27] D. Pollok, S. R. Waldvogel, 'Electro-Organic Synthesis – a 21st Century Technique', *Chem. Sci.* **2020**, *11*, 12386–12400.

[28] M. C. Leech, K. Lam, 'A Practical Guide to Electrosynthesis', *Nat. Rev. Chem.* **2022**, *6*, 275–286.

[29] M. Masui, K. Hosomi, K. Tsuchida, S. Ozaki, 'Electrochemical Oxidation of Olefins Using N-Hydroxyphthalimide as a Mediator', *Chem. Pharm. Bull.* **1985**, *33*, 4798–4802.

[30] A. Guirado, G. P. Moss, J. H. P. Utley, 'Selective Allylic Electro-Oxidation of α- and β-ionones', *J. Chem. Soc., Chem. Commun.* **1987**, *1987*, 41-42.

[31] E. J. Horn, B. R. Rosen, Y. Chen, J. Tang, K. Chen, M. D. Eastgate, P. S. Baran, 'Scalable and Sustainable Electrochemical Allylic C–H Oxidation', *Nature* **2016**, *533*, 77–81.

[32] Z. Zheng, F. Florit, B. Jin, H. Wu, S.-C. Li, K. Y. Nandiwale, C. A. Salazar, J. G. Mustakis, W. H. Green, K. F. Jensen, 'Integrating Machine Learning and Large Language Models to Advance Exploration of Electrochemical Reactions', *Angew. Chem., Int. Ed.* **2024**, *64*, e202418074.

[33] T. Shen, J. Zhao, X. Ren, Z.-Q. Liu, S. Liu, 'Metal-Free Electrochemical Allylic C–H Aerobic Oxidation', *J. Org. Chem.* **2025**, *90*, 1148–1158.

[34] M. Yan, Y. Kawamata, P. S. Baran, 'Synthetic Organic Electrochemical Methods Since 2000: On the Verge of a Renaissance', *Chem. Rev.* **2017**, *117*, 13230–13319.

[35] A. Wiebe, T. Gieshoff, S. Möhle, E. Rodrigo, M. Zirbes, S. R. Waldvogel, 'Electrifying Organic Synthesis', *Angew. Chem., Int. Ed.* **2018**, *57*, 5594–5619.

[36] S. Möhle, M. Zirbes, E. Rodrigo, T. Gieshoff, A. Wiebe, S. R. Waldvogel, 'Modern Electrochemical Aspects for the Synthesis of Value-Added Organic Products', *Angew. Chem., Int. Ed.* **2018**, *57*, 6018–6041.

[37] S. R. Waldvogel, B. Janza, 'Renaissance of Electrosynthetic Methods for the Construction of Complex Molecules', *Angew. Chem., Int. Ed.* **2014**, *53*, 7122–7123.

[38] N. E. S. Tay, D. Lehnherr, T. Rovis, 'Photons or Electrons? A Critical Comparison of Electrochemistry and Photoredox Catalysis for Organic Synthesis', *Chem. Rev.* **2022**, *122*, 2487–2649.

[39] C. Zhu, N. W. J. Ang, T. H. Meyer, Y. Qiu, L. Ackermann, 'Organic Electrochemistry: Molecular Syntheses with Potential', *ACS Cent. Sci.* **2021**, *7*, 415–431.

[40] H.-C. Xu, K. D. Moeller, 'Electrochemistry in Synthetic Organic Chemistry', *J. Org. Chem.* **2021**, *86*, 15845–15846.

[41] R. D. Little, 'A Perspective on Organic Electrochemistry', *J. Org. Chem.* **2020**, *85*, 13375–13390.

[42] D. M. Heard, A. J. J. Lennox, 'Electrode Materials in Modern Organic Electrochemistry', *Angew. Chem., Int. Ed.* **2020**, *59*, 18866–18884.

[43] R. Francke, R. D. Little, 'Redox Catalysis in Organic Electrosynthesis: Basic Principles and Recent Developments', *Chem. Soc. Rev.* **2014**, *43*, 2492–2521.

[44] R. Francke, M. Májek, *Sustainable and Functional Redox Chemistry, Chapter 6: Mediated Electron Transfer in Electrosynthesis: Concepts, Applications, and Recent Influences from Photoredox Catalysis*, The Royal Society of Chemistry, London **2022**, pp. 119–153.

[45] J. R. Long, 'Perchlorate safety: Reconciling inorganic and organic guidelines', *Chem. Health Saf.* **2002**, *9*, 12–18.

[46] L. G. Gombos, J. Nikl, S. R. Waldvogel, 'Dual Roles of Supporting Electrolytes in Organic Electrosynthesis', *ChemElectroChem* **2024**, *11*, e202300730.

[47] M.-A. Müller, C. Schäfer, G. Litta, A.-M. Klünter, M. G. Traber, A. Wyss, T. Ralla, M. Eggersdorfer, W. Bonrath, 1'00 Years of Vitamin E: From Discovery to Commercialization', *Eur. J. Org. Chem.* **2022**, *2022*, e202201190.

[48] E. Widmer, 'Synthetic Advances in the Carotenoid Field', *Pure Appl. Chem.* **1985**, *57*, 741–752.

[49] C. Gütz, B. Klöckner, S. R. Waldvogel, 'Electrochemical Screening for Electroorganic Synthesis', *Org. Process Res. Dev.* **2016**, *20*, 26–32.

[50] M. M. Hielscher, B. Gleede, S. R. Waldvogel, 'Get Into Flow: Design of Experiments as a Key Technique in the Optimization of Anodic Dehydrogenative C,C Cross-Coupling Reaction of Phenols in Flow Electrolyzers', *Electrochim. Acta* **2021**, *368*, 137420.

[51] M. Dörr, M. M. Hielscher, J. Proppe, S. R. Waldvogel, 'Electrosynthetic Screening and Modern Optimization Strategies for Electrosynthesis of Highly Value-Added Products', *ChemElectroChem* **2021**, *8*, 2621–2629.

[52] S. B. Beil, D. Pollok, S. R. Waldvogel, 'Reproducibility in Electroorganic Synthesis—Myths and Misunderstandings', *Angew. Chem., Int. Ed.* **2021**, *60*, 14750–14759.

[53] J. Nikl, K. Hofman, S. Mossazghi, I. C. Möller, D. Mondeshki, F. Weinelt, F.-E. Baumann, S. R. Waldvogel, 'Electrochemical Oxo-Functionalization of Cyclic Alkanes and Alkenes Using Nitrate and Oxygen', *Nat. Commun.* **2023**, *14*, 4565.

[54] F. Sprang, J. D. Herszman, S. R. Waldvogel, 'Electrochemical Oxidation of Phenols in Flow: A Versatile and Scalable Access to Para-Benzoquinones', *Green Chem.* **2022**, *24*, 5116–5124.

[55] A.-K. Seitz, P. J. Kohlpaintner, T. van Lingen, M. Dyga, F. Sprang, M. Zirbes, S. R. Waldvogel, L. J. Gooßen, 'Peroxodicarbonate as a Green Oxidizer for the Selective Degradation of Kraft Lignin Into Vanillin', *Angew. Chem., Int. Ed.* **2022**, *61*, e202219217.

[56] S. Möhle, S. Herold, N. D. Hillerson, S. R. Waldvogel, 'Anodic Formation of Aryl Mesylates Through Dehydrogenative Coupling Reaction', *ChemElectroChem* **2019**, *6*, 121–125.

[57] T. Rundlöf, M. Mathiasson, S. Bekiroglu, B. Hakkarainen, T. Bowden, T. Arvidsson, 'Survey and Qualification of Internal Standards for Quantification by 1H NMR Spectroscopy', *J. Pharm. Biomed. Anal.* **2010**, *52*, 645–651.

[58] S. Lips, S. R. Waldvogel, 'Use of Boron-Doped Diamond Electrodes in Electro-Organic Synthesis', *ChemElectroChem* **2019**, *6*, 1649–1660.

[59] J. D. Lasso, D. J. Castillo-Pazos, C.-J. Li, 'Green Chemistry Meets Medicinal Chemistry: A Perspective on Modern Metal-Free Late-Stage Functionalization Reactions', *Chem. Soc. Rev.* **2021**, *50*, 10955–10982.

[60] J.-G. Cui, L. Fan, L.-L. Huang, H.-L. Liu, A.-M. Zhou, 'Synthesis and Evaluation of Some Steroidal Oximes as Cytotoxic Agents: Structure/Activity Studies (I)', *Steroids* **2009**, *74*, 62–72.

[61] D. Lehnherr, L. Chen, 'Overview of Recent Scale-Ups in Organic Electrosynthesis (2000–2023)', *Org. Process Res. Dev.* **2024**, *28*, 338–366.

[62] M. C. Leech, A. D. Garcia, A. Petti, A. P. Dobbs, K. Lam, 'Organic Electrosynthesis: From Academia to Industry', *React. Chem. Eng.* **2020**, *5*, 977–990.

[63] L. Lennartz, P. Stenner, S. B. Beil, S. R. Waldvogel, 'Electrochemical Processes for the Chemical Industry', *Chem. Eng.* **2022**, *22*, 22–26.

[64] F. Weinelt, F. E. Baumann, S. R. Waldvogel, S. Hofmann, J. Nikl, *Electrochemical oxidation of cycloalkenes to form α, ω-dicarboxylic acids and ketocarboxylic acids, WO2023186658A1*, **2023**.

[65] M. Klein, S. R. Waldvogel, 'Counter Electrode Reactions—Important Stumbling Blocks on the Way to a Working Electro-organic Synthesis', *Angew. Chem., Int. Ed.* **2022**, *61*, e202204140.

[66] W. L. F. Armarego, *Purification of Laboratory Chemicals*, Butterworth-Heinemann, Oxford **2017**.

[67] A. Saib, R. Goy, J. Medlock, B. Wüstenberg, G. Kociok-Köhn, C. L. Lyall, J. P. Lowe, U. Hintermair, 'Catalyst Speciation and Deactivation in the Ruthenium-Mediated Transformation of Ethynyl-β-ionol to α,β-unsaturated Esters for Vitamin A Synthesis', *Catal. Sci. Technol.* **2025**, *15*, 355–375.

[68] G. R. Fulmer, A. J. M. Miller, N. H. Sherden, H. E. Gottlieb, A. Nudelman, B. M. Stoltz, J. E. Bercaw, K. I. Goldberg, 'NMR Chemical Shifts of Trace Impurities: Common Laboratory Solvents, Organics, and Gases in Deuterated Solvents Relevant to the Organometallic Chemist', *Organometallics* **2010**, *29*, 2176–2179.

[69] K. Izutsu, *Electrochemistry in Nonaqueous Solutions*, Wiley, Weinheim **2002**.

[70] N. Elgrishi, K. J. Rountree, B. D. McCarthy, E. S. Rountree, T. T. Eisenhart, J. L. Dempsey, 'A Practical Beginner's Guide to Cyclic Voltammetry', *J. Chem. Educ.* **2018**, *95*, 197–206.

[71] R. G. Compton, C. E. Banks, *Understanding Voltammetry*, World Scientific, New Jersey **2025**.

[72] M. Tavanti, F. Parmeggiani, J. R. G. Castellanos, A. Mattevi, N. J. Turner, 'One-Pot Biocatalytic Double Oxidation of α-Isophorone for the Synthesis of Ketoisophorone', *ChemCatChem* **2017**, *9*, 3338–3348.

[73] V. B. Kharitonov, E. Podyacheva, D. Chusov, Y. V. Nelyubina, D. V. Muratov, D. A. Loginov, 'Planar Chiral Rhodium Complex Based on the Tetrahydrofluorenyl Core for Enantioselective Catalysis', *Org. Lett.* **2023**, *25*, 8906–8911.

[74] T. J. Kuczmera, P. Puylaert, B. J. Nachtsheim, 'Oxidation of Benzylic Alcohols to Carbonyls Using N-heterocyclic Stabilized λ3-iodanes', *Beilstein J. Org. Chem.* **2024**, *20*, 1677–1683.

[75] S. Serra, 'MnO2/TBHP: A Versatile and User-Friendly Combination of Reagents for the Oxidation of Allylic and Benzylic Methylene Functional Groups', *Eur. J. Org. Chem.* **2015**, *2015*, 6472–6478.

[76] D. Clemente-Tejeda, A. López-Moreno, F. A. Bermejo, 'Non-heme Iron Catalysis in C=C, C–H, and CH2 Oxidation Reactions. Oxidative Transformations on Terpenoids Catalyzed by Fe(bpmen)(OTf)2', *Tetrahedron* **2013**, *69*, 2977–2986.

[77] C. Zanato, A. Pelagalli, K. F. M. Marwick, M. Piras, S. Dall'Angelo, A. Spinaci, R. G. Pertwee, D. J. A. Wyllie, G. E. Hardingham, M. Zanda, 'Synthesis, Radio-Synthesis and In Vitro Evaluation of Terminally Fluorinated Derivatives of HU-210 and HU-211 as Novel Candidate PET Tracers', *Org. Biomol. Chem.* **2017**, *15*, 2086–2096.

[78] W. S. Grainger, E. J. Parish, 'Allylic Oxidation of Steroidal Olefins by Vanadyl Acetylacetonate and tert-butyl Hydroperoxide', *Steroids* **2015**, *101*, 103–109.

[79] V. Amountzias, D. Abatis, N. Aligiannis, 'Chemical Constituents from the Fruits of Paliurus spina-christi', *Chem. Nat. Compd.* **2024**, *60*, 714–716.

[80] Y. Zhao, Y.-Y. Yeung, 'An Unprecedented Method for the Generation of tert-Butylperoxy Radical Using DIB/TBHP Protocol: Solvent Effect and Application on Allylic Oxidation', *Org. Lett.* **2010**, *12*, 2128–2131.

[81] S. Nurfazilah Wan Yusop, S. Imran, M. Ilham Adenan, K. Ashraf, S. Sultan, 'Biocatalytic Modifications of Ethynodiol Diacetate by Fungi, Anti-Proliferative Activity, and Acetylcholineterase Inhibitory of its Transformed Products', *Steroids* **2021**, *171*, 108832.

Received April 8, 2025
Revised April 30, 2025