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Electrochemical Synthesis of Isoxazoles and Isoxazolines via Anodic Oxidation of Oximes

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Isoxazol(in)es are widely featured structural motifs in natural products, agrochemicals, and pharmaceuticals. The first intermolecular approach for a direct electrochemical synthesis from readily available aldoximes is reported. Isoxazoles and isoxazolines were obtained in yields up to 81%. The synthesis is carried out in an undivided cell as the simplest electrochemical set-up and requires only the use of electric current as traceless oxidizing agent. The application of inexpensive and widely available electrode materials in combination with recyclable supporting electrolytes and solvents paves the path for translation of the presented reaction onto preparative scale. This is underlined by successful scale-up to multi-gram runs.

Introduction

Five-membered heterocycles, especially isoxazoles and isoxazolines, are widely found in natural products and among important structural motifs in medicinal chemistry and agrochemistry (Figure 1). Ibotenic acid (**1**), for example, naturally occurring in *Amanita muscaria* (fly agaric), is a prodrug of psychoactive muscimol. The orthosteric agonist for $GABA_A$ receptors exhibits hallucinogenic and sedative-hypnotive psychoactivity.[1] Moreover, a variety of non-steroidal anti-inflammatory drugs,[2] antibiotics (e.g. cloxacillin, **2**),[3] as well as some promising candidates for immuno- and chemo-therapeutics feature isoxazol(in)es.[4] In the field of agrochemicals, isoxazoles and isoxazolines find frequently application as herbicides (fenoxasulfone, **3**),[5] fungicides (hymexazol, **4**),[6] and insecticides (fluxametamid, **5**).[7]

Conventionally, isoxazoles and isoxazolines can be accessed via intramolecular oxidative cyclization of allyl aldehyde oximes,[8] propargyl hydroxylamines[9] or propargyl aldehyde oximes.[10] In general, these methods require terminal oxidizers and eventually transition metal catalysts. Furthermore, commonly used methods start from easily accessible benzaldehyde oximes. Conversion to the desired isoxazol(in)es requires initial oxidation to their respective nitrile oxides and subsequent 1,3-dipolar cycloaddition with alkenes or alkynes. Therefore, hazardous and strong oxidizers such as *m*-CPBA in combination with iodobenzene,[11] hypervalent iodine reagents[12] or organo nitrites[13] need to be employed. Another route involves formation of *N*-hydroximidoyl halides which undergo base-promoted formation of nitrile oxides. These strategies require the use of hazardous halogenation reagents[14] and sometimes even additional use of transition metal catalysts,[15] resulting in significant amounts of reagent waste.

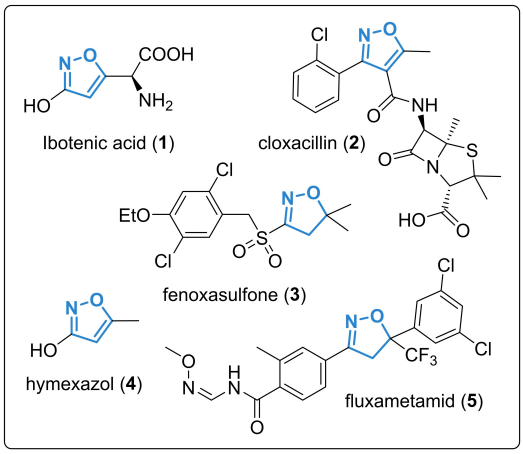

Figure 1. Important examples of isoxazoles and isoxazolines in natural products, pharmaceuticals, and agrochemicals.

As a greater awareness for sustainability of chemical processes is generated, modern chemical transformations aim for greener approaches. Electrochemistry fulfils many principles of green chemistry.[16] Hazardous redox reagents can be substituted with electric current and in combination with recyclable solvents and supporting electrolytes the generation of waste can be strongly diminished.[17] For translation of a synthetic protocol to a larger scale, the downstream processing must be considered, which is often costlier than the electrosynthetic step.[18] Moreover, electrochemical approaches in-

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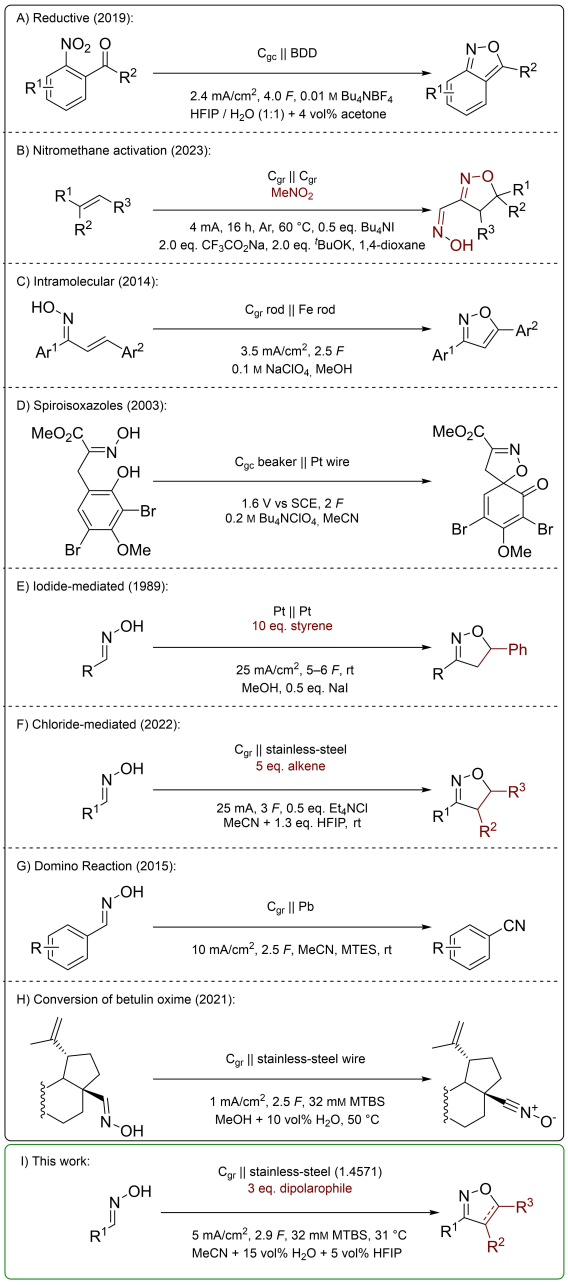
crease the safety of processes, as the constraint of the initial electron transfer to the electrode surface allows for precise reaction control.[19]

The synthesis of isoxazoles and isoxazolines as well as the generation of nitrile oxides has caught the interest of the electrochemical community for decades. Four examples granting access to isoxazole(in)es via intramolecular approaches are reported in literature. Synthesis of 2,1-benzoxazoles was enabled by reductive cyclization of *o*-nitrobenzaldehydes or -acetophenones (Scheme 1, A).[20] Noteworthy, such reductive conversions can be accompanied by cathodic corrosion making other approaches highly desired.[21] Recently, an electrochemical approach for the synthesis of isoxazoline aldoximes via nitromethane activation was established (Scheme 1, B).[22] Anodic oxidation of α,β-unsaturated oximes led to intramolecular cyclization, leading to 3,5-substituted isoxazoles (Scheme 1, C).[23] Furthermore, oxidation of phenols via constant potential electrolysis allowed for synthesis of spiroisoxazoles (Scheme 1, D).[24] Back in 1989, the first iodide-mediated synthesis of nitriles from aldoximes was reported (Scheme 1, E).[25] To prove the formation of nitrile oxides as intermediates, styrene was added as a trapping agent, yielding the corresponding isoxazoline. About 30 years later, a deeper mechanistic study of chloride-mediated aldoxime oxidation and subsequent isoxazoline formation was provided and a broad scope was presented (Scheme 1, F).[26] Furthermore, halide-free synthetic access to nitriles from aldoximes was achieved via a domino oxidation-reduction reaction (Scheme 1, G).[27] Thereby, anodic oxidation led to formation of nitrile oxides as intermediates, which were subsequently reduced to the corresponding nitrile at the counter-electrode. Recently, even highly lipophilic betulin oxime was successfully oxidized at a graphite anode in a quasi-divided set-up, resulting in the formation of stable nitrile oxides, while hydrogen evolution occurred at the cathode (Scheme 1, H).[28]



Scheme 1. Electrochemical approaches for conversion of aldoximes to isoxazol(in)es.

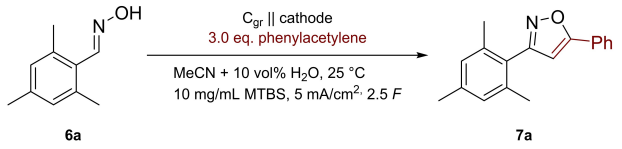
We developed an approach for the synthesis of isoxazoles and isoxazolines via direct anodic oxidation of aldoximes (Scheme 1, I). A simple undivided galvanostatic set-up with inexpensive graphite and stainless-steel electrodes was used. Using a solvent system of acetonitrile/water with HFIP as additive enabled the synthesis of isoxazol(in)es in moderate to very good yields. Moreover, the scalability of the reaction was demonstrated by multi-gram scale electrolysis. The recovery and reuse of electrolyte components supports the green nature of the approach.

Results and Discussion

Initially, the reaction was investigated in an undivided cell using 2,4,6-trimethylbenzaldehyde oxime (**6a**) as test substrate and phenylacetylene as dipolarophile. As the use of graphite anodes for successful oxidation of oximes has been thoroughly studied, graphite was chosen as anode and no further investigation was performed.[23,27–30] Based on previous results, acetonitrile and water with methyltributylammonium methylsulfate (MTBS) were chosen as supporting electrolyte.[27,29–30] First, different cathode materials suitable for hydrogen evolution as the desired counter reaction were screened (Table 1), since the counter electrode can have a significant impact on the overall performance of the electrolysis.[31]

Amongst the tested cathode materials, the metals proved superior to carbon-based cathodes. The latter allowed for synthesis of isoxazole **7a** in yields of 42–49%. Within the tested metals, nickel gave the lowest isoxazole **7a** yield of 56%, whereas platinum and stainless-steel provided comparable product yields of 60% and 59%, respectively. Thus, further reaction optimization was carried out using inexpensive and widely available stainless-steel as cathode.

Table 1. Screening for different cathode materials.



6a 7a

Cathode	NMR yield[a]
Stainless-steel (1.4571)	59%
Platinum	60%
Nickel	56%
Graphite (C_{gr})	49%
Glassy carbon (C_{gc})	42%
Boron-doped diamond (BDD)	46%

Reaction was carried out using a 5 mL screening cell and 0.5 mmol oxime. [a] Quantification using ^{1}H NMR with 1,3,5-trimethoxybenzene as internal standard.

Reaction Optimization

A detailed evaluation and optimization of the targeted reaction was carried out using Design of Experiments (DoE).[32] Besides the electrochemical parameters such as current density (*j*) and amount of applied charge (*Q*), concentration of the starting material, equivalents of dipolarophile, amount of water as additive and reaction temperature were investigated. For investigation of those 6 parameters, a fractional factorial design was chosen (2^{6-2}, resolution IV with central point and rotatable axis points, each data point acquired twice). The observation of curvature within the main effects plot necessitated expansion to a response surface design (For detailed information see ESI, Table S2, Figure S1–2). Target optimization with regards to maximization of the isoxazole yield led to the following optimum reaction conditions: 5 mA/cm^2 as current density, an amount of applied charge of 2.9 *F*, 3 eq. of dipolarophile, 31 °C, 10 vol% water as additive in MeCN, and an optimum amount of aldoxime of 0.5 mmol.

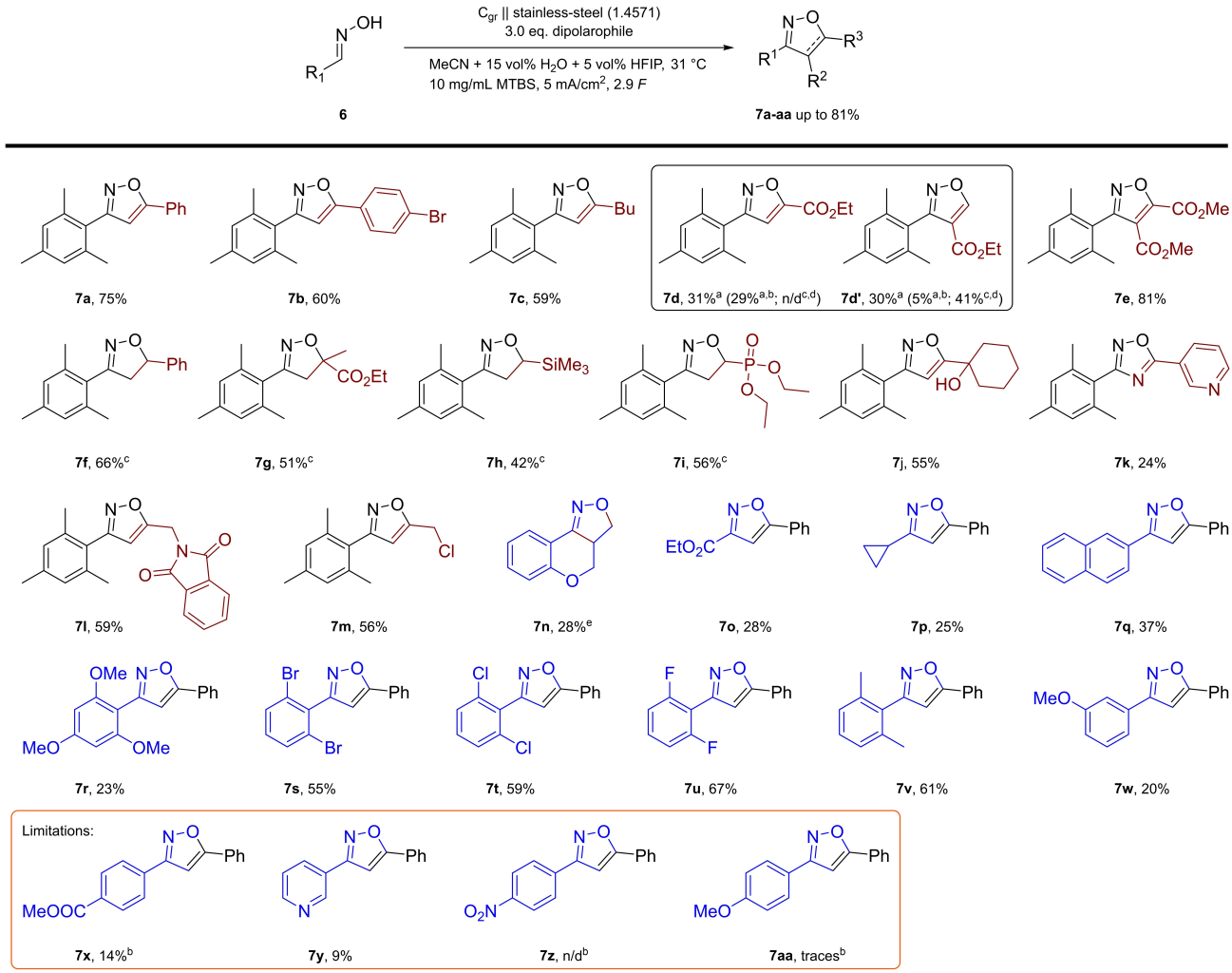
Unfortunately, for the latter two parameters no clear optima were obtained. Thus, subsequent linear optimization (one variable at a time, OVAT) for the amount of water as additive as well as the starting material concentration was carried out. Decreasing the concentration of **6a** did not improve the yield of **7a**. However, the reaction proved stable in the range of 0.45 mmol–0.5 mmol starting material yielding 57% of isoxazole **7a**. Thus, a substrate concentration of 0.1 M (0.5 mmol) was chosen for further optimization.

Furthermore, the reaction time with regards to post-electrolysis stirring was investigated. Although generation of the 1,3-dipole is determined by the electrolysis time, the slower cycloaddition reaction might occur during the post-electrolysis stirring. For initial reaction optimization, a total reaction time of 24 h (19 h post-electrolysis stirring) was chosen in order to compensate for any potential effects of post-electrolysis stirring. This yielded isoxazole **7a** in 63% yield. Indeed, directly after the electrolysis isoxazole **7a** was obtained in only 45% yield, which gradually increased over time and the maximum of 63% was finally reached after 4 h of post-electrolysis stirring.

Last, the solvent system was investigated. First, the amount of water as an additive in acetonitrile was increased as indicated by the DoE results. The optimum was reached at 15 vol% water in MeCN, yielding 66% isolated yield of **7a**. Further increase to 20 vol% or 25 vol% water resulted in a drop in yield to 60%. As the anodic oxidation of aldoximes to nitrile oxides occurs overall via a two-electron transfer, the process could potentially benefit from a (radical) stabilizing additive. 1,1,1,3,3,3-Hexafluoroisopropanol (HFIP) is a well-known solvent and additive due to its unique physical and chemical properties and outstanding ability of engaging organic transformations.[33,34] HFIP exhibits high polarity,[35] a strong hydrogen-bond donor ability[36] and extraordinary (electro−)chemical stability.[37] Not only, but especially in electro-organic synthesis, HFIP is known for its potency of stabilizing ionic and radical intermediates and has proven to boost selectivity as well as yield for numerous reactions.[26,33,38] Indeed, addition of only 5 vol% HFIP to the solvent system of MeCN + 15 vol% H_2O led to an increase in yield, enabling access to product **7a** in a good isolated yield of 75%. Next, the scope of the reaction was investigated applying the following optimized conditions: graphite anode, stainless steel cathode, 0.1 M oxime, 10 mg/mL MTBS in MeCN + 15 vol% H_2O + 5 vol% HFIP, 5 mA/cm^2, 2.9 *F*, 3 eq. of dipolarophile, 31 °C (Scheme 2).

Scope and Limitations

First, the applicability of different dipolarophiles with 2,4,6-trimethylbenzaldehyde oxime (**7a**) as substrate was evaluated. 4-Bromophenylacetylene and 1-hexyne enabled access to products **7b** and **7c** in comparable yields of 60% and 59%, respectively. Interestingly, conversion of 1-hexyne allowed for a regioselective reaction. In contrast, ethyl propiolate gave a 1.03:1 mixture of the 3,5-disubstituted product **7d** (31%) and 3,4-disubstituted **7d'** (30%). Switching the solvent system to solely MeCN + 15 vol% HFIP allowed for an enhanced regioselective ratio of 5.8:1 (**7d**:**7d'**), yielding 29% of **7d** and only 5% of **7d'**. However, the combined yield of both isomers decreased from 61% to 34%. Nonetheless, a regioselective reaction yielding solely the 3,4-substituted derivative **7d'** (41%) was achieved when ethyl (*E*)-3-(piperidin-1-yl)acrylate was employed as dipolarophile. Thus, application of such acrylates could offer a general strategy for achieving a reversed regioselectivity within this electrochemical approach. To our delight, electron poor dimethyl acetylendicarboxylate yielded 3,4,5-trisubstituted product **7e** in a very good yield of 81%. Generally, a good functional group tolerance was observed at the propargylic position and yields of up to 59% were obtained for derivatives **7j**–**7m**. Noteworthy, even phthalimide-substituted **7l** (59%) and chloro-substituted derivate **7m** (56%) were obtained. Furthermore, 3-cyano-pyridine was successfully employed as dipolarophile, enabling access to oxadiazole **7k** in 24% yield. Moreover, the synthesis of various isoxazolines was achieved by application of different alkenes. To prevent sensitive alkenes



Scheme 2. Scope of isoxazoles and isoxazolines. 0.5 mmol scale, 4 h post-electrolysis stirring, isolated yields. [a] regioisomers. [b] MeCN + 15 vol% HFIP as solvent. [c] dipolarophile added after the electrolysis. [d] ethyl (*E*)-3-(piperidin-1-yl)acrylate as dipolarophile. [e] w/o phenylacetylene, intramolecular cyclization.

like styrene from undergoing side reactions, e.g. polymerizations, an ex-cell approach was established. Thus, the respective alkene was added after the electrolysis and the reaction mixture was stirred for 4 h. Derivatives **7f–l** were obtained in fair yields of up to 66%. Besides dipolarophiles like styrene (**7f**, 66%) and ethyl methacrylate (**7g**, 51%), even trimethyl vinylsilane (**7h**, 42%) and diethyl vinylphosponate (**7i**, 56%) were successfully converted to the corresponding isoxazolines. Application of different oximes in the reaction proved that steric protection of the intermediary formed nitrile oxide is beneficial. Naphthyl- and ester-substituted derivatives **7q** and **7o** were obtained in moderate yields of 37% and 28%. Furthermore, conversion of cyclopropyl carbaldehyde oxime gave access to the corresponding isoxazole **7p** in a comparable yield of 25%. Thereby, no byproducts indicating ring-opening reactions of the cyclopropyl-ring were detected. Attempted synthesis of isoxazole **7y** from rather electron-deficient pyridine-3-carbaldehyde oxime resulted in a poor yield of 9%.

2,6-Disubstituted benzaldoximes were converted successfully due to steric protection of the intermediates (**7s–7v**, up to 67%). Within the halogen-substituted isoxazoles **7s–7u**, a trend of decrease in yield with decreasing electronegativity for higher homologues was observed (Br (55%) < Cl 59%) < F (67%)). An exception was found for conversion of electron-rich 2,4,6-trimethoxybenzaldoxim, yielding the corresponding isoxazole **7r** in a rather poor yield of 23%. Thus, successful conversion is most likely not only related to sufficient steric protection of the intermediary formed nitrile oxide, but also a matter of reactivity and electronic stabilization of any formed radical and ionic intermediates. Generally, synthesis of isoxazoles bearing electron-rich arenes in 2-position was restricted to *ortho*- and *meta*-substituted benzaldoximes in mediocre yields. Intramolecular cyclization of salicylaldehyde-derived oxime enabled synthesis of isoxazoline **7n** in 28% yield and *meta*-methoxy benzaldoxime yielded 20% of the corresponding isoxazole **7w**. However, after application of *para*-methoxybenzaldoxime only traces of the desired product **7aa** as well as the corresponding benzaldehyde were detected by GC-MS analysis (see Figure S6–S7, supporting information). Generally, application of *para*-substituted benzaldoximes in the reaction proved challenging.

Para-nitro derivative **7z** could not be obtained, most likely due to the electrochemical sensitivity of the nitro-group tending to undergo electrochemical reduction.[39] Only *para*-(methoxycarbonyl) benz-aldoxime derived isoxazole **7x** was successfully isolated in a poor yield of 14%. However, a change of the solvent system to water-free MeCN + 15 vol% HFIP was required, as otherwise no product was obtained. Thus, the reaction was investigated using cyclic voltammetry (CV, Figure 2). No distinct oxidative peak could be observed for *para*-(methoxycarbonyl)benzaldoxime (**6x**) in the initially used aqueous solvent system.

However, the incipient oxidation is overlapping with the oxidative wave for the electrolyte. On the contrary, a clear oxidative peak for substrate **6x** was observed in the MeCN/HFIP-based solvent system, supporting the experimental findings. Furthermore, CV studies of test substrate **6a** in aqueous MeCN with and without HFIP as additive did not show any significant differences. Hence, these findings support the assumption that HFIP does not directly engage in the oxidation, but functions as a stabilizing agent for occurring intermediates. Therefore, application of HFIP as additive allows for higher yields of the target products due to protection of intermediates and thus promotes the desired subsequent cycloaddition reaction.

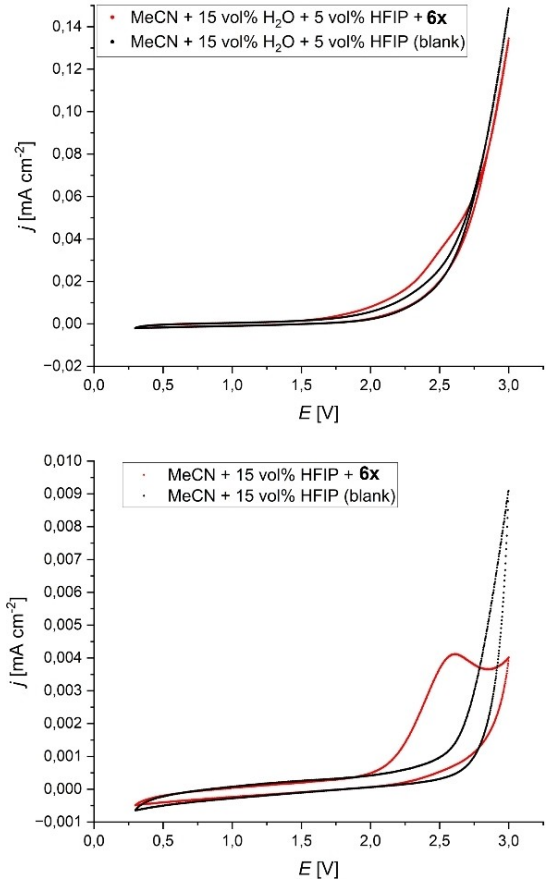
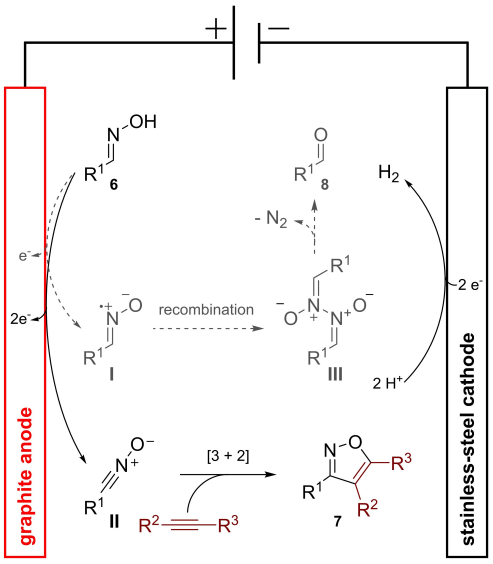


Figure 2. Cyclic voltammograms of *para*-(methoxycarbonyl)benzaldoxime (**6x**) in organic-aqueous (top) and organic (bottom) solvent systems. Working electrode: glassy carbon, counter electrode: Pt, reference electrode: Ag/AgCl in sat. LiCl/EtOH. Scan rate: 100 mV/s. Supporting electrolyte: 0.5 M MTBS; *c*(**6x**) = 5.0 mM.

Mechanistic Considerations

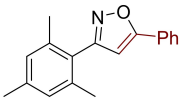
In accordance with literature and our experimental results, we propose anodic oxidation of the aldoximes followed by a conventional [3 + 2] dipolar cycloaddition (Scheme 3). Anodic oxidation of oxime **6** via two-electron transfer results in formation of nitrile oxide **II**. Coinciding with cathodic hydrogen evolution base is generated, which might engage in the deprotonation occurring in this step. Nitrile oxide **II** undergoes subsequent cycloaddition reaction with the added dipolarophile, resulting in formation of the desired isoxazole **7**. For 2,6-disubstituted aryl aldoximes, the corresponding nitrile oxide is sterically protected. Thus, the nitrile oxide of test substrate **6a** was detected by GC-MS (see Figure S8–S9, supporting information), supporting the hypothesis of isoxazole synthesis via conventional [3 + 2] cycloaddition. Formation of corresponding benzaldehydes as byproducts can be explained via initial one-electron oxidation of the aldoxime. According to literature, formation of iminoxyl-radicals (**I**) occurs which rapidly undergo recombination to intermediate (**III**).[27,40] Elimination of nitrogen finally yields the corresponding aldehyde **8**.

The nitrile oxides of *para*-substituted benzaldehyde oximes could not be observed by any analytical method. This could simply be a result of their lack of steric protection resulting in greater reactivity. However, DFT calculations and experimental findings indicate a radical mechanism for a chloride-mediated intermolecular electrochemical synthesis of isoxazolines according to literature.[25] Thus, in case of sterically non-protected aldoximes a radical reaction pathway might need to be considered alternatively to the conventional [3 + 2] cycloaddition as well. As no nitrile formation was observed in any case,



Scheme 3. Proposed reaction mechanism for formation of isoxazoles (black, plain) and aldehydes as potential byproducts (grey, dashed).

Table 2. Scale-up of the synthesis of **7a**.

Product				
 7a	75%[a] 0.33 mmol 87 mg	72%[a] 1.81 mmol 476 mg	73–77%[a, b] 3.64–3.88 mmol 961 mg–1.02 g	67%[a] 13.4 mmol 3.53 g

[a] Isolated yields given. Reaction conditions: graphite anode, stainless-steel (1.4571) cathode, 10 mg/mL MTBS in MeCN + 15 vol% H_2O + 5 vol% HFIP, 31 °C, 5 mA/cm^2, 2.9 *F*, 3.0 eq. phenylacetylene, 4 h post-electrolysis stirring. [b] results obtained from solvent recycling; experiment replicated twice.

we propose solely hydrogen evolution serves as the cathodic counter reaction.

Scale-up and Solvent Recycling

Last, the scalability of the reaction was investigated using test substrate **6a** (Table 2). Initially, the reaction was transferred from screening-scale to a batch-type electrolysis via 5-fold scale-up. To our delight, isoxazole **7a** was obtained in 72% with almost no loss in yield. This could be maintained on 5.00 mmol-scale (815 mg **6a**), yielding 73% of isoxazole **7a**. Usually, the exemplary reuse of the supporting electrolyte is chosen to prove the sustainability of a process and its resource efficiency. Thus, the recyclability of tetraalkylammonium-based supporting electrolytes via extraction and recrystallization is widely demonstrated in literature.[41] As the application of HFIP as additive might be seen as a limiting factor of this procedure in particular, the recyclability of the employed mixed solvent system (MeCN + 15 vol% H_2O + 5 vol% HFIP) was investigated (Figure 3). Therefore, the solvent mixture was distilled under reduced pressure during work-up, which allowed for quantitative recycling, and reused for a second run. The targeted product **7a** was obtained without any loss in yield (73%). Even a third run with the recycled solvent mixture could be achieved without affecting the course of the reaction, yielding 77% of product **7a**. Hence, the recyclability of the used solvent mixture by simple vacuum distillation was proven. Moreover, the option of multiple reuses contributes to the sustainability of the established reaction, as the amount of solvent waste can be minimized. Thus, the use of small quantities of HFIP to improve the reaction's performance, which might appear to be a disadvantage at first, can be justified.

Last, a multi-gram scale electrolysis was performed. In a 40-fold scale-up, the desired product could still be obtained in a comparable yield of 67%, demonstrating the general translation of this electrosynthetic method to a preparative-relevant scale.

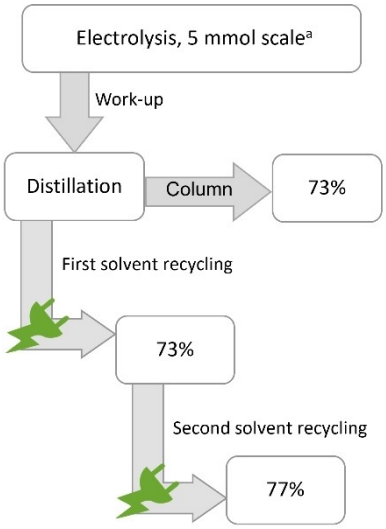


Figure 3. Demonstration of solvent recyclability.

Conclusions

An electrochemical method for the synthesis of isoxazoles and isoxazolines from readily available aldoximes in up to 81% yield was established. Constant current electrolysis was carried out in the simplest set-up in an undivided cell. Direct anodic oxidation of aldoximes in up to multi-gram scale with solely electric current as traceless oxidant minimizes reagent waste. Moreover, application of inexpensive and widely available electrode materials and the recyclability of solvents and supporting electrolyte contribute to an environmentally benign method that still captivates with cost-efficiency. The possibility of variation as an in-cell or ex-cell process allowed for application of a broad variety of alkynes and alkenes, highlighting a significant functional group tolerance. Furthermore, the applicability of heteroatomic dipolarophiles was demonstrated by exemplary synthesis of an oxadiazole. Thus, further development of the presented method might enable greener access to a broad variety of heterocyclic compounds in the future.

Experimental Section

General Procedure for the Synthesis of Isoxazoles

The respective oxime (0.5 mmol, 1 eq.) and dipolarophile (1.5 mmol, 3 eq.) were placed in a 5 mL PTFE cell and dissolved in 5 mL of tributylmethylammonium methylsulfate (MTBS, 10 mg/mL) in acetonitrile + 15 vol% water + 5 vol% 1,1,1,3,3,3-hexafluoroisopropanol (HFIP). The mixture was subjected to galvanostatic electrolysis at 31 °C under moderate stirring (magnetic stirrer set to approx. 500 rpm) using a current density of 5 mA/cm^2, a graphite anode and a stainless-steel (1.4571) cathode with a relevant surface area of 1.5 cm^2 (surface: 70 mm×10 mm, immersion depth of 1.5 cm), until an amount of charge of 2.9 *F* (142.3 C) was applied. The reaction mixture was stirred at 31 °C until the cycloaddition-reaction was completed (approx. 4 h). The mixture was transferred to a flask and evaporated to dryness under reduced pressure. The crude product was purified by recrystallisation or flash column chromatography.

General Procedure for the Synthesis of Isoxazolines

The respective oxime (0.5 mmol, 1 eq.) was placed in a 5 mL PTFE cell and dissolved in 5 mL of MTBS (10 mg/mL) in acetonitrile + 15 vol% water + 5 vol% HFIP. The mixture was subjected to galvanostatic electrolysis at 31 °C under moderate stirring (magnetic stirrer set to approx. 500 rpm) using a current density of 5 mA/cm^2, a graphite anode and a stainless-steel (1.4571) cathode with a relevant surface area of 1.5 cm^2 (surface: 70 mm×10 mm, immersion depth of 1.5 cm), until an amount of charge of 2.9 *F* (142.3 C) was applied. The respective dipolarophile (1.5 mmol, 3 eq.) was added and the mixture was stirred at 31 °C until the cycloaddition-reaction was completed (approx. 4 h). The mixture was transferred to a flask and evaporated to dryness under reduced pressure. The crude product was purified by recrystallisation or flash column chromatography.

General Procedure for Scale-up

The respective oxime (2.00 mmol or 5.00 mmol, 1 eq.) and dipolarophile (6.00 mmol or 15.00 mmol, 3 eq.) was placed in a 50 mL jacketed beaker-type cell, equipped with a cross-shaped stirring bar and dissolved in 25 mL or 50 mL of tributylmethylammonium methylsulfate (MTBS, 10 mg/mL) in acetonitrile + 15 vol% water + 5 vol% 1,1,1,3,3,3-hexafluoroisopropanol (HFIP). The mixture was subjected to galvanostatic electrolysis at 31 °C under moderate stirring (magnetic stirrer set to approx. 500 rpm) using a current density of 5 mA/cm^2, a graphite anode and a stainless-steel (1.4571) cathode with a relevant surface area of 5 cm^2 (surface: 25 mm×20 mm, immersion depth of 2.5 cm) or 7 cm^2 (surface: 35 mm×20 mm, immersion depth of 3.5 cm), until an amount of charge of 2.9 *F* was applied. The mixture was stirred at 31 °C until the cycloaddition-reaction was completed (approx. 4 h), transferred to a flask and evaporated to dryness under reduced pressure. The crude product was purified by recrystallisation or flash column chromatography.

Supporting Information

Further experimental details and CV studies as well as data regarding the characterization of products is included in the Supporting Information of this article. The authors have cited additional references within the Supporting Information.[42–59]

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Conflict of Interests

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: electrosynthesis · cycloaddition · anodic oxidation · oximes · isoxazoles

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