



Sustainable Electrocatalytic Oxidation Method for Synthesis of Imines and Nitriles

Students' Scientific Conference

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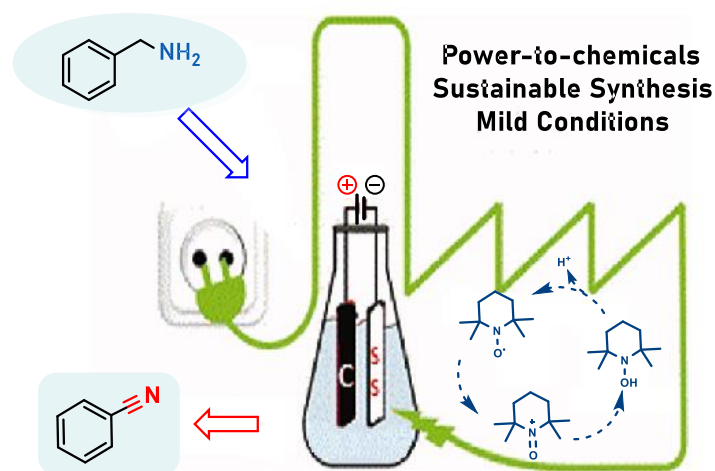
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1. Abstract

The high applicability of imines and nitriles in numerous fields, including pharmaceuticals, agriculture, materials science, and polymers, coupled with their versatility in several reactions, such as nucleophilic addition, reduction, and cross-coupling reactions, allows for elevating the organic synthesis of complex molecules. The synthesis of imines and nitriles using innovative methods represents a promising research direction in the present era. The oxidation process by electrosynthesis is regarded as a sustainable and productive cleansing methodology, offering an alternative to the traditional redox techniques. In contrast to the employment of toxic reagents and the necessity for harsh conditions inherent to the redox transfer method, electrochemical oxidation is a technique that numerous scientists have selected due to its cost-effectiveness and eco-friendliness.

Over the past few decades, various electrochemical oxidation reactions have been deeply investigated. However, the reaction mechanisms have not been thoroughly figured out due to the complex direction of various electron-donating (EDG) or electron-withdrawing groups (EWG) in substituted compounds, yielding inconsistent results. In some cases, electrochemical oxidation of amines is known, applying transition metal electrodes, special alloys, or expensive electrodes with modified surfaces, however, only a few amines were investigated, mostly primary ones.¹ This project represents a comprehensive analysis of the diverse electrocatalytic transformation of various amines, including primary amines, *N*-substituted benzylamines, and further secondary amines by applying inexpensive electrodes in mild conditions. Consequently, using appropriate conditions with catalytic amounts of nitroxyl radical, cost-effective electrodes such as graphite and stainless steel were successfully employed to produce stable imine and nitrile products with high yields (>99%), selectivity (up to 99%) and high Faradic efficiency.



2. *List of abbreviations*

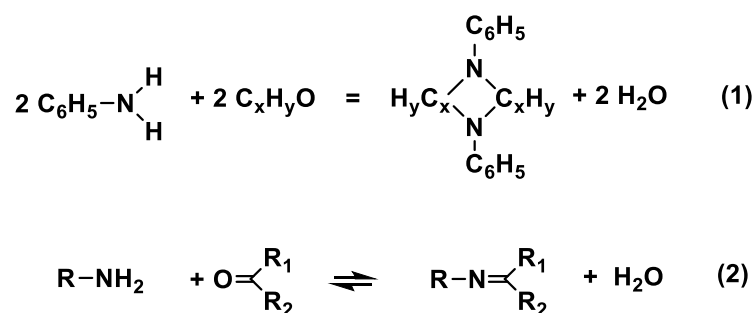
Abbreviation	Explanation
^1H NMR	Proton nuclear magnetic resonance
^{13}C NMR	Carbon-13 nuclear magnetic resonance
^{19}F NMR	Fluorine-19 nuclear magnetic resonance
ABS	Acrylonitrile butadiene styrene copolymer
Bn	Benzyl group
C	Graphite (electrode)
CD_3CN	Deuterated acetonitrile
CDCl_3	Deuterated chloroform
CE	Counter electrode
CV	Cyclic voltammetry
DCM	Dichloromethane
DDQ	2,3-Dichloro-5,6-dicyanobenzoquinone
DMSO-d_6	Deuterated dimethyl sulfoxide
EDG	Electron-donating group
ESI	Electrospray ionization
EWG	Electron-withdrawing group
HER	Hydrogen evolution reaction
HMBC	Heteronuclear Multiple Bond Correlation
HSQC	Heteronuclear Single Quantum Coherence
LC-MS	Liquid chromatography-mass spectrometry
MeCN	Acetonitrile
NMR	Nuclear magnetic resonance spectroscopy
NNO	Nortropine <i>N</i> -oxyl
Ph	Phenyl group
PMMA	Poly(methyl methacrylate)
RE	Reference electrode
ROESY	Rotating Frame Overhauser Enhancement Spectroscopy
HPLC	High-performance liquid chromatography
S.S.	Stainless steel (electrode)
SAN	Styrene-acrylonitrile resin
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
TFA	Trifluoroacetic acid
THIQ	1,2,3,4-Tetrahydroisoquinoline
WE	Working electrode

3. Introduction

3.1. Theoretical background of imines and nitriles

3.1.1. Historical overview and advances in imine chemistry: From early discoveries to modern applications

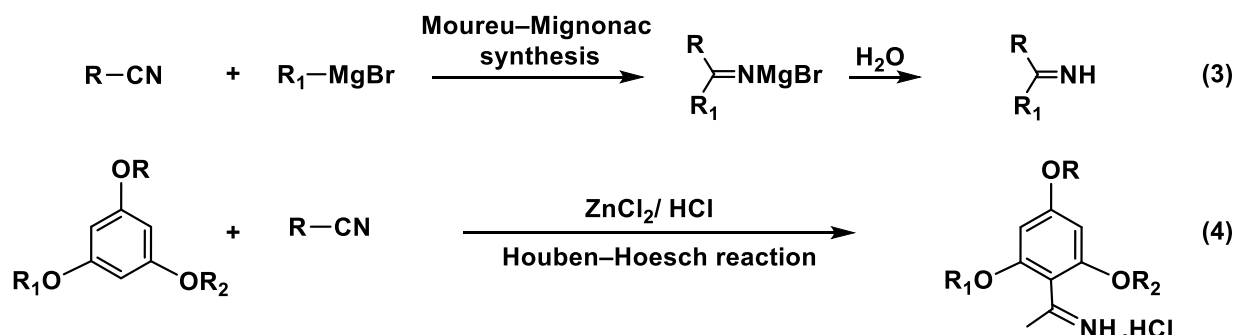
The term “imine“ was first defined in 1883 by the German scientist Albert Ladenburg, who investigated the chemical functional group containing the carbon-nitrogen double bond (C=N) in compounds designated as $R_1R_2C=NR_3$ where R_1 , R_2 , and R_3 are alkyl, aryl substituents or hydrogen.²⁻³ Nevertheless, some reviews suggest that the initial identification of compounds containing the imino bond (C=N) and group $R^3 \neq H$ named *Schiff bases* was first obtained by Hugo Schiff when he conducted a study employing the condensation formation of aldehydes and aniline (**Scheme 1**, top) and published an article entitled “Mittheilungen aus dem Universitäts-laboratorium in Pisa” in 1864 in the journal *Annalen der Chemie und Pharmacie*.⁴⁻⁶ After Schiff's experiments, Ladenburg also conducted intensive work on forming imine by substituting the aryl group with hydrogen or other substituents (**Scheme 1**, bottom).⁷ This investigation widely contributed to the organic synthesis and classified compounds containing the C=N double bond, thus completing a remarkable point in organic chemistry.



Scheme 1. The condensation reaction between aniline and aldehyde illustrated from Schiff's work in 1864 (eq. 1),⁵ and condensation between amine with aldehyde or ketone as a contemporary perspective using modern fonts (eq. 2).⁴ R_1 , R_2 , R_3 are alkyl, aryl groups or H.

Following Schiff and Ladenburg's seminal contributions to imines, numerous scientists have refined and expanded the way for synthesizing these compounds through various techniques. Moureu-Mignonac successfully synthesized ketimine, a derivative of imine in 1913 based on the first experiment in 1901 by Blaise, through the reaction of aryl or alkyl Grignard reagents with aryl nitrile.⁸ Subsequently, by replacing Grignard reagents with phenols or their ethers and catalyzing the reaction with hydrogen chloride or zinc chloride, Hoesch and Houben

significantly increased the yield of ketimine salt formation as shown in **Scheme 2**.^{9–11} In addition, many progressive methods involving a wide range of compounds, such as the dehydrogenation of amines, reduction of oximes, the reaction of nitroso compounds with active hydrogen compounds, or the combination of metal amides with aromatic ketones, have markedly enhanced the synthesis of imines.³



Scheme 2. Moureu–Mignonac synthesis (eq.3)⁸ and Houben–Hoesch ketimine formation (eq.4).¹¹ R, R₁, R₂ are alkyl, aryl groups or H.

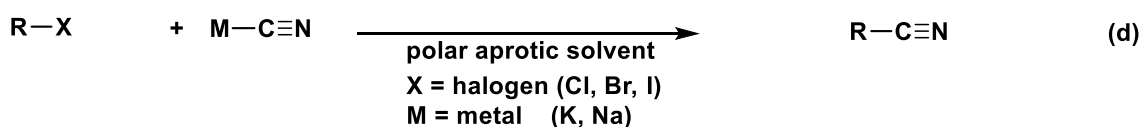
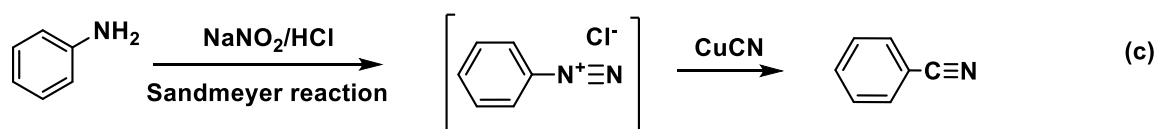
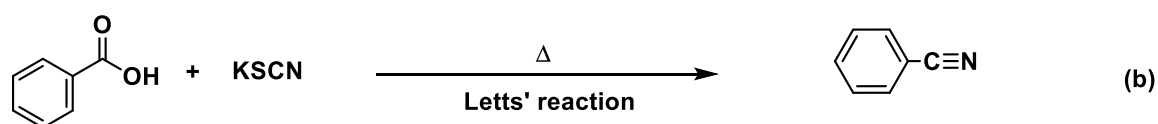
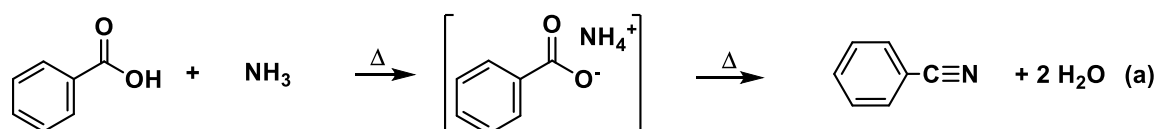
Based on the prior foundational work, numerous researchers have developed imines as a crucial intermediate in the synthesis of further valuable compounds. In 1957, the scientist J.H. Billman employed natural primary amine to synthesize bulky secondary amines of the *N*-aryl substituted benzhydryl type compounds by reducing their intermediate imines with lithium aluminium hydride (LiAlH₄). This method proved useful in establishing a new route for producing a variety of amines from imines in the field of organic synthesis.¹²

In the field of polymers, numerous scientists have emphasized the high potential of polyimines (PIs) for a multitude of major industries, including not only fibers and film-forming polymers¹³ but also semiconductors and electronic materials.¹⁴ D’Alelio et al. (1967) successfully established polymeric Schiff bases as a valuable research topic based on developing twelve types of polyimine derivatives, involving related conjugated, pseudoconjugated, and nonconjugated forms, with thermal stability due to their high-resonance energy structures.¹⁵ Thereafter, other derivatives namely polyazomethines (PAMs), polyazines (PAZs), polyketamines, and polyketazines were also created from imines, representing a significant breakthrough in the area.¹⁶

3.1.2. Nitrile chemistry: The historical developments and their industrial applications

Nitrile is the designation for organic compounds comprising the $\text{-C}\equiv\text{N}$ functional group.¹⁷ However, the precursor to nitrile compounds is the highly toxic hydrogen cyanide, the simplest

inorganic nitrile, which was prepared by C. W. Scheele by treating Prussian blue with sulfuric acid in 1782 and represents an important early step in the field of organic chemistry.¹⁸ Half a century later, German scientists Friedrich Wöhler and Justus von Liebig successfully produced the first organic nitrile – benzonitrile in low yield.¹⁹ Following over a decade of research, Hermann Fehling successfully produced benzonitrile by heating ammonium benzoate, enabling him to generate sufficient yield for analysis (**Scheme 3, a**). He created the functional group of this newly identified compound, which was named "nitrile".¹⁷

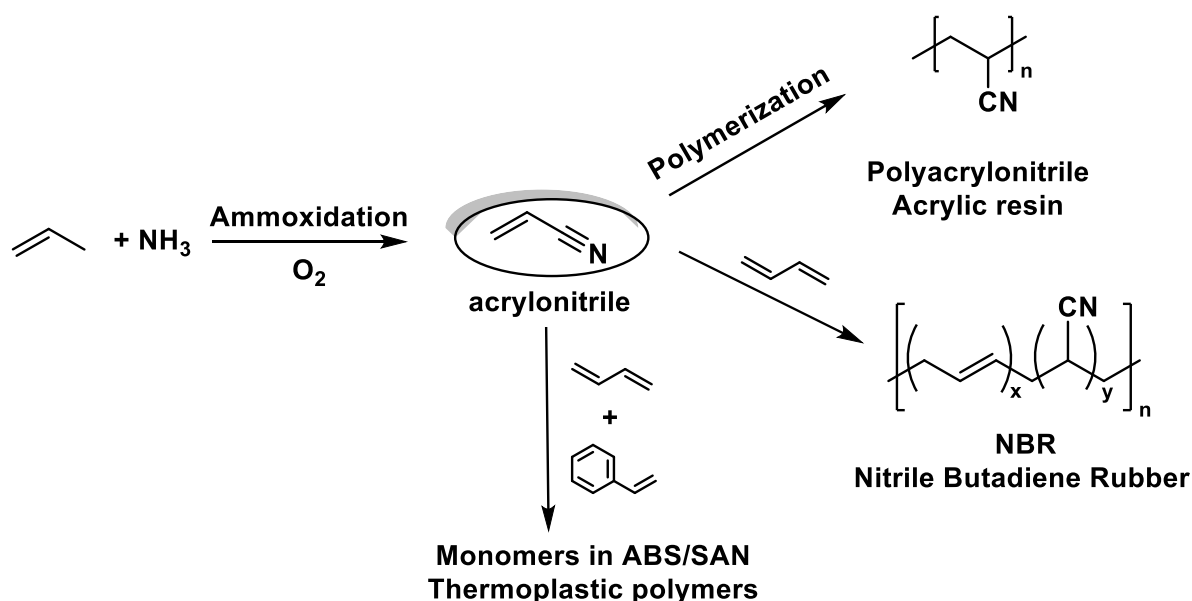


Scheme 3. (a) Benzonitrile synthesis depicted from Fehling's experiment,¹⁷ (b) Lett's nitrile synthesis,²⁰ (c) Sandmeyer reaction,^{21,22} and (d) Kolbe's nitrile preparations.²³

Definitions of nitrile have prompted many scientists to conduct in-depth research to synthesize nitriles from different precursors. Subsequently, in 1872, another substitution reaction utilizing a base was conducted by Edmund A. Letts when he reacted benzoic acid with potassium thiocyanate and heated it for several hours, producing nitrile in 40% yield (**Scheme 3, b**).²⁰ Another type of reaction is the radical-nucleophilic aromatic substitution, which was discovered by Traugott Sandmeyer. In 1884, he converted aryl diazonium salts to aryl nitriles, providing a new synthetic route for producing aromatic nitriles (**Scheme 3, c**).^{21,22} During that period, Kolbe successfully developed a straightforward and effective procedure for preparing

nitriles from alkyl halides and inorganic cyanide salts using a polar solvent through an S_N2 substitution reaction (**Scheme 3, d**).²³

From the early research, which involved significant toxicity and low efficiency in the late 19th century, the process of studying and producing nitriles gradually improved in the following years. Notable methods for synthesizing acrylonitriles by the Sohio process (1950s),²⁴ utilized environmentally friendly chemicals and achieved high efficiency, leading to the production of precursors for the acrylic fiber, rubber, and thermoplastic polymers industries in the modern century (**Scheme 4**).²⁵



Scheme 4. Sohio's process to prepare acrylonitrile and its application.^{24,25}

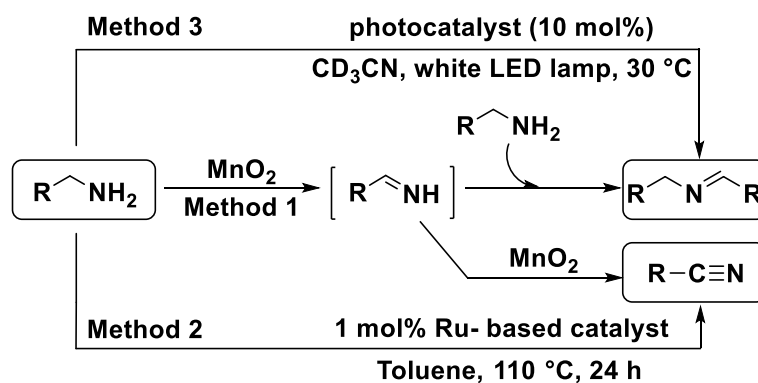
Furthermore, various nitriles have been employed in areas of human endeavor, including dyeing, pharmaceuticals, the production of nylon, and the manufacture of pesticides and fungicides. **Table 1** below provides a comprehensive overview of nitrile precursors in industrial applications.²⁶

Table 1. The most relevant industrial applications of nitriles.²⁶

Nitrile precursor	Industrial application
Saturated nitriles	
Acetonitrile (CH ₃ CN)	Solvent in pharmaceuticals
Propionitrile (CH ₃ CH ₂ CN)	Organic intermediate in pharmaceuticals
Isobutyronitrile (CH ₃) ₂ CHCN)	Amprolium drugs, insecticides
Saturated dinitriles	
Malononitrile (NC-CH ₂ -CN)	Key intermediate in pharmaceuticals, pesticides, fungicides, dyes
Succinonitrile (NC-CH ₂ -CH ₂ -CN)	Pharmaceutical intermediate, electrochromic devices, plasticizers, nylon
Adiponitrile (NC(CH ₂) ₄ CN)	Production of nylon 6,6 for fibers and resins
Unsaturated nitriles	
Acrylonitrile (CH ₂ =CHCN)	Precursor of plastics, rubber, resin
Allyl cyanide (CH ₂ =CH-CH ₂ CN)	Intermediate in organic synthesis, rubber chemicals, and pesticides
Methacrylonitrile (CH ₂ =C(CH ₃)CN)	Production of transparent plastics (PMMA)
Aromatic nitriles	
Phenylacetoneitrile (C ₆ H ₅ CH ₂ CN)	Anti-inflammatory drugs (penicillins or barbiturates)
Benzonitrile (C ₆ H ₅ CN)	Production of azo dyes, pharmaceuticals, and herbicides

3.2. Traditional oxidation of amines to nitriles and imines

Nitriles and imines are crucial derivatives of amines, employed widely in organic synthesis as well as industrial applications. Numerous scientists have successfully achieved those derivatives through traditional oxidation methods. One of the most classical techniques is amine oxidation by effective oxidizing agents such as MnO₂ or KMnO₄ (**Method 1, Scheme 5**). Depending on the specific conditions, primary amine can be converted to imine or nitrile. Meanwhile, secondary amines are predominantly oxidized to Schiff base. Tertiary amines undergo oxidative fragmentation to form imine.^{27,28}



*Scheme 5. Three different approaches to the synthesis of nitriles and imines: **Method 1** traditional oxidation,^{27,28} **Method 2** transition-metal catalysis,²⁹ and **Method 3** photocatalytic methods.³⁰*

Although this redox methodology is rapid and straightforward, it still exhibits limited selectivity and low atom economy due to the over-oxidizing of undesired products.^{27,28} Consequently, a novel strategy is widely exploited to generate better conversion using transition-metal complex catalysts. Catalyst complexes, such as ruthenium, rhodium, and gold, promote amine dehydrogenation (**Method 2, Scheme 5**).²⁹ In 1979, the irreversible oxidation reaction of amines was demonstrated by Toshikatsu et al. under the application of active rhodium catalysts under ambient conditions, resulting in the formation of corresponding nitriles. However, the authors concluded that the yields obtained from active rhodium-based reactions were not too high.³¹ Later, N. K. Szymczak et al. conducted a similar dehydrogenation of amine by utilizing ruthenium hydride complex catalysts. This investigation suggests that the reaction catalyzed by an active ruthenium-base complex can obtain better selectivity and yield.²⁹

Nevertheless, further investigation indicates that using transition-metal catalysts for dehydrogenation has some limitations due to the necessity for an aerobic environment, and harsh conditions.²⁹⁻³¹ A green pathway that utilizes a photocatalyst to drive amine oxidation directly has been developed, allowing the selective oxidation of amines to nitriles or imines under mild and environmentally friendly conditions (**Method 3, Scheme 5**).^{30,32} L. Kia-Sheun et al. prepared an environmentally benign approach by performing oxidation amine to imine through mesoporous $\text{SiO}_2/\text{BiVO}_4/\text{CuO}_x$ nanospheres. The combination of bismuth, vanadate copper, and oxide-silica provides a high absorption area and enhanced photocatalytic results of amine dehydrogenation.³⁰

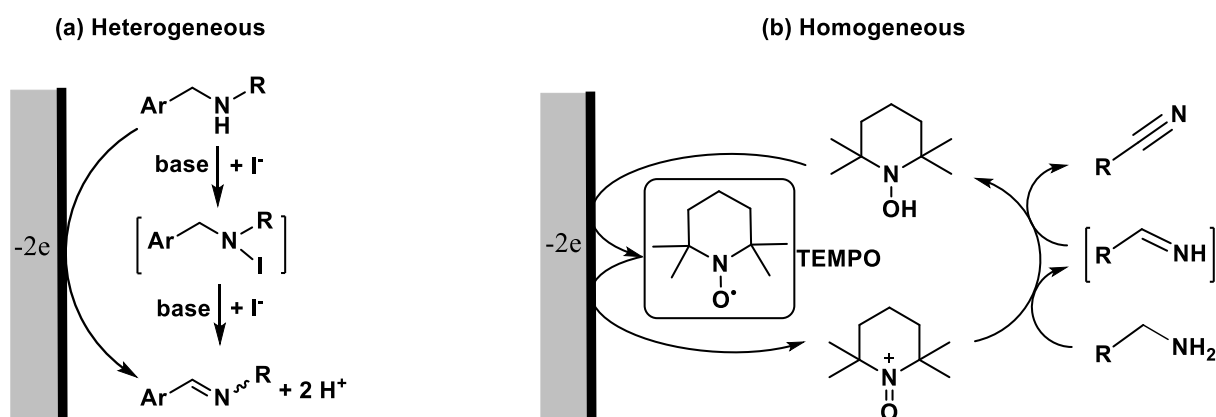
Traditional techniques to produce nitrile or imine which rely on oxidizing agents, catalytic oxidation, or photocatalysts, have marked a pivotal development in organic chemistry despite the aforementioned limitations.²⁷⁻³⁴ Considering the increasingly prioritized green

chemistry, and sustainable and environmentally friendly transformations, new solutions such as applying electrochemistry or biocatalyst will offer promising approaches in future research.³⁵⁻⁵²

3.3. Electrochemical oxidation of amine to nitriles and imines

To avoid using hazardous reagents and generate fewer by-products in traditional oxidation reactions, many scientists have investigated more eco-friendly and sustainable approaches through the application of electrosynthesis.³⁵⁻⁴⁰ This mild and safe technique uses electric current in trace amounts and electrode potential as a continuously variable driving force to deliver the reaction in a reactor simply as a cell.^{37,38,40} Some parameters are considered to enhance the selectivity and efficiency of electrochemical oxidation reactions, including temperature, electrolytes, electrodes, and cell types. However, the most widely used investigation employs electrocatalysis to facilitate the electron transfer via chemical interaction.⁴²

The earliest appearance of heterogeneous electrocatalysis can be attributed to the use of platinum (Pt) as an anodic electrode where electron transfer (ET) between the substrate and the anode takes place at the surface during electrochemical reactions.^{43,44} Due to its high stability, corrosion resistance, and excellent conductivity, the Pt electrode serves as one of the most effective solid catalysts for amine electrocatalysis oxidation.⁴⁵ Mitsuhiro et al. employ a platinum net as an anode and a nickel coil as a cathode in mild conditions to oxidize a variety of benzylamine derivatives, thereby achieving the corresponding imines in good yields (**Scheme 6a**).⁴⁶



Scheme 6. (a) Heterogeneous electrochemical oxidation of benzylamines,⁴⁶ (b) Homogeneous electrocatalysis oxidation of various amines using TEMPO mediator.⁴⁷

Due to the scarcity and high cost of platinum, many scientists have attempted alternative methods for reducing the reliance on Pt electrodes. Modified electrodes such as robust nickel-

based electrodes,⁴⁸ metal-organic frameworks (MOFs),⁴⁹ and transition metal combined with Pt trace electrode⁵⁰ have been developed to obtain higher conversion and enhanced electrochemical performance. In the case of metal-organic frameworks (MOFs), Xu's group researched that oxidation of primary amine with coupling HER in a bimetallic-electrode system (t-Ni/Co MOF || Pt) can be selective to corresponding aliphatic and aromatic nitriles and with higher Faraday efficiency (FE) and better yield.⁴⁹

Besides the sustainability and reusability of heterogeneous electrocatalysis, homogeneous electrocatalysis is also a unique approach by eliminating kinetic inhibition, enhancing selectivity, and preventing electrode passivation in electrosynthesis. Different from the electron transfer in the surface electrode of the heterogeneous process, in a homogeneous manner, electron transfer occurs through the interaction of catalyst and substance in the bulk solution.⁴² The pioneering and notable redox organic mediator is TEMPO, 2,2,6,6-tetramethylpiperidine-1-yloxy, along with other *N*-oxyl radicals which can be used in various electrochemical oxidation reactions of amine and alcohol.^{47,51} In 1983, M. F. Semmelhack applied electrochemical reagents in the oxidation of various amines. By conducting the electrolysis amine in "H" cell with Pt electrode in the solution of LiClO₄ in freshly distilled MeCN and using TEMPO as a catalyst, the desired nitrile is produced with high efficiency, and the imine intermediate expected (**Scheme 6b**).⁴⁷

In addition to the wide use of organic mediators such as TEMPO,⁴⁷ NNO,⁵¹ triaryl amine,⁵² and DDQ,⁵³ some researchers have grown an interest in the application of inorganic mediators for amine oxidation due to their cost-effectiveness and availability in both industrial and laboratory scales. For instance, the use of halides and hypohalites has been shown to promote amine oxidation with remarkable efficiency and high selectivity.^{35,36} In 1984, Tatsuya Shono's group demonstrated the potential of bromine ion sources in indirect electrooxidation of amine to effectively obtain the desired nitriles in high yield (95%).³⁵

Although utilizing heterogeneous or homogeneous electrocatalysis has shown powerful approaches, it can be observed that the commonly used electrodes are often platinum or other modified expensive materials that make costly limits in the accessibility and scalability of these methods.³⁵⁻⁵³ Therefore, based on their satisfactory catalytic performance, affordability, and availability, by investigating further alternative electrode materials such as graphite and stainless steel electrodes in the electrooxidation field, this oxidation process can be accessible for sustainable organic chemistry and broader adoption in various industrial applications.⁵⁴

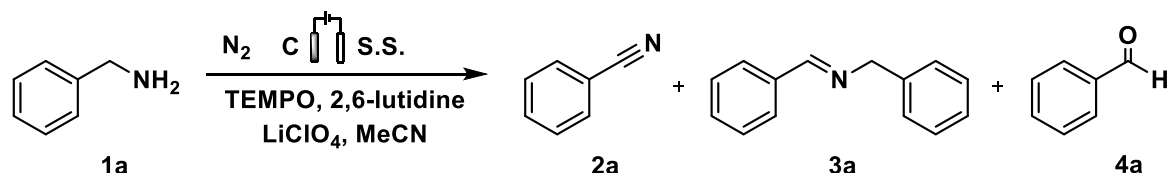
4. Results and discussion

The aim of the project was the oxidation of amines under electrocatalytic conditions using unmodified, cheap electrodes and a simple, undivided cell, which is generally more sustainable than traditional chemical oxidation method, to reduce the need of stoichiometric oxidants and the generation of hazardous by-products. In 1983, M. F. Semmelhack successfully synthesized nitrile with high, around 90% Coulomb efficiency in the oxidation of various amines applying an “H” cell with Pt electrode serving as both working electrode (WE) and counter electrode (CE), using a electrolyte as solution of anhydrous LiClO_4 in anhydrous MeCN, 2,6-lutidine as a weak base, and using TEMPO as catalytic mediator which is mostly used in green chemistry.⁴⁷ In this project, similar electrolyte, base, solvent and additives were applied, however, cheap and simple electrodes and simple undivided cell were used, lowering energy and material requirements compared to divided cells. In the first reaction, I have chosen stainless steel as the CE and graphite as the WE, offering a sustainable choice due to their abundant, lower-cost and smaller environmental footprint than precious metals for the electrooxidation of amines under very low current (1 mA) at room temperature, minimizing energy consumption. This approach aims to compare their efficiency and selectivity against previous methods, maximize the yield of the desired product, and minimize waste, which could contribute to developing accessible oxidation processes for sustainable organic synthesis.

4.1. Preparation of nitrile from electrocatalytic oxidation of benzylamine derivatives

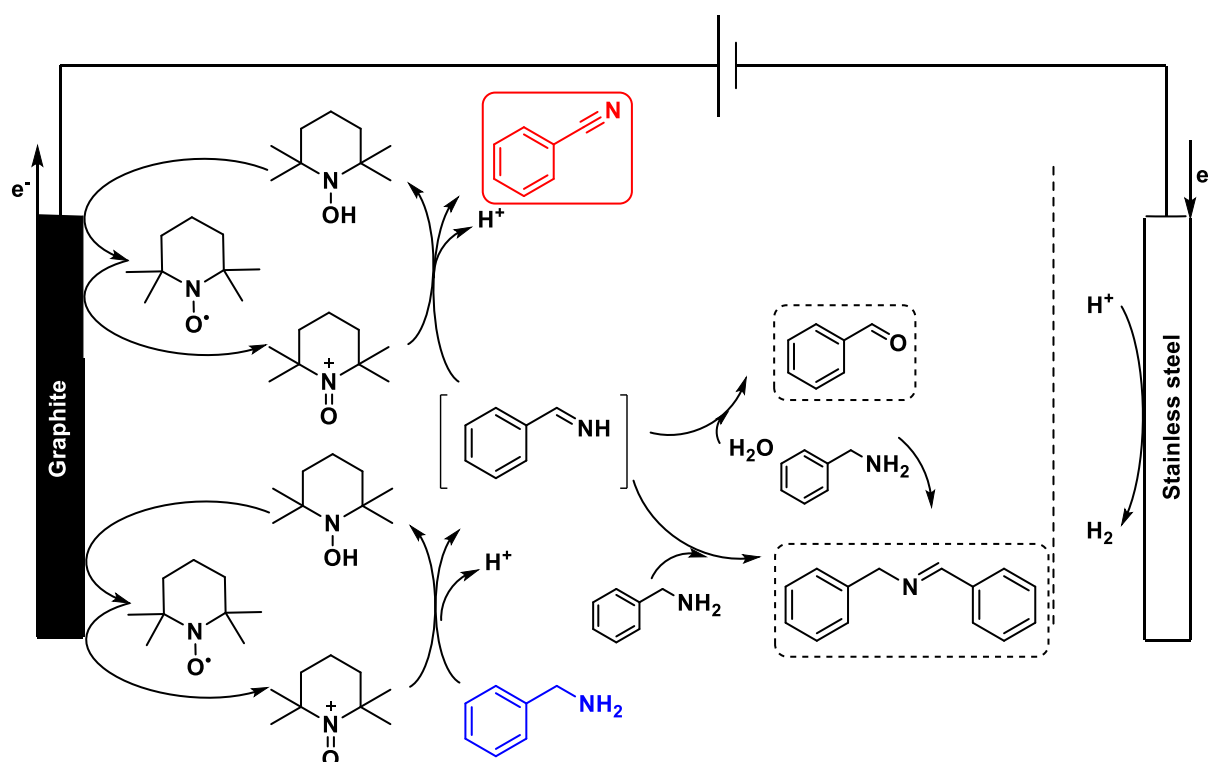
4.1.1. Electrocatalytic oxidation of benzylamine as a model substrate

In the first step, the electrooxidation of benzylamine (**1a**) was investigated. Model substrate **1a** was applied in a 0.25 mmol scale, the reaction was carried out using constant current (1 mA), over 28 hours (0.52 mmol electron transfer). The desired reaction and relevant coproducts were illustrated in **Scheme 7**.



*Scheme 7. Electrocatalytic oxidation of benzylamine (**1a**) under inert conditions. S.S.: stainless steel; C: graphite electrode.*

After 28 hours, we successfully synthesized benzonitrile (**2a**) in high yield (97%), which was determined by analyzing the crude product with multiple methods. LC-MS and NMR measurements were carried out. The NMR spectra indicated a relatively high conversion of the starting material (>99%) due to the elimination of the benzylic peak (3.83 ppm) in the ^1H NMR spectrum (see Section 5.2.1.1).⁵⁵ The formation of benzaldehyde (**4a**) and *N*-benzyl-1-phenylmethanimine (**3a**) coproducts could be observed in traces (**Scheme 8**). The formation of **2a** was also proved by ^{13}C NMR measurement (Section 5.2.1.1).⁵⁶ The yields of the crude products were calculated by ^1H NMR investigations (**2a**: 97%, **3a**: 2 %, **4a**: 1%).



*Scheme 8. The suggested mechanism of the product (highlighted in red, **2a**) and co-product (dashed) formation reactions on the electrochemical oxidation of benzylamine (highlighted in blue, **1a**).*

The reaction starts with the oxidation in the benzylic position of amine facilitated by TEMPO^+ oxidant to form the imine intermediate. In the next step, further oxidation occurred, and the imine transformed into the desired nitrile. A possible side reaction involves the nucleophilic attack of amine to the imines, leading to diaryl compound. Additionally, in the presence of traces of water, hydrolysis of imine occurs and forms aldehyde which can react with unreacted amine to produce the diaryl compound.

4.1.2. Optimization of reaction conditions

Following the initial reaction, we modified reaction parameters such as applying different electrodes, reaction time, different reactant ratios, or reaction conditions to observe how impact of those factors on the yield and reaction efficiency. The results are summarized in **Table 2**. The optimization indicates the influence of reaction conditions in the electrooxidation of benzylamine **1a**. The inert condition intensively enhances the formation of desired nitrile while the effect of air can act as a co-oxidant, enhancing the generation of dimerization. The graphite anode is essential for TEMPO-mediated due to its high conductivity and excellent electrocatalytic efficiency compared to stainless steel to regenerate the active TEMPO radical species from its reduced form (TEMPOH) by transferring electrons. Longer reaction time also improved the selectivity (from 76% to 97%).

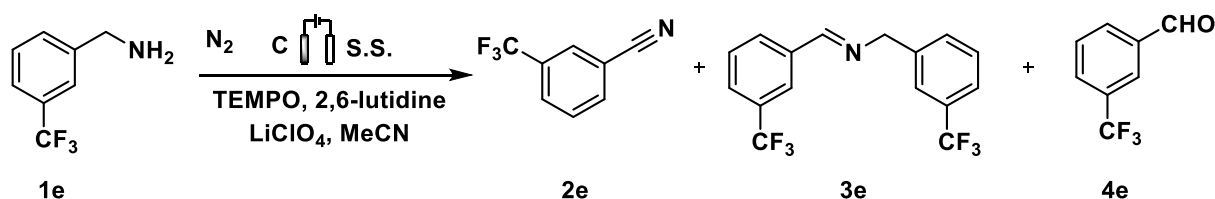
Table 2. Optimization of reaction parameters in electrooxidation reaction of **1a**.

BA amount (mmol)	TEMPO equivalent	Anode (WE)	Cathode (CE)	Current (mA)	Time (h)	Atmosphere	Conv. (%)	Yield ¹ (%)		
								2a	3a	4a
0.25	0.1	-	-	-	20	Air	<5	-	-	-
0.25	0.1	Graphite	S.S.	1	20	Air	>99	27	65	8
0.25	0.1	S.S.	Graphite	1	20	Inert (N ₂)	<5	-	-	-
0.25	0.1	Graphite	S.S.	1	20	Inert (N ₂)	>99	76	11	13
0.25	0.1	Graphite	S.S.	1	14	Inert (N ₂)	>99	26	69	5
0.25	0.1	Graphite	S.S.	1	28	Inert (N₂)	>99	97	2	1
0.5	0.1	Graphite	S.S.	1	56	Inert (N ₂)	>99	81	5	14

¹ Yields were determined by ¹H NMR analysis of the reaction mixture relative to 2,6-lutidine as internal standard.

Based on these modifications, significant differences in yield of product and selectivity were observed. By conducting the reaction under inert conditions, and applying appropriate time, we can successfully produce the desired product in high yield (**2a**, 97%) and selectivity with minimized byproduct formation.

4.1.2.1. Current effect on the electrochemical oxidation



Scheme 9. Electrocatalytic oxidation of 1e under inert conditions. S.S.: stainless steel; C: graphite electrode

Encouraged by previous promising results, we deeply investigate further exploration into the synthesis of nitrile by oxidation of 3-(trifluoromethyl)benzonitrile (**1e**) (**Scheme 9**), taking advantage of the convenience of determination of the composition of the reaction mixture using ^{19}F NMR spectroscopy. By fine-tuning the reaction parameters, based on the literature data,⁵⁷ we increased the current from 1 mA to 10 mA to reduce the reaction time (from 28 h to 2.8 h). Consequently, these adjustments enabled the production of 3-(trifluoromethyl)benzonitrile (**2e**) with an excellent yield of 94%. (**Table 3**). This optimization highlights an important and effective scale-enlarging step in this novel electrochemical oxidation method.

Table 3. Current effect on electrooxidation reaction reaction of 3-(trifluoromethyl)benzylamine.

Substrate (mmol)	TEMPO equivalent	Anode (WE)	Cathode (CE)	Current (mA)	Time (h)	Atmosphere	Conv. (%)	Yield ¹ (%)		
								2e	3e	4e
0.25	0.1	Graphite	SS	1	28	Inert (N ₂)	>99	95	5	-
0.25	0.1	Graphite	SS	2	14	Inert (N ₂)	>99	91	9	-
0.25	0.1	Graphite	SS	10	2.8	Inert (N₂)	>99	94	5	1
0.25	0.1	Graphite	SS	10	3.2	Inert (N ₂)	>99	87	5	8
0.25	0.1	Graphite	SS	10	3.6	Inert (N ₂)	>99	85	6	9

¹ Yields were determined by ^{19}F NMR analysis of the reaction mixture using benzonitrile as an internal standard.

4.1.2.2. Water effect on the electrochemical oxidation

Previously, we hypothesized water could generate the relevant amount of side products (**Scheme 8**). To access the effect of water, parallel experiments of the electrocatalytic oxidation

1e were carried out in the presence of varying amounts of distilled water. Water may hydrolyze the imine intermediate to aldehyde which may subsequently react with unreacted amine to form the diaryl compound, thereby hindering further oxidation to the desired nitrile. This hydrolysis effect is illustrated in **Table 4**. As we can see, the inherent water content of dry acetonitrile results in the low amount of coproduct (**3e**, 5%, **4e**, 1%). Later, the addition of 2 equivalents of distilled water caused a slight impact, resulting in a higher yield of side products (**3e**, 10%, **4e**, 2%). The yield of **3e** increased sharply to 35% when the 20 equivalents of distilled water was added. Notably, using technical grade MeCN, which contains 2.3 equivalents of water, allowed the oxidation of **1e** to proceed efficiently, achieving a good yield of 3-(trifluoromethyl)benzonitrile (**2e**, 88%). This result emphasizes the method's potential for industrial-scale applications.

*Table 4. Effect of water on the electrochemical 3-(trifluoromethyl)benzylamine **1e** oxidation*

Substrate (mmol)	TEMPO equivalent	Anode (WE)	Cathode (CE)	Current (mA)	Time (h)	Solvent	Conv. (%)	Yield ¹ (%)		
								2e	3e	4e
0.25	0.1	Graphite	SS	10	2.8	Dry MeCN	>99	94	5	1
0.25	0.1	Graphite	SS	10	2.8	technical grade MeCN²	>99	88	10	2
0.25	0.1	Graphite	SS	10	2.8	Dry MeCN +2 eq. water	>99	88	10	2
0.25	0.1	Graphite	SS	10	2.8	Dry MeCN +20 eq. water	>99	63	35	2

¹ Yields were determined by ¹⁹F NMR analysis of the reaction mixture using benzonitrile as an internal standard.

² Technical grade acetonitrile contains 2.3 equivalents of water determined by NMR measurements.

4.1.2.3. Effect of the amount of TEMPO catalyst on the electrochemical oxidation

To evaluate the effect of the TEMPO mediator on electrochemical oxidation reaction of **1e**, we reduced the amount of TEMPO catalyst. Initially, 0.1 equivalent of TEMPO was used.

Thereafter, the TEMPO concentration was progressively lowered to 0.05 equivalent, 0.01 equivalent, and finally to a condition without TEMPO. As can be seen from **Table 5**, the insufficient amount of TEMPO fails to fully oxidize the imine intermediate to target 3-(trifluoromethyl)benzonitrile **2e**, while significantly increasing the yield of the coproduct **3e** (from 5% to 38%). In the absence of TEMPO, the heterogeneous electrocatalytic reaction of **1e** proceeded, yielding notable amounts of coproducts (**3e**, 24% and **4e**, 8%).

Table 5. Effect of TEMPO catalyst on the electrochemical 3-(trifluoromethyl)benzylamine oxidation

Substrate (mmol)	TEMPO equivalent	Anode (WE)	Cathode (CE)	Current (mA)	Time (h)	Atmosphere	Conv. (%)	Yield ¹ (%)		
								2e	3e	4e
0.25	0.1	Graphite	SS	10	2.8	Inert (N ₂)	>99	94	5	1
0.25	0.05	Graphite	SS	10	2.8	Inert (N ₂)	>99	66	33	1
0.25	0.01	Graphite	SS	10	2.8	Inert (N ₂)	>99	50	38	2
0.25	0	Graphite	SS	10	2.8	Inert (N ₂)	>99	68	24	8

¹ Yields were determined by ¹⁹F NMR analysis of the reaction mixture using benzonitrile as an internal standard.

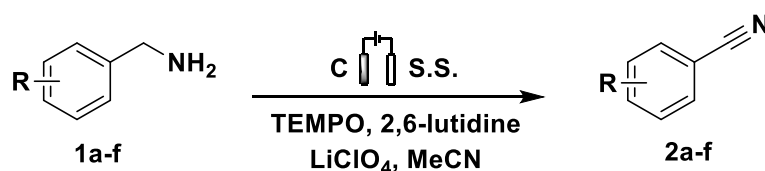
The investigations of applied current, time, the amount of TEMPO additive, and the presence of water through electrocatalytic oxidation of 3-(trifluoromethyl)benzylamine **1e** were carried out. Increasing the current from 1 mA to 10 mA, correspondingly reducing the reaction time by the same factor while maintaining selective oxidation of amine, highlights the scalability and reproducibility of this strategy. The presence of water slightly decreases the yield of the desired product. Additionally, the role of the amount of TEMPO additive in the oxidation reaction was ascertained to ensure the maximum yield of the target nitrile.

4.1.3. Substrate scope investigation of benzylamine derivatives in electrocatalytic oxidation

After successful electrochemical oxidation of **1a**, the substituent effect was investigated. Both electron-withdrawing (EWGs) and electron-donating (EDGs) groups were selected. Under using conditions (nitrogen atmosphere) which resulted in the best yield of reaction of **1a**, 4-

chlorobenzylamine (**1b**), 4-methoxybenzylamine (**1c**), 2-fluorobenzylamine (**1d**), 3-(trifluoromethyl)benzylamine **1e**, and 2-methoxybenzylamine (**1f**) were oxidized, and crude products were analyzed by NMR and LC-MS measurements (**Scheme 10**).

The products and the results of the oxidation of these compounds are summarized in **Table 6** (Section 5.2.1). All the tested substances show excellent conversion (>99%) under the applied mild conditions. By choosing the unsubstituted benzylamine as a reference (97% yield), we can determine the influence of various substituents on the reaction. The EDG groups, particularly in the para position (4-OMe) generally facilitate the nucleophilicity of the aromatic ring and make it more reactive toward the electrophilic attack during oxidation, resulting in the high yield (94%), while ortho positions (2-OMe) cause the steric hindrance that may affect the accessibility of the substrate to the oxidizing agent and result in the lower yield (77%). In addition, the EWGs, such as chloro, fluoro, or trifluoromethyl groups, decrease the reactivity of substrates during oxidation and result in lower yield.



*Scheme 10. Electrocatalytic oxidation of benzylamines **1a-f** in the presence of TEMPO.*

*Table 6. The yield of benzylamine derivatives referenced to **1a** using similar conditions in section 5.2.1.*

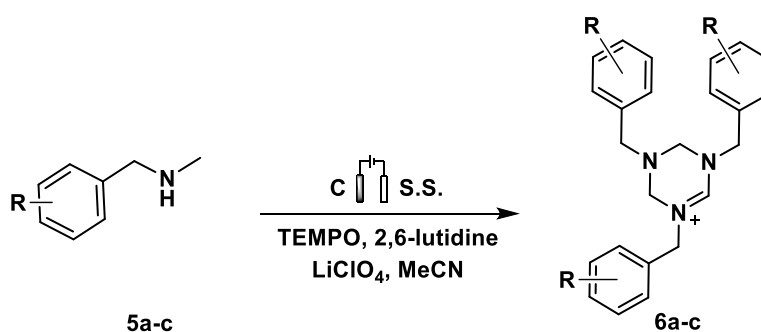
Substrate	R	Main product	Conversion (%)	Yield ¹ (%)
1a	H	2a	>99	97
1b	4-Cl	2b	>99	83
1c	4-OMe	2c	>99	94
1d	4-F	2d	>99	70
1e	3-CF ₃	2e	>99	82
1f	2-OMe	2f	>99	77

¹Yields were determined by ¹H NMR analysis of the reaction mixture relative to 2,6-lutidine as internal standard.

4.2. One-pot heterocyclic iminium compound formation from *N*-methylbenzylamines

Following the preliminary results, a study on the electrochemical oxidation of *N*-substituted benzylamines, such as 4-methoxy-*N*-methylbenzylamine (**5a**) was investigated. In these reactions, under oxidation conditions, the aliphatic amine such as **5a** might undergo the dehydrogenation from nitrogen atom and the adjacent carbon atom (benzyl or alkyl position), resulting in corresponding imine.

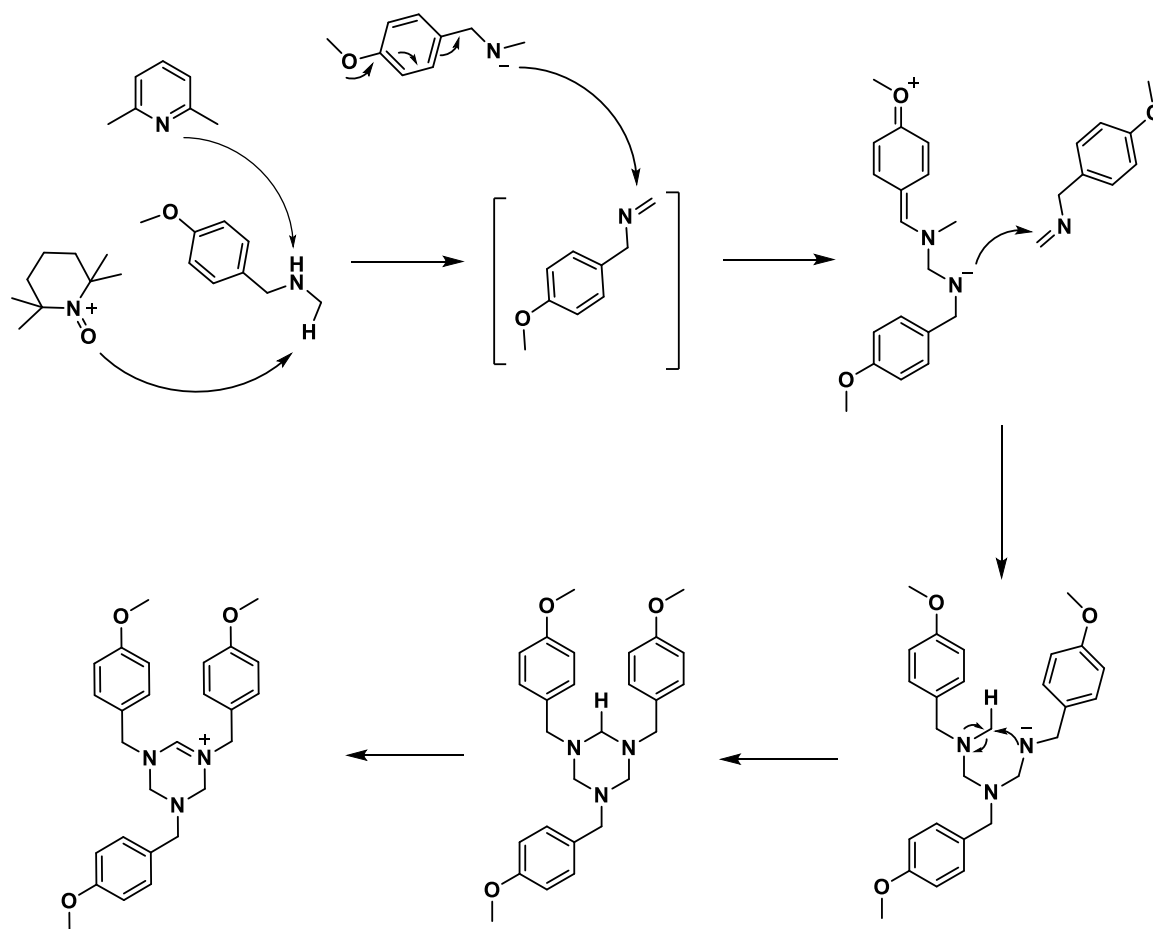
After 14 hours of oxidation (regarding 2 electrons transfer) of **5a**, the reaction mixture was analyzed by ^1H NMR measurement. Based on the analysis, a complex mixture was observed with a main product and further coproducts. Further purification was needed to identify the desired products. After the workup, purification utilizing preparative HPLC was carried out. Three different products were isolated (**Table 10**, section 5.2.2.2). Interestingly, the main product was a trimer (**Scheme 11**), its structure was determined by Dr. Gábor Turczel using ^1H , ^{13}C NMR, ROESY, HMBC, HSQC measurements, and LC-MS.



*Scheme 11. Electrochemical oxidation of *N*-methylbenzylamines (**6a-c**) in the presence of TEMPO additive.*

This reaction is unknown in the literature. However, C. A. Florea proved if the *N*-substituted secondary amine was oxidized to imine in a traditional synthesis, it could be transformed to its cyclic “trimer”, the 1,3,5-triazacyclohexane derivative due to its poor stability.⁵⁸ Independently, C. Ganter showed the ability to convert 1,3,5-triazacyclohexane derivative to the corresponding amidinium cation after workup in analytically pure form.⁵⁹ These works were in good correlation with our results. We determined the trimer iminium product (**6a**) as the main product formed during the electrochemical oxidation of **5a**. The proposed mechanism is illustrated in **Scheme 12**. The oxidation begins with the dehydrogenation at the N atom and adjacent C of alkyl group to form the imine intermediate. Then, the nucleophilic attack of another amine leads to dimerization. Subsequently, the third

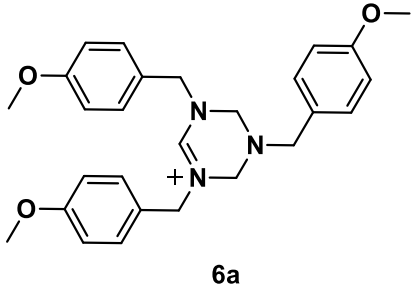
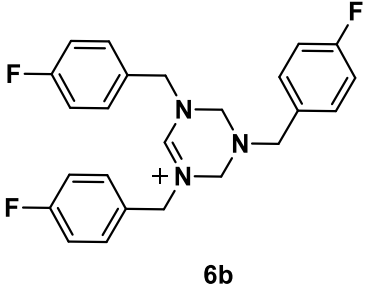
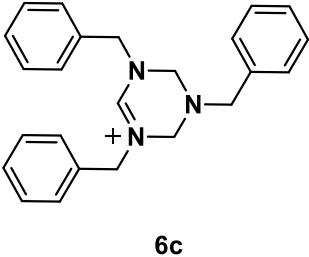
amine molecule attaches to the dimer intermediate which favors the stabilized trimer by cyclic arrangement and conjugation of imine bond over oligomeric form.



Scheme 12. Proposed mechanism of the 1,3,5-triazacyclohexane ring formation from 4-methoxy-N-methylbenzylamine (5a) followed by a further oxidation resulting in the isolated product.

The 1,3,5-triazacyclohexene derivatives have high relevance synthesis, as the skeleton of the formed product is patented as a valuable intermediate in herbicides.⁶⁰ We aimed to investigate the extensibility of the reaction, and further substituted derivatives were tested. 4-Fluoro-N-methylbenzylamine (5b), and N-methylbenzylamine (5c) were also investigated. Following the previous procedure, the purification step using preparative HPLC and subsequent analysis by LC-MS, the results indicated the formation of iminium ion trimer in all three cases as shown in **Table 7**.

Table 7. The yields and the structure of the products in the electrochemical oxidation of 5a-c.

Entry	R	Main product	Conversion (%)	Yield (%)
5a	4-MeO	 6a	>99	57 ¹
5b	4-F	 6b	>99	70 ²
5c	H	 6c	>99	54 ¹

¹Yields were determined by ¹H NMR analysis of the reaction mixture relative to 2,6-lutidine as an internal standard.

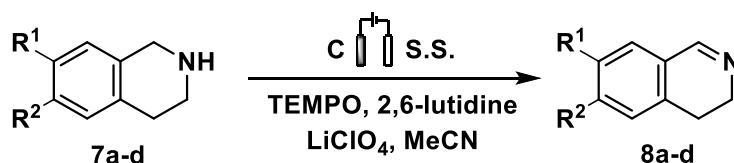
²Yield was determined by ¹⁹F NMR analysis of the reaction mixture using (trifluoromethyl)benzene as an internal standard.

Based on these experiments, presented in **Table 7**, it is found that the oxidation of *N*-methylbenzylamine and its derivative results in high yields (54 to 70%). Notably, in the case of *N*-methyl-4-fluorobenzylamine, three parallel experiments were carried out, and the yields were found to be consistent (69% to 71%). This result indicates the reproducibility of this oxidation process, reinforcing the reliability of the results of the oxidation reaction, and the possibility of this reliable methodology for future research.

4.3. Preparation of 3,4-dihydroisoquinolines by electrocatalytic oxidation of 1,2,3,4-tetrahydroisoquinolines

Following the studies on *N*-methylbenzylamine, cyclic secondary amines were also investigated. During oxidation, due to different structures and steric hindrance around the nitrogen atom along with the ring strain, conjugation, and steric effects of the cyclic compound can be investigated, providing a diversity of products formed during oxidation.

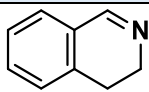
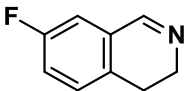
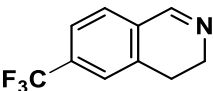
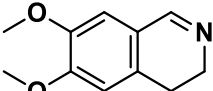
1,2,3,4-Tetrahydroisoquinoline (THIQ, **7a**) has been selected as standard substrate. In the presence of cyclic form, it was supposed that the oxidation might result in the formation of Schiff base due to the conjugation of carbon-carbon double bonds with the aromatic ring. As a result, we successfully synthesized 3,4-dihydroisoquinoline (**8a**) with high yield (96%) and conversion (up to 99%). Due to the stable conjugation between the imine bond in the heterocyclic ring and aromatic ring, the reaction could not undergo oxidative fragmentation, and the product was predominantly produced in imine formation.^{61,62} The formation of the desired imine is described in **Scheme 13**.



Scheme 13. Electrocatalytic oxidation of 1,2,3,4-tetrahydroisoquinolines (7a-d).

Based on the quantity of ¹H and ¹³C NMR measurements (Section 5.2.3.1), we can define the structure of the product and conversion along with the calculation of the yield by ¹H integral ratio. Based on ¹H NMR, the conversion is high, up to 99% in the case of **7a**, and the formation of **8a** was high (96%), which was also confirmed by ¹H NMR and ¹³C NMR measurements (section 5.2.3.1). Following this preliminary study, we turned our attention to oxidize THIQ derivatives. Different substituents were investigated, including 7-fluoro-1,2,3,4-tetrahydroisoquinoline (**7b**), 6-(trifluoromethyl)-1,2,3,4-tetrahydroisoquinoline (**7c**) and 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**7d**). The results are summarized in **Table 8**.

Table 8. Result of the electrocatalytic oxidation of 1,2,3,4-tetrahydroisoquinolines **7a-d**.

Entry	R	Product	Conversion (%)	Yield ¹ (%)
7a	R ¹ =H; R ² =H	 8a	>99	96
7b	R ¹ =F; R ² =H	 8b	>99	94
7c	R ¹ =H; R ² =CF ₃	 8c	>99	96
7d	R ¹ =OMe; R ² =OMe	 8d	>99	95

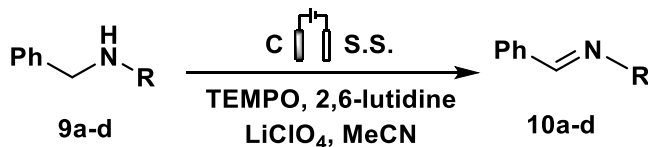
¹Yields were determined by ¹H NMR analysis relative to 2,6-lutidine as internal standard.

As can be seen in **Table 8**, relatively high conversion (>99%) for all substrates indicates the effectiveness of oxidizing THIQs under mild conditions (1 mA current and TEMPO catalytic amount). This suggests that TEMPO is a mild oxidant, that leads predominantly to DHIQs by one-step selective dehydrogenation of THIQs without extensive over-oxidation. The yield range (94-96%) indicates the efficiency of the oxidation as well as the selectivity of the reaction to get the desired products. By using THIQ as a baseline for comparison, the steric effect of EDG and EWG has shown minor influence on the final product due to the substituents being located far from the oxidation site, along with the stability provided by the conjugation of carbon-carbon double bonds within the aromatic ring and the formation of imine.

4.4. Synthesis of imines by electrocatalytic oxidation of benzylamines

The *N*-methyl-substituted nitrogen atom in the section 4.2 facilitates the formation of trimer cyclic iminium structure due to the flexibility in the molecular structure and lower steric hindrance, enabling better conformational arrangements (**Scheme 14**). To elucidate the influence of these bulkier substituents adjacent to the nitrogen atom on the formation and

stability of *E/Z* isomers, and whether steric hindrance from larger substituents preferentially stabilized one configuration over the other, several benzylamines (**9a-d**) oxidized using the similar condition of section 5.2.3. The electrooxidation conversion of benzylamines into the corresponding imines (**10a-d**) is summarized in **Table 9**.



Scheme 14. Electrocatalytic oxidation of N-substituted benzylamines (9a-d).

NMR spectra of the products were compared with the literature data,⁶³ it can be declared that in all the cases the imines were formed in *E* configuration. The preference for this configuration can be attributed to the steric and electron density effect, favoring the arrangement with minimal steric hindrance and high stability. In addition, the high yield observed from those experiments (85-99 %) highlights the efficiency and reproducibility of this oxidation process.

Table 9. The results of the electrocatalytic oxidation of N-substituted benzylamines (9a-d).

Entry	R	Product	Conversion (%)	Yield ¹ (%)
9a	Bn	 10a	>99	98
9b	Ph	 10b	>99	98
9c	α -methyl benzyl	 10c	>99	99
9d	Cyclohexyl	 10d	>99	85

¹Yields were determined by ¹H NMR analysis of the reaction mixture relative to 2,6-lutidine as an internal standard.

5. Experimental

5.1. Materials and methods

5.1.1. Chemicals

All substances, including amines (Merck), TEMPO (Sigma-Aldrich), and inorganic salts (VWR Hungary) were purchased. All electrochemical measurements were conducted in anhydrous solvents. 2,6-Lutidine was distilled over calcium hydride under nitrogen and stored in a glovebox. Other chemicals were used without any purification. Dry solvents were purchased from Merck and stored in a glovebox. Deuterated solvents were provided by Eurisotop.

5.1.2. Electrochemical reactor

Electrochemical experiments were performed on IKA ElectraSyn 2.0 reactor (**Scheme 15**) was used equipped with electrodes. The used undivided electrochemical cells were a glass vial and the electrode-equipped Teflon-lid, supplied from IKA.



Scheme 15. IKA ElectraSyn 2.0 Package used for electrocatalytic oxidation of amines.

5.1.3. Characterization and purification methods

NMR spectroscopy

^1H , ^{19}F and $^{13}\text{C}\{^1\text{H}\}$ spectra were recorded at 25°C using Varian Unity INOVA spectrometer operating at an equivalent ^1H frequency of 300 MHz with a 5 mm inverse detection tunable dual-broadband probe equipped with Z-gradient. Samples were prepared by dissolving approximately 50 mg of product or diluted 50 μl of reaction mixture in 400 μl DMSO- d_6 or CDCl_3 solvents. Notations for the ^1H NMR spectral splitting patterns include singlet (s), doublet (d), triplet (t), quartet (q), broad (br) and multiplet/overlapping peaks (m). Chemical shifts of the resonances are given as δ values in ppm and coupling constants (J) are expressed in Hertz.

High-performance liquid chromatography – Mass spectroscopy (HPLC-MS)

Shimadzu LC-40D XR UPLC-MS system was used equipped with a SIL-40C XR autosampler, SPD-M40 photo diode array detector, RF-20A XS fluorescent detector and an LCMS-2020 DUIS Mass Spectrometer operated in negative and positive ionisation modes. The separation was carried out on Ascentis® Express C18, 2 μ m UHPLC column (L $\times$ I.D. 5 cm $\times$ 2.1 mm), at 40 °C provided by a CTO-40s column oven. Gradient elution was used with either using 0.1% v/v TFA in water and 0.1% v/v TFA in MeCN.

Purification by preparative HPLC

In the case of 1,3,5-triazacyclohexane derivative synthesis, the crude product was purified by preparative HPLC (Armen Spot Prep II) on a Phenomenex Gemini C18, 250 $\times$ 50.00 mm; 10 μ m, 110A column. Gradient elution was applied using 0.2% v/v TFA in water (A) and MeCN (B) as the mobile phase components. The pure fractions were collected, and MeCN was removed under vacuum. The residual aqueous solution was lyophilized to obtain the TFA salt of the desired product, which is stable during storage at room temperature.

5.2. Synthetic methods

In the experiments, amines were selected as substrates, TEMPO as an additive, 2,6-lutidine as a base, and lithium perchlorate (LiClO₄) as a carrier electrolyte in dry acetonitrile (MeCN).

The precise quantities of the amine, 2,6-lutidine, LiClO₄ were measured to the undivided cell under argon atmosphere in an MBraun (Labmaster PRO) glovebox at 25 °C, 3 mL acetonitrile was added. TEMPO was measured in a distinct screw-capped vial within a glovebox, 2 mL acetonitrile was added. Both the closed cell and vial with TEMPO were removed from the glovebox. The cell was fitted to the IKA Electrasyn 2.0 reactor. TEMPO solution was added to the electrochemical cell using a syringe, then the reaction was started using a preliminary programmed method. The reaction was conducted at room temperature for varying periods of time, dependent upon the number of electrons transferred in each reaction. The reaction was carried out for 14 hours for two equivalents of electrons and for 28 hours for four equivalents of electrons. The current is maintained at a constant 1 mA, with other parameters set in accordance with the standard reaction conditions specified for use with IKA equipment. Once the reaction was completed, internal standard was added if needed. ¹H NMR and/or ¹⁹F NMR measurement was carried out using 50 μ L of the crude product diluted with 500 μ L deuterated solvent. If the reaction was successful, the reaction mixture was transferred into the round-bottom flask. The solvent is subsequently removed by vacuum evaporation. The residue was dissolved in 25 ml of DCM, washed with distilled water (3 $\times$ 10 mL). The combined organic

phase was dried over sodium sulfate, filtered then concentrated under reduced pressure. The product was analyzed by further measurements, such as ^1H and ^{13}C NMR, and LC-MS.

5.2.1. *Electrochemical oxidation of benzylamine and its substituted derivatives*

Procedure A: Into an undivided electrochemical cell equipped with a stainless steel counter electrode (CE) and graphite working electrode (WE), 53.2 mg of LiClO_4 (0.5 mmol), 3 mL of anhydrous MeCN was measured to prepare the electrolyte solution. Meanwhile, a catalytic mediator, 3.9 mg (0.025 mmol) of TEMPO was dissolved in 2 mL of MeCN in a distinct screw-capped vial. Subsequently, 58.4 μL (0.5 mmol) of 2,6-lutidine and a precise amount of starting material (0.25 mmol) were sequentially added to the electrolyte solution, and finally, TEMPO solution was added. The reaction was stirred in the IKA reactor and applied 1 mA in a 28-hour reaction at room temperature.

Electrochemical oxidation of benzylamine 1a to benzonitrile (2a)

2a was prepared according to Procedure A from benzylamine **1a** (27.3 μL - 0.25 mmol) resulting 25.1 mg (97% yield) **2a** as a colorless oil. MS: $[\text{M}+\text{H}^+]$ 104 m/z.

^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 7.82 (d, $J = 6.9$ Hz, 2H), 7.71 (t, $J = 7.0$ Hz, 1H), 7.57 (t, $J = 8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$) δ 133.21, 132.13, 129.37, 118.63, 111.26.

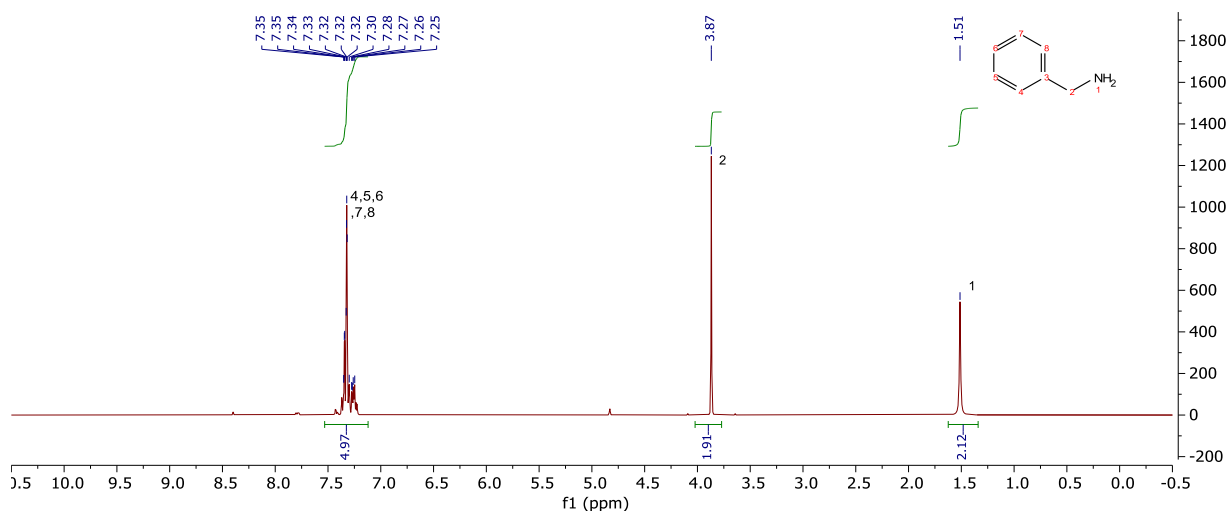


Figure 1. The ^1H NMR spectrum of benzylamine (**1a**) in CDCl_3 .

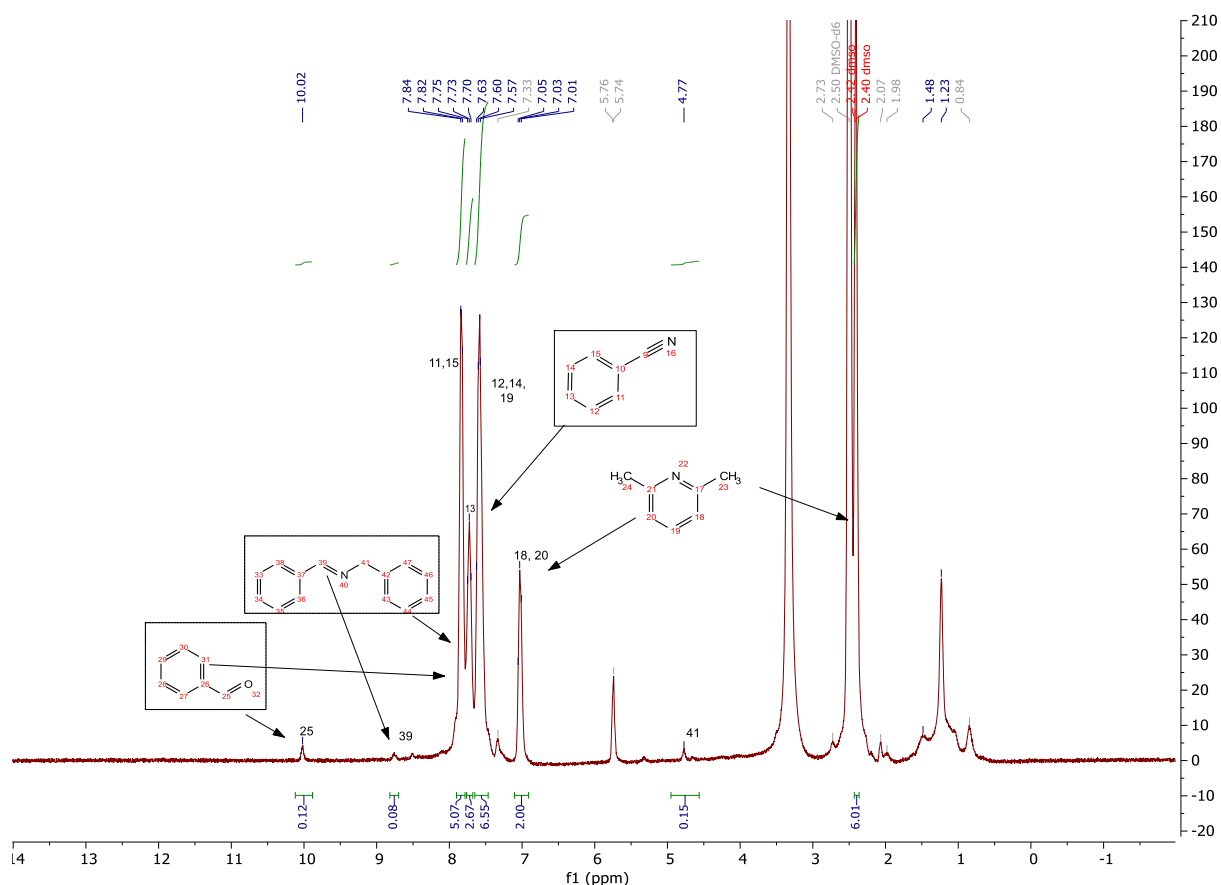


Figure 2. The ^1H NMR spectrum of the crude product of electrocatalytic oxidation of **1a** in DMSO-d_6 .

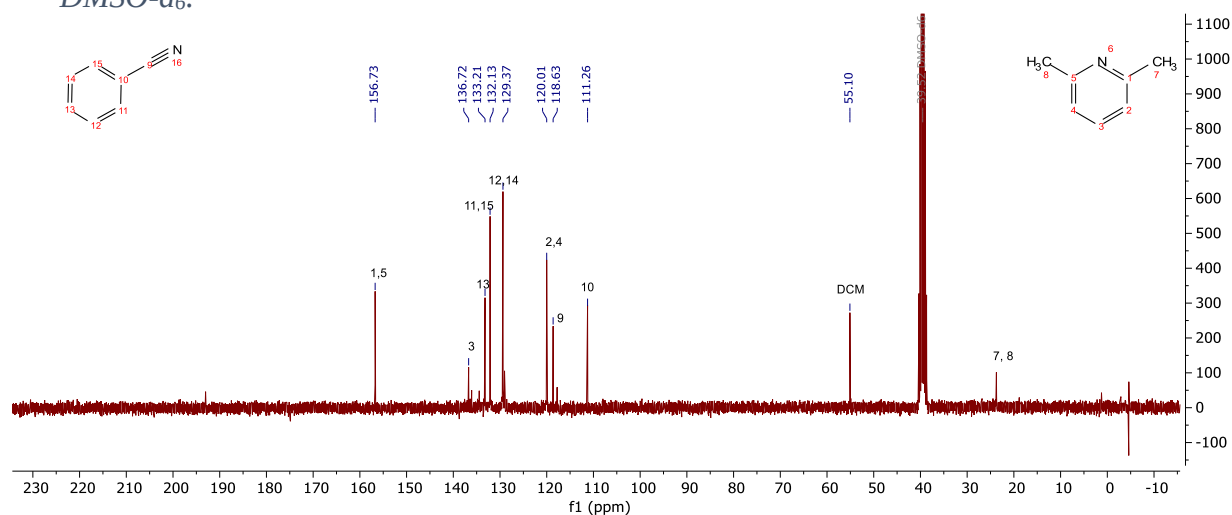


Figure 3. The ^{13}C NMR spectrum of the crude product of electrocatalytic oxidation of **1a** in DMSO-d_6 .

Electrochemical oxidation of **1b** to **2b**

The product **2b** was prepared according to Procedure A from 4-chlorobenzylamine (**1b**, 30.4 μL , 0.25 mmol), resulting in 28.5 mg (83% yield) **2b** as a colorless oil. MS: $[\text{M}+\text{H}^+]$ 138 m/z.

^1H NMR (300 MHz, DMSO- d_6) δ 7.89 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 8.4 Hz, 2H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 138.93, 134.57, 130.19, 118.48, 110.63.

Electrochemical oxidation of 1c to 2c

Compound **2c** was prepared according to Procedure A from 4-methoxybenzylamine (**1c**, 32.7 μl , 0.25 mmol), resulting in 31.3 mg (94% yield) **2c** as a colorless oil. MS: $[\text{M}+\text{H}^+]$ 134 m/z.

^1H NMR (300 MHz, DMSO- d_6) δ 7.74 (d, J = 8.3 Hz, 2H), 7.09 (d, J = 8.8 Hz, 2H), 3.82 (s, 3H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 163.15, 134.61, 119.61, 115.56, 103.20, 55.31.

Electrochemical oxidation of 1d to 2d

2d was synthesized according to Procedure A from 2-fluorobenzylamine (**1d**, 28.6 μl , 0.25 mmol) resulting in **2d** (21.2 mg, colorless oil, 70% yield). MS: $[\text{M}+\text{H}^+]$ 122 m/z.

^1H NMR (300 MHz, DMSO- d_6) δ 7.88 (t, J = 7.2 Hz, 1H), 7.77 (dd, J = 6.8 Hz, 1H), 7.47 (t, J = 9.1 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 164.57, 161.18, 136.68, 136.43, 134.15, 125.90, 117.04, 116.8, 114.31, 100.32, 100.20. ^{19}F NMR (282 MHz, DMSO- d_6) δ -108.39.

Electrochemical oxidation of 1e to 2e

2e was prepared according to Procedure A from 3-(trifluoromethyl)benzylamine (**1e**, 35.8 μl , 0.25 mmol) resulting in 35.1 mg (82% yield) of **2e** as a colorless oil. MS: $[\text{M}+\text{H}^+]$ 172 m/z.

^1H NMR (300 MHz, Chloroform- d) δ 7.93 (s, 1H), 7.87 (bs, J = 7.7, 4.1 Hz, 2H), 7.66 (t, J = 7.9 Hz, 1H). ^{13}C NMR (75 MHz, Chloroform- d) δ 135.31, 132.22, 129.99, 129.53, 129.07, 122.09, 117.31, 113.51. ^{19}F NMR (282 MHz, Chloroform- d) δ -63.24.

Electrochemical oxidation of 1f to 2f

2f was synthesized according to Procedure A from 2-methoxybenzylamine (**1f**, 32.6 μl , 0.25 mmol) resulting in 25.6 mg (77% yield) of **2f** as colorless oil. MS: $[\text{M}+\text{H}^+]$ 134 m/z.

^1H NMR (300 MHz, DMSO- d_6) δ 7.75 – 7.61 (m, 2H), 7.23 (dd, J = 8.4, 4.2 Hz, 1H), 7.08 (td, J = 7.5, 4.4 Hz, 1H), 3.91 (bs, J = 1.7 Hz, 3H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 161.28, 134.10, 133.54, 120.45, 116.89, 111.65, 100.72, 56.68.

5.2.2. *Electrochemical oxidation of 4-methoxy-N-methylbenzylamine (5a) and its substitutes.*

Procedure B: Dissolve 53.2 mg of LiClO₄ (0.5 mmol) in an electrochemical undivided vial fitted with a stainless steel electrode (CE) and graphite (WE) by 3 mL of dry MeCN to form an electrolyte solution. Meanwhile, 2 mL of MeCN is introduced into 3.9 mg (0.025 mmol) of TEMPO as the catalytic mediator in a screw-cap vial. Then a strong base 2,6-lutidine 29.2 μ L (0.25 mmol) is added to buffer the solution, followed by the addition of an amount of starting material corresponding to 0.25 mmol into the working chamber. Finally, TEMPO solution is added into the cell and the reaction starts at room temperature with 1mA current in 14 hours. After the evaporation of solvents by rotary evaporator, the residue was dissolved in a 10 ml mixture of methanol, and acetonitrile (1:1), then injected onto prep. HPLC (section 5.1). Acetonitrile from the pure fractions was evaporated and the aqueous residue was lyophilized after freezing. The pure fractions were further analyzed by NMR and LC-MS measurements.

Electrochemical oxidation of 5a to 6a

Table 10: The results of LC-MS measurements from three fractions separated by preparative HPLC from the crude product of 5a oxidation.

Prep HPLC fraction	Amount (mg)	Retention time (t_R) (min)	Molar mass (g/mol)
fr19	4.6	2.43	166
fr44-49	9.6	3.92	446
fr59-60	0.1	3.81	286

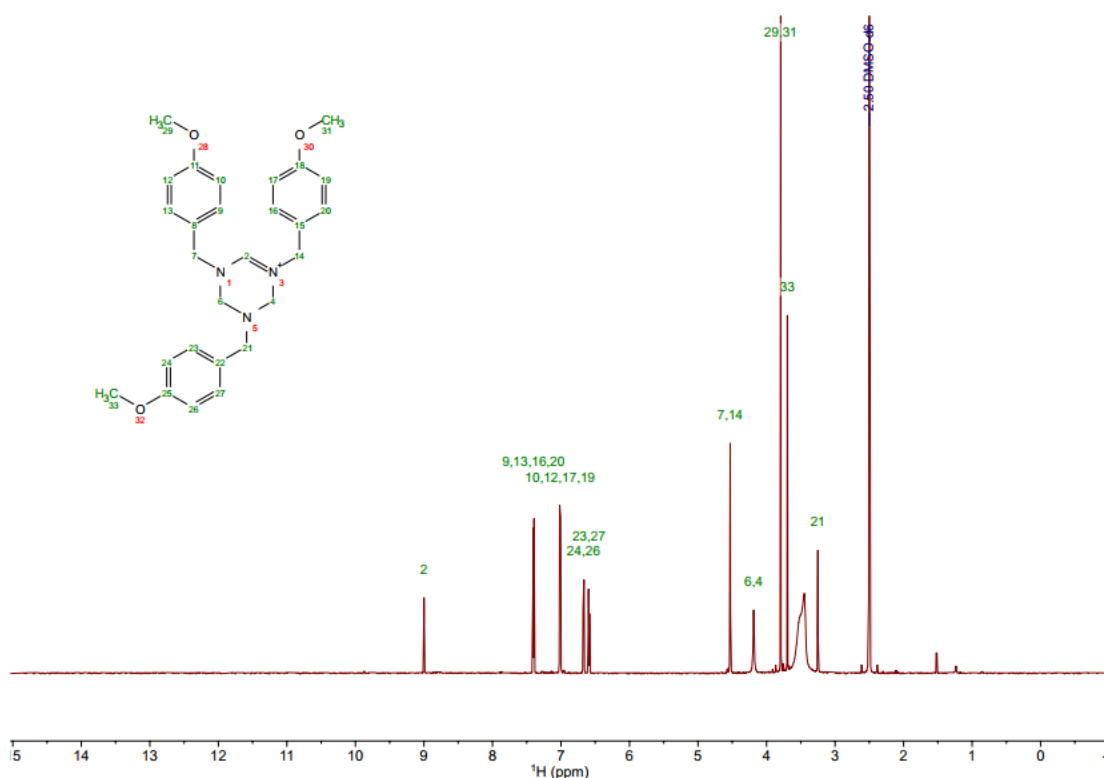


Figure 4. The ^1H NMR spectrum of the purified product in $\text{DMSO}-d_6$ solvent when electrocatalytic oxidized **5a**.

6a was prepared according to procedure B from 4-methoxy *N*-methylbenzylamine (**5a**, 37.5 μL , 0.25 mmol), resulting in 21.2 mg (57% yield) **6a** as a colorless oil. MS: $[\text{M}+\text{H}^+]$ 446 m/z.

^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ 9.00 (s, 1H), 7.40 (d, J = 8.6 Hz, 4H), 7.01 (d, J = 8.6 Hz, 4H), 6.67 (d, J = 8.7 Hz, 2H), 6.59 (d, J = 8.6 Hz, 2H), 4.53 (s, 4H), 4.19 (s, 4H), 3.79 (s, 6H), 3.70 (s, 3H), 3.25 (s, 2H). ^{13}C NMR (151 MHz, $\text{DMSO}-d_6$) δ 159.64, 158.58, 152.95, 130.30, 129.97, 128.11, 125.94, 114.33, 113.49, 61.87, 55.26, 54.96, 54.81, 53.64.

Electrochemical oxidation of **5b** to **6b**

6b was obtained according to procedure B from 4-fluoro *N*-methylbenzylamine (**5b**, 32.9 μL , 0.25 mmol), resulting in 23.9 mg (70% yield) **6b** as a colorless oil. MS: $[\text{M}+\text{H}^+]$ 410 m/z.

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.98 (s, 1H), 7.55 – 7.47 (m, 4H), 7.31 – 7.24 (m, 4H), 7.01 – 6.93 (m, 2H), 6.84 – 6.73 (m, 2H), 4.59 (s, 4H), 4.21 (s, 4H), 3.39 (s, 2H). ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ 162.53 (d, J = 245.2 Hz), 161.64 (d, J = 243.5 Hz), 153.71, 132.61 (d, J = 3.0 Hz), 131.27 (d, J = 8.5 Hz), 130.59 (d, J = 8.1 Hz), 130.42 (d, J = 3.0 Hz), 116.00 (d, J =

21.6 Hz), 115.18 (d, $J = 21.3$ Hz), 62.33, 54.78, 53.56. ^{19}F NMR (376 MHz, $\text{DMSO-}d_6$) δ -113.28 (tt, $J = 9.0, 5.4$ Hz), -114.76 (tt, $J = 9.1, 5.5$ Hz).

Electrochemical oxidation of 5c to 6c

6c was prepared according to procedure B from *N*-methylbenzylamine (**5c**, 32.3 μL , 0.25 mmol), resulting in 16.1 mg (54% yield) **6c** as a colorless oil. MS: $[\text{M}+\text{H}^+]$ 356 m/z.

^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 9.08 (s, 1H), 7.51 – 7.40 (m, 10H), 7.21 – 7.15 (m, 1H), 7.15 – 7.09 (m, 2H), 6.75 – 6.53 (m, 2H), 4.63 (s, 4H), 4.24 (s, 4H), 3.34 (s, 3H). ^{13}C NMR (101 MHz, $\text{DMSO-}d_6$) δ 153.93, 136.64, 134.48, 129.46, 129.21, 129.16, 129.06, 128.68, 128.01, 62.77, 55.81, 54.77.

5.2.3. Electrochemical oxidation of 1,2,3,4-tetrahydroisoquinoline (7a) and substituted THIQs

Procedure C: To prepare the electrolyte solution, 53.2 mg of LiClO_4 (0.5 mmol) is dissolved in 3 mL of water-free MeCN solvent in an undivided vial equipped with a stainless steel counter electrode and a graphite working electrode. Separately, introduce 2 mL of MeCN into 3.9 mg (0.025 mmol) of TEMPO to form a mediating solution in another flask. Continue to add 29.2 μL (0.25 mmol) of 2,6-lutidine dropwise to the electrolyte solution, and an amount of starting material corresponding to 0.25 mmol into the working cell. The reaction is conducted by the addition of TEMPO solution to the mixture and stirring at room temperature with 1mA current for 14 hours. After workup, the product is dissolved in $\text{DMSO-}d_6$ and measured in NMR equipment.

Electrochemical oxidation of 7a to 8a

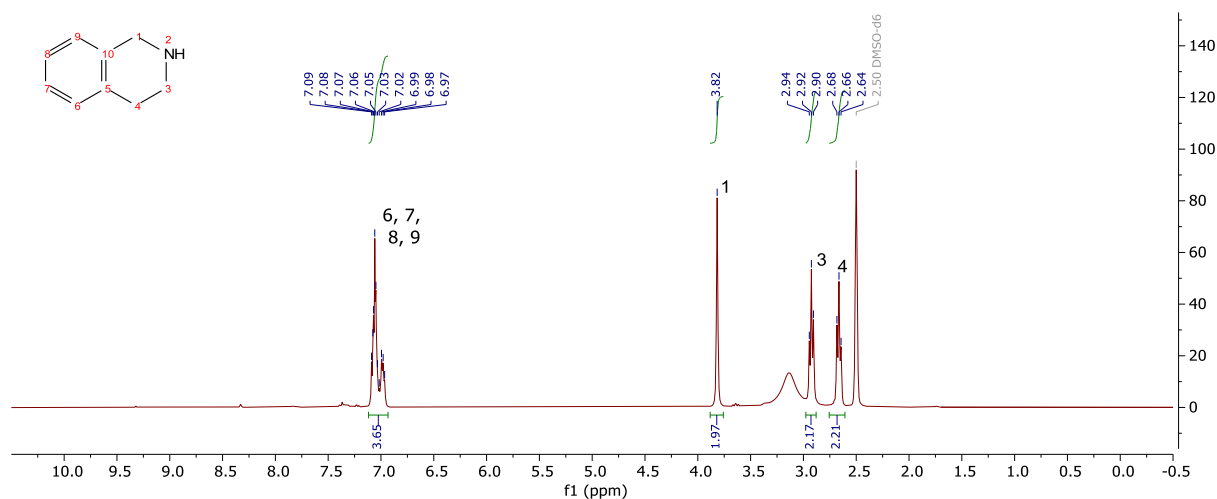


Figure 5. The ^1H NMR spectrum of **7a** in $\text{DMSO}-d_6$ solvent.

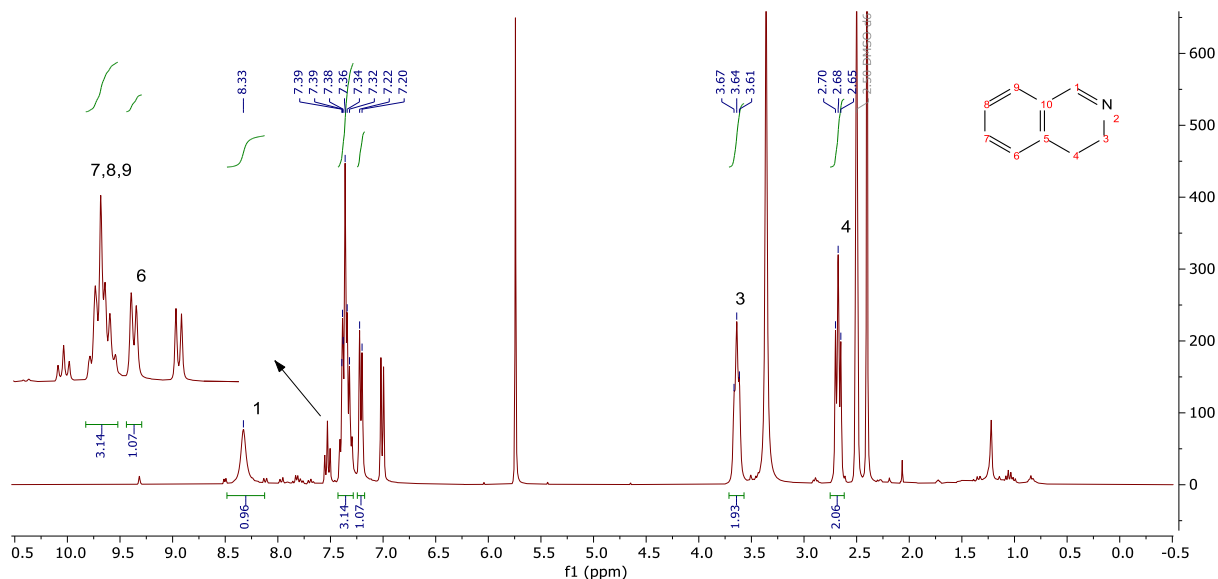


Figure 6. The ^1H NMR spectrum of the crude product in $\text{DMSO}-d_6$ solvent when electrocatalytic oxidized **7a** was used.

8a was prepared according to procedure C from 1,2,3,4-tetrahydroisoquinoline **7a** (31.3 μL , 0.25 mmol), resulting in 31.4 mg (96% yield) **8a** as a colorless oil. MS: $[\text{M}+\text{H}^+]$ 132 m/z.

^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 8.33(bs, 1H) 7.45 – 7.30 (m, 3H), 7.21 (d, J = 7.0 Hz, 1H), 3.64 (t, J = 7.7 Hz, 2H), 2.68 (t, J = 7.6 Hz, 2H). ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$) δ 159.93, 137.06, 131.47, 128.84, 127.84, 127.56, 127.53, 47.28, 24.82.

Electrochemical oxidation of **7b** to **8b**

8b was synthesized according to procedure C from 7-fluoro-1,2,3,4-tetrahydroisoquinoline (**7b**, 34.1 μL , 0.25 mmol), resulting in 35.1 mg (94% yield) **8b** as a colorless oil. MS: $[\text{M}+\text{H}^+]$ 150 m/z.

^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 8.30 (bs, 1H), 7.20 (bs, J = 10.3 Hz, 3H), 3.61 (t, J = 7.7 Hz, 3H), 2.63 (t, J = 7.6 Hz, 3H). ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$) δ 163.11, 159.11, 132.34 (d, J = 3.2 Hz), 129.79, 129.68, 118.13 (d, J = 21.6 Hz), 114.17 (d, J = 22.4 Hz), 47.45, 24.21 (d, J = 25.3 Hz). ^{19}F NMR (282 MHz, $\text{DMSO}-d_6$) δ -115.18.

Electrochemical oxidation of 7c to 8c

8c was prepared according to procedure C from 6-(trifluoromethyl)-1,2,3,4-tetrahydroisoquinoline (**7c**, 50.3 mg, 0.25 mmol), resulting in 47.8 mg (96% yield) **8c** as a colorless oil. MS: $[M+H]^+$ 200 m/z.

1H NMR (300 MHz, DMSO- d_6) δ 8.50 (s, 1H), 7.81 – 7.38 (m, 3H), 3.72 (bs, 2H), 2.81 (t, 2H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 158.84, 137.70, 132.14(q), 130.08, 128.05, 126.14, 124.55 (q), 122.53, 46.98, 24.37. ^{19}F NMR (282 MHz, DMSO- d_6) δ -61.37.

Electrochemical oxidation of 7d

8d was obtained according to procedure C from 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**7d**, 48.3 mg, 0.25 mmol), resulting in 44.9 mg (95% yield) **8d** as a colorless oil. MS: $[M+H]^+$ 192 m/z.

1H NMR (300 MHz, DMSO- d_6) δ 8.24 (bs, 1H), 7.05 (s, 1H), 6.85 (s, 1H), 3.79 (s, 3H), 3.75 (s, 3H), 3.60 (bs, 2H), 2.62 (t, J = 7.7 Hz, 2H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 159.62, 151.44, 147.58, 129.70, 120.88, 111.36, 110.93, 55.85, 55.75, 46.39, 24.14.

5.2.4. Electrochemical oxidation of N-substituted benzylamines

By conducting similar conditions with procedure C, the summarized data, presented below, highlights the consistency and producibility in facilitating benzylamines to their corresponding imines.

Electrochemical oxidation of dibenzylamine (9a)

10a was prepared according to procedure C from dibenzylamine (**9a**, 48.1 μ l, 0.25 mmol), resulting in 47.8 mg (98% yield) **10a** as a colorless oil. MS: $[M+H]^+$ 196 m/z.

1H NMR (300 MHz, DMSO- d_6) δ 8.49 (s, 1H), 7.79 (dd, J = 6.8, 2.9 Hz, 2H), 7.48 – 7.41 (m, 3H), 7.25 – 7.20 (m, 5H), 4.77 (s, 2H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 162.14, 140.05, 136.52, 131.14, 129.07, 128.77, 128.42, 128.32, 127.19, 64.49.

Electrochemical oxidation of N-phenylbenzylamine (9b)

10b was prepared according to procedure C from *N*-phenylbenzylamine (**9b**, 45.8 mg, 0.25 mmol), resulting in 44.3 mg (98% yield) **10b** as a colorless oil. MS: $[M+H]^+$ 182 m/z.

^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 8.63 (s, 1H), 7.96 (d, J = 5.0 Hz, 2H), 7.54 (m, 3H), 7.43 (m, 2H), 7.27 (m, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 161.16, 151.96, 136.51, 131.98, 129.70, 129.32, 129.18, 126.48, 121.48.

Electrochemical oxidation of (S)-(-)-N-benzyl- α -methylbenzylamine (9c)

10c was prepared according to procedure C from (S)-(-)-N-Benzyl- α -methyl-benzylamine (**9c**, 52.3 μL , 0.25 mmol), resulting in 51.7 mg (99% yield) **10c** as a colorless oil. MS: $[\text{M}+\text{H}^+]$ 210 m/z.

^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 8.47 (s, 1H), 7.78 (dd, J = 6.6, 2.9 Hz, 2H), 7.49 – 7.38 (m, 5H), 7.33 (t, J = 7.4 Hz, 2H), 7.28 – 7.17 (m, 1H), 4.57 (q, J = 6.5 Hz, 1H), 1.48 (d, J = 6.5 Hz, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 159.89, 145.64, 136.57, 131.16, 129.12, 128.79, 128.43, 127.17, 126.95, 69.04, 25.27.

Electrochemical oxidation of N-benzylcyclohexanamine (9d)

10d was prepared according to procedure C from N-benzylcyclohexanamine (**9d**, 48.8 μL , 0.25 mmol), resulting in 39.7 mg (85% yield) **10d** as a colorless oil. MS: $[\text{M}+\text{H}^+]$ 188 m/z.

^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 8.34 (s, 1H), 7.77 – 7.65 (m, 2H), 7.42 (m, 3H), 3.20 (tt, J = 9.6, 4.1 Hz, 1H), 1.76 – 1.12 (m, 10H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 158.32, 136.34, 130.38, 128.55, 127.79, 68.64, 34.10, 25.25, 24.16.

6. Conclusions

In this project, the electrocatalytic oxidation of various amines was successfully carried out with high selectivity and productivity. Using a sustainable and economical method, mild conditions were applied utilizing electricity as a green reagent.

To avoid the toxic transition metals, harsh conditions, and strong oxidation reagent, a simple electrochemical method was applied with graphite and stainless steel electrodes, the natural base 2,6-lutidine, and a catalytic amount of TEMPO as an additive. The effect of traces of water, and the effect of the amount of additive was investigated. The reaction optimization was carried out in the case of the applied current and reaction time. Using nitrogen atmosphere, relevant increase in the yield was observed. Selectively six nitriles were prepared from primary amines. Imines were obtained from further secondary amines.

Surprisingly, in the case of *N*-methylbenzylamines, 1,3,5-triazacyclohexane derivatives were prepared. These products may have high relevance in the herbicide industry.

One of the most remarkable aspects of this method is the ability to avoid the formation of harmful byproducts. The obtained products can be easily purified by simple distillation, while other reagents can be reused, minimizing the environmental impact and highlighting the broader applicability of this electrocatalytic method.

These approaches not only demonstrate an eco-friendly alternative for nitrile and imine synthesis but also provide a one-step synthesis of a heterocyclic aromatic compound with high relevance in agriculture and pharmaceutical applications.

The promising results achieved in this work can be considered as a clean procedure for fine chemical industrial applications.

7. References

- (1) Xu, Z.; Kovács, E. Beyond Traditional Synthesis: Electrochemical Approaches to Amine Oxidation for Nitriles and Imines. *ACS Org. Inorg. Au* **2024**, 4 (5), 471–484. <https://doi.org/10.1021/acsorginorgau.4c00025>.
- (2) Tehrani, K. A.; Kimpe, N. De. Product Class 7: Imines. In *Compounds with Two Carbon Heteroatom Bonds*; Padwa, A., Bellus, D., Eds.; Georg Thieme Verlag KG: Stuttgart, 2005; pp 245–312. <https://doi.org/10.1055/b-00000101>.
- (3) Delanty, G. The Chemistry of Imine. *Lit. Imagin.* **2010**, 12 (3), 289–290. <https://doi.org/10.1093/litimag/imq040>.
- (4) Fabbrizzi, L. Beauty in Chemistry: Making Artistic Molecules with Schiff Bases. *J. Org. Chem.* **2020**, 85 (19), 12212–12226. <https://doi.org/10.1021/acs.joc.0c01420>.
- (5) Schiff, H. Mittheilungen Aus Dem Universitätslaboratorium in Pisa: Eine Neue Reihe Organischer Basen. *Justus Liebigs Ann. Chem.* **1864**, 131 (1), 118–119. <https://doi.org/10.1002/jlac.18641310113>.
- (6) Moss, G. P.; Smith, P. A. S.; Tavernier, D. Glossary of Class Names of Organic Compounds and Reactive Intermediates Based on Structure (IUPAC Recommendations 1995). *Pure Appl. Chem.* **1995**, 67 (8–9), 1307–1375. <https://doi.org/10.1351/pac199567081307>.
- (7) Ladenburg, A. “Ueber Die Imine” [About Imines]. *Berichte der Dtsch. Chem. Gesellschaft* **1883**, 16 (1), 1125–1694. <https://doi.org/10.1002/cber.188301601259>.
- (8) Wang, Z. Moureau-Mignonac Ketimine Synthesis. In *Comprehensive Organic Name Reactions and Reagents*; Wang, Z., Ed.; John Wiley & Sons, Inc., 2010; pp 1988–1990. <https://doi.org/10.1002/9780470638859.conrr446>.
- (9) Hoesch, K. Eine Neue Synthese Aromatischer Ketone. I. Darstellung Einiger Phenol-Ketone. *Berichte der Dtsch. Chem. Gesellschaft* **1915**, 48 (1), 1122–1133. <https://doi.org/10.1002/cber.191504801156>.
- (10) Houben, J. Über Die Kern-Kondensation von Phenolen Und Phenol-Äthern Mit Nitrilen Zu Phenol- Und Phenol-Äther-Ketimiden Und -Ketonen (I.). *Berichte der Dtsch. Chem. Gesellschaft* **1926**, 11 (59), 2878–2891. <https://doi.org/10.1002%2Fcbcr.19260591135>.
- (11) Jeffery, E. A.; Satchell, D. P. N. A Kinetic Study of the Formation of Ketimine Hydrochlorides. The Mechanism of the Houben–Hoesch Reaction. *J. Chem. Soc. B Phys. Org.* **1966**, 5, 579–586. <https://doi.org/10.1039/J29660000579>.
- (12) Billman, J. H.; Tai, K. M. Reduction of Schiff Bases. II. Benzhydrylamines and

- Structurally Related Compounds. *J. Org. Chem.* **1958**, 23 (4), 535–539. <https://doi.org/10.1021/jo01098a009>.
- (13) Morgan, P. W.; Kwolek, S. L.; Pletcher, T. C. Aromatic Azomethine Polymers and Fibers. *Macromolecules* **1987**, 20 (4), 729–739. <https://doi.org/10.1021/ma00170a006>.
- (14) Burroughes, J. H.; Bradley, D. D. C.; Brown, A. R.; Marks, R. N.; Mackay, K.; Friend, R. H.; Burns, P. L.; Holmes, A. B. Light-Emitting Diodes Based on Conjugated Polymers. *Nature* **1990**, 347 (6293), 539–541. <https://doi.org/10.1038/347539a0>.
- (15) D'alelio, G. F.; Crivello, J. V.; Schoenig, R. K.; Huemmer, T. F. Polymeric Schiff Bases. I. The Synthesis and Evaluation of Polymeric Schiff Bases Prepared by Schiff Base Exchange Reactions. *J. Macromol. Sci. Part A - Chem.* **1967**, 1 (7), 1161–1249. <https://doi.org/10.1080/10601326708053766>.
- (16) Grigoras, M.; Catanescu, C. O. Imine Oligomers and Polymers. *J. Macromol. Sci.* **2004**, 44 (2), 131–173. <https://doi.org/10.1081/MC-120034152>.
- (17) Fehling, H. "Ueber Die Zersetzung Des Benzoësauren Ammoniaks Durch Die Wärme (On the Decomposition of Ammonium Benzoate by Heat). *Justus Liebigs Ann. Chem.* **1844**, 49 (1), 91–97. <https://doi.org/10.1002/jlac.18440490106>.
- (18) Schulz, A.; Surkau, J. Main Group Cyanides: From Hydrogen Cyanide to Cyanido-Complexes. *Rev. Inorg. Chem.* **2023**, 43 (1), 49–188. <https://doi.org/10.1515/revic-2021-0044>.
- (19) Mowry, D. T. The Preparation of Nitriles. *Chem. Rev.* **1948**, 42 (2), 189–283. <https://doi.org/10.1021/cr60132a001>.
- (20) Reid, E. E. Studies in the Preparation of Nitriles. *Am. Chem. J.* **1910**, 43 (2), 162–181.
- (21) Sandmeyer, T. Ueber Die Ersetzung Der Ueber Die Ersetzung Der Amidgruppe Durch Chlor in Den Aromatischen Substanzen. *Berichte der Dtsch. Chem. Gesellschaft* **1884**, 17 (2), 1633–1635. <https://doi.org/10.1002/cber.18840170219>.
- (22) Hodgson, H. H. The Sandmeyer Reaction. *Chem. Rev.* **1947**, 40 (2), 251–277. <https://doi.org/10.1021/cr60126a003>.
- (23) Wang, Z. Kolbe Nitrile Synthesis. *Compr. Org. Name React. Reagents* **2010**, 1661–1663. <https://doi.org/10.1002/9780470638859.conrr370>.
- (24) Guvendik, G.; Bosgelmez, I. I. Acrylonitrile. *Ankara Univ. Eczac. Fak. Derg.* **2000**, 29 (1), 31–58. https://doi.org/10.1501/Eczfak_0000000341.
- (25) Mark C. Cesa, J. F.; Brazdil, Lynn M. Moravcik, Frederick A. Pesa, Wilfrid G. Shaw, A.; A. Kozlowski, J. M.; Jones, P. R. Sohio Acrylonitrile Process. *National Historic Chemical Landmark, American Chemical Society*. Washington, D.C. September 1996,

- pp 1–8. <https://www.acs.org/content/dam/acsorg/education/whatischemistry/landmarks/acrylonitrile/sohio-acrylonitrile-process-commemorative-booklet-1996.pdf>.
- (26) Pollak, P.; Romeder, G.; Hagedorn, F.; Gelbke, H.-P. Nitriles. *Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH, 2000; Vol. 24, pp 251–265. https://doi.org/10.1002/14356007.a17_363.
 - (27) Kim, Y. H.; Hwang, S. K.; Lee, Y. S.; Kim, J. W. Selective Oxidation of Amines to Imines or Nitriles by Manganese Dioxide in Air. *Appl. Chem. Eng.* **2014**, 25 (2), 215–221. <https://doi.org/10.14478/ace.2014.1017>.
 - (28) Rawalay, S. S.; Shechter, H. Oxidation of Primary, Secondary, and Tertiary Amines with Neutral Permanganate. A Simple Method for Degrading Amines to Aldehydes and Ketones. *J. Org. Chem.* **1967**, 32 (10), 3129–3131. <https://doi.org/10.1021/jo01285a042>.
 - (29) Tseng, K. N. T.; Rizzi, A. M.; Szymczak, N. K. Oxidant-Free Conversion of Primary Amines to Nitriles. *J. Am. Chem. Soc.* **2013**, 135 (44), 16352–16355. <https://doi.org/10.1021/ja409223a>.
 - (30) Ng, L. K. S.; Tan, E. J. C.; Goh, T. W.; Zhao, X.; Chen, Z.; Sum, T. C.; Soo, H. Sen. Mesoporous SiO₂/BiVO₄/CuO_x Nanospheres for Z-Scheme, Visible Light Aerobic C–N Coupling and Dehydrogenation. *Appl. Mater. Today* **2019**, 15, 192–202. <https://doi.org/10.1016/j.apmt.2019.01.010>.
 - (31) Yoshida, T.; Okano, T.; Otsuka, S. Catalytic Hydrogenation of Nitriles and Dehydrogenation of Amines with the Rhodium(I) Hydrido Compounds [RhH(PⁱPr₃)₃] and [Rh₂H₂(μ-N₂){P(Cyclohexyl)₃}₄]. *J. Chem. Soc. Chem. Commun.* **1979**, 1 (19), 870–871. <https://doi.org/10.1039/C39790000870>.
 - (32) Zhu, P.; Zhang, J.; Wang, J.; Kong, P.; Wang, Y.; Zheng, Z. Photocatalytic Selective Aerobic Oxidation of Amines to Nitriles over Ru/γ-Al₂O₃: The Role of the Support Surface and the Strong Imine Intermediate Adsorption. *Catal. Sci. Technol.* **2020**, 10 (2), 440–449. <https://doi.org/10.1039/C9CY01916B>.
 - (33) Murahashi, S.; Imada, Y. Amine Oxidation. *ChemInform* **2005**, 36 (45), 497–507. <https://doi.org/10.1002/chin.200545240>.
 - (34) Schümperli, M. T.; Hammond, C.; Hermans, I. Developments in the Aerobic Oxidation of Amines. *ACS Catal.* **2012**, 2 (6), 1108–1117. <https://doi.org/10.1021/cs300212q>.
 - (35) Shono, T.; Matsumura, Y.; Inoue, K. Indirect Electrooxidation of Amines to Nitriles Using Halogen Ions as Mediators. *J. Am. Chem. Soc.* **1984**, 106 (20), 6075–6076. <https://doi.org/10.1021/ja00332a052>.
 - (36) Zhang, Y.; Zhao, J.; Cheng, J.; Wang, X.; Wang, H.; Shao, Y.; Mao, X.; He, X. Bromine-

- Mediated Strategy Endows Efficient Electrochemical Oxidation of Amine to Nitrile. *Chem. Commun.* **2024**, 60 (17), 2369–2372. <https://doi.org/10.1039/d3cc05861a>.
- (37) Frontana-Urbe, B. A.; Little, R. D.; Ibanez, J. G.; Palma, A.; Vasquez-Medrano, R. Organic Electrosynthesis: A Promising Green Methodology in Organic Chemistry. *Green Chem.* **2010**, 12 (12), 2099–2119. <https://doi.org/10.1039/c0gc00382d>.
- (38) Horn, E. J.; Rosen, B. R.; Baran, P. S. Synthetic Organic Electrochemistry: An Enabling and Innately Sustainable Method. *ACS Cent. Sci.* **2016**, 2 (5), 302–308. <https://doi.org/10.1021/acscentsci.6b00091>.
- (39) Pollok, D.; Waldvogel, S. R. Electro-Organic Synthesis-a 21st Century Technique. *Chem. Sci.* **2020**, 11 (46), 12386–12400. <https://doi.org/10.1039/d0sc01848a>.
- (40) Schäfer, H. J. Contributions of Organic Electrosynthesis to Green Chemistry. *Comptes Rendus Chim.* **2011**, 14 (7–8), 745–765. <https://doi.org/10.1016/j.crci.2011.01.002>.
- (41) Yan, M.; Kawamata, Y.; Baran, P. S. Synthetic Organic Electrochemical Methods since 2000: On the Verge of a Renaissance. *Chem. Rev.* **2017**, 117 (21), 13230–13319. <https://doi.org/10.1021/acs.chemrev.7b00397>.
- (42) Francke, R.; Little, R. D. Redox Catalysis in Organic Electrosynthesis: Basic Principles and Recent Developments. *Chem. Soc. Rev.* **2014**, 43 (8), 2492–2521. <https://doi.org/10.1039/c3cs60464k>.
- (43) Triaca, W. E.; Luna, A. M. C.; Arví, A. J. The Electrocatalytic Oxidation of Ethylene on Platinized Platinum at Different Saturation Pressures. *J. Electrochem. Soc.* **1980**, 127 (4), 827–833. <https://doi.org/10.1149/1.2129765>.
- (44) Austin, D. S.; Polta, J. A.; Polta, T. Z.; Tang, A. P.-C.; Cabelka, T. D.; Johnson, D. C. Electrocatalysis at Platinum Electrodes for Anodic Electroanalysis. *J. Electroanal. Chem. Interfacial Electrochem.* **1984**, 168 (1), 227–248. [https://doi.org/10.1016/0368-1874\(84\)87101-4](https://doi.org/10.1016/0368-1874(84)87101-4).
- (45) Barnes, K. K.; Mann, C. K. Electrochemical Oxidation of Primary Aliphatic Amines. *J. Org. Chem.* **1967**, 32 (5), 1474–1479. <https://doi.org/10.1021/jo01280a037>.
- (46) Okimoto, M.; Takahashi, Y.; Numata, K.; Nagata, Y.; Sasaki, G. Electrochemical Oxidation of Benzylic Amines into the Corresponding Imines in the Presence of Catalytic Amounts of KI. *Synth. Commun.* **2005**, 35 (15), 1989–1995. <https://doi.org/10.1081/SCC-200066648>.
- (47) Semmelhack, M. F.; Schmid, C. R. Nitroxyl-Mediated Electro-Oxidation of Amines to Nitriles and Carbonyl Compounds. *J. Am. Chem. Soc.* **1983**, 105 (22), 6732–6734. <https://doi.org/10.1021/ja00360a042>.

- (48) Mondal, I.; Hausmann, J. N.; Vijaykumar, G.; Mebs, S.; Dau, H.; Driess, M.; Menezes, P. W. Nanostructured Intermetallic Nickel Silicide (Pre)Catalyst for Anodic Oxygen Evolution Reaction and Selective Dehydrogenation of Primary Amines. *Adv. Energy Mater.* **2022**, *12* (25), 2200269. <https://doi.org/10.1002/aenm.202200269>.
- (49) Xiang, M.; Xu, Z.; Wu, Q.; Wang, Y.; Yan, Z. Selective Electrooxidation of Primary Amines over a Ni/Co Metal-Organic Framework Derived Electrode Enabling Effective Hydrogen Production in the Membrane-Free Electrolyzer. *J. Power Sources* **2022**, 535, 231461. <https://doi.org/10.1016/j.jpowsour.2022.231461>.
- (50) Yang, W.; Cheng, P.; Li, Z.; Lin, Y.; Li, M.; Zi, J.; Shi, H.; Li, G.; Lian, Z.; Li, H. Tuning the Cobalt–Platinum Alloy Regulating Single-Atom Platinum for Highly Efficient Hydrogen Evolution Reaction. *Adv. Funct. Mater.* **2022**, *32* (39), 1–8. <https://doi.org/10.1002/adfm.202205920>.
- (51) Semmelhack, M. F.; Chou, C. S.; Cortes, D. A. Nitroxyl-Mediated Electrooxidation of Alcohols to Aldehydes and Ketones. *J. Am. Chem. Soc.* **1983**, *105* (13), 4492–4494. <https://doi.org/10.1021/ja00351a070>.
- (52) Pletcher, D.; Zappi, G. D. The Indirect Anodic Oxidation of Amines Mediated by Brominated Aryl Amines. *J. Electroanal. Chem.* **1989**, *265* (1–2), 203–213. [https://doi.org/10.1016/0022-0728\(89\)80190-1](https://doi.org/10.1016/0022-0728(89)80190-1).
- (53) Luca, O. R.; Wang, T.; Konezny, S. J.; Batista, V. S.; Crabtree, R. H. DDQ as an Electrocatalyst for Amine Dehydrogenation, a Model System for Virtual Hydrogen Storage. *New J. Chem.* **2011**, *35* (5), 998–999. <https://doi.org/10.1039/c0nj01011a>.
- (54) Kisszekelyi, P.; Hardian, R.; Vovusha, H.; Chen, B.; Zeng, X.; Schwingenschlögl, U.; Kupai, J.; Szekely, G. Selective Electrocatalytic Oxidation of Biomass-Derived 5-Hydroxymethylfurfural to 2,5-Diformylfuran: From Mechanistic Investigations to Catalyst Recovery. *ChemSusChem* **2020**, *13* (12), 3127–3136. <https://doi.org/10.1002/cssc.202000453>.
- (55) Liu, L.; Li, J.; Ai, Y.; Liu, Y.; Xiong, J.; Wang, H.; Qiao, Y.; Liu, W.; Tan, S.; Feng, S.; Wang, K.; Sun, H.; Liang, Q. A Ppm Level Rh-Based Composite as an Ecofriendly Catalyst for Transfer Hydrogenation of Nitriles: Triple Guarantee of Selectivity for Primary Amines. *Green Chem.* **2019**, *21* (6), 1390–1395. <https://doi.org/10.1039/c8gc03595d>.
- (56) Exner, O.; Buděšínský, M. Correlation of Carbon-13 Substituent-Induced Chemical Shifts Revisited: Meta- and Para-Substituted Benzonitriles. *Magn. Reson. Chem.* **1989**, *27*, 27–36. <https://doi.org/10.1002/mrc.1260270106>.

- (57) Dargó, G.; Kis, D.; Ráduly, A.; Farkas, V.; Kupai, J. Furandicarboxylic Acid (FDCA): Electrosynthesis and Its Facile Recovery From Polyethylene Furanoate (PEF) via Depolymerization. *ChemSusChem* **2024**, 202401190, 1–9. <https://doi.org/10.1002/cssc.202401190>.
- (58) Florea, C.; Hîrtopeanu, A.; Stavarache, C.; Petricle, H. RuO₄-Mediated Oxidation of Secondary Amines 2. Imines as Main Reaction Intermediates. *J. Serbian Chem. Soc.* **2017**, 82 (6), 627–640. <https://doi.org/10.2298/jsc160914055f>.
- (59) Makhloufi, A.; Frank, W.; Ganter, C. Diamino- and Mixed Amino-Amido-*N*-Heterocyclic Carbenes Based on Triazine Backbones. *Organometallics* **2012**, 31 (5), 2001–2008. <https://doi.org/10.1021/om201275z>.
- (60) Giacomelli, G.; Porcheddu, A. 1,3,5-Triazines. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R., Ramsden, C. A., Scriven, E. F. V, Taylor, R. J. K., Eds.; Elsevier: Oxford, 2008; pp 197–290. <https://doi.org/10.1016/B978-008044992-0.00803-8>.
- (61) Li, P.; Tian, Y.; Tian, L.; Wang, Y. Selective Electrochemical Acceptorless Dehydrogenation Reactions of Tetrahydroisoquinoline Derivatives. *Org. Biomol. Chem.* **2024**, 22 (4), 725–730. <https://doi.org/10.1039/d3ob01930f>.
- (62) Zhou, Z.; Pan, X.; Sun, L.; Xie, Y.; Zheng, J.; Li, L.; Zhao, G. Boosting Hydrogen Production via Selective Two-Electron Mild Electrochemical Oxidation of Tetrahydroisoquinolines Completely to Dihydroisoquinolines. *Angew. Chemie - Int. Ed.* **2023**, 62 (11), e202216347. <https://doi.org/10.1002/anie.202216347>.
- (63) Tian, H.; Yu, X.; Li, Q.; Wang, J.; Xu, Q. General, Green, and Scalable Synthesis of Imines from Alcohols and Amines by a Mild and Efficient Copper-Catalyzed Aerobic Oxidative Reaction in Open Air at Room Temperature. *Adv. Synth. Catal.* **2012**, 354 (14–15), 2671–2677. <https://doi.org/10.1002/adsc.201200574>.