THE JOURNAL OF PHYSICAL CHEMISTRY C
A JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

pubs.acs.org/JPCC Article

Bromonium-Mediated Electrochemical Synthesis of 3-Pyridinol from Biomass-Derived Furfurylamine

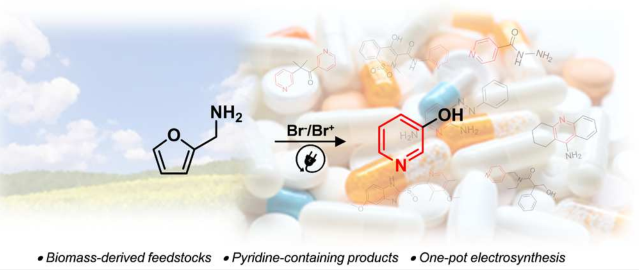
Published as part of The Journal of Physical Chemistry virtual special issue "Early-Career and Emerging Researchers in Physical Chemistry Volume 2".

Kaili Yan, Hyuna Kwon, Morgan Huddleston, De-en Jiang,* and Yujie Sun*

Cite This: *J. Phys. Chem. C* 2023, 127, 10107−10113 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: Electrocatalytic biomass valorization has attracted increasing interest over the years. Amongst many possible products from biomass upgrading, pyridine-containing chemicals are rarely reported. Herein, we describe an electrochemical synthesis of 3-pyridniol from biomass-derived furfurylamine in 0.1 M H_2SO_4, taking advantage of the Br^-/Br^+ redox cycle and the strong acidic condition in driving the final dehydration step. Such an electrosynthesis approach was able to achieve a 97% yield of 3-pyridinol from the nearly complete conversion of furfurylamine. A number of control experiments aided by computational investigation were carried out to elucidate the key mechanistic steps of the "one-pot" conversion of furfurylamine to 3-pyridinol.



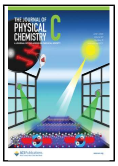
■ INTRODUCTION

The catalytic transformation of biomass into value-added products will play an important role in developing sustainable chemical industries. As a promising substitute of traditional fossil fuels, biomass has numerous advantages, such as earth abundance, eco-friendliness, potentially lower costs, and zero net-carbon emission.[1] The conventional approach of biomass conversion is thermocatalysis, which typically requires demanding conditions, such as high pressure, elevated temperature, and external oxidants/reductants.[2] As a potentially greener alternative approach, electrocatalytic biomass valorization has attracted increasing attention more recently because electricity can be produced from renewable energy sources (e.g., solar and wind) and electrochemical reactions are usually conducted under ambient conditions without the utilization of stoichiometric oxidants/reductants.[3] In addition, another advantage of electrocatalytic conversion is that the reaction selectivity and rate can be readily controlled via a variety of electrochemical parameters (e.g., applied potential, current, and electrocatalyst). Therefore, there is emerging interest in developing innovative electrocatalytic approaches for the upgrading of biomass-derived feedstock chemicals, like furanics, to highly valuable products, such as heterocycles.

In 2021, we reported an electrocatalytic Achmatowicz reaction for the synthesis of hydropyranone from furfuryl alcohol using an immobilized nickel-containing electrocatalyst.[4] This strategy does not require any expensive oxidants or tedious separation steps. If furfurylamine is used as the starting compound, the analogous aza-Achmatowicz reaction is able to produce piperidone. Notably, the acid-catalyzed aromatization of piperidinone can result in the formation of pyridine-containing molecules.

It is well known that substituted pyridines are important building blocks in fine chemicals, pharmaceuticals, polymers, and functional materials.[5−9] Traditional approaches of pyridine synthesis entail the involvement of multiple components, such as condensation of 1,3-dicarbonyls with a vinylogous amide, Diels−Alder cycloaddition between α,β-unsaturated ketoximes and alkynes, and the Hantzsch reaction.[10−13] A common nature of these conventional methods is the requirement of noble metal-based catalysts and relatively harsh conditions. Moreover, many reactions involve tedious steps and burdensome workups, which may lead to lower yields and higher cost of the final products. In contrast, as shown in Figure 1a, the oxidative ring expansion of substituted α-furyl amine followed by treatment with Lewis acid in either Et_3N or MeOH will yield substituted pyridines, albeit stoichiometric meta-chloroperoxybenzoic acid (*m*-CPBA) or *N*-bromosuccinimide (NBS) are consumed.[14,15] A more economically attractive and electricity-driven synthesis was reported by Clauson-Kaas et al., who demonstrated that the electro-

Received: April 4, 2023
Revised: May 4, 2023
Published: May 22, 2023



https://doi.org/10.1021/acs.jpcc.3c02245
J. Phys. Chem. C 2023, 127, 10107−10113

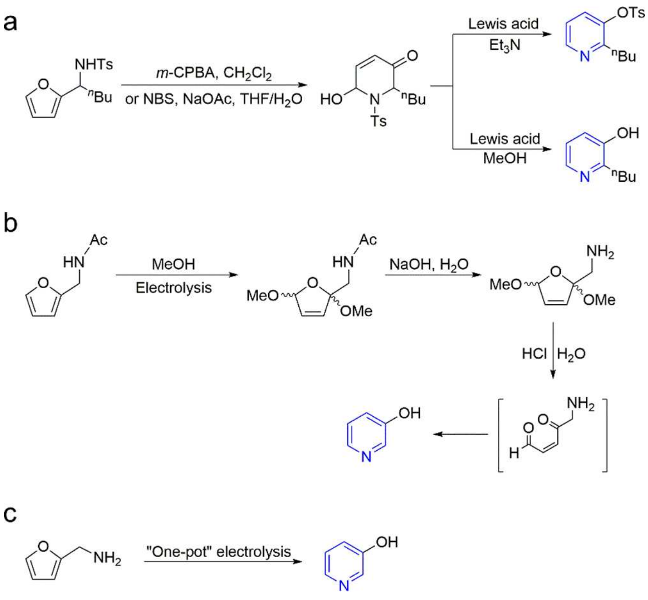


Figure 1. Reported chemical synthesis of substituted pyridines from oxidative ring expansion of substituted α-furyl amine followed by Lewis acid treatment (a) and electricity-assisted synthesis of 3-pyridiol from 2-(acetamidomethyl)-furan in methanol (b). (c) Our proposed "one-pot" electrosynthesis of 3-pyridinol from furfurylamine in 0.1 M H_2SO_4 mediated by the Br^-/Br^+ redox cycle.

chemical oxidation of 2-(acetamidomethyl)-furan in methanol would lead to 3-pyridiol after consecutive base and acid treatments (Figure 1b).[16] It was proposed that this reaction proceeds via a *cis*-dicarbonyl amine intermediate, which was unstable and would go through an acid-promoted aromatization step to form 3-pyridinol. Even though this strategy avoids the utilization of stoichiometric oxidants, the requirement of two additional hydrolysis steps renders it economically less attractive for large-scale production.

Inspired by a recent work reporting Br^+ as a possible active species for the Achmatowicz reaction,[17] and also recognizing that reactive brominating species can be generated from the electrochemical oxidation of Br^-,[18,19] we hypothesize that 3-pyridinol can be electrosynthesized from furfurylamine by a judicious choice of a bromine redox couple. Pursuing this idea, here, we report a new electricity-driven aza-Achmatowicz reaction, which, when carried out in an acidic electrolyte (e.g., 0.1 M H_2SO_4), is able to realize the "one-pot" synthesis of 3-pyridinol from furfurylamine under ambient conditions using the Br^-/Br^+ redox cycle. Mechanistic investigations aided by computational studies rationalize that Br^+ is the true active species, similar to the reported Br^+-driven Achmatowicz reaction. Overall, this work demonstrates the effectiveness and robustness of the Br^-/Br^+ redox cycle in the electrochemical synthesis of pyridines from biomass-derived and readily achievable furfurylamines, paving the way for the production of highly valuable pyridine-containing chemicals from renewable biomass-derived feedstocks.

■ EXPERIMENTAL SECTION

All the chemicals used in this study were purchased from commercial vendors and used without further purification. Furfurylamine, 3-pyridinol, pent-4-enoic acid, lithium perchlorate ($LiClO_4$), and tetrabutylammonium bromide (n-Bu_4NBr) were purchased from Ambeed. Sodium bromide (NaBr), *N*-bromosuccinimide (NBS), and bromine were purchased from LabChem. Sulfuric acid, acetonitrile, and acetic acid (AcOH) were purchased from Sigma-Aldrich.

Cyclic voltammetry (CV) and chronoamperometry experiments were performed at room temperature using a VMP-3 potentiostat (Biologic Science Instrument). The CV experi-

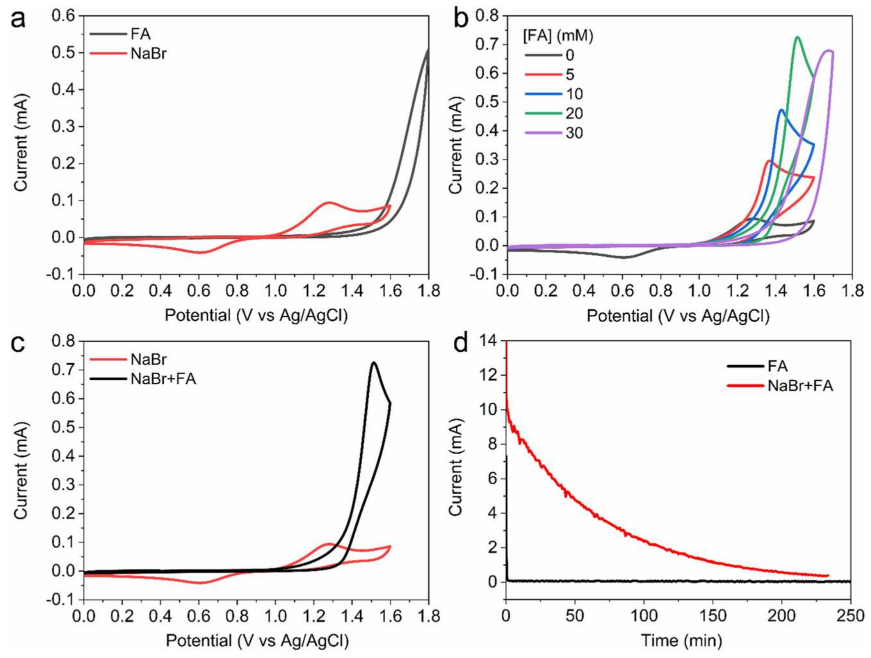


Figure 2. (a) Cyclic voltammograms (CVs) of individual 5 mM furfurylamine (FA) and 5 mM NaBr in 0.1 M H_2SO_4. (b) CVs of 5 mM NaBr along with the increasing addition of furfurylamine in 0.1 M H_2SO_4. (c) CV comparison of 5 mM NaBr in the absence (red) and presence (black) of 20 mM furfurylamine in 0.1 M H_2SO_4. (d) Current evolution over time during chronoamperometry electrolysis of 20 mM furfurylamine at 1.2 V vs Ag/AgCl in 0.1 M H_2SO_4 in the absence (black) and presence (red) of 5 mM NaBr.

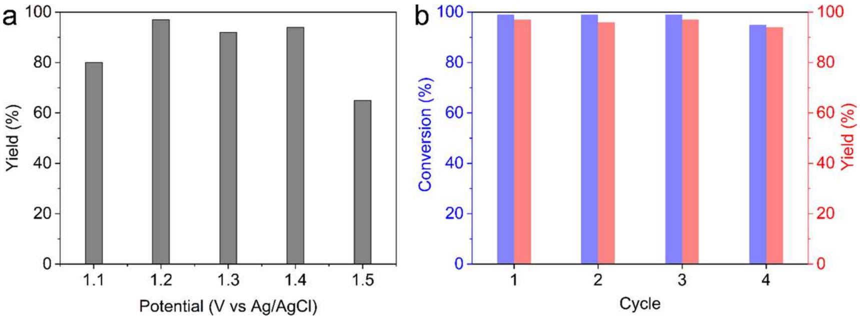


Figure 3. (a) Yields of 3-pyridinol from electrolysis performed at different applied potentials from 1.1 to 1.5 V vs Ag/AgCl using 20 mM furfurylamine and 5 mM NaBr in 0.1 M H_2SO_4 for each electrolysis. (b) Yields of 3-pyridinol from electrolysis in 0.1 M H_2SO_4 at 1.2 V vs Ag/AgCl using the same amount of NaBr (5 mM) with replenished 20 mM furfurylamine for each cycle.

ments were carried out in a three-electrode configuration with a glassy carbon (GC) as the working electrode, Ag/AgCl (or Ag/Ag^+) as the reference electrode, and a Pt wire as the counter electrode. Electrolysis experiments were performed in a two-compartment electrochemical cell with a proton exchange membrane (Nafion 211, Fuel Cell Store). At the anode chamber, 10 mL of 0.1 M H_2SO_4 containing 20 mM furfurylamine was used as the starting material for electrolysis. For electrolysis, a carbon rod was used as the working electrode, Ag/AgCl as the reference electrode, and a Pt wire as the counter electrode. For the quantification of furfurylamine and 3-pyridinol during electrolysis, 50 μL of the anolyte was collected and diluted with 950 μL of deionized water. The mixture was analyzed via high-performance liquid chromatography (HPLC) equipped with a C18 column using 80% 5 mM ammonium acetate and 20% methanol as the eluent with a flow rate of 0.8 mL/min. When the electrolysis was performed in the organic electrolyte (e.g., 0.1 M $LiClO_4$ in CH_3CN), an organic anion exchange membrane (Fumasep FAB-PK-130) was used, and n-Bu_4NBr was used as the bromine source instead of NaBr. ^1H NMR spectra were recorded on a Bruker 400 MHz spectrometer.

For the Br^+ trapping experiment, CVs were collected in a one-compartment cell with a GC, an Ag/AgCl electrode, and a Pt wire as the working, reference, and counter electrodes, respectively, and 0.1 M H_2SO_4 as the electrolyte. The bromine source and substrate were 5 mM NaBr and 5 mM pent-4-enoic acid, respectively. The electrolysis was conducted in a two-compartment electrochemical cell separated by a proton exchange membrane (Nafion 211, Fuel Cell Store). After electrolysis, the anolyte was evaporated and analyzed via ^1H NMR.

All calculations were carried out using the Gaussian 09 package.[20] The geometries of compounds were optimized using density functional theory (DFT) at the level of B3LYP hybrid functional with the 6-311+G(2d,2p) basis set and the default convergence criteria. Vibrational frequencies were computed to confirm no imaginary frequencies.[21] D3 correction[22] was employed to account for dispersion correction, and the SMD solvation model[23] was applied to account for the solvation free energy, where water was employed as a solvent.

■ RESULTS AND DISCUSSION

Synthesis of 3-Pyridinol from Furfurylamine in an Acidic Electrolyte Containing NaBr. Since acid-catalyzed aromatization is critical for the transformation from the aza-Achmatowicz reaction product piperidinone to the desirable 3-pyridinol, we hypothesized that it might be feasible to realize "one-pot" electrochemical synthesis of 3-pyridinol from furfurylamine if an acidic electrolyte could be employed. Therefore, 0.1 M H_2SO_4 was selected as the electrolyte. In addition, NaBr was used as an inexpensive bromine source. As shown in Figure 2a, the cyclic voltammogram of furfurylamine suggests that it will not be oxidized on a GC working electrode before 1.5 V vs Ag/AgCl in 0.1 M H_2SO_4. However, an anodic feature at ∼1.3 V vs Ag/AgCl could be observed from the cyclic voltammogram of 5 mM NaBr under the same condition, which could be ascribed to the oxidation of Br^- to Br_2.[19] It is known that the in situ generated Br_2 in the aqueous environment will react with H_2O to yield HOBr and Br^-. HOBr is a weak acid that can dissociate to produce H^+ and OBr^-. The OBr^- ion can be oxidized to form Br^+ in a strong oxidation environment or under highly acidic conditions.[24] As a result, when an oxidation potential is applied, the active species become Br^+ instead of HOBr. As expected, the cathodic feature at 0.6 V vs Ag/AgCl resulted from the reduction of Br_2 back to Br^-.

Figure 2b presents the evolution of cyclic voltammograms of 5 mM NaBr upon the continuous addition of furfurylamine (5−30 mM). When 1 equiv of furfurylamine was added, an apparent anodic current rise was observed with a slightly positive peak shift to ∼1.35 V vs Ag/AgCl. In the meantime, the original reduction feature at ca. 0.6 V vs Ag/AgCl completely disappeared, suggesting that the in situ generated bromine species was consumed in the reaction with furfurylamine. Further increasing the addition of furfurylamine to 20 mM led to enhanced anodic current accompanied with a slightly positive shift of the anodic peak. Once 30 mM furfurylamine was added, a decrease in the anodic current was observed. Therefore, 5 mM NaBr and 20 mM furfurylamine were employed in all the following electrochemical experiments unless noted otherwise. Figure 2c compares the cyclic voltammograms of 5 mM NaBr before and after the addition of 20 mM furfurylamine in 0.1 M H_2SO_4, showing nearly 7 times enhancement in the maximum anodic current and the disappearance of the reduction feature at 0.6 V vs Ag/AgCl once furfurylamine was added.

Next, controlled potential electrolysis was carried out using a carbon rod as the working electrode. The cyclic voltammograms of relevant species are shown in Figure S1. The electrolysis potential was set at 1.2 V vs Ag/AgCl, right before the onset of furfurylamine oxidation on the carbon electrode. Indeed, as shown in Figure 2d, no appreciable oxidation current was observed from furfurylamine oxidation at an

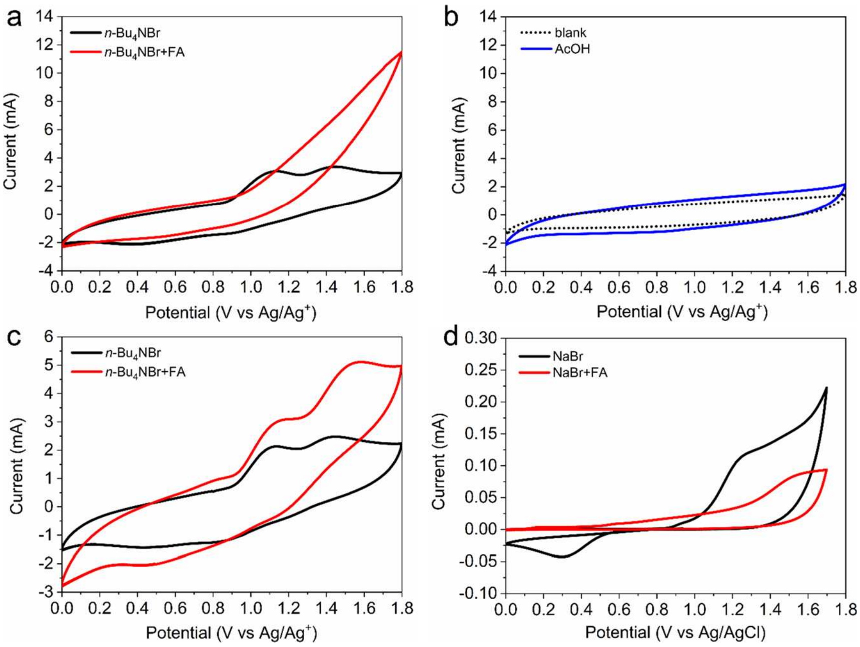


Figure 4. (a) Cyclic voltammograms (CVs) of 5 mM *n*-Bu_4NBr oxidation in the absence (black) and presence (red) of 20 mM furfurylamine (FA) in 0.1 M $LiClO_4$ CH_3CN. (b) CVs of 100 mM AcOH oxidation in 0.1 M $LiClO_4$ CH_3CN. (c) CVs of 5 mM *n*-Bu_4NBr oxidation in 0.1 M $LiClO_4$ MeCN with 100 mM AcOH in the absence (black) and presence (red) of 20 mM furfurylamine. (d) CVs of 5 mM NaBr oxidation in 0.1 M KPi in the absence (black) and presence (red) of 20 mM furfurylamine (FA).

applied potential of 1.2 V vs Ag/AgCl. In sharp contrast, once 5 mM NaBr was added to the electrolyte, over 10 mA oxidation current was detected, which gradually decayed to the capacitance current level after 4 h electrolysis at 1.2 V vs Ag/AgCl. HPLC analysis (Figures S2 and S3) of the post-electrolysis electrolyte confirmed that furfurylamine was completely consumed, and the primary product was 3-pyridinol with a yield of 97%. In contrast, no 3-pyridinol was detected in the absence of NaBr, and furfurylamine remained as the main species (Figure S4), indicating that 1.2 V vs Ag/AgCl was not able to drive its direct oxidation, consistent with the cyclic voltammetry results of Figures 2a and S1.

When varying the applied potential for electrolysis from 1.1 to 1.5 V vs Ag/AgCl (Figure S5), it was found that furfurylamine could always be consumed with over 90% conversion and 3-pyridinol was consistently produced as the primary product (Figures 3a and S6). The highest yield of 3-pyridinol of 97% was achieved when the applied potential was 1.2 V vs Ag/AgCl. It should be noted that in the absence of NaBr, furfural was produced as the primary oxidation product during the electrolysis at 1.5 V vs Ag/AgCl (Figure S7). In contrast, when 5 mM NaBr was utilized, 3-pyridinol was detected as the main product at the same applied potential (Figure S7). Figure S8 shows how the Faradaic efficiency of 3-pyridinol production varies with different levels of applied electrolysis potentials. The results indicate that the highest efficiency of 97% is attained when the constant potential is set at 1.2 V vs Ag/AgCl.

Under the optimal applied potential of 1.2 V vs Ag/AgCl, we next explored the stability of NaBr for four consecutive electrolysis cycles. For these electrolysis experiments, 5 mM NaBr was used as the bromine source, and the initial furfurylamine concentration was 20 mM. After each electrolysis cycle (Figure S9), the produced amount of 3-pyridinol was measured via HPLC (Figure S10), and fresh furfurylamine was added to retain its original concentration as 20 mM prior to the next electrolysis cycle. Figure 3b illustrates that 3-pyridinol was consistently produced in high yields (>90%) for all the four consecutive electrolysis cycles, highlighting the excellent stability and efficacy of our system in the electrochemical synthesis of 3-pyridinol.

Control Experiments To Elucidate the Necessity of Water and an Acidic Condition. The above results prompted us to investigate the key factors that are contributing to the successful synthesis of 3-prydinol from furfurylamine. Herein, we conducted a series of control experiments to elucidate the necessity of two factors, water and an acidic condition. The first control experiment was conducted in the absence of both water and H^+, using *n*-Bu_4NBr as the bromine source and 0.1 M $LiClO_4$ in CH_3CN as the electrolyte. As shown in Figure 4a, the oxidation of *n*-Bu_4NBr (5 mM) shows two anodic features, which could be assigned to the oxidation of Br^- to Br_3^- and Br_2 consecutively.[18] Upon the addition of 20 mM furfurylamine, an anodic current took off at ~1.0 V vs Ag/AgCl. However, controlled potential electrolysis experiments performed at an applied potential of either 1.0 or 1.5 V vs Ag/Ag^+ (Figure S11a) did not produce detectable 3-pyridinol (Figure S12).

Our second control experiment was set to carry out electrochemical oxidation in the presence of an acid but no H_2O (or a limited amount of H_2O). AcOH was employed as the acid. Cyclic voltammograms in Figure 4b demonstrate that AcOH was not oxidized in CH_3CN within the potential window of 0−1.8 V vs Ag/Ag^+. In the presence of AcOH, *n*-Bu_4NBr still exhibited two anodic features (Figure 4c), which could be attributed to the formation of Br_3^- and Br_2. Since H_2O was nearly absent in the electrolyte, the in situ formed Br_2 would not be able to react with H_2O to yield Br^+. Two controlled potential electrolysis experiments conducted at 1.0 and 1.4 V vs Ag/Ag^+ (Figure S11b), which were corresponding

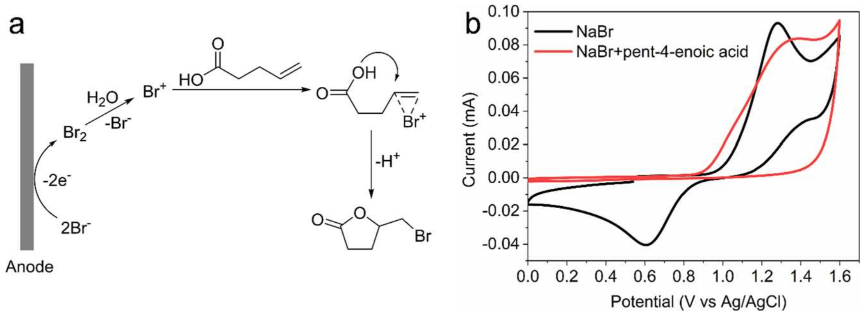


Figure 5. (a) Schematic formation of 5-(bromomethyl)dihydrofuran-2(3*H*)-one from the reaction between Br^+ and pent-4-anoic acid. (b) Cyclic voltammograms of 5 mM NaBr oxidation in the absence (black) and presence (red) of 5 mM pent-4-anoic acid in 0.1 M H_2SO_4.

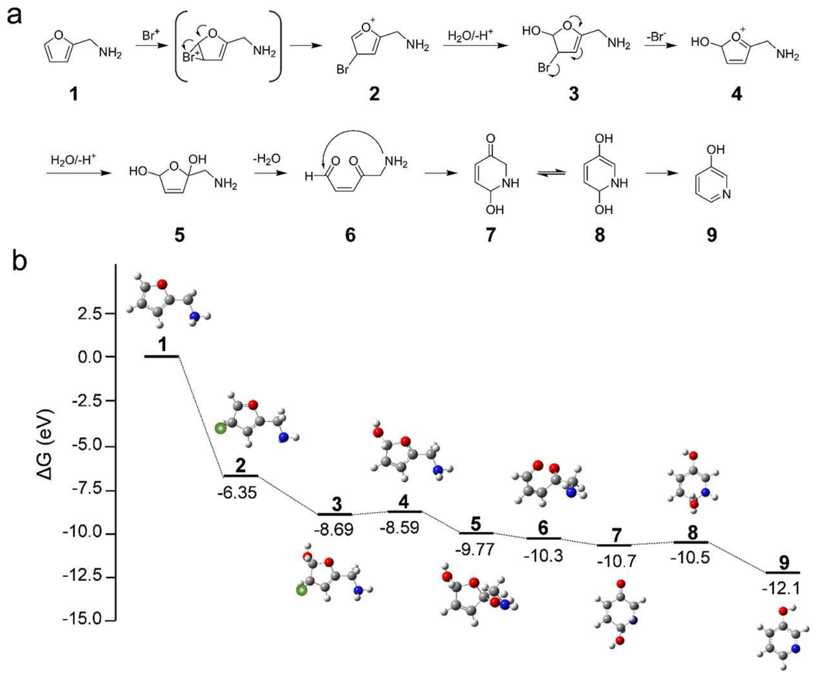


Figure 6. (a) Proposed reaction pathway and (b) the DFT-computed free energies of corresponding species along the pathway for the electrochemical synthesis of 3-pyridinol from furfurylamine initiated by Br^+. C, gray; H, white; O, red; Br, green.

to the formation of Br_3^- and Br_2, respectively, produced no desirable 3-pyridinol (Figure S13). The results of the above control experiments suggest that neither Br_3^- nor Br_2 was able to drive the conversion of furfurylamine to 3-pyridinol in an organic electrolyte, regardless of the presence of an acid source.

Finally, we tested the electrochemical oxidation of furfurylamine in a neutral aqueous electrolyte 0.1 M phosphate buffer (KPi) using 5 mM NaBr as the bromine source. As shown in Figure 4d, the oxidation of NaBr showed an oxidation peak at 1.2 V vs Ag/AgCl and a reduction peak at 0.3 V vs Ag/AgCl. However, upon the addition of 20 mM furfurylamine, a suppressed anodic current was observed, probably due to the competing adsorption of furfurylamine on the working electrode. Controlled potential electrolysis at an applied potential of 1.2 V vs Ag/AgCl (Figure S11c) again did not result in the detectable formation of 3-hdyroxylpyridine (Figure S14). Collectively, the aforementioned control results prompted us to hypothesize that both water and a strong acidic condition were required for the production of 3-pyridinol and the real active bromine species was Br^+ from the reaction between in situ formed Br_2 and water.

To verify whether Br^+ was indeed generated from Br^- oxidation in 0.1 M H_2SO_4 under our condition, a control experiment employing pent-4-enoic acid as the substrate was carried out. It has been well documented that pent-4-enoic acid will selectively react with Br^+ to form a lactone, 5-(bromomethyl)dihydrofuran-2(3*H*)-one (Figure 5a).[17] As presented in Figure 5b, the reduction feature of Br_2 back to Br^- completely disappeared once 5 mM pent-4-enoic acid was added to the solution of 5 mM NaBr in 0.1 M H_2SO_4. Controlled potential electrolysis carried out at 1.2 V vs Ag/AgCl (Figure S15) unambiguously confirmed the production of 5-(bromomethyl)dihydrofuran-2(3*H*)-one (Figure S16).[25] Therefore, it was proved that Br^+ could be generated from the electrochemical oxidation of Br^- in 0.1 M H_2SO_4.

Computational Investigation of the Reaction Mechanism. DFT calculations were further performed to shed light on the possible transformation from furfurylamine to 3-pyridinol initiated by Br^+. As shown in Figure 6a, Br^+ initially attacks a C=C bond on the furan ring to form **2** with highly favorable energetics (Figure 6b). Subsequent hydroxylation at the 5′-position of the cationic intermediate **2** will form a neutral species **3** in another downhill step. The next step is debromination, which is only slightly uphill by about 0.1 eV to yield a new cationic intermediate **4**. A second hydroxylation step at its 2′-position results in the formation of **5**, which is also energetically favorable. Next, dehydration of **5** furnishes the cis-dicarbonyl amine (**6**), which immediately goes through a condensation step for ring closure to yield piperidinone **7**, the aza-Achmatowicz product. The steps from **5** to **7** are also downhill. The isomerization of **7** to form **8** is slightly uphill by 0.2 eV but followed by a very downhill dehydration step to form the final product, 3-pyridinol (**9**). Overall, the DFT-computed energy profile of the key intermediates in Figure 6 indicates that once Br^+ is generated electrochemically, the subsequent steps of transforming of furfurylamine to 3-pyridinol in an aqueous acidic environment will be thermodynamically very favorable, thereby corroborating our experimental findings.

■ CONCLUSIONS

A new system for producing pyridines through electrocatalysis using Br^-/Br^+ as a mediator has been developed. This method is superior to traditional approaches due to its one-step synthesis process. By optimizing the conditions of the electrolysis process, furfurylamine was converted at a rate of nearly 100%, and a 97% yield of pyridines was achieved. The effectiveness of Br^-/Br^+ was further confirmed through four consecutive electrolysis runs. Controlled experiments and DFT calculations have demonstrated that the electrosynthesis of pyridines requires the presence of protons and Br^+.

■ ASSOCIATED CONTENT

SI Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.jpcc.3c02245.

Methods for the synthesis, characterization, and electrochemical studies and NMR and HPLC spectra of organic compounds involved in this study (PDF)

Bromonium-mediated electrochemical synthesis of 3-Ppyridinol (TIF)

■ AUTHOR INFORMATION

Corresponding Authors

De-en Jiang − *Department of Chemical and Biomolecular Engineering, Vanderbilt University, Nashville, Tennessee 37212, United States;* orcid.org/0000-0001-5167-0731; Email: de-en.jiang@vanderbilt.edu

Yujie Sun − *Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 43221, United States;* orcid.org/0000-0002-4122-6255; Email: yujie.sun@uc.edu

Authors

Kaili Yan − *Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 43221, United States*

Hyuna Kwon − *Department of Chemical and Environmental Engineering, University of California, Riverside, California 92521, United States;* orcid.org/0000-0002-4828-8598

Morgan Huddleston − *Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 43221, United States*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.jpcc.3c02245

Author Contributions

Y.S. conceived and designed this research. K.Y. performed the electrocatalytic experiments with the assistance of M.H. H.K. and D.J. conducted the theoretical computation. All authors contributed to the analysis and interpretation of the results. K.Y. and Y.S. wrote the manuscript.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Y.S. acknowledges the support of the National Science Foundation (CHE-1914546 and CHE-2102220) and the Herman Frasch Foundation (820-HF17). DFT computation (D.J.) was sponsored by the National Science Foundation (CHE-2102191).

■ REFERENCES

(1) Gupta, K.; Rai, R. K.; Singh, S. K. Metal catalysts for the efficient transformation of biomass derived HMF and furfural to value added chemicals. *ChemCatChem* **2018**, *10*, 2326−2349.

(2) Goyal, H. B.; Seal, D.; Saxena, R. C. Bio-fuels from thermochemical conversion of Renewable resources: a review. *Renew. Sustain. Energy Rev.* **2008**, *12*, 504−517.

(3) Li, K.; Sun, Y. Electrocatalytic upgrading of biomass-derived intermediate compounds to value-added products. *Eur. J. Chem.* **2018**, *24*, 18258−18270.

(4) Liu, X.; Li, B.; Han, G.; Liu, X.; Cao, Z.; Jiang, D. E.; Sun, Y. Electrocatalytic synthesis of heterocycles from biomass-derived furfuryl alcohols. *Nat. Commun.* **2021**, *12*, 1868.

(5) O'Hagan, D. Pyrrole, pyrrolidine, pyridine, piperidine and tropane alkaloids. *Nat. Prod. Rep.* **2000**, *17*, 435−446.

(6) Taylor, R. D.; MacCoss, M.; Lawson, A. D. G. Rings in drugs. *J. Med. Chem.* **2014**, *57*, 5845−5859.

(7) Vitaku, E.; Smith, D. T.; Njardarson, J. T. Analysis of the structural diversity, substitution patterns, and frequency of nitrogen heterocycles among US FDA approved pharmaceuticals. *J. Med. Chem.* **2014**, *57*, 10257−10274.

(8) Van Der Pijl, F.; Harmel, R. K.; Richelle, G. J.; Janssen, P.; van Delft, F. L.; Rutjes, F. P. Organocatalytic entry into 2, 6-disubstituted aza-Achmatowicz piperidinones: application to (−)-sedacryptine and its epimer. *Org. Lett.* **2014**, *16*, 2038−2041.

(9) Ciufolini, M. A.; Hermann, C. Y. W.; Dong, Q.; Shimizu, T.; Swaminathan, S.; Xi, N. Nitrogen heterocycles from furans: The aza-Achmatowicz reaction. *Synlett* **1998**, *1998*, 105−114.

(10) Kelly, T. R.; Lebedev, R. L. Synthesis of some unsymmetrical bridged terpyridines. *J. Org. Chem.* **2002**, *67*, 2197−2205.

(11) Antonyraj, C. A.; Kannan, S. Hantzsch pyridine synthesis using hydrotalcites or hydrotalcite like materials as solid base catalysts. *Appl. Catal. A: Gen.* **2008**, *338*, 121−129.

(12) Hill, M. D. Recent strategies for the synthesis of pyridine derivatives. *Eur. J. Chem.* **2010**, *16*, 12052−12062.

(13) Parthasarathy, K.; Jeganmohan, M.; Cheng, C. H. Rhodium-catalyzed one-pot synthesis of substituted pyridine derivatives from *α*, *β*-unsaturated ketoximes and alkynes. *Org. Lett.* **2008**, *10*, 325−328.

(14) Hodgson, R.; Kennedy, A.; Nelson, A.; Perry, A. Synthesis of 3-sulfonyloxypyridines: Oxidative ring expansion of *α*-furylsulfonamides and N→O sulfonyl transfer. *Synlett* **2007**, *2007*, 1043−1046.

(15) Zhou, W. S.; Lu, Z. H.; Wang, Z. M. An efficient preparation of optically active *α*-furfuryl amide by kinetic resolution using the modified Sharpless asymmetric epoxidation reagents. *Tetrahedron* **1993**, *49*, 2641−2654.

(16) Clauson-Kaas, N.; Elming, N.; Tyle, Z.; Caglieris, A. Preparation of 3-pyridols from furans. *Acta Chem. Scand.* **1955**, *9*, 1−8.

(17) Zhao, G.; Liang, L.; Wang, E.; Tong, R. Fenton Chemistry for Achmatowicz Rearrangement. *ACS Catal.* **2021**, *11*, 3740−3748.

(18) Tariq, M. Electrochemistry of Br−/Br_2 Redox Couple in Acetonitrile, Methanol and Mix Media of Acetonitrile−Methanol: An Insight into Redox Behavior of Bromide on Platinum (Pt) and Gold (Au) Electrode. *Z. Phys. Chem.* **2020**, *234*, 295−312.

(19) Natarajan, P.; Vagicherla, V. D.; Vijayan, M. T. Indirect electrochemical oxidation of substituted polycyclic aromatic hydrocarbons to corresponding para-quinones with potassium bromide in water-chloroform medium. *Tetrahedron Lett.* **2014**, *55*, 5817−5821.

(20) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09, Revision B.01*; Gaussian, Inc.: Wallingford CT, 1993.

(21) Becke, A. D. Density-functional exchange-energy approximation with correct asymptotic behavior. *Phys. Rev. A* **1988**, *38*, 3098−3100.

(22) Grimme, S.; Ehrlich, S.; Goerigk, L. Effect of the damping function in dispersion corrected density functional theory. *J. Comput. Chem.* **2011**, *32*, 1456−1465.

(23) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal solvation model based on solute electron density and on a continuum model of the solvent defined by the bulk dielectric constant and atomic surface tensions. *J. Phys. Chem. B* **2009**, *113*, 6378−6396.

(24) Thasan, R.; Kumarasamy, K. Electrochemical bromination and oxidation of alkyl aromatic compounds by two-phase electrolysis. *Korean J. Chem. Eng.* **2014**, *31*, 365−373.

(25) Lu, Y.; Liu, Q.; Wang, Z. X.; Chen, X. Y. Alkynyl Sulfonium Salts Can Be Employed as Chalcogen-Bonding Catalysts and Generate Alkynyl Radicals under Blue-Light Irradiation. *Angew. Chem., Int. Ed.* **2022**, *134*, No. e202116071.

https://doi.org/10.1021/acs.jpcc.3c02245
J. Phys. Chem. C 2023, 127, 10107−10113