JACS Au
AN OPEN ACCESS JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

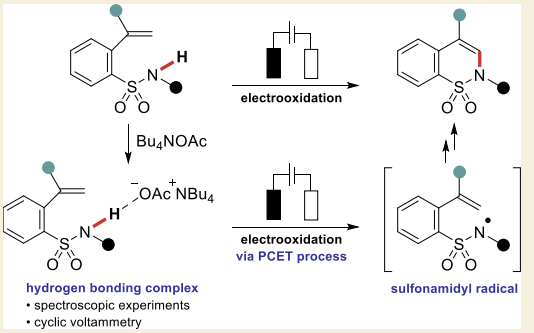
pubs.acs.org/jacsau
Article

Electrochemical Generation of Sulfonamidyl Radicals via Anodic Oxidation of Hydrogen Bonding Complexes: Applications to Electrosynthesis of Benzosultams

Yasuyuki Okumura, Eisuke Sato, Koichi Mitsudo,* and Seiji Suga*

Cite This: https://doi.org/10.1021/jacsau.5c00619
Read Online

ABSTRACT: Amidyl radicals and sulfonamidyl radicals are widely used in the field of organic synthesis. In particular, the electrochemical oxidation of amides in the presence of bases is one of the most practical methods for generating amidyl radicals. However, it is often difficult to observe the "true" radical precursor, such as an amide anion and/or a hydrogen bonding complex with an amide and a base. We found that a sulfonamide and Bu_4NOAc form a 1:1 hydrogen bonding complex by spectroscopic experiments. Cyclic voltammetry suggested that 1:1 hydrogen bonding complexes should be oxidized predominantly under the optimized conditions to afford a sulfonamidyl radical via the proton-coupled electron transfer (PCET) process by the oxidation of the complex. Thus-generated sulfonamidyl radicals could be used in the electrochemical synthesis of a variety of benzosultams.



KEYWORDS: *electrochemical generation, sulfonamidyl radicals, hydrogen bonding complexes, anodic oxidation, proton-coupled electron transfer, electrosynthesis, benzosultams, cyclization*

Amidyl radicals and sulfonamidyl radicals, which are classified as electrophilic *N*-centered radicals, are widely used in the field of organic synthesis.[1] Because of the electrophilic nature of these radicals, intramolecular radical cyclization or intermolecular radical addition to a π-system or an electrophilic functional group occurs (Figure 1A).[2] Amidyl radicals also act as hydrogen abstractors due to the high bond dissociation energies of amide N−H bonds. These radicals induce an intramolecular remote hydrogen atom transfer (HAT) or an intermolecular HAT from an aliphatic C−H bond.[3] Therefore, efficient synthetic methods using amidyl radicals and sulfonamidyl radicals have been reported.[4−6]

General methods for generating amidyl radicals are classified into three categories: homolytic cleavage of an N−heteroatom bond,[4] reductive cleavage of an N−heteroatom bond,[5] and oxidation of amides in the presence of a base (Figure 1B).[6] Homolytic cleavage of an N−halogen bond has long been studied as Hofmann−Löffler−Freytag-type reactions since the 1880s.[7] This type of bond cleavage occurs with photoirradiation or heating, or with the use of transition metals. Reductive cleavage reaction of N−heteroatom bonds has been studied intensively with the rise of photochemical synthesis using photoredox catalysts.[8] Reductive cleavage involves a single electron transfer (SET) to an *N*-substituted amide, which gives rise to the formation of an amidyl radical. Oxidation of amides in the presence of a base is one of the most common methods for generating amidyl radicals without prefunctionalization of amides. There are two possible pathways for the oxidation of amides; proton transfer, then an electron transfer (PT-ET) process, or a proton-coupled electron transfer (PCET) process.[9] The PT-ET process consists of proton transfer of amides forming amide anions and electron transfer of amide anions generating amidyl radicals. In contrast, in the PCET process, deprotonation of amides and SET proceed in concert. Therefore, in the oxidative formation of an amidyl radical, it is very challenging to investigate the process of radical formation, including the involvement a "true" radical precursor, such as the amide anion and/or a hydrogen bonding complex with an amide and a base.

Electrochemical oxidation is a useful method for generating heteroatom radicals under mild conditions without the use of a stoichiometric amount of chemical oxidants and transition metals.[10] In particular, the cyclization reaction via electrogenerated amidyl radicals is a well-known robust strategy (Figure 1C).[11] For instance, in 2008, Moeller and co-worker reported the electrochemical synthesis of pyrrolidine derivatives via sulfonamidyl radicals generated by the anodic oxidation of sulfonamide anions.[12] In 2018, Lei and co-

Received: May 16, 2025
Revised: June 27, 2025
Accepted: July 17, 2025
Published: July 24, 2025

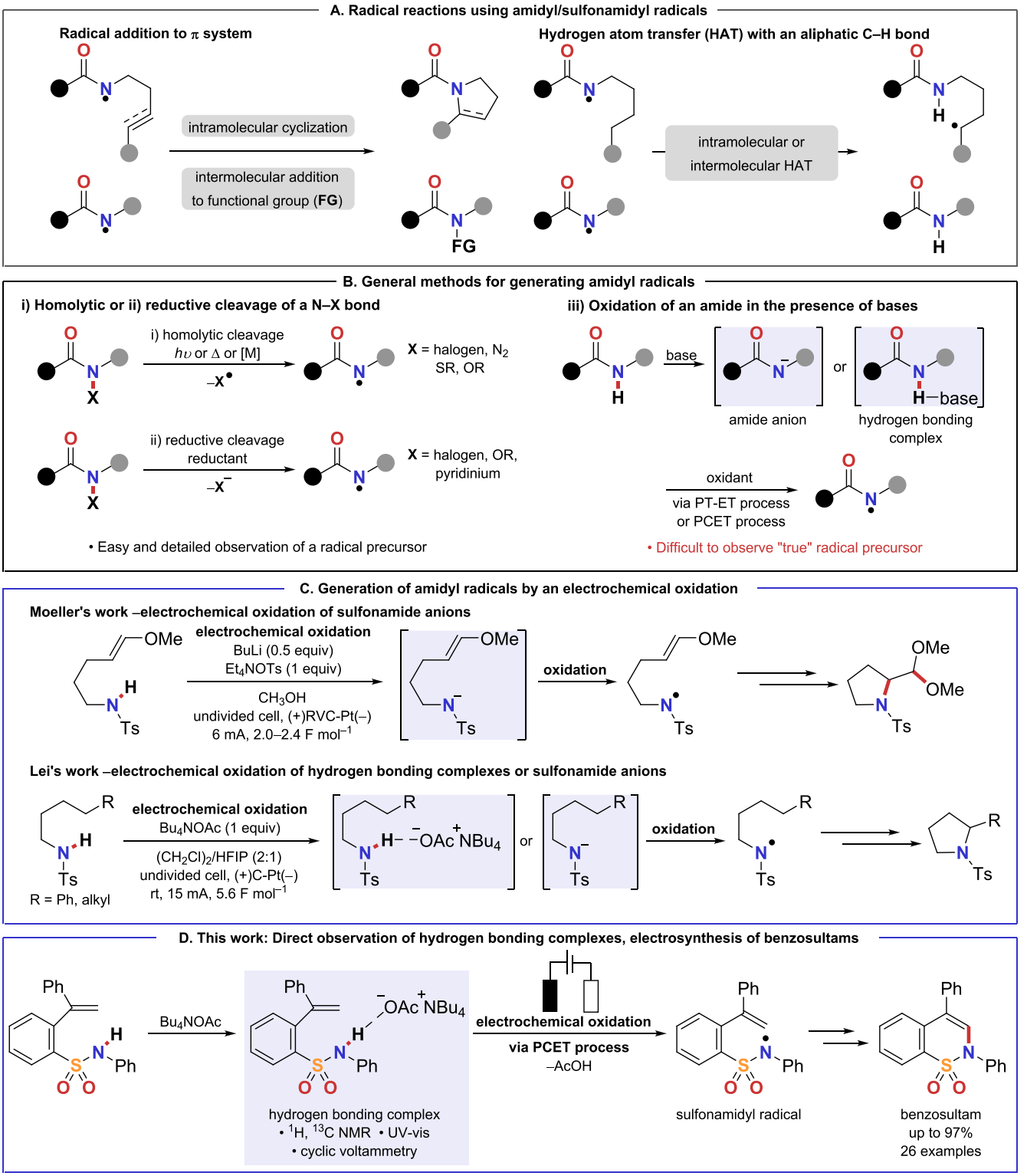


Figure 1. (A) Radical reactions using amidyl/sulfonamidyl radicals. (B) General methods for generating amidyl radicals. (C) Generation of amidyl radicals by an electrochemical oxidation. (D) This work: Direct observation of hydrogen bonding complexes and electrosynthesis of benzosultams; PT = proton transfer, ET = electron transfer, PCET = proton-coupled electron transfer, HFIP = 1,1,1,3,3,3-hexfluoropropan-2-ol.

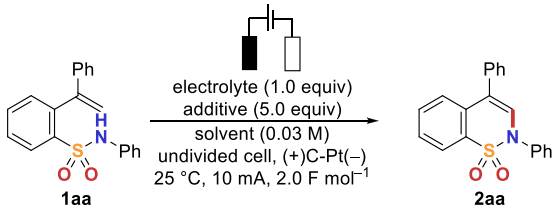
workers reported the synthesis of five-membered *N*-heterocyclic compounds by an anodic oxidation of sulfonamide.[13] They suggested that the reactions involve sulfonamide anions or hydrogen bonding complexes with sulfonamides and Bu_4NOAc. Formation of the complex was only observed by ^1H NMR measurements. In the field of organic synthesis using electrochemical methods, several studies have suggested that hydrogen bonding complexes may be the actual species undergoing oxidation.[14] However, very few studies have investigated the complexes in detail. Elucidation of the chemical properties of hydrogen bonding complexes would be key for the development of an electrochemical synthesis.

https://doi.org/10.1021/jacsau.5c00619
JACS Au XXXX, XXX, XXX−XXX

Meanwhile, sultams have been recognized as important frameworks in pharmaceuticals and biologically active molecules.[15] Thus, efficient methods for synthesizing sultams are in high demand. In recent years, electrochemical reactions have received considerable attention as environmentally friendly methods in organic synthesis. Although several electrochemical methods for the formation of sultam skeletons have been reported, there have been no reports on the electrochemical synthesis of sultams via sulfonamidyl radicals.[16] Herein, we developed an electrochemical synthesis of benzosultams via electro-generated sulfonamidyl radicals. The key intermediate is the hydrogen bonding complex with a sulfonamide and an acetate. Formation of the complex was elucidated by chemical and electrochemical means, and the subsequent molecular transformation was found to proceed via oxidation through a PCET pathway.

We first chose sulfonamide **1aa** as a model substrate and optimized the reaction conditions for the electrochemical synthesis of benzosultam **2aa** (Table 1). In methanol, constant current electrolysis of **1aa** with Bu_4NOAc (1.0 equiv) was carried out in an undivided cell equipped with a carbon rod anode and a platinum cathode. After the passage of electricity (10 mA, 2 F mol^{-1}), **2aa** was obtained in 36% yield and **1aa** was recovered in 12% yield (entry 1). Moreover, methoxide adduct product was obtained in 58% yield (Table S1). This result suggests that the dibenzyl cation species would be generated during electrolysis. Anodic oxidation of **1aa** in 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP) and 2,2,2-trifluoroethanol (TFE) was ineffective, however, the alkoxide adducts were not observed due to the low nucleophilicity of these alkoxides (entries 2 and 3). In CH_2Cl_2, the yield of **2aa** was increased (50% yield, entry 4). Electrolyte screening revealed that the use of Bu_4NOAc was essential, while the use of Bu_4NOTf, Bu_4NClO_4, Bu_4NBF_4 or Bu_4NBr was ineffective (entries 5−8). The effect of anode materials is illustrated in Table S3 (see the Supporting Information). The yield of **2aa** drastically decreased with a reticulated vitreous carbon (RVC) electrode (8% yield). The use of a glassy carbon (GC) electrode and a platinum electrode as an anode did not yield **2aa**. The addition of 5 equiv of alcohols or acetic acid as sacrificial reagents which were reduced on the cathode was effective (entries 9−11). In particular, the use of 5 equiv of acetic acid gave **2aa** in the highest yield (83% ^{1}H NMR yield, 78% isolated yield, entry 11). We next examined the reaction on a 1 mmol scale, and **2aa** was obtained in 78% yield (entry 12).

Table 1. Optimization of the Reaction Conditions[a]



1aa **2aa**

entry	solvent	electrolyte	additive	**2aa** (%)[b]
1	CH_3OH	Bu_4NOAc	—	36
2	HFIP	Bu_4NOAc	—	25
3	TFE	Bu_4NOAc	—	2
4	CH_2Cl_2	Bu_4NOAc	—	50
5	CH_2Cl_2	Bu_4NOTf	—	27
6	CH_2Cl_2	Bu_4NClO_4	—	N.D.[c]
7	CH_2Cl_2	Bu_4NBF_4	—	N.D.
8	CH_2Cl_2	Bu_4NBr	—	4
9	CH_2Cl_2	Bu_4NOAc	HFIP	77
10	CH_2Cl_2	Bu_4NOAc	TFE	68
11	CH_2Cl_2	Bu_4NOAc	AcOH	83 (78)[d]
12[e]	CH_2Cl_2	Bu_4NOAc	AcOH	(78)[d]

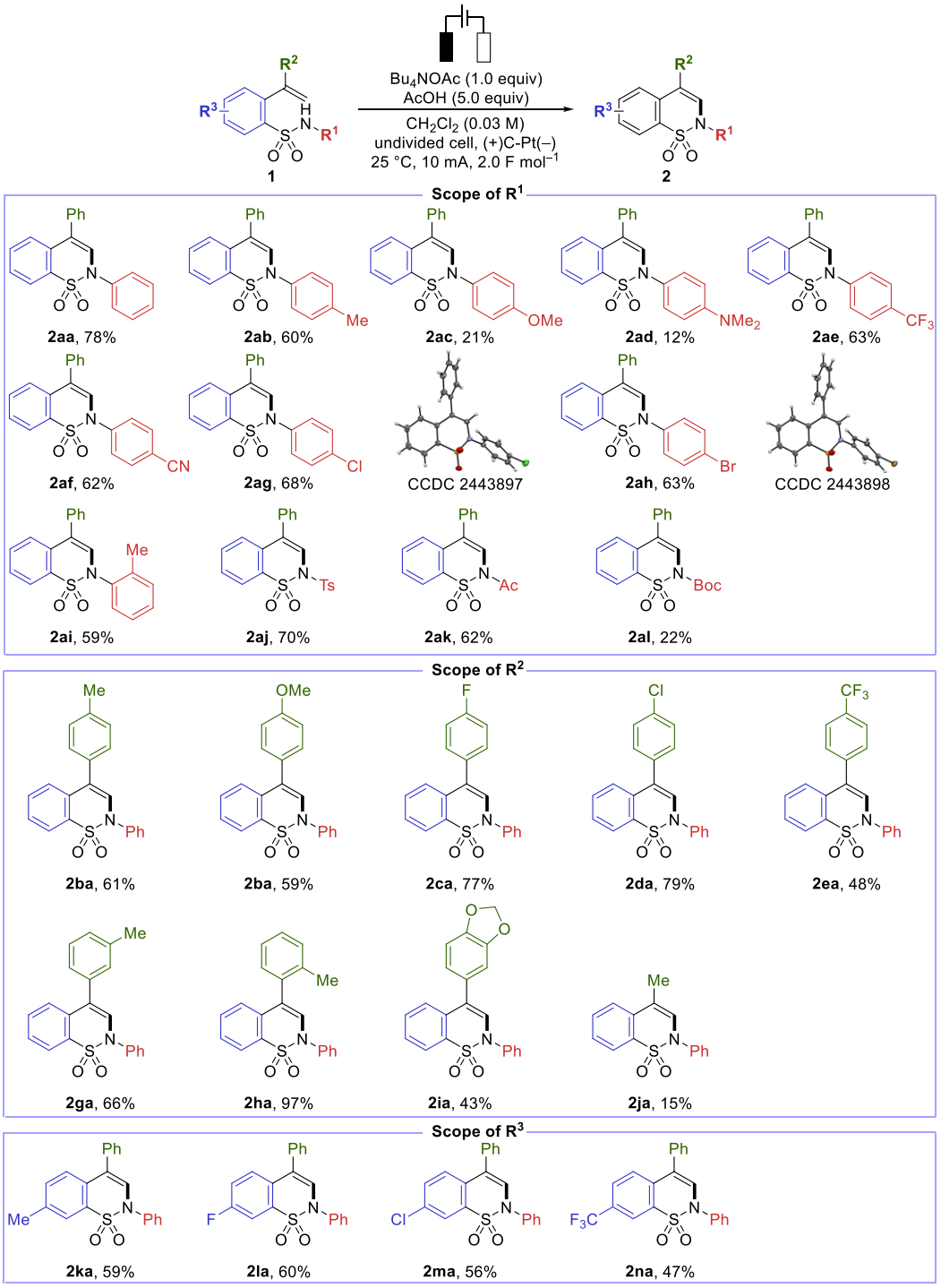
[a]Reaction conditions: **1aa** (0.2 mmol), electrolyte (0.2 mmol), additive (1.0 mmol), solvent (0.03 M), undivided cell, (+)C−Pt(−), 25 °C, 10 mA, 2.0 F mol^{-1}. [b]Determined by ^{1}H NMR with 1,1,2,2-tetrachloroethane as an internal standard. [c]N. D. = Not Detected. [d]Isolated yield. [e]Performed on a 1.0 mmol scale; TFE = trifluoroethanol.

Under the optimized conditions, we examined the scope of the reactions (Scheme 1). We first assessed the substituent on the phenyl ring of the *N*-phenyl moiety. The reactions of precursors bearing an electron-donating (Me, OMe, NMe_2) or electron-withdrawing group (CF_3, CN, Cl, Br) at the *p*-position gave the desired benzosultams **2ab**−**2ah** in moderate yields, although the yields of the products were low in some cases (**2ac** and **2ad**). The benzosultam with a methyl group at the *o*-position was also obtained (**2ai**, 59% yield). We next examined the *N*-protecting groups. Sulfonamides protected by tosyl (Ts), acetyl (Ac) and *tert*-butoxycarbonyl (Boc) groups on the nitrogen atom were tolerated under the reaction conditions (**2aj**−**2al**). However, *N*-free, *N*-alkyl and *N*-benzyl (Bn) protected benzosultams were not obtained (**2am**−**2ap**, Table S6). We also assessed the substituents on the phenyl ring of R^2. The electrolysis of substrates bearing electron-donating groups (Me, OMe) or electron-withdrawing groups (F, Cl, CF_3) at the *p*-position afforded the products in moderate yields (**2ba**−**2fa**). Benzosultams with methyl groups at the *m*- or *o*-positions could be used in the reaction; especially **2ha** was obtained in an excellent yield (**2ga**, 66% yield; **2ha**, 97% yield). We also successfully obtained an electron-rich heterocycle-substituted benzosultam **2ia** (43% yield). The product bearing a methyl group **2ja** was obtained in 15% yield. The reaction of sulfonamide with various substituents on the phenyl ring of R^3 gave the products in moderate yields (**2ka**−**2na**).

As mentioned above, Bu_4NOAc as an electrolyte is highly significant. To investigate further details of the interaction between sulfonamide **1aa** and Bu_4NOAc, a series of experiments were performed (Figure 2). We performed a ^{1}H NMR analysis of a 1:1 mixture of **1aa** and Bu_4NOAc in CD_2Cl_2 (Figure 2A,B; the full-scale version, see the Supporting Information for details). The peaks corresponding to H_a, H_e protons of **1aa** and an amide proton showed downfield shifts in the presence of 1 equiv of Bu_4NOAc. The peaks of other protons of **1aa** (H_b, H_c, H_d, H_g) showed only a slight upfield shift. The upfield shifts of the signals that were derived from Bu_4N^+ were observed with 1 equiv of **1aa**. The chemical shift of the methyl proton of acetate was 0.02 ppm downfield in comparison with that of $^-$OAc, and 0.16 ppm upfield comparing the chemical shift of the 1:1 complex to that of AcOH. These ^{1}H NMR measurements indicate that a 1:1 hydrogen bonding complex would form between **1aa** and Bu_4NOAc. We next performed a Job plot analysis using **1aa** and Bu_4NOAc dissolved in $CDCl_3$ with ^{1}H NMR spectroscopy, and the maximum chemical shift difference appeared at 50% (Figure 2C).[17] This suggests that a 1:1 complex formed between **1aa** and Bu_4NOAc. By UV−vis spectroscopy, in CH_2Cl_2, the Job plot also gave a maximum difference at a molar fraction of 50% (see the Supporting Information). We

https://doi.org/10.1021/jacsau.5c00619
JACS Au XXXX, XXX, XXX−XXX

Scheme 1. Synthesis of Several Benzosultams 2 under the Optimized Condition[a]



[a]Reaction conditions: **1** (0.2 mmol), Bu_4NOAc (0.2 mmol), AcOH (1.0 mmol), CH_2Cl_2 (0.03 M), undivided cell, (+)C–Pt(−), 25 °C, 10 mA, 2.0 F mol^{-1}.

next used the Beneshi–Hildebrand method with ^1H NMR, and the associated constant K_a of 18.1 M^{-1} in CD_2Cl_2 was calculated (Figure 2D).[18] All of the spectroscopic experiments strongly suggest that a 1:1 hydrogen bonding complex would form between **1aa** and Bu_4NOAc (Figure 2E).

Additional mechanistic studies are illustrated in Figure 3. We first performed cyclic voltammetry. The onset of the oxidation potential of **1aa**, Bu_4NOAc, and complex **I** was observed at 1.10, 0.61, and −0.06 V (vs Fc/Fc^+), respectively (Figure 3A). These results indicate that the oxidation of complex **I** proceeds predominantly under the reaction conditions.[19] The cyclic voltammogram of amide anion Bu_4N^+**1aa**$^-$ shows that the onset of its oxidation potential was much lower than that of complex **I** (Figure 3B). These voltammograms strongly suggest that the amide anion hardly exists in solution under the reaction conditions, and the sulfonamidyl radical should be generated via a PCET process.[20] To clarify these reactions in greater detail, we carried out the radical clock experiment

https://doi.org/10.1021/jacsau.5c00619
JACS Au XXXX, XXX, XXX−XXX

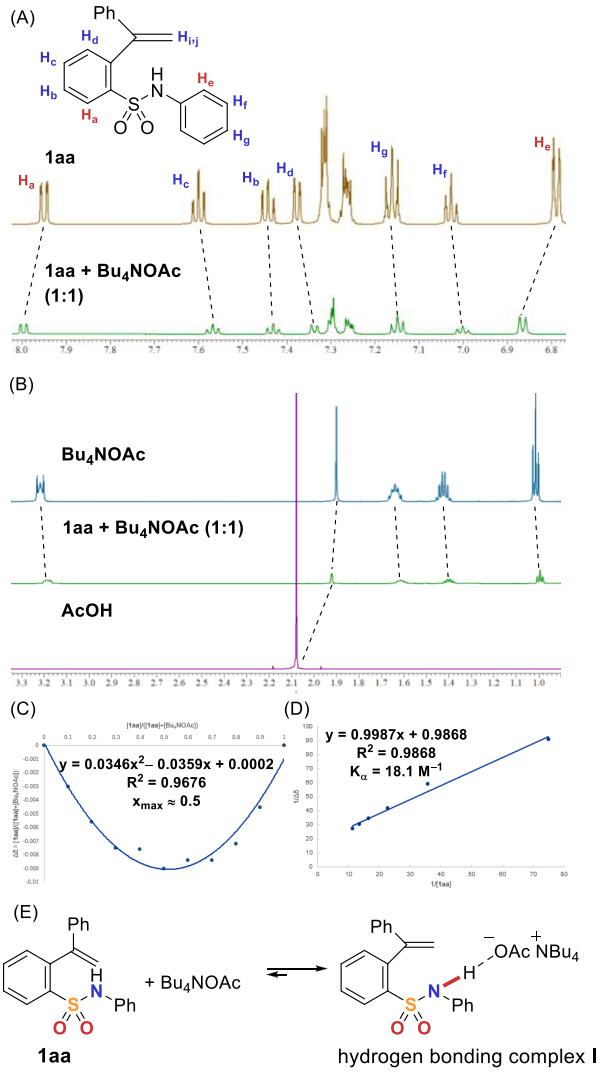


Figure 2. (A) ^{1}H NMR analysis (in CD_2Cl_2); (Top) **1aa**, (Bottom) the complex between **1aa** and Bu_4NOAc. (B) ^{1}H NMR analysis (in CD_2Cl_2); (Top) Bu_4NOAc, (Center) the complex between **1aa** and Bu_4NOAc, (Bottom) AcOH. (C) Job plot analysis (in $CDCl_3$). (D) Determination of association constant (in CD_2Cl_2). (E) Formation of the hydrogen bonding complex **I** with sulfonamide **1aa** and Bu_4NOAc.

(Figure 3C). The electrolysis of sulfonamide **1oa** afforded nonring-opening product **2oa** and ring-opening product **2oa′** (**2oa**, 28% yield; **2oa′**, 18% yield). We considered that the formation of **2oa′** occurred via the radical coupling reaction with an alkyl radical generated by a ring-opening and an acetoxyl radical. This strongly suggests that this reaction would proceed via a benzyl radical. The formation of **2oa** is probably due to the relatively higher stability of the generated cyclopropyl benzyl radical.[21] We next performed a radical trapping experiment. With 2,6-di-*tert*-butyl-4-methylphenol (BHT), the yield of **2aa** drastically decreased, and the BHT adduct was detected by HRMS (Figure 3D). This suggests that a sulfonamidyl radical would be generated in this reaction system. We also carried out electron paramagnetic resonance (EPR) experiments. When the electrolysis was performed with 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO) under the optimal conditions without acetic acid, the formation of a nitroxyl radical, resulting from the trapping of a radical intermediate,

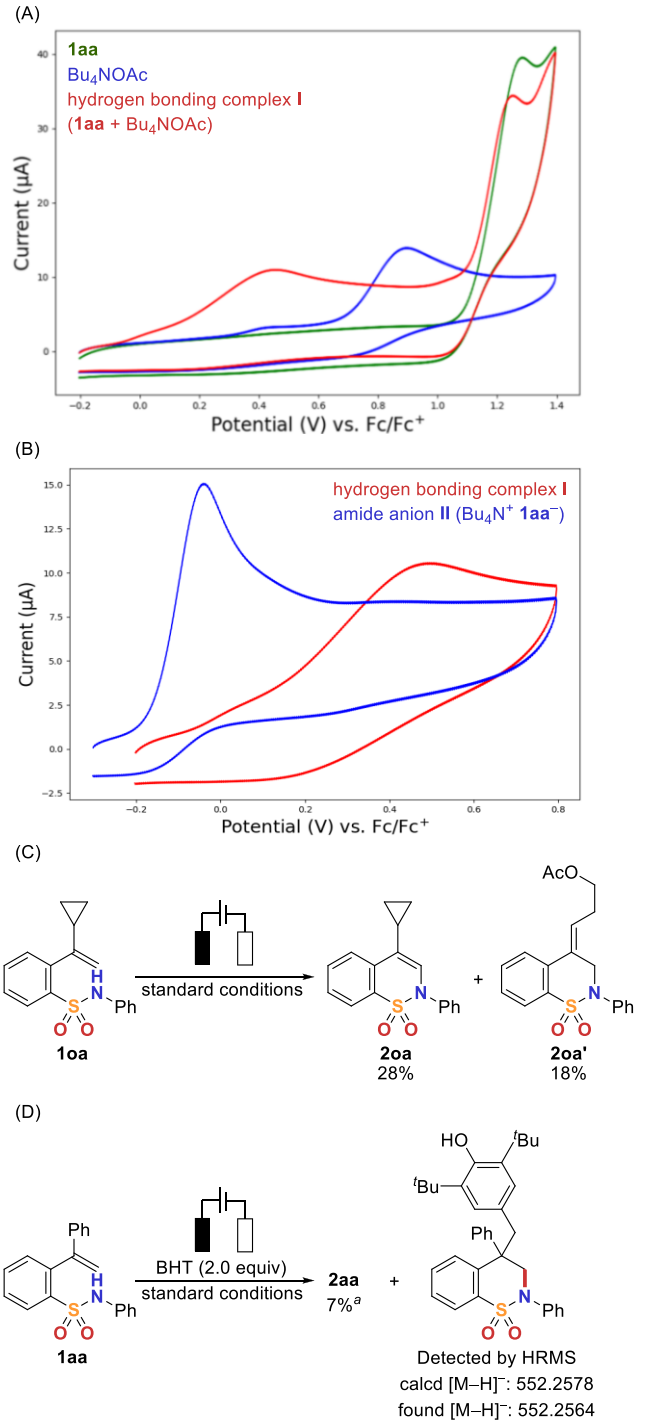


Figure 3. Mechanistic studies. (A) Cyclic voltammograms of sulfonamide **1aa** (green), Bu_4NOAc (blue), and hydrogen bonding complex I (red). The following conditions were applied; solvent: CH_2Cl_2, supporting electrolyte: Bu_4NPF_6 (0.1 M), substrate concentration: 1 mM, working electrode: GC, counter electrode: Pt coil, reference electrode: Ag/Ag^+ (CH_2Cl_2), standard: Fc/Fc^+, scan rate: 100 mV s^{-1}. (B) Cyclic voltammograms of hydrogen bonding complex **I** (red) and amide anion **II** (Bu_4N^+**1aa**$^-$; blue). (C) Radical clock experiment. (D) Radical trapping experiment with BHT. [a]Determined by ^{1}H NMR with 1,1,2,2-tetrachloroethane as an internal standard.

was confirmed by EPR spectroscopy and HRMS (see the Supporting Information). These results also suggested that this reaction would proceed via a radical mechanism.

https://doi.org/10.1021/jacsau.5c00619
JACS Au XXXX, XXX, XXX−XXX

Based on these experiments, a plausible mechanism for the electrochemical synthesis of benzosultam **2** is illustrated in Figure 4. In the presence of **1aa** and Bu_4NOAc, hydrogen

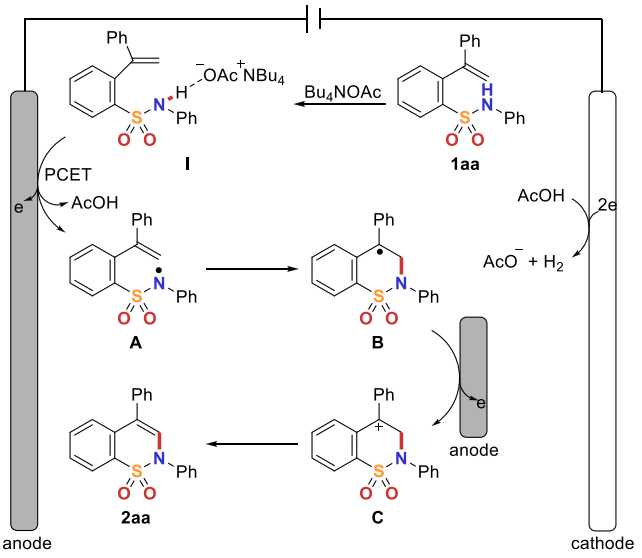


Figure 4. Plausible mechanism for the electrochemical synthesis of benzosultam **2**.

bonding complex **I** forms. Anodic oxidation of **I** generates amidyl radical **A** via a PCET process. The intramolecular cyclization of **A** gives radical intermediate **B**. Subsequent anodic oxidation of **B** forms dibenzyl cation **C**, which is then deprotonated to yield benzosultam **2aa**. On the cathode, the reduction of AcOH occurs.

To confirm this plausible reaction mechanism, we performed density functional theory (DFT) calculations (CPCM-(CH_2Cl_2)/(U)M06-2*X*/6-31+G(d,p)) (Figure 5). In the optimized structure of complex **I** between **1aa** and Bu_4NOAc, the bond length of the amide N−H bond was 1.10 Å (Figure 5A). The distance between the acetate oxygen and the amide proton was 1.49 Å. These results suggest that the hydrogen bond would be formed between the amido moiety of **1aa** and acetate. We next compared the Gibbs free energies of neutral **1aa**, hydrogen bonding complex **I**, and amide anion **II** (Figure 5B). The free energy of the hydrogen bonding complex was the lowest among them. Therefore, hydrogen bonding complex **I** would be thermodynamically dominant among the three states. These calculations were consistent with ^1H NMR experiments. We also calculated the energy profile of the cyclization from sulfonamidyl radical **A** to radical intermediate **B**, and found that the activation energy of this step is 12.4 kcal mol^{-1}, indicating that this cyclization would occur even at room temperature (Figure 5C). All of the calculated data are in good agreement with the experimental results.

In summary, we achieved the electrochemical synthesis of benzosultams via the anodic oxidative cyclization of hydrogen bonding complexes with sulfonamides **1** and Bu_4NOAc. A wide variety of benzosultams were obtained under the optimized conditions. We also clarified the behavior of hydrogen bonding complexes **I** by a series of spectroscopic and electrochemical analyses. These hydrogen bonding complexes would be oxidized to sulfonamidyl radicals via a PCET process under the reaction conditions. DFT calculations supported these experimental results. In this study, we clearly

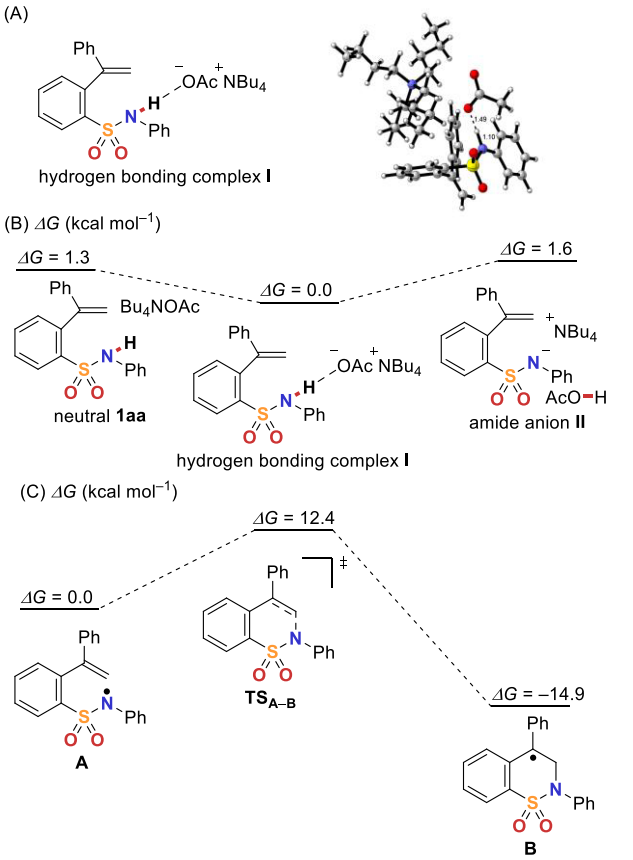


Figure 5. DFT calculations. (A) Energy-minimized structure of hydrogen bonding complex **I**. (B) Comparison of the free energy of each state. (C) Activation energy of the radical cyclization at the CPCM(CH_2Cl_2)/(U)M06-2*X*/6-31+G(d,p) levels of theory.

demonstrated that radical generation and cyclization reactions proceed efficiently via a PCET mechanism even in organic electrochemical reactions. We aim to investigate the generality of this phenomenon and hope that our findings will contribute to the development of novel and efficient electrochemical reactions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacsau.5c00619.

Synthetic experiments, data for compound characterization, crystal data of **2ag** and **2ah**, and DFT calculations (PDF)

Accession Codes

Deposition Numbers 2443897−2443898 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via the joint Cambridge Crystallographic Data Centre (CCDC) and Fachinformationszentrum Karlsruhe Access Structures service.

■ AUTHOR INFORMATION

Corresponding Authors

Koichi Mitsudo − *Division of Applied Chemistry, Graduate School of Environmental, Life, Natural Science and Technology, Okayama University, Okayama 700-8530,*

https://doi.org/10.1021/jacsau.5c00619
JACS Au XXXX, XXX, XXX−XXX

Japan; orcid.org/0000-0002-6744-7136; Email: mitsudo@okayama-u.ac.jp

Seiji Suga − *Division of Applied Chemistry, Graduate School of Environmental, Life, Natural Science and Technology, Okayama University, Okayama 700-8530, Japan*; orcid.org/0000-0003-0635-2077; Email: suga@cc.okayama-u.ac.jp

Authors

Yasuyuki Okumura − *Division of Applied Chemistry, Graduate School of Environmental, Life, Natural Science and Technology, Okayama University, Okayama 700-8530, Japan*

Eisuke Sato − *Division of Applied Chemistry, Graduate School of Environmental, Life, Natural Science and Technology, Okayama University, Okayama 700-8530, Japan*; orcid.org/0000-0001-6784-138X

Complete contact information is available at: https://pubs.acs.org/10.1021/jacsau.5c00619

Author Contributions

Y.O., K.M. and S.S. conceived the projects and analyzed the experimental results with the assistance of E.S. Y.O. performed all experiments. Y.O. and K.M. performed X-ray analysis. Y.O. wrote the manuscript with the feedback from all authors. CRediT: **Yasuyuki Okumura** conceptualization, data curation, formal analysis, funding acquisition, investigation, visualization, writing - original draft; **Eisuke Sato** formal analysis, funding acquisition, writing - review & editing; **Koichi Mitsudo** conceptualization, formal analysis, funding acquisition, investigation, project administration, resources, supervision, writing - review & editing; **Seiji Suga** conceptualization, formal analysis, funding acquisition, project administration, resources, supervision, writing - review & editing.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank Prof. Tadashi Ema (Okayama University) and Dr. Chihiro Maeda for their kind help with UV−vis analysis. The authors also thank Prof. Yuta Nishina (Okayama University) and Dr. Riki Kato for their assistance with EPR measurement. The computation was partially performed using Research Center for Computational Science, Okazaki, Japan (projects: 23-IMS-C120, 24-IMS-C115, and 25-IMS-C116). This work was supported by JSPS KAKENHI grant numbers JP25KJ1850 (to Y.O.), JP23K13748 (to E.S.), JP22H02122 (to K.M.), JP23K17917 (to K.M.), JP22K05115 (to S.S.), JP21H05214 (Digitalization-driven Transformative Organic Synthesis) (to S.S.), and OU-SPRING (to Y.O.).

■ REFERENCES

(1) (a) Zard, S. Z. Recent progress in the generation and use of nitrogen-centred radicals. *Chem. Soc. Rev.* **2008**, *37*, 1603−1608. (b) Kärkäs, M. D. Photochemical Generation of Nitrogen-Centered Amidyl, Hydrazonyl, and Imidyl Radicals: Methodology Developments and Catalytic Applications. *ACS Catal.* **2017**, *7*, 4999−5022. (c) Kwon, K.; Simons, T.; Nandakumar, M.; Roizen, J. L. Strategies to Generate Nitrogen-centered Radicals That May Rely on Photoredox Catalysis: Development in Reaction Methodology and Applications in Organic Synthesis. *Chem. Rev.* **2022**, *122*, 2353−2428. (d) Pratley, C.; Fenner, S.; Murphy, J. A. Nitrogen-Centered Radicals in Functionalization of sp^2 Systems: Generation, Reactivity, and Applications in Synthesis. *Chem. Rev.* **2022**, *122*, 8181−8260.

(2) (a) Lessard, J.; Griller, D.; Ingold, K. U. The structure of amidyl radicals. An investigation by variable-temperature electron paramagnetic resonance spectroscopy. *J. Am. Chem. Soc.* **1980**, *102*, 3262−3264. (b) Zhao, Y.; Xia, W. Recent advances in radical-based C−N bond formation via photo-/electrochemistry. *Chem. Soc. Rev.* **2018**, *47*, 2591−2608. (c) Jiang, H.; Studer, A. Chemistry With N-Centered Radicals Generated by Single-Electron Transfer-Oxidation Using Photoredox Catalysis. *CCS Chem.* **2019**, *1*, 38−49.

(3) (a) Baldwin, S. W.; Doll, R. J. Synthesis of the 2-aza-7-oxatricyclo[4.3.2.$0^{4,8}$]undecane nucleus of some gelsemium alkaloids. *Tetrahedron Lett.* **1979**, *35*, 3275−3278. (b) Choi, G. J.; Zhu, Q.; Miller, D. C.; Gu, C. J.; Knowles, R. R. Catalytic alkylation of remote C−H bonds enabled by proton-coupled electron transfer. *Nature* **2016**, *539*, 268−271. (d) Chu, J. C. K.; Rovis, T. Amide-directed photoredox-catalyzed C−C bond formation at unactivated sp^3 C−H bonds. *Nature* **2016**, *539*, 272−275. (e) Fazekas, T. J.; Alty, J. W.; Neidhart, E. K.; Miller, A. S.; Leibfarth, F. A.; Alexanian, E. J. Diversification of aliphatic C−H bonds in small molecules and polyolefins through radical chain transfer. *Science* **2022**, *375*, 545−550.

(4) (a) Mackiewicz, P.; Furstoss, R.; Waegell, B.; Cote, R.; Lessard, J. Peroxide-initiated cyclizations of olefinic N-chloro amides. Electronic configuration of amido radicals. *J. Org. Chem.* **1978**, *43*, 3746−3750. (b) Lu, H.; Li, C. Facile cyclization of amidyl radicals generated from *N*-acyltriazenes. *Tetrahedron Lett.* **2005**, *46*, 5983−5985. (c) Gagosz, F.; Moutrille, C.; Zard, S. Z. A New Tin-Free Source of Amidyl Radicals. *Org. Lett.* **2002**, *4*, 2707−2709. (d) Moutrille, C.; Zard, S. Z. A new, practical access to amidyl radicals. *Chem. Commun.* **2004**, 1848−1849. (e) Foo, K.; Sella, E.; Thomé, I.; Eastgate, M. D.; Baran, P. S. A Mild, Ferrocene-Catalyzed C−H Imidation of (Hetero)Arenes. *J. Am. Chem. Soc.* **2014**, *136*, 5279−5282.

(5) (a) Greulich, T. W.; Daniliuc, C. G.; Studer, A. *N*-Aminopyridinium Salts as Precursors for N-Centered Radicals − Direct Amidation of Arenes and Heteroarenes. *Org. Lett.* **2015**, *17*, 254−257. (b) Qin, Q.; Yu, S. Visible-Light-Promoted Remote C(sp^3)−H Amidation and Chlorination. *Org. Lett.* **2015**, *17*, 1894−1897. (c) Miyazawa, K.; Koike, T.; Akita, M. Regiospecific Intermolecular Aminohydroxylation of Olefins by Photoredox Catalysis. *Chem. - Eur. J.* **2015**, *21*, 11677−11680. (d) Davies, J.; Svejstrup, T. D.; Reina, D. F.; Sheikh, N. S.; Leonori, D. Visible-Light-Mediated Synthesis of Amidyl Radicals: Transition-Metal-Free Hydroamination and *N*-Arylation Reactions. *J. Am. Chem. Soc.* **2016**, *138*, 8092−8095.

(6) (a) Forrester, A. R.; Ingram, A. S.; Thomson, R. H. Persulphate oxidations. Part VI. Oxidation of biphenyl-2-carboxamides. *J. Chem. Soc., Perkin Trans.* **1972**, *1*, 2847−2853. (b) Glover, S. A.; Goosen, A. *N*-Iodo-amides: mechanism of intramolecular reactions with aromatic rings of amido-radicals in Σ- and Π- electronic states. *J. Chem. Soc., Perkin Trans.* **1977**, *1*, 1348−1356. (c) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L.; Barluenga, S.; Hunt, K. W.; Kranich, R.; Vega, J. A. Iodine(V) Reagents in Organic Synthesis. Part 3. New Routes to Heterocyclic Compounds via *o*-Iodoxybenzoic Acid-Mediated Cyclizations: Generality, Scope, and Mechanism. *J. Am. Chem. Soc.* **2002**, *124*, 2233−2244. (d) Choi, G. J.; Knowles, R. R. Catalytic Alkene Carboaminations Enabled by Oxidative Proton-Coupled Electron Transfer. *J. Am. Chem. Soc.* **2015**, *137*, 9226−9229.

(7) (a) Hofmann, A. W. Ueber die Einwirkung des Broms in Alkalicher Lösung auf die Amine. *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 558−560. (b) Löffler, K.; Freytag, C. Über eine neue Bildungsweise von *N*-alkylierten Pyrrolidinen. *Ber. Dtsch. Chem. Ges.* **1909**, *42*, 3427−3431.

(8) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis. *Chem. Rev.* **2013**, *113*, 5322−5363.

(9) (a) Warren, J. J.; Tronic, T. A.; Mayer, J. M. Thermochemistry of Proton-Coupled Electron Transfer Reagents and its Implications. *Chem. Rev.* **2010**, *110*, 6961−7001. (b) Qiu, G.; Knowles, R. R.

Understanding Chemoselectivity in Proton-Coupled Electron Transfer: A Kinetic Study of Amide and Thiol Activation. *J. Am. Chem. Soc.* **2019**, *141*, 16574−16578.
(10) (a) Yan, M.; Kawamata, Y.; Baran, P. S. Synthetic Organic Electrochemical Methods Since 2000: On the Verge of a Renaissance. *Chem. Rev.* **2017**, *117*, 13230−13319. (b) Novaes, L. F. T.; Liu, J.; Shen, Y.; Lu, L.; Meinhardt, J. M.; Lin, S. Electrocatalysis as an enabling technology for organic synthesis. *Chem. Soc. Rev.* **2021**, *50*, 7941−8002. (c) Liu, C.; Liu, J.; Li, W.; Lu, H.; Zhang, Y. *Org. Chem. Front.* **2023**, *10*, 5309−5330. (d) Okumura, Y.; Sato, E.; Mitsudo, K.; Suga, S. Electrochemical synthesis of heterocyclic compounds via carbon−heteroatom bond formation: direct and indirect electrolysis. *Chem. Lett.* **2024**, *53*, upae146.
(11) (a) Zhu, L.; Xiong, P.; Mao, Z.-Y.; Wang, Y.-H.; Yan, X.; Lu, X.; Xu, H.-C. Electrocatalytic Generation of Amidyl Radicals for Olefin Hydroamidation: Use of Solvent Effects to Enable Anilide Oxidation. *Angew. Chem., Int. Ed.* **2016**, *55*, 2226−2229. (b) Gieshoff, T.; Schollmeyer, D.; Waldvogel, S. R. Access to Pyrazolidin-3,5-diones through Anodic N−N Bond Formation. *Angew. Chem., Int. Ed.* **2016**, *55*, 9437−9440. (c) Li, J.; Huang, W.; Chen, J.; He, L.; Cheng, Xu.; Li, G. Electrochemical Aziridination by Alkene Activation Using a Sulfamate as the Nitrogen Source. *Angew. Chem., Int. Ed.* **2018**, *57*, 5695−5698. (d) Kehl, A.; Breising, V. M.; Schollmeyer, D.; Waldvogel, S. R. Electrochemical Synthesis of 5-Aryl-phenanthridin-6-one-by Dehydrogenative N. *C Bond Formation. Chem. Eur. J.* **2018**, *24*, 17230−17233. (e) Wang, F.; Stahl, S. S. Merging Photochemistry with Electrochemistry: Functional-Group Tolerant Electrochemical Amination of C(sp^3)−H Bonds. *Angew. Chem., Int. Ed.* **2019**, *58*, 6385−6390. (f) Xiong, P.; Xu, H.-C. Chemistry with Electrochemically Generated N-Centered Radicals. *Acc. Chem. Res.* **2019**, *52*, 3339−3350. (g) Huang, C.; Li, Z.-Y.; Song, J.; Xu, H.-C. Catalyst- and Reagent-Free Formal Aza-Wacker Cyclizations Enabled by Continuous-Flow Electrochemistry. *Angew. Chem., Int. Ed.* **2021**, *60*, 11237−11241. (h) Zheng, Y.-T.; Song, J.; Xu, H.-C. Electrocatalytic Dehydrogenative Cyclization of 2-Vinylanilides for the Synthesis of Indoles. *J. Org. Chem.* **2021**, *86*, 16001−16007. (i) Shi, Z.; Li, Y.; Li, N.; Wang, W.-Z.; Lu, H.-K.; Yan, H.; Yuan, Y.; Zhu, J.; Ye, K.-Y. Electrochemical Migratory Cyclization of *N*-Acylsulfonamides. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202206058.
(12) Xu, H.-C.; Moeller, K. D. Intramolecular Anodic Olefin Coupling Reactions: The Use of a Nitrogen Trapping Group. *J. Am. Chem. Soc.* **2008**, *130*, 13542−13543.
(13) Hu, X.; Zhang, G.; Bu, F.; Nie, L.; Lei, A. Electrochemical-Oxidation-Induced Site-Selective Intramolecular C(sp^3)−H Amination. *ACS Catal.* **2018**, *8*, 9370−9375.
(14) (a) Costero, A. M.; Rodríguez-Muñiz, G. M.; Gaviña, P.; Gil, S.; Domenech, A. Biphenylthioureas as organocatalysts for electrochemical reductions. *Tetrahedron Lett.* **2007**, *48*, 6992−6995. (b) Gamboa-Valero, N.; Astudillo, P. D.; González-Fuentes, M. A.; Leyva, M. A.; Rosales-Hoz, M. J.; González, F. J. Hydrogen bonding complexes in the quinone-hydroquinone system and the transition to a reversible two-electron transfer mechanism. *Electrochem. Acta* **2016**, *188*, 602−610. (c) Lan, L.; Xu, K.; Zeng, C. The merger of electroreduction and hydrogen bonding activation for a radical Smiles rearrangement. *Chem. Sci.* **2024**, *15*, 13459−13465. (d) Zhao, B; Zeng, D-B; He, X; Li, J-H; Lin, Y; Ye, K-Y Electrochemical Conversions of Sulfenamides into Sulfonimidoyl and Sulfondiimidoyl Fluorides. *JACS Au.* **2025**, *5*, 2359.
(15) (a) Majumdar, K. C.; Mondal, S. Recent Developments in the Synthesis of Fused Sultams. *Chem. Rev.* **2011**, *111*, 7749−7773. (b) Debnath, S.; Mondal, S. Sultams: Recent Syntheses and Applications. *Eur. J. Org. Chem.* **2018**, *2018*, 933−956. (c) Reetu, R.; Gujjarappa, R.; Malakar, C. C. Recent Advances in the Synthesis and Medicinal Evaluation of 1,2-Benzothiazine Analogues. *Asian J. Org. Chem.* **2022**, *11*, No. e202200163.
(16) (a) Herold, S.; Bafaluy, D.; Muñiz, K. Anodic benzylic C(sp^3)−H amination: unified access to pyrrolidines and piperidines. *Green Chem.* **2018**, *20*, 3192−3196. (b) Cao, Y.; Yuan, Y.; Lin, Y.; Jiang, X.; Weng, Y.; Wang, T.; Bu, F.; Zeng, L.; Lei, A. Cobalt catalyzed electrochemical [4 + 2] annulation for the synthesis of sultams. *Green Chem.* **2020**, *22*, 1548−1552. (c) Liu, A.; Guo, T.; Zhang, S.; Yang, H.; Zhang, Q.; Chai, Y.; Zhang, S. Structurally Diverse Synthesis of Five-, Six-, and Seven-Membered Benzosultams through Electrochemical Cyclization. *Org. Lett.* **2021**, *23*, 6326−6331. (d) Choi, I.; Trenerry, M. J.; Lee, K. S.; King, N.; Berry, J. F.; Schomaker, J. M. Divergent C−H Amidations and Imidations by Tuning Electrochemical Reaction Potentials. *ChemSusChem* **2022**, *15*, No. e2022201662. (e) Zhang, Y.; Cai, Z.; Zhao, C.; Zheng, H.; Ackermann, L. Electrosynthesis of bridged or fused sulfonamides through complex radical cascade reactions: divergence in medium-sized ring formation. *Chem. Sci.* **2023**, *14*, 3541−3547. (f) Reddy, C. R.; Shivudu, M.; Rathaur, A. An entry to spiro-fused sultams *via* electrochemical brominative *ipso*-annulation of *N*-aryl alkynyl sulphonamides. *Tetrahedron Lett.* **2024**, *152*, No. 155330.
(17) (a) Ostromisslensky, I. Über eine neue, auf dem Massenwirkungsgesetz fuβende Analysenmethode einiger binären Verbindungen. *Ber. Dtsch. Chem. Ges.* **1911**, *44*, 268−273. (b) Job, P. Formation and Stability of Inorganic Complexes in Solution. *Ann. Chim.* **1928**, *9*, 113−203.
(18) (a) Foster, R.; Fyfe, C. A. Interaction of electron acceptors with bases. Part 15.—Determination of association constants of organic charge-transfer complexes by n.m.r. spectroscopy. *Trans. Faraday Soc.* **1965**, *61*, 1626−1631. (b) Thordarson, P. Determining association constants from titration experiments in supramolecular chemistry. *Chem. Soc. Rev.* **2011**, *40*, 1305−1323.
(19) We also carried out cyclic voltammetry of ferrocene with hydrogen bonding complex **I**. As a result, a catalytic current and disappearance of a reduction wave of ferrocene were observed (see the Supporting Information). The voltammograms indicate that the complex itself would be a chemical species that undergoes electron transfer.
(20) When we performed the electrolysis of Bu_4N^+**1aa**$^-$, **2aa** was obtained in 23% yield along with several unidentified byproducts. While the reason for this result is not yet clear, we assumed that a sulfonamidyl radical was generated at a higher concentration and might have caused undesired intermolecular reactions.
(21) (a) Taniguchi, T.; Zaimoku, H.; Ishibashi, H. A Mild Oxidative Aryl Radical Addition into Alkenes by Aerobic Oxidation of Arylhydrazines. *Chem. - Eur. J.* **2011**, *17*, 4307−4312. (b) Zhang, S.; Li, L.; Wu, P.; Gong, P.; Liu, R.; Xu, K. Substrate-Dependent Electrochemical Dimethoxylation of Olefins. *Adv. Synth. Catal.* **2019**, *361*, 485−489. (c) Chen, Z.; Xue, F.; Liu, T.; Wang, B.; Zhang, Y.; Jin, W.; Xia, Y.; Liu, C. Synthesis of *β*-hydroxysulfides *via* visible-light-driven and EDA complex-promoted hydroxysulfenylation of styrenes with heterocyclic thiols in EtOH under photocatalyst-free conditions. *Green Chem.* **2022**, *24*, 3250−3256. (d) Biswas, P.; Maity, A.; Figgins, M. T.; Powers, D. C. Aziridine Group Transfer via Transient *N*-Aziridinyl Radicals. *J. Am. Chem. Soc.* **2024**, *146*, 30796−30801.

NOTE ADDED AFTER ASAP PUBLICATION

This paper was published ASAP on July 24, 2025, with an error in the Supporting Information. The corrected version was reposted on July 30, 2025.

https://doi.org/10.1021/jacsau.5c00619
JACS Au XXXX, XXX, XXX−XXX