Site-Selective Synthesis of N-Benzyl 2,4,6-Collidinium Salts by Electrooxidative C–H Functionalization

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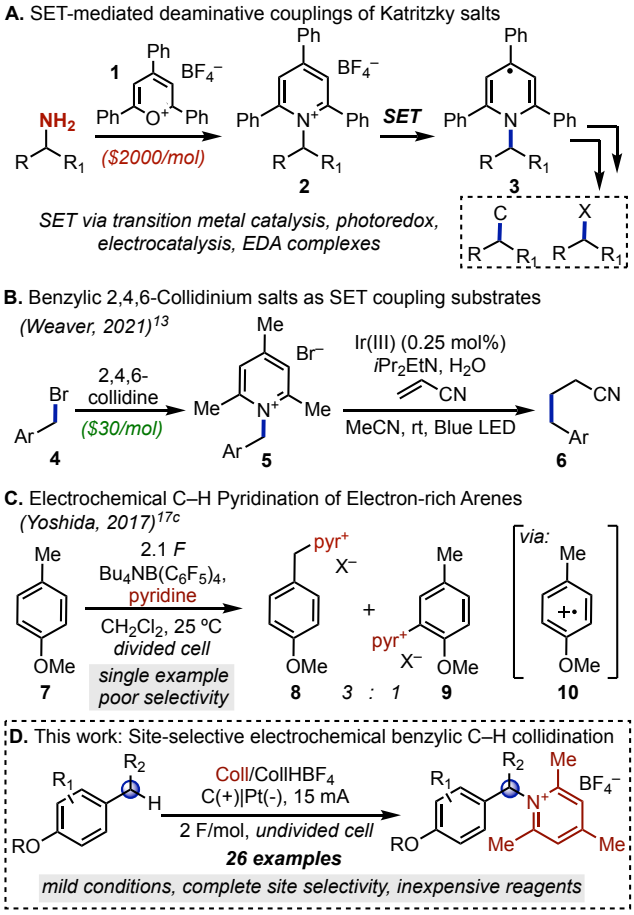
ABSTRACT: 2,4,6-Trisubstituted pyridinium salts have emerged as versatile pseudohalides for SET-mediated radical cross couplings. However, the widely utilized 2,4,6-triphenylpyridinium Katrtizky salt is plagued by poor atom economy and high cost of synthesis. Thus, there is a growing need for developing more practical scaffolds, along with novel strategies for pyridinium salt formation that will support both diverse heterocyclic motifs and substrates. A recent report demonstrated 2,4,6-collidinium salts as more atom-economical and cost-effective electron-acceptors, however their steric hinderance limits their synthesis via traditional nucleophilic substitution. Herein, we report the synthesis of benzylic 2,4,6-collidinium salts via the electrooxidative C–H functionalization of electron-rich arenes. The method proceeds under mild conditions, has broad functional group tolerance, is applicable to the synthesis of both primary and secondary collidinium salts, and uses an inexpensive, recoverable collidine-based electrolyte system. The resulting salts can be isolated via trituration and directly used in subsequent coupling reactions. This method represents the first synthesis of alkyl pyridinium salts via a net C–H functionalization, providing a complementary approach to traditional substitution and condensation reactions of pre-functionalized substrates.

N-alkyl pyridinium salts are scaffolds of diverse biological and synthetic importance.[1] In organic chemistry they serve as oxidants,[2] ionic liquids,[3] and phase transfer catalysts[4] as well as versatile synthetic intermediates en route to functionalized nitrogen heterocycles.[1] The pyridinium core can also be found in marine sponge secondary metabolites,[5] as well as a cellular cofactor in the NAD^+/NADH electron transport chain.[6] Their role as electron acceptors also formed the basis of the recent pioneering work of Watson, who in 2017 first reported deaminative radical couplings via single electron transfer (SET) to a 2,4,6-triphenyl pyridinium (**2**), or "Katritzky salt", using low-valent nickel catalysis (Scheme 1A).[7] Since Watson's seminal reports, this area has seen tremendous growth and now also includes diverse examples employing nickel catalysis,[8] photoredox catalysis,[9] electrocatalysis,[10] and photoexcited electron donor-acceptor complexes,[11] with these strategies allowing formation of diverse carbon-carbon and carbon-heteroatom bonds from amine precursors.[12] However, a persistent limitation in this chemistry is the need for the 2,4,6-triphenylpyridinium salt. Formed via condensation of an amine with 2,4,6-triphenylpyrylium tetrafluoroborate (**1**), this scaffold suffers from poor atom economy and high cost of the oxopyrylium ($2,000/mol), making process and other large-scale applications impractical. Furthermore, this constrains the application of pyridinium-based radical couplings to the presence of a substrate amine.

A recent report from Weaver posited that the utility of pyridinium salts may extend beyond deaminative processes, serving as a useful class of redox active pseudohalides with more normalized redox potentials than their halogen counterparts.[13] The potential for such broad utility further magnifies the need to develop more practical pyridinium scaffolds for SET coupling processes,[14] as well as methods for their incorporation that move beyond amine-pyrylium condensation. In a key advance, the Weaver report utilizes benzylic 2,4,6-collidinium salts (**5**) in iridium-mediated radical Giese reactions, providing the first evidence that this scaffold is competent in SET coupling processes (Scheme 1B). The collidinium scaffold is attractive as it is more atom economical than the Katritzky salt and cost effective as the salts can be generated using inexpensive 2,4,6-collidine ($30/mol). Unfortunately, the steric hinderance of the collidine nucleophile means the required substitution reactions require forcing conditions, are restricted to primary leaving groups and still rely on prefunctionalized halides (**4**), leaving significant opportunity for improvement.[13]

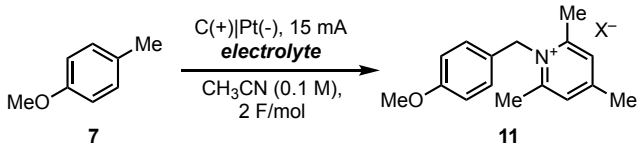
Our laboratory has a growing interest in developing novel oxidative strategies for the conversion of alkenes and C–H bonds directly to *N*-alkyl and *N*-aryl pyridinium salts.[15] Inspired by the Weaver report, we felt that a method enabling the direct synthesis of benzylic pyridinium salts via oxidative C–H amination would be of high value. Such a method could broaden the scope of accessible pyridinium scaffolds as well as obviate the need for prefunctionalized benzylic halides and potentially proceed under more mild conditions. Electrochemical oxidation has been demonstrated as an effective means of achieving benzylic C–H functionalization via single electron transfer,[16,17] and offers the advantages of being mild, green, and precisely tunable.[18] A 2017 report from Yoshida provided a single example of a electrochemical benzylic C–H pyridination of electron-rich arenes, however the reaction proceeded with poor site-selectivity for benzylic versus arene amination and no further studies were reported (Scheme 1C).[17c] It has been shown that site-selectivity in arene radical cation reactions can be modulated based on sterics of the nucleophile,[19] and we hypothesized that use of 2,4,6-substituted pyridines could lead to a benzylic selective methdology. Herein, we report the synthesis of benzylic 2,4,6-collidinium salts via site-selective electrooxidative C–H functionalization of activated arenes (Scheme 1D). The reaction proceeds under mild conditions, has broad scope and features an inexpensive and recyclable collidinium electrolyte system, making it attractive for large scale applications. Furthermore, secondary collidinium salts are accessible in good yields, compounds not amenable to synthesis via nucleophilic substitution.

Scheme 1. *N*-Alkyl 2,4,6-Trisubstituted Pyridinium Salts



Using 4-Me-anisole (**7**) as a model substrate, we began our study by using slightly modified Yoshida's conditions and replacing pyridine with 2,4,6-collidine (Table 1, entry 1). Encouragingly, the use of the more sterically hindered collidine nucleophile did result in complete selectivity for the benzylic position to give collidinium **11** in good yield. Unfortunately, separation of **11** from the tetrabutylammonium electrolyte proved extremely challenging, and using our electrochemical setup,[20] we were only able to achieve constant current up to 3 mA under these conditions. In considering alternative electrolytes, we turned to collidine/collidineH$^+$, which would serve as both electrolyte and source of nucleophile.[21] We also hypothesized that switching to a protic system would allow us to run the reaction in an undivided cell as facile cathodic H_2 production would suppress any competitive reduction of the collidinium product. Use of 0.6 M collidine/collidine•$HClO_4$ at 15 mA constant current gave a 70% yield of **11** (entry 2), which was now readily isolable via simple Et_2O trituration. A switch to the Coll•HBF_4 salt gave an improved 88% yield and also avoided use of potentially explosive perchlorates (entry 3). Notably, the Coll•HBF_4 salt can be readily prepared on multigram scale and isolated as a free-flowing white powder, and the 0.6 M electrolyte solution can be prepared in batches and stored for several months on the benchtop. Lower electrolyte concentrations led to reduction in yields (entries 4, 5) along with formation of 4-anisaldehyde, believed to be from addition of adventitious water or oxygen to the intermediate cation or radical respectively.[22] The higher concentrations of electrolyte also allowed the use of higher current, reducing reaction times, and the excess collidine can be readily recovered and reused. The scalability and robustness of the reaction is demonstrated as a 1 mmol scale reaction using recycled electrolyte under "precaution-free" conditions (no care to exclude air or moisture), gave **11** in a comparable 82% yield (entry 6).

Table 1. Reaction Optimization

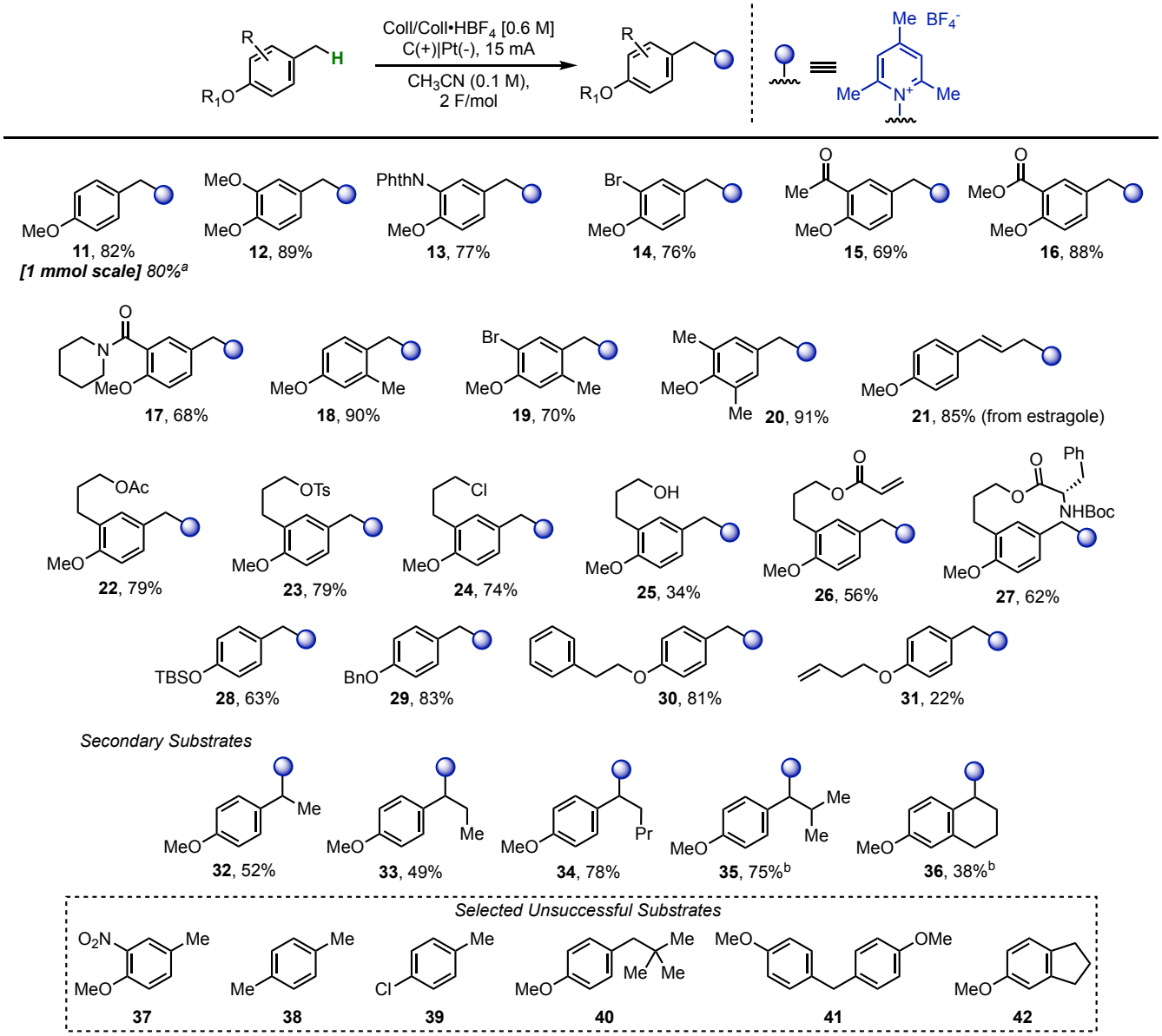


Entry	Conditions/Electrolyte	Yield[a]
1	$TBABF_4$ (0.1 M, CH_2Cl_2), collidine (10 equiv)[b,c]	77%
2	Coll/Coll•$HClO_4$ (0.6M)	70%
3	Coll/Coll•HBF_4 (0.6M)	88% (82%)[d]
4	Coll/Coll•HBF_4 (0.3M)	73%
5	Coll/Coll•HBF_4 (0.1M)	59%
6	Recycled Coll/Coll•HBF_4 (0.6M), precaution-free[e, f]	82% (80%)[d]

[a]Yields via ^{1}H-NMR with CH_2Br_2 internal standard. [b]Modification of Yoshida procedure: $TBABF_4$ used in place of $TBAB(C_6F_5)_3$ [c]C(+)||Pt(-), 3 mA. [d]Isolated yield. [e]Use of non-anhydrous solvent and no inert atmosphere [f]1 mmol scale.

With optimized conditions in hand, the scope of the collidination reaction was examined, beginning with electronic variation about the anisole ring (Table 2). More electron-rich substrates performed well, with 2-methoxy and 2-phthalimide substitution giving collidinium salts **12** and **13** in 89% and 77% yield respectively. The reaction was compatible with an aryl bromide, giving **14** in 76% yield, which possesses complimentary functional handles for subsequent cross coupling. Moving to electron-withdrawing groups, ketone, ester, and amide substitution all gave collidinium salts in high yield (**15**–**17**). Notably the amide was completely selective for collidination of the benzylic C–H bond, with no Shono-type oxidation products detected. A more electron-withdrawing nitro-substitution shut down reactivity (see **37**, inset). Site-selectivity in substrates with multiple benzylic positions was then examined, as these would be challenging substrates for complimentary processes for benzylic functionalization, such as those relying on radical C–H abstraction. The reaction was found to be completely selective for *para*-collidination over both *meta*- (**18**, **19**) and *ortho*-Me (**20**) groups relative to the methoxy substituent. Site- and chemoselectivity were then probed in substrates containing competing sites of reactivity or sensitive functional groups. Use of estragole gave terminal collidinium salt **21** in 85% yield, via isomerization of the putative intermediate allylic cation. Primary –OAc, –OTs, and –Cl groups all gave clean conversion to the benzylic collidinium salts **22**–**24** with no observation of competitive S_N2 displacement. Reactive functional groups including a nucleophilic alcohol (**25**), reducible acrylate (**26**), and an N-Boc-phenylalanine (**27**) containing an N–H bond and an additional benzylic methylene all gave desired salts in moderate to good yields, demonstrating the utility of mild and selective electrochemical oxidation. Finally, while a *para*-oxygen substituent was found to be required (see **38**, **39**, inset), the methyl ether could be varied to include silyl (**28**), benzyl or homobenzyl (**29**, **30**), or homoallyl ethers (**31**).

Table 2. Benzylic C–H 2,4,6-Collidination Scope[a]



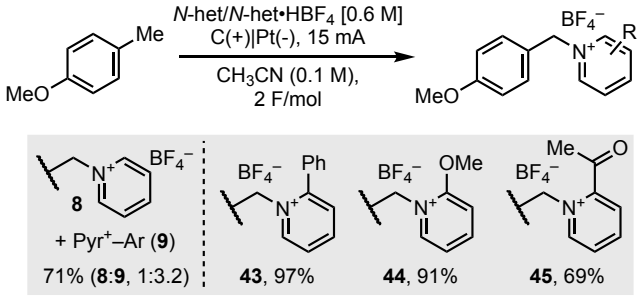
[a]All reactions run on 0.3 mmol scale using an IKA ElectraSyn 2.0. Products isolated via trituration with Et_2O. [b]Yield via ^{1}H-NMR with CH_2Br_2 internal standard due to contamination with inseparable protonated collidine.

We then examined the synthesis of secondary collidinium salts, products that would be exceptionally challenging to access via traditional nucleophilic substitution. Beginning with extended linear alkyl chains, we were pleased to find the reaction still gave moderate to good yields of salts **32**–**34**. Perhaps surprisingly, the sterically-hindered isobutyl substrate gave high yields of collidinium **35**, which we hypothesize is due to the sterically hindered methine β C-H bond inhibiting elimination pathways of either cationic intermediates or product. In support of this hypothesis, tetralin-derived collidinium **36** was obtained in decreased yield, along with styrenyl byproducts, as restricted rotational freedom allowed for more facile elimination. The limits of the secondary scope included a more hindered *t*-butyl group (**40**) and the diarylmethane (**41**), both of which returned exclusively starting material and indane **42** which provided product that rapidly decomposed during isolation.

Having established a broad arene scope, we revisited those examples that were unsuccessful on the basis of arene electronics (**37**–**39**, inset). The requirement of a *para*-oxygen substituent is consistent with prior reports of oxidative arene radical cation functionalization.[17a,23] A study from Waldvogel[24] indicated that under our conditions, the presence of an *N*-heterocycle may be suppressing arene oxidation in less activated substrates. CV measurements on **7**, **37**, **38**, and **39** in 0.1 M $TBABF_4$ compared with 0.1 M Coll•HBF_4 with 15mM collidine found that while the oxidation peak of **7** was still present, those of **37**–**39**, with oxidation onset > ~2.0 V, were completely suppressed in the presence of collidine (see SI for details). While we currently can not explain this effect, it does provide a simple tool for preliminary assessment of potential substrates.

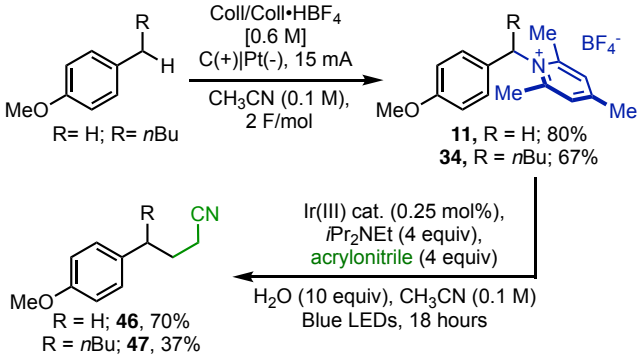
As the high level of site-selectivity was attributed to steric modulation of the pyridine nucleophile, we then examined the use of differentially substituted pyridines, in the interest of establishing a steric limit for achieiving high levels of benzylic selectivity. Under our conditions, simple pyridine gave 71% yield of a 1:3.2 mixture of benzylic to arene pyridination (**8**:**9**, Scheme 2); interestingly, this ratio is the inverse of that observed in Yoshida's prior report (*vide supra*).[17c] However, it was found that a single substituent at C2 of the pyridine ring was sufficient to completely suppress arene amination, and 2-phenyl, 2-methoxy, and 2-acyl-pyridine were all found to give exclusively the benzylic pyridinium salts (**43**–**45**) in excellent to high yields. This methodology could therefore also be applied to the direct electrochemical synthesis of oxidatively-masked 2-substituted piperidines[25] via subsequent derivatization of the pyridinium salts.[1]

Scheme 2. Steric Effects on Benzylic Site-Selectivity



a. In each case the electrolyte solution was generated using the corresponding *N*-heterocycle/*N*-heterocycle•HBF_4 salt. b. Reactions run on 0.3 mmol scale.

Scheme 3. 2,4,6-Collidinium Salts in Iridium-Catalyzed Giese Reaction



a. Electrochemical collidination run on 1 mmol scale.

Finally, we wished to demonstrate that the electrochemically generated collidinium salts were effective in subsequent coupling reactions. To this end, both primary (**11**, R= H) and secondary (**34**, R= *n*Bu) collidinium salts were synthesized via the standard method and, with no purification beyond simple trituration, subjected to conditions of Weaver for iridium-catalyzed Giese reaction with acrylonitrile.[13] 4-Me-anisole derived salt **11** gave **47** in 70% yield, on par with that reported by Weaver for the corresponding chloride salt. While no secondary collidinium salts were included in the prior scope,[26] 4-pentyl-anisole salt **34** successfully gave **48** in modest 37% yield without optimization.

In conclusion, we report the synthesis of benzylic 2,4,6-collidinium salts via the electrooxidative C–H functionalization of electron-rich arenes. The reaction proceeds with complete site-selectivity, proceeds under mild conditions, uses a cheap and recoverable 2,4,6-collidine electrolyte system, and does not require chromatography. The broad scope includes both primary and secondary collidinium salts, the latter being effectively inaccessible via traditional nucleophilic substitution. The resulting 2,4,6-collidinium salts represent an emerging scaffold for SET-mediated pyridinium cross couplings, offering improved atom economy, cost, and versatility in synthesis over the established Katrizky salts This method represents the first synthesis of alkyl pyridinium salts via a net C–H functionalization, providing a complementary approach to traditional substitution and condensation reactions of pre-functionalized substrates. Future studies aim to extend this platform to additional heterocycles and alkyl positions to provide a general oxidative strategy to these valuable motifs.

ASSOCIATED CONTENT

Experimental procedures, full characterization data for all new compounds, NMR spectra, and cyclic voltammetry. The Supporting Information material is available free of charge via the Internet at http://pubs.acs.org.

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Funding Sources

The authors are grateful to the National Science Foundation (NSF CAREER 152244) and National Institutes of Health (NIH R01 GM123098) for financial support of this work.

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

The authors thank Dr. Charles DeBrosse (Temple University) for NMR spectroscopic assistance and Dr. Charles W. Ross III, Director: Automated Synthesis and Characterization at University of Pennsylvania Chemistry for providing high-resolution mass spectral data.

REFERENCES

(1) Sowmiah, S.; Esperança, J. M. S. S.; Rebelo, L. P. N.; Afonso, C. A. M. Pyridinium Salts: From Synthesis to Reactivity and Applications. *Org. Chem. Front.* **2018**, *5* (3), 453–493.

(2) Umemoto, T.; Tomita, K. N-Fluoropyridinium Triflate and Its Analogs, the First Stable 1:1 Salts of Pyridine Nucleus and Halogen Atom. *Tetrahedron Lett.* **1986**, *27* (28), 3271–3274.

(3) Welton, T. Room-Temperature Ionic Liquids. Solvents for Synthesis and Catalysis. *Chem. Rev.* **1999**, *99* (8), 2071–2083.

(4) Brunelle, D. J.; Singleton, D. A. N-Alkyl-4-(N′,N′-Dialkylamino)Pyridinium Salts: Thermally Stable Phase Transfer Catalysts for Nucleophilic Aromatic Displacement. *Tetrahedron Lett.* **1984**, *25* (32), 3383–3386.

(5) Sepčić, K. Bioactive Alkylpyridinium Compounds From Marine Sponges. *Journal of Toxicology: Toxin Reviews* **2000**, *19* (2), 139–160.

(6) Yang, Y.; Sauve, A. A. NAD+ Metabolism: Bioenergetics, Signaling and Manipulation for Therapy. *Biochim. Biophys. Acta - Proteins Proteomics* **2016**, *1864* (12), 1787–1800.

(7) Basch, C. H.; Liao, J.; Xu, J.; Piane, J. J.; Watson, M. P. Harnessing Alkyl Amines as Electrophiles for Nickel-Catalyzed Cross Couplings via C–N Bond Activation. *J. Am. Chem. Soc.* **2017**, *139* (15), 5313–5316.

(8) (a) Liao, J.; Guan, W.; Boscoe, B. P.; Tucker, J. W.; Tomlin, J. W.; Garnsey, M. R.; Watson, M. P. Transforming Benzylic Amines into Diarylmethanes: Cross-Coupling of Benzylic Pyridinium Salts via C–N Bond Activation. *Org. Lett.* **2018**, *20*, 3030–3033. (b) Guan, W.; Liao, J.; Watson, M. P. Vinylation of Benzylic Amines via C–N Bond Functionalization of Benzylic Pyridinium Salts. *Synthesis*, **2018**, *50*, 3231–3237. (c) Yue, H.; Zhu, C.; Shen, L.; Geng, Q.; Hock, K. J.; Yuan, T.; Cavallo, L.; Rueping, M. Nickel-Catalyzed C–N Bond Activation: Activated Primary Amines as Alkylating Reagents in Reductive Cross-Coupling. *Chem. Sci.* **2019**, *10* (16), 4430–4435. (d) Plunkett, S.; Basch, C. H.; Santana, S. O.; Watson, M. P. Harnessing Alkylpyridinium Salts as Electrophiles in Deaminative Alkyl-Alkyl Cross-Couplings. *J. Am. Chem. Soc.* **2019**, *141* (6), 2257–2262. (e) Liao, J.; Basch, C. H.; Hoerrner, M. E.; Talley, M. R.; Boscoe, B. P.; Tucker, J. W.; Garnsey, M. R.; Watson, M. P. Deaminative Reductive Cross-Electrophile Couplings of Alkylpyridinium Salts and Aryl Bromides. *Org. Lett.* **2019**, *21* (8), 2941–2946. (f) Hoerrner, M. E.; Baker, K. M.; Basch, C. H.; Bampo, E. M.; Watson, M. P. Deaminative Arylation of Amino Acid-Derived Pyridinium Salts. *Org. Lett.* **2019**, *21* (18), 7356–736. (g) Baker, K. M.; Lucas Baca, D.; Plunkett, S.; Daneker, M. E.; Watson, M. P. Engaging Alkenes and Alkynes in Deaminative Alkyl-Alkyl and Alkyl-Vinyl Cross-Couplings of Alkylpyridinium Salts. *Org. Lett.* **2019**, *21* (23), 9738–9741. (h) Martin-Montero, R.; Yatham, V. R.; Yin, H.; Davies, J.; Martin, R. Ni-Catalyzed Reductive Deaminative Arylation at Sp^3 Carbon Centers. *Org. Lett.* **2019**, *21* (8), 2947–2951. (i) Sun, S. Z.; Romano, C.; Martin, R. Site-Selective Catalytic Deaminative Alkylation of Unactivated Olefins. *J. Am. Chem. Soc.* **2019**, *141* (41), 16197–16201. (j) Wang, J.; Hoerrner, M. E.; Watson, M. P.; Weix, D. J. Nickel-Catalyzed Synthesis of Dialkyl Ketones from the Coupling of N-Alkyl Pyridinium Salts with Activated Carboxylic Acids. *Angew. Chemie Int. Ed.* **2020**, *59* (32), 13484–13489. (k) Bercher, O. P.; Plunkett, S.; Mortimer, T. E.; Watson, M. P. Deaminative Reductive Methylation of Alkylpyridinium Salts. *Org. Lett.* **2021**, *23* (18), 7059–7063. (l) Xu, J.; Twitty, J. C.; Watson, M. P. Nickel-Catalyzed Deaminative Cyanation: Nitriles and One-Carbon Homologation from Alkyl Amines. *Org. Lett.* **2021**, *23* (16), 6242–6245.

(9) (a) Klauck, F. J. R.; James, M. J.; Glorius, F. Deaminative Strategy for the Visible-Light-Mediated Generation of Alkyl Radicals. *Angew. Chemie Int. Ed.* **2017**, *56* (40), 12336–12339. (b) Ociepa, M.; Turkowska, J.; Gryko, D. Redox-Activated Amines in C(Sp3)-C(Sp) and C(Sp3)-C(Sp2) Bond Formation Enabled by Metal-Free Photoredox Catalysis. *ACS Catal.* **2018**, *8* (12), 11362–11367. (c) Klauck, F. J. R.; Yoon, H.; James, M. J.; Lautens, M.; Glorius, F. Visible-Light-Mediated Deaminative Three-Component Dicarbofunctionalization of Styrenes with Benzylic Radicals. *ACS Catal.* **2019**, *9* (1), 236–241. (d) Yi, J.; Badir, S. O.; Kammer, L. M.; Ribagorda, M.; Molander, G. A. Deaminative Reductive Arylation Enabled by Nickel/Photoredox Dual Catalysis. *Org. Lett.* **2019**, *21*, 3346–3351.

(10) Liu, Y.; Tao, X.; Mao, Y.; Yuan, X.; Qiu, J.; Kong, L.; Ni, S.; Guo, K.; Wang, Y.; Pan, Y. Electrochemical C–N Bond Activation for Deaminative Reductive Coupling of Katritzky Salts. *Nat. Commun. 2021 121* **2021**, *12* (1), 1–7.

(11) (a) James, M. J.; Strieth-Kalthoff, F.; Sandfort, F.; Klauck, F. J. R.; Wagener, F.; Glorius, F. Visible-Light-Mediated Charge Transfer Enables C−C Bond Formation with Traceless Acceptor Groups. *Chem. – A Eur. J.* **2019**, *25* (35), 8240–8244. (b) Wu, J.; Grant, P. S.; Li, X.; Noble, A.; Aggarwal, V. K. Catalyst-Free Deaminative Functionalizations of Primary Amines by Photoinduced Single-Electron Transfer. *Angew. Chemie Int. Ed.* **2019**, *58* (17), 5697–5701. (c) Wu, J.; He, L.; Noble, A.; Aggarwal, V. K. Photoinduced Deaminative Borylation of Alkylamines. *J. Am. Chem. Soc.* **2018**, *140* (34), 10700–10704.

(12) For recent reviews see: (a) Pang, Y.; Moser, D.; Cornella, J. Pyrylium Salts: Selective Reagents for the Activation of Primary Amino Groups in Organic Synthesis. *Synthesis (Stuttg).* **2019**, *52* (04), 489–503. (b) Kong, D.; Moon, P. J.; Lundgren, R. J. Radical Coupling from Alkyl Amines. *Nat. Catal. 2019 26* **2019**, *2* (6), 473–476. (c) Li, Y. N.; Xiao, F.; Guo, Y.; Zeng, Y. F. Recent Developments in Deaminative Functionalization of Alkyl Amines. *European J. Org. Chem.* **2021**, *2021* (8), 1215–1228.

(13) Rathnayake, M. D.; Weaver, J. D. Coupling Photocatalysis and Substitution Chemistry to Expand and Normalize Redox-Active Halides. *Org. Lett.* **2021**, *23* (6), 2036–2041.

(14) Tcyrulnikov, S.; Cai, Q.; Cameron Twitty, J.; Xu, J.; Atifi, A.; Bercher, O. P.; Yap, G. P. A.; Rosenthal, J.; Watson, M. P.; Kozlowski, M. C. Dissection of Alkylpyridinium Structures to Understand Deamination Reactions. *ACS Catal.* **2021**, *11*, 8456–8466.

(15) Tierno, A. F.; Walters, J. C.; Vazquez-Lopez, A.; Xiao, X.; Wengryniuk, S. E. Heterocyclic Group Transfer Reactions with I(III) N-HVI Reagents: Access to N-Alkyl(Heteroaryl)Onium Salts via Olefin Aminolactonization. *Chem. Sci.* **2021**, *12* (18), 6385–6392.

(16) For a recent review see: Oliva, M.; Coppola, G. A.; Van der Eycken, E. V.; Sharma, U. K. Photochemical and Electrochemical Strategies towards Benzylic C−H Functionalization: A Recent Update. *Adv. Synth. Catal.* **2021**, *363* (7), 1810–1834.

(17) (a) Morofuji, T.; Shimizu, A.; Yoshida, J. I. Direct C-N Coupling of Imidazoles with Aromatic and Benzylic Compounds via Electrooxidative C-H Functionalization. *J. Am. Chem. Soc.* **2014**, *136* (12), 4496–4499. (b) Hayashi, R.; Shimizu, A.; Yoshida, J. The Stabilized Cation Pool Method: Metal- and Oxidant-Free Benzylic C–H/Aromatic C–H Cross-Coupling. *J. Am. Chem. Soc.* **2016**, *138* (27), 8400–8403. (c) Hayashi, R.; Shimizu, A.; Song, Y.; Ashikari, Y.; Nokami, T.; Yoshida, J. Metal-Free Benzylic C−H Amination via Electrochemically Generated Benzylaminosulfonium Ions. *Chem. – A Eur. J.* **2017**, *23* (1), 61–64.

(18) For recent reviews see: (a) 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. (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* (14), 7941–8002.

(19) Schlesener, C. J.; Kochi, J. K. Stoichiometry and Kinetics of P-Methoxytolueneoxidation by Electron Transfer. Mechanistic Dichotomy between Side Chain and Nuclear Substitution. *J. Org. Chem.* **1984**, *49* (17), 3142–3150.

(20) Reaction run using IKA ElectraSyn 2.0 ProDivide.

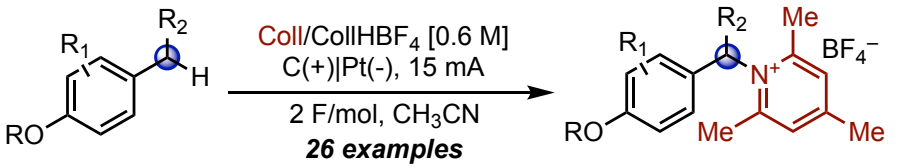
(21) Rafiee, M.; Wang, F.; Hruszkewycz, D. P.; Stahl, S. S. N-Hydroxyphthalimide-Mediated Electrochemical Iodination of Methylarenes and Comparison to Electron-Transfer-Initiated C-H Functionalization. *J. Am. Chem. Soc.* **2018**, *140* (1), 22–25.

(22) Li, X.; Bai, F.; Liu, C.; Ma, X.; Gu, C.; Dai, B. Selective Electrochemical Oxygenation of Alkylarenes to Carbonyls. *Org. Lett.* **2021**, *23* (19), 7445–7449.

(23) For representative examples of (a) Morofuji, T.; Shimizu, A.; Yoshida, J. I. Electrochemical C-H Amination: Synthesis of Aromatic Primary Amines via N -Arylpyridinium Ions. *J. Am. Chem. Soc.* **2013**, *135* (13), 5000–5003. (b) Wang, H.; Zhang, D.; Bolm, C. Sulfoximidations of Benzylic C−H Bonds by Photocatalysis. *Angew. Chemie Int. Ed.* **2018**, *57* (20), 5863–5866. (c) Joolee, B.; Deglopper, S.; Yoon, T. P.; Lee,] B J; Deglopper, K. S.; Yoon, P. R. T. P. Site-Selective Alkoxylation of Benzylic C−H Bonds by Photoredox Catalysis. *Angew. Chemie Int. Ed.* **2020**, *59* (1), 197–202. (d) Hou, Z. W.; Li, L.; Wang, L. Organocatalytic Electrochemical Amination of Benzylic C–H Bonds. *Org. Chem. Front.* **2021**, *8* (17), 4700–4705. (e) Ruan, Z.; Huang, Z.; Xu, Z.; Zeng, S.; Feng, P.; Sun, P. H. Late-Stage Azolation of Benzylic C–H Bonds Enabled by Electrooxidation.

Sci. China Chem. 2021 645 **2021**, *64* (5), 800–807.
(24) Herold, S.; Möhle, S.; Zirbes, M.; Richter, F.; Nefzger, H.; Waldvogel, S. R. Electrochemical Amination of Less-Activated Alkylated Arenes Using Boron-Doped Diamond Anodes. *European J. Org. Chem.* **2016**, *2016* (7), 1274–1278.
(25) Yoshida, J. I.; Shimizu, A.; Hayashi, R. Electrogenerated Cationic Reactive Intermediates: The Pool Method and Further Advances. *Chem. Rev.* **2018**, *118* (9), 4702–4730.
(26) For secondary substrates in the previously reported Ir(III) Giese reaction, 4-methylpyridinium salts were used in place of 2,4,6-collidinium salts (ref. 13).

Authors are required to submit a graphic entry for the Table of Contents (TOC) that, in conjunction with the manuscript title, should give the reader a representative idea of one of the following: A key structure, reaction, equation, concept, or theorem, etc., that is discussed in the manuscript. Consult the journal's Instructions for Authors for TOC graphic specifications.



– mild conditions –complete site selectivity –inexpensive reagents –primary and secondary collidinium salts