A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition

GDCh

Chemie

www.angewandte.org

Accepted Article

Title: Pyridyl Radical Cation for C–H Amination of Arenes

Authors: Erick Moran Carreira, Simon Rössler, Benson Jelier, Pascal Tripet, Andrej Shemet, Gunnar Jeschke, and Antonio Togni

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.201810261
Angew. Chem. 10.1002/ange.201810261

Link to VoR: http://dx.doi.org/10.1002/anie.201810261
http://dx.doi.org/10.1002/ange.201810261

WILEY-VCH

10.1002/anie.201810261

WILEY-VCH

Pyridyl Radical Cation for C–H Amination of Arenes

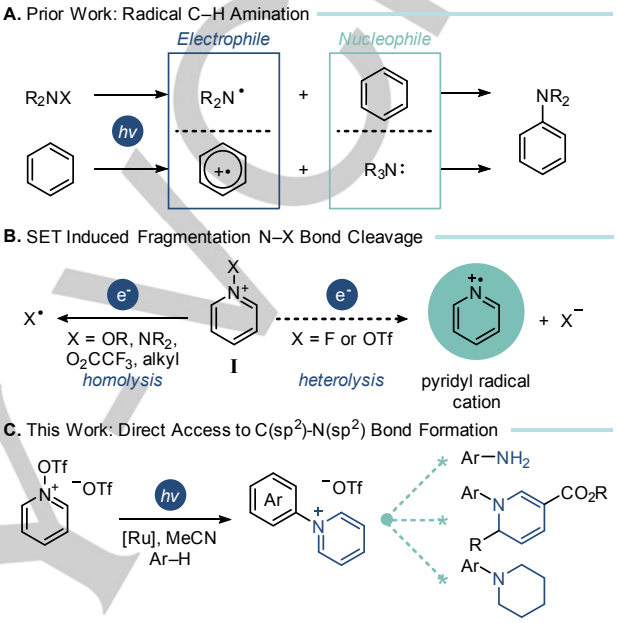
Simon L. Rössler,[+] Benson J. Jelier,[+] Pascal F. Tripet, Andrej Shemet, Gunnar Jeschke, Antonio Togni,* and Erick M. Carreira*

Abstract: Electron-transfer photocatalysis provides access to the elusive and unprecedented *N*-pyridyl radical cation from selected *N*-substituted pyridinium reagents. The resulting C(sp^2)–H functionalization of hetero(arenes) furnishes versatile intermediates for the development of valuable aminated aryl scaffolds. Mechanistic studies that include the first spectroscopic evidence of a spin-trapped *N*-pyridyl radical adduct implicate SET-triggered, pseudo-mesolytic cleavage of the N–X pyridinium reagents triggered by visible light.

Nitrogen containing motifs are among the most eminent structural components in discovery programs.[1] Radical mediated C–H functionalization of (hetero)arenes provides direct methods for elaborating (hetero)aryl frameworks without requiring prior manipulation of the structural core.[2] In particular, nitrogen-centered radicals have long captured the interest of the synthetic community for late-stage C–H amination of a wide range of substrates.[3] However, available methods are typically limited by harsh conditions,[4] the requirements for multiple equivalents of a valuable arene substrate,[5] or only provide anilines and their protected derivatives.[6] Herein, we describe visible light-mediated generation of pyridinium radicals for direct C–H pyridination of arenes and hetarenes. The method affords *N*-aryl pyridinium adducts, enabling divergent access to anilines, dihydropyridines, and substituted piperidines.

Photoredox catalysis has led to powerful strategies for radical functionalization chemistry and serves as an attractive approach to forge new disconnections including those applicable to the amination of arenes. In one approach commonly employed (Scheme 1A), electrophilic imidyl,[7] amidyl,[8] and ammonium radicals[9] aminate sufficiently electron-rich arenes. As an alternative, nucleophilic amines have been reported to trap aryl radical cations generated by electrochemical or photoredox processes.[10]

N-functionalized pyridinium reagents (**I**) have been explored as convenient precursors to radicals (X$^{\bullet}$), following single electron transfer (SET) reduction and subsequent homolysis (Scheme 1B).[11] Pioneering work carried out by the Kodak company focused on *N*-alkoxypyridinium salts for photoinduced polymerizations.[12] Recent advances in photoredox processes have enabled the facile reduction of diverse *N*-functionalized pyridinium salts to yield a wide array of radicals. Oxygen-, nitrogen, and carbon-based radicals generated from such pyridinium compounds have been leveraged for direct perfluoroalkylation,[13] trifluoromethoxylation,[14] amination,[5d] and alkylation,[15] of arenes and hetarenes.



Scheme 1. Visible light-mediated generation of a pyridiyl radical cation for direct C–H amination of arenes and hetarenes. Tf = trifluoromethylsulfonyl.

We have been interested in exploring an alternative fragmentation pathway for pyridiniums, specifically, N–X cleavage leading to an *N*-centered pyridyl radical cation (Scheme 1B). In this respect the selection of X might influence the fragmentation if the ensuing X anion is energetically favored over the corresponding radical.[14] In the presence of suitable arenes, these reactive intermediates could undergo C–H amination. Ritter and co-workers have utilized Selectfluor® to generate nitrogen-centered radicals for the introduction of N-(chloromethyl)triethylenediamine) (TEDA) radical into arenes.[6] Likewise, we reasoned that *N*-fluoropyridinium reagents when triggered by single electron reduction could afford *N*-centered pyridyl radical cation with concomitant expulsion of energetically favored fluoride anion.[16] Similarly, *N*-sulfonyloxypyridiniums could provide an alternative source of the pyridyl radical cation (Scheme 1). Advantages to the latter include convenient synthesis from inexpensive precursors (pyridine-*N*-oxide and triflic anhydride) and opportunities for structural and electronic variation of the pyridinium fragment.[17]

The C–H amination of arenes with pyridyl radical cations would enable direct access to a versatile class of *N*-arylpyridinium products. First disclosed over a century ago by Zincke,[18] pyridiniums have been exploited in a wide range of synthetic transformations.[19] Contemporary efforts have showcased the ability of pyridinium substrates to undergo Ni-catalyzed coupling reactions, deaminative borylation, and

[*] S. L. Rössler, A. Shemet, Prof. Dr. E. M. Carreira
Laboratory of Organic Chemistry
E-mail: erickm.carreira@org.chem.ethz.ch
Dr. B. J. Jelier, P. F. Tripet, Prof. Dr. A. Togni,
Laboratory of Inorganic Chemistry
E-mail: antonio.togni@inorg.chem.ethz.ch
Prof. Dr. G. Jeschke
Laboratory of Physical Chemistry
ETH Zürich, Vladimir-Prelog-Weg, 8093 Zürich, Switzerland

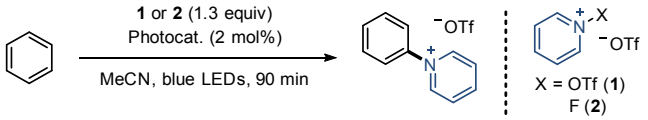
[+] These authors contributed equally to this work.

Supporting information for this article is given via a link at the end of the document.

10.1002/anie.201810261

heterocycle functionalization as well as their use in alkaloid synthesis.[20] An *N*-centered pyridyl radical cation could provide straightforward access to such products.[21]

Table 1. Exploration of Reaction Conditions.[a]



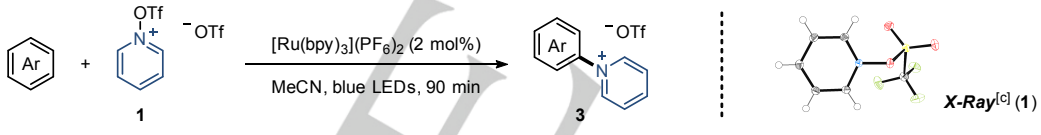
entry	reagent (equiv)	equiv PhH	Photocat.[b]	yield (%)[c]
1	**1** (1.3 equiv)	1	[Ru]	64
2	**1** (1.0 equiv)	3	[Ru]	86
3	**1** (1.0 equiv)	10	[Ru	94
4	**2** (1.3 equiv)	1	[Ir]	11
5[d]	**2** (1.3 equiv)	1	[Ir]	19
6[d]	**2** (1.0 equiv)	3	[Ir]	20
7[d]	**2** (1.0 equiv)	10	[Ir]	30
8[d]	**2** (1.0 equiv)	10	[Ru]	22
9	**2** (1.3 equiv)	1	[Ru]	57
10	no catalyst; or no light; or 80 °C and no light			0

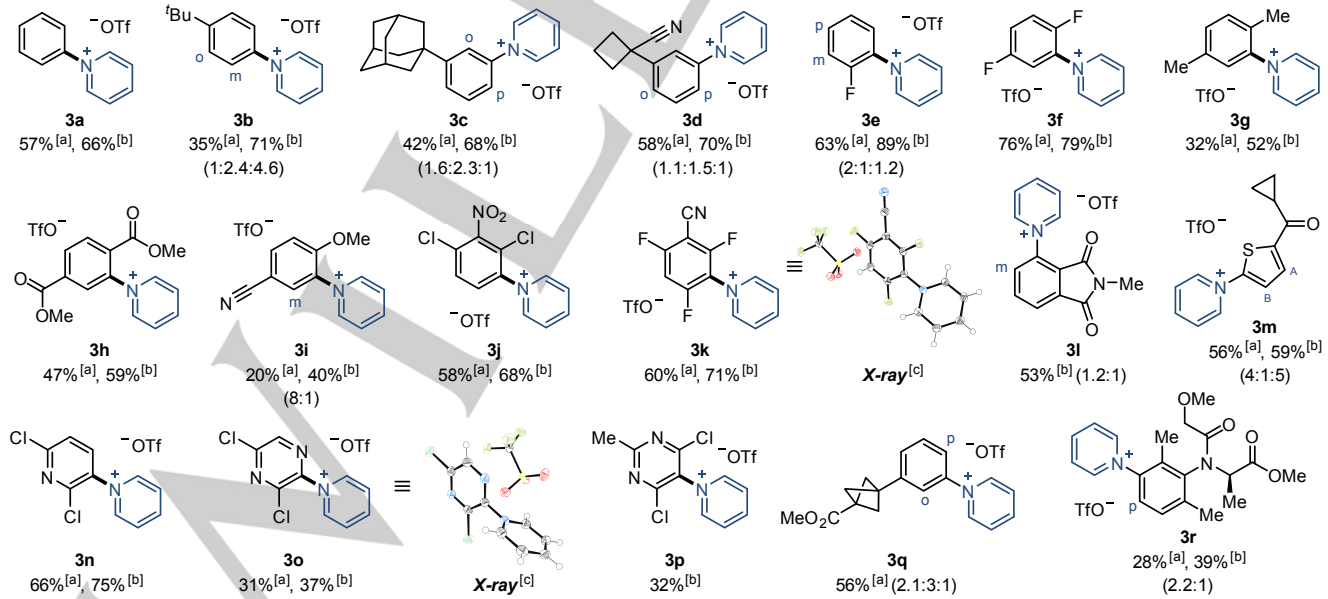
[a] Reactions were conducted on 0.2 mmol scale. [b] [Ru] = $[Ru(bpy)_3](PF_6)_2$; [Ir] = $[Ir(dtbbpy)(ppy)_2]PF_6$ (2 mol%) was employed. [c] Determined by ^1H NMR analysis of the unpurified reaction mixture. [d] Reaction run for 20 h. bpy = 2,2'-bipyridine, dtbbpy = 2,2'-di-*t*-butyl-2,2'-dipyridine, ppy = 2-phenylpyridine

Our investigations commenced by evaluating the reactivity of pyridinium salts **1** and **2** with benzene in the presence of photocatalyst under irradiation of the reaction mixture with blue LEDs (Table 1). Detailed experimentation allowed the identification of an optimal reaction system consisting of $[Ru(bpy)_3](PF_6)_2$ (2 mol%) in anhydrous acetonitrile in combination with arene as the limiting reactant and a slight excess of triflyloxypyridinium **1** (entry 1). For comparative purposes, a threefold excess of arene with **1** as the limiting reactant was also employed (entry 2). The *N*-fluoropyridinium triflate **2** effects the amination reaction in 11% yield with arene as limiting reactant (entry 4); marginally improved yields were observed (19-30%) only with excess of arene (entry 5-7), significantly more expensive Ir-based photocatalyst (entry 8), and extended reaction times. Control experiments confirmed that both light and catalyst are crucial for amination; in the absence of either no product formation is observed (entry 10).

Having established optimal reaction conditions, we explored the scope of pyridination. A salient feature of this transformation is that the arene substrate is employed as limiting reactant, however, for comparative purposes to the state of the art we include yields of reactions conducted with 3 equivalents of arenes. The parent *N*-phenylpyridinium salt **3a** was isolated in good yields under both conditions. Sterically encumbered alkyl groups were observed to exert little influence on the regioselectivity (**3b-d**). Particularly noteworthy is the success of this transformation with electron-poor arenes, thus providing a complementary amination approach to current methods, which are mostly limited to sufficiently electron-rich arenes. For example, electron deficient PET monomer undergoes pyridination to afford **3h**.

Table 2. Scope of the C–H pyridination.



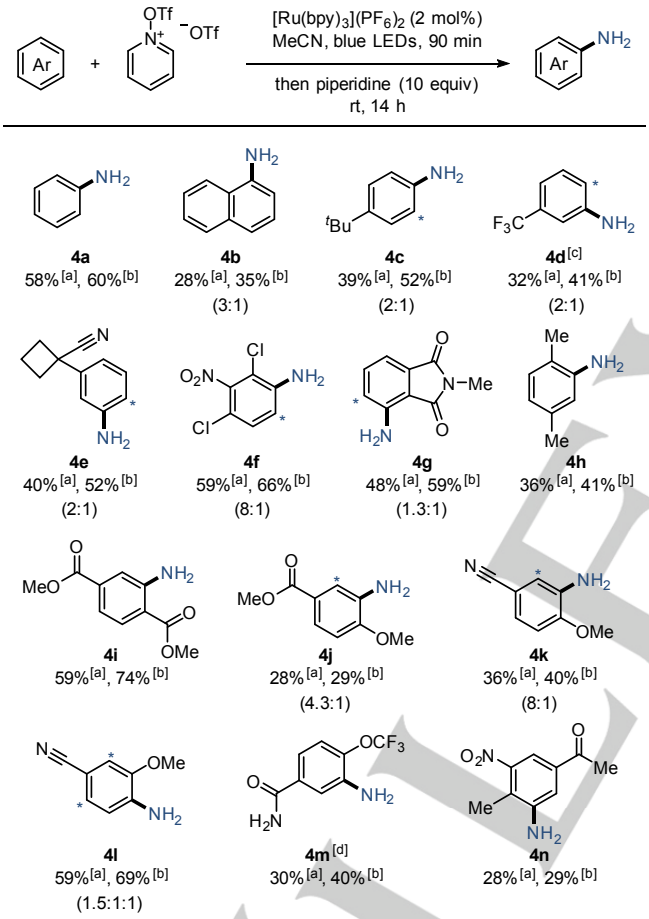


[a] Performed with arene (1.0 equiv), reagent (1.3 equiv), $[Ru(bpy)_3](PF_6)_2$ (2 mol%) in anhydrous MeCN (0.2 M), yield after isolation by column chromatography, regioisomeric ratio after isolation given in brackets as (ortho/meta/para). [b] Arene (3.0 equiv), reagent (1.0 equiv). [c] Thermal ellipsoids are shown at the 50% probability level. Counterions in **1** have been omitted for clarity. CCDC codes: 1865356 (**1**), 1865357 (**3a**), 1865358 (**3h**), 1865359 (**3k**), 1865360 (**3o**).

10.1002/anie.201810261

Electron-rich substrates such as xylene are also suitable, furnishing product **3g** in diminished yield presumably due to competing radical-mediated homodimerization of xylene. Functional groups such as nitriles, ethers, nitro, and esters were tolerated, furnishing the corresponding products (**3i**, **3j**, **3k**, **3l**). Hetarenes also underwent amination to yield pyridinylated pyridine **3n** and pyrazine **3o**. However, pyrimidine **3p** could only be obtained in low yields since isolation was hampered by hydrolysis of one of the chlorides. The pyridination of arylated bicyclopentane proceeded smoothly to **3q**, providing a point of diversification for the recently popularized bicyclopentane building blocks.[22] Additionally, pyridination of Metalaxyl furnished derivative **3r** of the systemic fungicide.

Table 3. Scope of the C–H pyridination-aminolysis sequence.

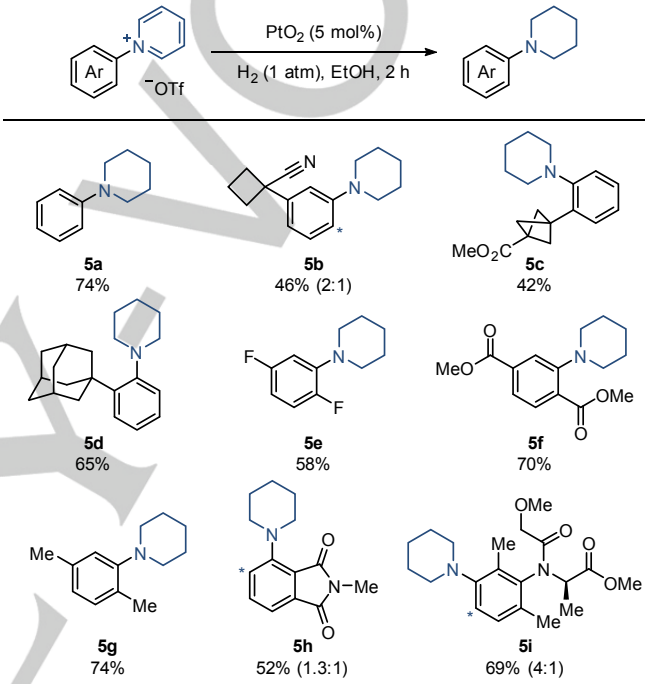


[a] Performed with arene (1.0 equiv), reagent (1.3 equiv), $[Ru(bpy)_3](PF_6)_2$ (2 mol%), piperidine (10 equiv) in anhydrous MeCN (0.2 M), yield after isolation by column chromatography, regioisomeric ratio after isolation given in brackets, minor regioisomer denoted with an asterisk. [b] arene (3.0 equiv), reagent (1.0 equiv). [c] Isolated as its HCl salt due to volatility. [d] Performed with TfOH (1 equiv with respect to arene).

We next examined the *in situ* conversion of pyridinium intermediates to anilines (Table 3). Quenching the pyridination reaction with piperidine initiates high-yielding Zincke aminolysis under ambient conditions over the course of 14 hours, enabling the direct synthesis of anilines. It is important to note that anilines **4b**, **4j**, **4l-n** in Table 3 represent an expansion of the substrate scope for the pyridinylation beyond that shown in Table 2. For the production of amide **4m**, optimal conditions necessitated the addition of acid to the pyridination reaction.

Adams demonstrated almost a century ago that pyridines could be subjected to reduction, following their activation by conversion to the corresponding pyridinium salts.[23] Accordingly, we found that *N*-arylpyridinium products of this study cleanly underwent hydrogenation in the presence of Adams' catalyst (PtO_2), furnishing a variety of *N*-arylated piperidines at room temperature within 2 hours (Table 4).

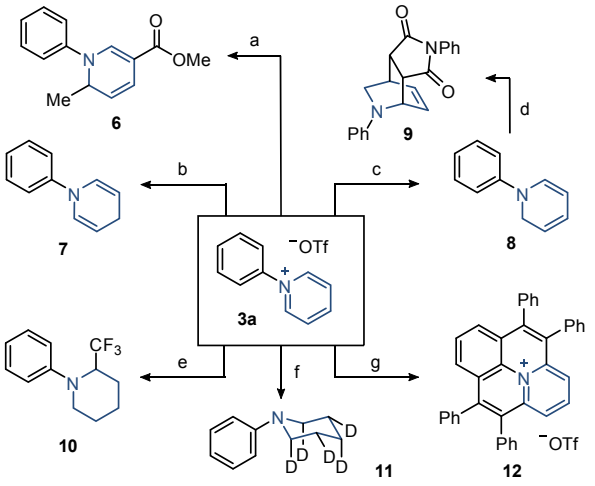
Table 4. Scope of the pyridinium salt hydrogenation.[a]



[a] Performed with arene (1.0 equiv), PtO_2 (0.05 equiv), H_2 (1 atm) in anhydrous EtOH (0.2 M), yield after isolation by column chromatography, regioisomeric ratio after isolation given in brackets, minor regioisomer denoted with an asterisk.

The pyridinium moiety produced herein constitutes a versatile handle for a myriad of further transformations, a selection of which is highlighted in Scheme 2. *N*-phenylpyridinium triflate **3a** was selectively reduced to the corresponding 1,2- and 1,4-dihydropyridines with sodium borohydride or sodium amalgam, respectively.[24] The resulting diene in **8** readily undergoes Diels-Alder cycloadditon to provide azabicyclooctane **9** in three steps from benzene. Treatment of **3a** with methyl Grignard leads to selective C2 alkylation, and subsequent methoxycarbonylation affords dihydropiperidine **6**.[25] In a similar fashion, trifluoromethylation followed by hydrogenation yields derivatized piperidine **10**.[26] Deuterated **3a**-d_5 undergoes hydrogenation furnishing partially deuterated piperidine **11**. Pyridinium **3a** efficiently underwent rhodium catalyzed C–H activation and annulation with diphenylacetylene to afford quinolinium **12**, which has been demonstrated to have applications as an optoelectronic material.[27]

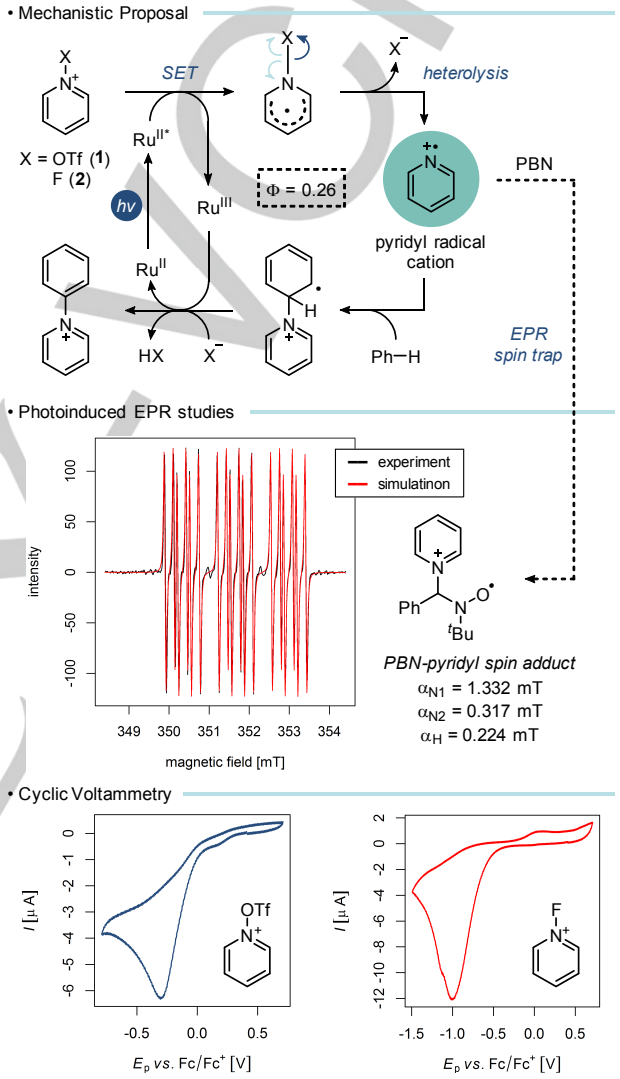
10.1002/anie.201810261



Scheme 2. Functionalization of *N*-phenylpyridinium triflate. Reagents and conditions: a) MeMgCl (6 equiv), THF, 0 °C, 2h; then TCAA (1.4 equiv), –78 °C to rt, 63%; NaOMe (1.5 equiv), MeOH/THF, 1 min, 76%. b) Na(Hg) (5 equiv), water, 14 h, 89%. c) $NaBH_4$ (0.4 equiv), KOH (2 equiv), water, 8 h, 86%. d) *N*-phenylmaleimide (1.1 equiv), Et_2O, rt, 4 h, 73%. e) $TMSCF_3$ (1.2 equiv), CsF (1.1 equiv), DCM, rt, 16 h; then H_2 (1 atm), Pd/C (0.1 equiv), EtOH, 8 h, 35%. f) from **3a**-d_5: H_2, PtO_2, EtOH, 2 h, 51%. g) 1,2-diphenylethyne (4 equiv), $[Cp^*RhCl_2]_2$ (0.05 equiv), $Cu(OAc)_2$ (4 equiv), NaOAc (4 equiv), DCE, 140 °C, 16 h, 52%. THF = tetrahydrofuran, TCAA = trichloroacetic acid, TMS = trimethylsilyl, DCM = dichloromethane, Cp = cyclopentadienyl, DCE = 1,2-dichloroethane.

A plausible mechanism for visible light-regulated radical pyridination is proposed in Scheme 3. After initial excitation of the photocatalyst under blue light irradiation (446 nm),[28] the resulting excited $Ru(bpy)_3^{2+*}$ (E_{red} = –1.2 V vs. $Fc^{0/+}$) would undergo oxidative quenching at a rate of 2.2 x 10^5 M^{-1} s^{-1} with respect pyridinium reagent **1** (E_{red} = –0.3 V vs. $Fc^{0/+}$) to afford $Ru(bpy)_3^{3+}$, as evidenced by Stern-Volmer quenching studies (see SI). The pyridyl radical resulting from this single electron transfer rapidly and irreversibly undergoes heterolytic N–X bond fragmentation to give a pyridyl radical cation and anionic X. For **1** and **2** this process is driven by the extrusion of a triflate or fluoride anion, respectively. DFT calculations support that heterolytic fragmentation is preferred by more than 10 kcal mol^{-1} for both reagents in preference to the homolytic cleavage to high-energy fluorine and triflyl radicals (see SI). Upon addition of the pyridyl radical cation to the arene, the subsequent oxidation and deprotonation of the cyclohexadienyl radical completes the catalytic cycle. The quantum yield (Φ = 0.26) indicates that the reaction is catalytic or conversely, operates under a highly inefficient radical chain process (see SI).[29] The absence of an isotope effect in an intramolecular competition experiment indicates that the final C–H bond cleavage is not rate-determining (see SI).[30]

The intermediacy of the elusive pyridyl radical cation is further corroborated by photo-induced EPR studies based on our earlier work on pyridinium reagent fragmentation.[14] A solution of **2**, Ir-photocatalyst and the spin trap PNB was monitored by EPR, and no signal was observed in the absence of light. Upon blue light irradiation, immediate formation of spin-trapped *N*-pyridyl radical cation adduct was evidenced by an intense signal with hyperfine couplings consistent with DFT simulations and those reported by Lagercrantz who documented a multistep synthesis of the PBN-pyridyl spin adduct from pyridine.[31] After the light was switched off, a weak signal was still detectable in the first scan, but not thereafter. The occurrence of misleading artifacts resulting from inverse-spin trapping or Forrester-Hepburn mechanism were excluded by control experiments (see SI).[32]



Scheme 3. Mechanistic proposal, EPR spectrum of PBN-spin trapped pyridyl radical cation and cyclic voltammetry measurements of reagents **1** and **2**. EPR = electron paramagnetic resonance, PBN = *N*-*tert*-butyl-α-phenylnitrone.

In summary, we have identified *N*-functionalized pyridinium reagents which produce the pyridyl radical cation upon single electron reduction. The pyridinium radical efficiently aminates arenes and hetereoarenes to furnish pyridinium salts, anilines or piperidenes and derivatives. The existence of the pyridinium radical was corroborated by EPR studies, which in combination with other experiments implicate a tenable mechanism. The work exploits for the first time the mechanistic duality of the

fragmentation process in pyridinium reagents, a process that has been largely overlooked.[33]

Acknowledgements

ETH Zürich is acknowledged for financial support. NSERC is thanked for a postdoctoral fellowship (B.J.). This research was supported by kind gifts from SpiroChem AG. Dr. Kissner and N. Kaeffer are thanked for cyclic voltammetry expertise and Dr. E. Meister for assistance with photospectroscopy. The authors thank Dr. N. Trapp and M. Solar for X-ray crystallographic analysis. We thank I. Franzoni and C. Gordon for advice regarding DFT computations.

Keywords: late-stage functionalization • amination • photoredox • pyridyl radical cation • radical mechanism

[1] E. Vitaku, D. T. Smith, J. T. Njardarson, *J. Med. Chem.* **2014**, *57*, 10257.

[2] a) J. Jiao, K. Murakami, K. Itami, *ACS Catal.* **2016**, *6*, 610; b) M. D. Kärkäs, *ACS Catal.* **2017**, *7*, 4999.

[3] For selected reviews, see: a) R. S. Neale, *Synthesis* **1971**, *1971*, 1; b) Y. L. Chow, W. C. Danen, S. F. Nelsen, D. H. Rosenblatt, *Chem. Rev.* **1978**, *78*, 243; c) S. Z. Zard, *Chem. Soc. Rev.* **2008**, *37*, 1603; d) T. Xiong, Q. Zhang, *Chem. Soc. Rev.* **2016**, *45*, 3069; e) L. Stella, in *Radicals in Organic Synthesis* (Ed.: P Renaud, M. P. Sibi), Wiley-VCH, **2008**, pp. 407.

[4] a) F. Minisci, *Synthesis* **1973**, *1973*, 1; b) U. Lüning, P. S. Skell, *Tetrahedron* **1985**, *41*, 4289.

[5] For selected examples that employ the unreactive arene as the limiting reactant, see: a) G. B. Boursalian, M.-Y. Ngai, K. N. Hojczyk, T. Ritter, *J. Am. Chem. Soc.* **2013**, *135*, 13278; b) K. Foo, E. Sella, I. Thomé, M. D. Eastgate, P. S. Baran, *J. Am. Chem. Soc.* **2014**, *136*, 5279; c) T. Kawakami, K. Murakami, K. Itami, *J. Am. Chem. Soc.* **2015**, *137*, 2460; d) W. Xie, J. H. Yoon, S. Chang, *J. Am. Chem. Soc.* **2016**, *138*, 12605; e) M. P. Paudyal, A. M. Adebesin, S. R. Burt, D. H. Ess, Z. Ma, L. Kürti, J. R. Falck, *Science* **2016**, *353*, 1144; f) L. Legnani, G. Prina Cerai, B. Morandi, *ACS Catal.* **2016**, *6*, 8162.

[6] For an exception, see: G. B. Boursalian, W. S. Ham, A. R. Mazzotti, T. Ritter, *Nat. Chem.* **2016**, *8*, 810.

[7] a) L. J. Allen, P. J. Cabrera, M. Lee, M. S. Sanford, *J. Am. Chem. Soc.* **2014**, *136*, 5607; b) H. Kim, T. Kim, D. G. Lee, S. W. Roh, C. Lee, *Chem. Commun.* **2014**, *50*, 9273; c) L. Song, L. Zhang, S. Luo, J.-P. Cheng, *Chem Eur. J.* **2014**, *20*, 14231; d) T. W. Greulich, C. G. Daniliuc, A. Studer, *Org. Lett.* **2015**, *17*, 254; e) E. Ito, T. Fukushima, T. Kawakami, K. Murakami, K. Itami, *Chem* **2017**, *2*, 383.

[8] a) Q. Qin, S. Yu, *Org. Lett.* **2014**, *16*, 3504; b) E. Brachet, T. Ghosh, I. Ghosh, B. König, *Chem. Sci.* **2015**, *6*, 987; c) K. Tong, X. Liu, Y. Zhang, S. Yu, *Chem. Eur. J.* **2016**, *22*, 15669; e) J. Davies, T. D. Svejstrup, D. Fernandez Reina, N. S. Sheikh, D. Leonori, *J. Am. Chem. Soc.* **2016**, *138*, 8092

[9] a) T. D. Svejstrup, A. Ruffoni, F. Juliá, V. M. Aubert, D. Leonori, *Angew. Chem. Int. Ed.* **2017**, *56*, 14948; b) K. A. Margrey, A. Levens, D. A. Nicewicz, *Angew. Chem. Int. Ed.* **2017**, *56*, 15644.

[10] a) T. Morofuji, A. Shimizu, J. Yoshida, *J. Am. Chem. Soc.* **2013**, *135*, 5000; b) N. A. Romero, K. A. Margrey, N. E. Tay, D. A. Nicewicz, *Science* **2015**, *349*, 1326; c) S. Möhle, S. Herold, F. Richter, H. Nefzger, S. R. Waldvogel, *ChemElectroChem* **2017**, *4*, 2196; d) A. Magomedov, E. Kasparavičius, K. Rakstys, S. Paek, N. Gasilova, K. Genevičius, G. Juška, T. Malinauskas, M. K. Nazeeruddin, V. Getautis, *J. Mater. Chem. C* **2018**, *6*, 8874.

[11] a) K. Y. Lee, J. K. Kochi, *J. Chem. Soc., Perkin Trans. 2* **1992**, *0*, 1011; b) T. M. Bockman, K. Y. Lee, J. K. Kochi, *J. Chem. Soc., Perkin Trans. 2* **1992**, *0*, 1581.

[12] a) D. P. Specht, C. G. Houle, S. Y. Farid, *Photopolymerizable Compositions Featuring Novel Co-Initiators*, **1981**, US4289844A. b) I. R. Gould, D. Shukla, D. Giesen, S. Farid, *Helv. Chim. Acta* **2001**, *84*, 2796.

[13] a) J. W. Beatty, J. J. Douglas, K. P. Cole, C. R. J. Stephenson, *Nature Communications* **2015**, *6*, 7919; b) J. W. Beatty, J. J. Douglas, R. Miller, R. C. McAtee, K. P. Cole, C. R. J. Stephenson, *Chem* **2016**, *1*, 456; c) Y. Ouyang, X.-H. Xu, F.-L. Qing, *Angew. Chem. Int. Ed.* **2018**, *57*, 6926.

[14] B. J. Jelier, P. F. Tripet, E. Pietrasiak, I. Franzoni, G. Jeschke, A. Togni, *Angew. Chem. Int. Ed.* **2018**, *57*, 13784.

[15] a) F. J. R. Klauck, M. J. James, F. Glorius, *Angew. Chem. Int. Ed.* **2017**, *56*, 12336; b) A. C. Sun, E. J. McClain, J. W. Beatty, C. R. J. Stephenson, *Org. Lett.* **2018**, *20*, 3487.

[16] T. Umemoto, S. Fukami, G. Tomizawa, K. Harasawa, K. Kawada, K. Tomita, *J. Am. Chem. Soc.* **1990**, *112*, 8563.

[17] C. Zhen-Chu, P. J. Stang, *Tetrahedron Letters* **1984**, *25*, 3923.

[18] T. Zincke, *Justus Liebigs Annalen der Chemie* **1904**, *330*, 361.

[19] S. Sowmiah, J. M. S. S. Esperança, L. P. N. Rebelo, C. A. M. Afonso, *Org. Chem. Front.* **2018**, *5*, 453.

[20] a) C. H. Basch, J. Liao, J. Xu, J. J. Piane, M. P. Watson, *J. Am. Chem. Soc.* **2017**, *139*, 5313; b) C. D. Vanderwal, *J. Org. Chem.* **2011**, *76*, 9555; c) D. Moser, Y. Duan, F. Wang, Y. Ma, M. J. O'Neill, J. Cornella, *Angew. Chem. Int. Ed.* **2018**, *57*, 11035.; d) J. Wu, L. He, A. Noble, V. K. Aggarwal, *J. Am. Chem. Soc.* **2018**, *140*, 10700.

[21] We recently became aware of Ritter and co-workers having independently and concurrently developed a similar approach.

[22] K. D. Bunker, N. W. Sach, Q. Huang, P. F. Richardson, *Org. Lett.* **2011**, *13*, 4746.

[23] T. S. Hamilton, R. Adams, *J. Am. Chem. Soc.* **1928**, *50*, 2260.

[24] M. Saunders, E. H. Gold, *J. Org. Chem.* **1962**, *27*, 1439.

[25] M.-L. Bennasar, T. Roca, M. Monerris, C. Juan, J. Bosch, *Tetrahedron* **2002**, *58*, 8099.

[26] R. Loska, M. Majcher, M. Makosza, *J. Org. Chem.* **2007**, *72*, 5574.

[27] Q. Ge, Y. Hu, B. Li, B. Wang, *Org. Lett.* **2016**, *18*, 2483.

[28] a) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322; b) J. J. Douglas, M. J. Sevrin, C. R. J. Stephenson, *Org. Process Res. Dev.* **2016**, *20*, 1134.

[29] M. A. Cismesia, T. P. Yoon, *Chem. Sci.* **2015**, *6*, 5426; b) M. Kärkäs, B. Matsuura, C. R. J. Stephenson, *Science* **2015**, 349, 1285**;** c) High intensity irradiation has been shown to diminish the observed quantum yield, see: S. Pitre, C. D. McTiernan, W. Vine, R. DiPucchio, M. Grenier, J. C. Scaiano, *Sci. Rep.* **2015**, 5, 16397.

[30] E. M. Simmons, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2012**, *51*, 3066.

[31] C. Lagercrantz, *Acta Chem. Scand.* **1993**, *47*, 734.

[32] A. R. Forrester, S. P. Hepburn, *J. Chem. Soc. C* **1971**, *0*, 701.

[33] The EPR results in conjunction with cyclic voltammetry data suggest that in their role as oxidants *N*-fluoropyridinium salts may not liberate fluorine radicals as classically proposed, but rather a highly oxidizing pyridyl radical cation. Hence, when a SET mechanism is invoked the exact nature of what is colloquially referred to as "F^+ oxidant" may need revising.

10.1002/anie.201810261

WILEY-VCH

COMMUNICATION

Simon L. Rössler, Benson J. Jelier, Pascal F. Tripet, Andrej Shemet, Gunnar Jeschke, Antonio Togni, and Erick M. Carreira**

Page No. – Page No.
Pyridyl Radical Cation for C–H Amination of Arenes

The road less travelled: Select pyridinium reagents undergo an unprecedented, heterolytic fragmentation upon single electron reduction to afford a synthetically viable *N*-pyridyl radical cation. This reactive species was leveraged for the C–H amination of (hetero)arenes to furnish N-aryl pyridinium products, which enable access to diverse nitrogen scaffolds.