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Electrochemical Intramolecular Aminooxygenation of Unactivated Alkenes

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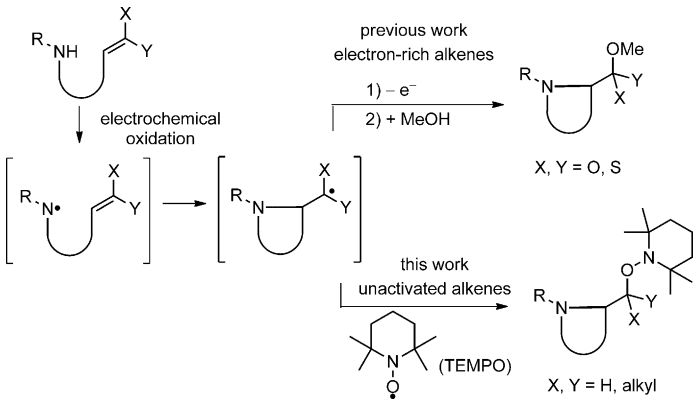
Abstract: An electrochemical approach to the intramolecular aminooxygenation of unactivated alkenes has been developed. This process is based on the addition of nitrogen-centered radicals, generated through electrochemical oxidation, to alkenes followed by trapping of the cyclized radical intermediate with 2,2,6,6-tetramethylpiperidine-*N*-oxyl radical (TEMPO). Difunctionalization of a variety of alkenes with easily available carbamates/amides and TEMPO affords aminooxygenation products in high yields and with excellent *trans* selectivity for cyclic systems (d.r. up to > 20:1). The approach provides a much-needed complementary route to existing *cis*-selective methods.

Direct aminooxygenation of alkenes provides straightforward and efficient access to the 1,2-aminoalcohol motif, which is present in a variety of bioactive molecules, natural products, and chiral reagents.[1] Current methods to promote alkene aminooxygenation typically involve either the use of catalysts containing precious and/or toxic transition metals[2] or rely on a stoichiometric amount of iodine-based oxidants.[3] Additionally, a general method for the *trans* aminooxygenation of cyclic alkenes with high regio- and stereoselectivity remains elusive.[4] Along those lines, Wardrop did discover that the aminooxygenation of cyclic *O*-alkyl hydroxamate facilitated by an iodine(III) reagent led to excellent *trans*-selectivity.[4a] Alexanian disclosed metal-free *trans* aminooxygenation via amidoxy radicals.[4b] Han observed *trans* difunctionalization of cycloalkenes in the studies of oxime and hydrazone radical addition reactions.[4c,d] Recently, Xu reported an iron-catalyzed method and demonstrated *trans* selectivity with a cyclohexenyl substrate.[4e]

Previous anodic cyclization studies[5] demonstrated the successful application of anodic oxidation[6] for the aminomethoxylation of electron-rich olefins (Scheme 1). In this process, the addition of the anode-generated, nitrogen-centered radical[7] to a tethered alkene leads to a new, carbon-centered radical, which is further oxidized to form a cation that is trapped with methanol to afford the final product. The electrochemical method obviates the use of stoichiometric quantities of chemical oxidants and can derive the energy it needs from renewable sources such as sunlight.[8] We surmised that, instead of an oxidation, interception of this carbon radical with a trapping reagent, such as 2,2,6,6-tetramethylpiperidine-*N*-oxyl radical (TEMPO),[9] would also lead to difunctionalization. Since no second oxidation would be needed in such a scenario, there would be no requirement for an electron-rich radical. Hence, the reaction might work with an unactivated olefin. Additionally, the alkoxyamine moiety of the TEMPO adduct could serve as a versatile functional group handle for various subsequent transformations (vide infra).[10] Herein, we report the successful development of an electrochemical method for the aminooxygenation of unactivated alkenes using carbamate and amide substrates and TEMPO as a trapping group.

Carbamate **1a** was selected as the model substrate and submitted to electrochemical aminooxygenation (Table 1). The standard reaction was run at 60 °C and a constant current of 10 mA in a three-necked round-bottom flask equipped with a reticulated vitreous carbon (RVC) anode and a platinum wire



Scheme 1. Electrochemical aminooxygenation of alkenes.

cathode (see the Supporting Information). A solution of 0.1 M Bu_4NBF_4 in H_2O/CH_3CN (1:19) was used as the supporting electrolyte and two equivalents of TEMPO were included. After 2.5 F mol^{-1} of electricity[11] was passed through the electrolysis cell, the substrate was consumed and the desired product **2a** was isolated in 70% yield as a single diastereomer (Table 1;

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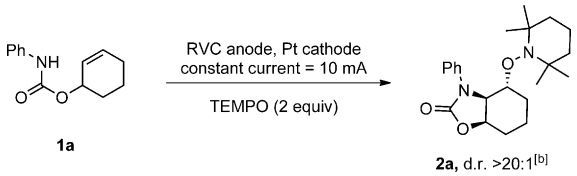
Table 1. Optimization of electrolysis conditions for aminooxygenation.[a]



1a **2a**, d.r. >20:1[b]

Entry	Electrolysis conditions	Yield [%][c]
1	Bu_4NBF_4 (0.1 M), H_2O/CH_3CN (1:19), 60 °C, 2.5 F mol^{-1}	70
2	Bu_4NBF_4 (0.1 M), LiOH (1 equiv), H_2O/CH_3CN (1:19), 60 °C, 2.8 F mol^{-1}	81
3	Bu_4NBF_4 (0.1 M), Cs_2CO_3 (1 equiv), H_2O/CH_3CN (1:19), 60 °C, 3.2 F mol^{-1}	80
4	Bu_4NBF_4 (0.1 M), Na_2CO_3 (1 equiv), H_2O/CH_3CN (1:19), 60 °C, 1.5 F mol^{-1}	90
5	Et_4NOTs (0.1 M), Na_2CO_3 (1 equiv), H_2O/CH_3CN (1:19), 60 °C, 3.9 F mol^{-1}	89
6[d]	Bu_4NBF_4 (0.1 M), Na_2CO_3 (1 equiv), CH_3CN, 60 °C, 5.2 F mol^{-1}	10
7	Bu_4NBF_4 (0.1 M), Na_2CO_3 (1 equiv), H_2O/CH_3CN (1:9), 60 °C, 3.0 F mol^{-1}	83
8	Bu_4NBF_4 (0.1 M), Na_2CO_3 (1 equiv), H_2O/CH_3CN (1:19), RT, 3.3 F mol^{-1}	61

[a] Reaction conditions: **1** (0.35 mmol), TEMPO (0.70 mmol), H_2O (0.5 mL), CH_3CN (9.5 mL), 60 °C. [b] Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [c] Isolated yield. [d] **1a** was recovered in 70% yield.

entry 1). The addition of a base such as LiOH, Cs_2CO_3, or Na_2CO_3 improved the yield to 81, 80, or 90%, respectively (entries 2–4). Moreover, Na_2CO_3 also reduced the amount of electricity needed for the complete consumption of **1a** (1.5 F mol^{-1}). However, substituting Bu_4NBF_4 with Et_4NOTs (entry 5), altering the water composition of the solvent system (entries 6–7), and conducting the reaction at a lower temperature (entry 8) all led to a less efficient reaction. Based on these results, it was concluded that the optimal reaction conditions would involve adding one equivalent of Na_2CO_3 to the Bu_4NBF_4 electrolyte solution in H_2O/CH_3CN (1:19) and conducting the electrolysis at 60 °C (entry 4).

The *N*-phenyl ring of **1a** was modified with various functional groups to investigate their effects on alkene aminooxygenation (Table 2). A broad spectrum of substituents with diverse electronic properties were found to be well-tolerated, including electron-donating groups, such as Me (Table 2; entry 1) and OMe (entries 2–3), halogens, such as F (entries 4–6) and Cl (entry 7), and electron-withdrawing groups such as CF_3 (entry 8), Ac (entry 9), and CN (entry 10). Carbamates with a 2,6-disubstituted phenyl group, previously reported to be incompatible with hypervalent iodine-mediated cyclization,[3a] also served as efficient substrates (entries 11–12). The introduction of a nitro group, however, led to less satisfactory results,[3a,12] which was probably caused by the decomposition of the product **2n** during the electrolysis.[13]

Further examination of the substrate scope revealed a broad tolerance of the electrochemical method to cyclic alkenes. Trisubstituted olefins could be efficiently difunctionalized to generate tetrasubstituted stereogenic centers that are difficult to construct with existing methods[4] (Table 2; entries 14–16). Notably, the electrolysis of **1o** was carried out on a gram-scale without difficulty and the reaction exhibited exclusive preference for the proximal double bond over the distal one (entry 14). Introduction of a nitrogen functionality into the cyclohexene ring was tolerated and led to the formation of a highly functionalized piperidine (entry 17). Cyclopentenyl carbamates (entries 18–19), which were found to be difficult for the Os-mediated method,[2d] also participated readily in the reaction, albeit with diminished diastereoselectivity for the trisubstituted olefin (entry 19). Further investigation revealed that *N*-aryl amides were also excellent substrates (entries 20–21).

The stereochemistry of the aminooxygenation was determined by a single-crystal X-ray diffraction study of **2h** and **2q**. In each case, a clear *trans* arrangement of the nitrogen atom relative to the alkoxyamine group (Figure 1) was found in the product. These findings were consistent with the preferential approach of TEMPO to the cyclization-derived cyclic carbon radical from the less hindered direction in the transition state of the radical-radical combination reaction. Hence, using cyclic alkenes as substrates, this electrochemical approach offers an efficient access to *trans*-configured products with a high level of regio- and stereochemical control, complementing the *cis*-selective Os-based strategy.[2c–e]

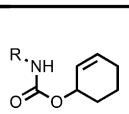
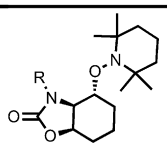
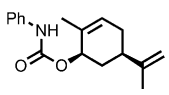
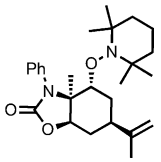
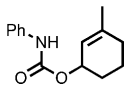
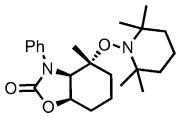
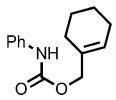
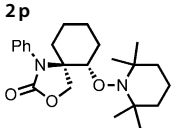
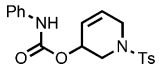
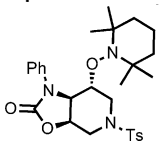
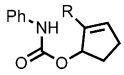
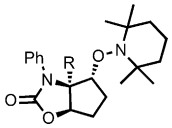
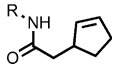
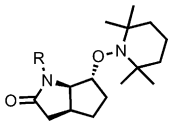
Following the success with cyclic alkenes, effort was extended to testing acyclic systems for their suitability as substrates (Table 3). As expected, the reaction proceeded in high yield with a multitude of tri-, and disubstituted olefins. Aminooxygenation of 1,2-disubstituted alkenes was, however, nonselective and afforded a mixture of diastereomers (entries 3–4). Furthermore, the monosubstituted alkene **3f** (Table 3; entry 6) seemed to necessitate significantly higher current usage compared to the other more substituted substrates.

As mentioned earlier, the TEMPO-derived alkoxyamine moiety can provide facile access to a variety of synthetically useful functionalities. For instance, when using **2a** and **2p** as the starting materials, the alkoxyamine group in these compounds can be readily transformed into a hydroxyl group by reductive cleavage of the N–O bond, a carbonyl group by oxidation,[3d] or a double bond by thermal elimination[10] (Scheme 2).

To confirm the hypothesis that the aminooxygenation reaction underwent a radical mechanism, compound **9** bearing a cyclopropane group as the radical probe[12,14] was synthesized and electrolyzed in the presence of TEMPO (Scheme 3). Indeed, the ring-opening product **10** was obtained in 52% yield, providing solid evidence for the involvement of a nitrogen-centered radical.

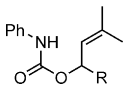
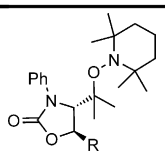
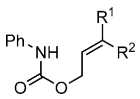
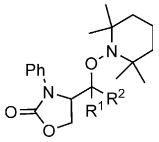
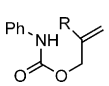
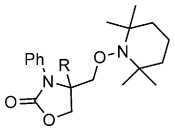
To give rise to the nitrogen radicals, the substrates could either be directly oxidized at the anode, or they could be oxidized by an oxoammonium ion that in turn originates from anodic oxidation of TEMPO[15] (Scheme 4). To test these possibilities, the oxidation potentials of TEMPO and **1a** were measured by cyclic voltammetry,[16] which indicated that the former

Table 2. Aminooxygenation of cyclic alkenes.[a]

Entry	Substrate	Product	Electricity [F mol^{-1}]	Yield [%],[b] d.r.[c]
				
1	**1b**, R = 4-MePh	**2b**	3.0	97, >20:1
2	**1c**, R = 4-OMePh	**2c**	2.2	94, >20:1
3	**1d**, R = 2-OMePh	**2d**	2.4	85, >20:1
4	**1e**, R = 4-FPh	**2e**	2.1	93, >20:1
5	**1f**, R = 3-FPh	**2f**	2.8	91, >20:1
6	**1g**, R = 2-FPh	**2g**	1.6	96, >20:1
7	**1h**, R = 4-ClPh	**2h**	1.3	88, >20:1
8	**1i**, R = 4-CF_3Ph	**2i**	1.4	83, >20:1
9	**1j**, R = 4-AcPh	**2j**	1.5	86, >20:1
10	**1k**, R = 4-CNPh	**2k**	2.0	87, >20:1
11	**1l**, R = 2,6-Me_2Ph	**2l**	1.9	93, >20:1
12	**1m**, R = 2,6-Cl_2Ph	**2m**	2.5	85, >20:1
13	**1n**, R = 4-NO_2Ph	**2n**	4.1	51, >20:1
				
14	**1o**	**2o**	3.4	81, >20:1
				
15	**1p**	**2p**	2.1	90, >20:1
				
16	**1q**	**2q**	1.5	96, >20:1
				
17	**1r**	**2r**	3.6	89, >20:1
				
18	**1s**, R = H	**2s**	1.4	86, >20:1
19	**1t**, R = Me	**2t**	3.0	81, 4:1
				
20	**1u**, R = Ph	**2u**	2.5	95, >20:1
21	**1v**, R = 4-MeOPh	**2v**	1.4	90, >20:1

[a] Reaction conditions: RVC anode, Pt cathode, 10 mA, **1** (0.35 mmol), TEMPO (0.70 mmol), Bu_4NBF_4 (1.0 mmol), Na_2CO_3 (0.35 mmol), H_2O (0.5 mL), CH_3CN (9.5 mL), 60 °C. [b] Isolated yield. [c] Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [d] 1.0 gram of **1o** was used.

Table 3. Aminooxygenation of acyclic alkenes.[a]

Entry	Substrate	Product	Electricity [F mol^{-1}]	Yield [%],[b] d.r.[c]
				
1	**3a**, R = H	**4a**	2.3	90
2	**3b**, R = Bn	**4b**	2.8	86, >20:1
				
3	**3c**, R^1 = *n*Pr, R^2 = H	**4c**	4.2	89, 1.4:1
4	**3d**, R^1 = H, R^2 = Et	**4d**	1.4	97, 1.4:1
				
5	**3e**, R = Me	**4e**	2.8	91
6[d]	**3f**, R = H	**4f**	12.1	58 (27)

[a] Reaction conditions: RVC anode, Pt cathode, 10 mA, **1** (0.35 mmol), TEMPO (0.70 mmol), Bu_4NBF_4 (1.0 mmol), Na_2CO_3 (0.35 mmol), H_2O (0.5 mL), CH_3CN (9.5 mL), 60 °C. [b] Isolated yield. [c] Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [d] % Recovered starting material shown in parenthesis.

was oxidized much more readily than the latter ($E_{p/2}$ = 0.70 and 1.53 V for TEMPO and **1a**, respectively, versus an Ag/AgCl reference electrode).

We then investigated the oxidation of **1a** with pre-synthesized oxoammonium salt **11**[17] (Scheme 5). The reaction was successful only when Cs_2CO_3 was added, but not when the reaction mixture contained Na_2CO_3 or was base-free.[4d] These findings suggested that the generation of the nitrogen radicals likely proceeded through the TEMPO-mediated pathway but required a base for efficiency. Despite the fact that Na_2CO_3 was previously found to be the best alkaline additive for the electrolysis, it was unlikely to be directly involved in the radical generation step because of its inability to induce substrate oxidation in an electricity-free environment. Based on this reasoning, we theorized that hydroxide, generated during electrolysis as a result of H_2O reduction at the cathode, facilitated the TEMPO-mediated electrochemical oxidation of the substrates (Scheme 4). The failure of Na_2CO_3 to promote the oxidation of the carbamate was probably caused by its relatively low solubility in the mixed solvent used.

In conclusion, electrooxidative formation of nitrogen-centered radicals and their addition to alkenes in the presence of TEMPO constitutes a general and mild approach to alkene aminooxygenation. Our method in this study relies on the dual role of TEMPO as both a redox mediator and a radical trap and offers much-needed complementation to existing *cis*-selective methods in the generation of *trans*-configured aminoalcohol motifs from cyclic alkenes.

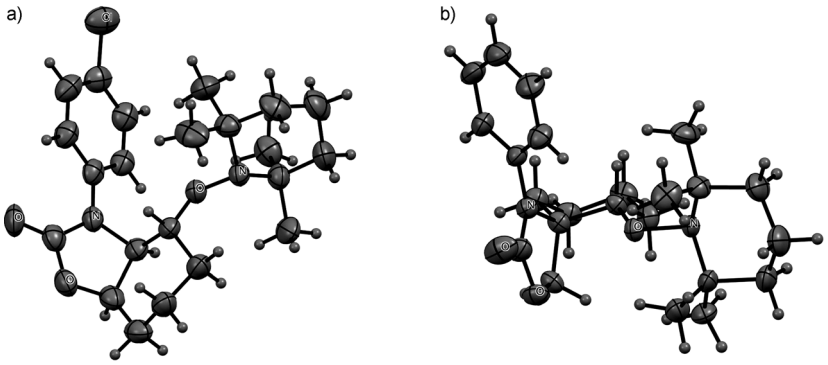
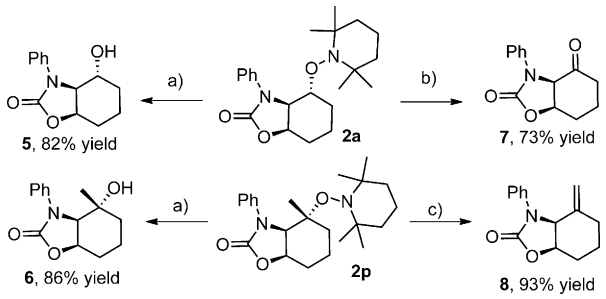
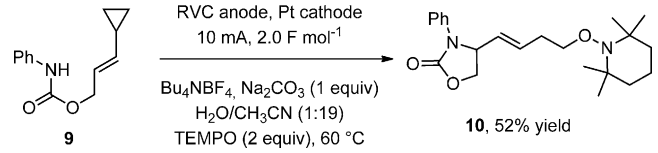


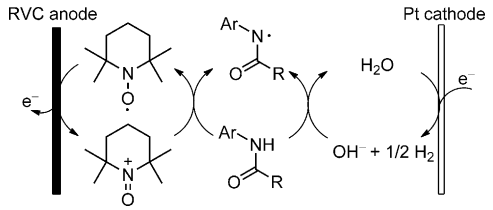
Figure 1. ORTEP representation of **2h** (a) and **2q** (b); thermal ellipsoids are shown at 50% probability.[18]



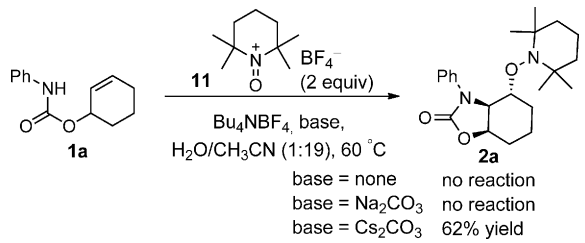
Scheme 2. Transformations of the aminooxygenation products. a) Zn (12 equiv), AcOH/THF/H_2O (3:1:1), 50 °C, 3 h; b) 3-Chloroperbenzoic acid (1.5 equiv), CH_2Cl_2, 0 °C, 0.5 h; c) *i*Pr_2NH (6.2 equiv), toluene, 150 °C, 12 h.



Scheme 3. Electrolysis of **9**.



Scheme 4. Mechanistic rationale for the generation of nitrogen radicals.



Scheme 5. Aminooxygenation using oxoammonium salt **11**.

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Keywords: amino alcohols · aminooxygenation · cyclization · electrochemical oxidation · radicals

[1] a) S. C. Bergmeier, *Tetrahedron* **2000**, *56*, 2561 – 2576; b) D. Nilov, O. Reiser, *Adv. Synth. Catal.* **2002**, *344*, 1169 – 1173; c) J. A. Bodkin, M. D. McLeod, *J. Chem. Soc. Perkin Trans. 1* **2002**, 2733 – 2746; d) T. J. Donohoe, C. K. A. Callens, A. Flores, A. R. Lacy, A. H. Rathi, *Chem. Eur. J.* **2011**, *17*, 58 – 76.

[2] For selected examples, see: Os: a) K. B. Sharpless, A. O. Chong, K. Oshima, *J. Org. Chem.* **1976**, *41*, 177 – 179; b) G. Li, H. T. Chang, K. B. Sharpless, *Angew. Chem.* **1996**, *108*, 449 – 452; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 451 – 454; c) T. J. Donohoe, P. D. Johnson, M. Helliwell, M. Keenan, *Chem. Commun.* **2001**, 2078 – 2079; d) T. J. Donohoe, P. D. Johnson, A. Cowley, M. Keenan, *J. Am. Chem. Soc.* **2002**, *124*, 12934 – 12935; e) T. J. Donohoe, M. J. Chughtai, D. J. Klauber, D. Griffin, A. D. Campbell, *J. Am. Chem. Soc.* **2006**, *128*, 2514 – 2515. Rh: f) A. Padwa, T. Stengel, *Org. Lett.* **2002**, *4*, 2137 – 2139; g) E. Levites-Agababa, E. Menhaji, L. N. Perlson, C. M. Rojas, *Org. Lett.* **2002**, *4*, 863 – 865; h) S. Beaumont, V. Pons, P. Retailleau, R. H. Dodd, P. Dauban, *Angew. Chem.* **2010**, *122*, 1678 – 1681; *Angew. Chem. Int. Ed.* **2010**, *49*, 1634 – 1637. Pd: i) E. J. Alexanian, C. Lee, E. J. Sorensen, *J. Am. Chem. Soc.* **2005**, *127*, 7690 – 7691; j) G. Liu, S. S. Stahl, *J. Am. Chem. Soc.* **2006**, *128*, 7179 – 7181; k) L. V. Desai, M. S. Sanford, *Angew. Chem.* **2007**, *119*, 5839 – 5842; *Angew. Chem. Int. Ed.* **2007**, *46*, 5737 – 5740; l) H. Zhu, P. Chen, G. Liu, *J. Am. Chem. Soc.* **2014**, *136*, 1766 – 1769. Pt: m) K. Mũniz, A. Iglesias, Y. Fang, *Chem. Commun.* **2009**, 5591 – 5593. Au: n) T. de Haro, C. Nevado, *Angew. Chem.* **2011**, *123*, 936 – 940; *Angew. Chem. Int. Ed.* **2011**, *50*, 906 – 910. Cu: o) D. J. Michaelis, C. J. Shaffer, T. P. Yoon, *J. Am. Chem. Soc.* **2007**, *129*, 1866 – 1867; p) P. H. Fuller, J. W. Kim, S. R. Chemler, *J. Am. Chem. Soc.* **2008**, *130*, 17638 – 17639; q) D. E. Mancheno, A. R. Thornton, A. H. Stoll, A. Kong, S. B. Blakey, *Org. Lett.* **2010**, *12*, 4110 – 4113. Fe: r) K. S. Williamson, T. P. Yoon, *J. Am. Chem. Soc.* **2010**, *132*, 4570 – 4571.

[3] a) K. C. Nicolaou, P. S. Baran, Y.-L. Zhong, S. Barluenga, K. W. Hunt, R. Kranich, J. A. Vega, *J. Am. Chem. Soc.* **2002**, *124*, 2233 – 2244; b) H. M. Lovick, F. E. Michael, *J. Am. Chem. Soc.* **2010**, *132*, 1249 – 1251; c) U. Farid, T. Wirth, *Angew. Chem.* **2012**, *124*, 3518 – 3522; *Angew. Chem. Int. Ed.* **2012**, *51*, 3462 – 3465; d) B. Zhang, A. Studer, *Org. Lett.* **2013**, *15*, 4548 – 4551.

[4] a) D. J. Wardrop, E. G. Bowen, R. E. Forslund, A. D. Sussman, S. L. Weerasekera, *J. Am. Chem. Soc.* **2010**, *132*, 1188 – 1189; b) V. A. Schmidt, E. J. Alexanian, *J. Am. Chem. Soc.* **2011**, *133*, 11402 – 11405; c) B. Han, X.-L. Yang, R. Fang, W. Yu, C. Wang, X.-Y. Duan, S. Liu, *Angew. Chem.* **2012**, *124*, 8946 – 8950; *Angew. Chem. Int. Ed.* **2012**, *51*, 8816 – 8820; d) X.-Y. Duan, N.-N. Zhou, R. Fang, X.-L. Yang, W. Yu, B. Han, *Angew. Chem.* **2014**, *126*, 3222 – 3226; *Angew. Chem. Int. Ed.* **2014**, *53*, 3158 – 3162; e) G.-S. Liu, Y.-Q. Zhang, Y.-A. Yuan, H. Xu, *J. Am. Chem. Soc.* **2013**, *135*, 3343 – 3346.

[5] a) H.-C. Xu, K. D. Moeller, *J. Am. Chem. Soc.* **2008**, *130*, 13542 – 13543; b) H.-C. Xu, K. D. Moeller, *J. Am. Chem. Soc.* **2010**, *132*, 2839 – 2844; c) H.-C. Xu, J. M. Campbell, K. D. Moeller, *J. Org. Chem.* **2014**, *79*, 379 – 391.

[6] For recent reviews on synthetic applications of anodic electrochemistry, see: a) K. D. Moeller, *Tetrahedron* **2000**, *56*, 9527 – 9554; b) A. J. Bard, M. Stratman, H. J. Schäfer, *Encyclopedia of Electrochemistry, Vol. 8, Organic*

Electrochemistry, Wiley-VCH, Weinheim, **2004**; c) J. B. Sperry, D. L. Wright, *Chem. Soc. Rev.* **2006**, *35*, 605 – 621; d) J. Yoshida, K. Kataoka, R. Horcajada, A. Nagaki, *Chem. Rev.* **2008**, *108*, 2265 – 2299.

[7] For recent reviews on nitrogen-centered radicals, see: a) J. L. Esker, M. Newcomb in *Advances in Heterocyclic Chemistry, Vol. 58*, (Ed.: A. R. Katritzky), Academic Press, New York, **1993**, pp. 1 – 45; b) A. G. Fallis, I. M. Brinza, *Tetrahedron* **1997**, *53*, 17543 – 17594; c) L. Stella in *Radicals in Organic Synthesis, Vol. 2* (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, **2001**, pp. 407 – 426; d) S. Z. Zard, *Chem. Soc. Rev.* **2008**, *37*, 1603 – 1618; e) A. Baralle, A. Baroudi, M. Daniel, L. Fensterbank, J.-P. Goddard, E. Lacote, M.-H. Larraufie, G. Maestri, M. Malacria, C. Ollivier, in *Encyclopedia of Radicals in Chemistry, Biology and Materials* (Eds.: C. Chatgilialoglu, A. Studer), Wiley, Chichester, **2012**, pp. 767 – 816.

[8] a) L. A. Anderson, A. Redden, K. D. Moeller, *Green Chem.* **2011**, *13*, 1652 – 1654; b) B. H. Nguyen, A. Redden, K. D. Moeller, *Green Chem.* **2014**, *16*, 69 – 72.

[9] For TEMPO-involved alkene aminooxygenation, see refs. [2p], [3d], [4c], and [4d]. For selected reviews on TEMPO, see: a) T. Vogler, A. Studer, *Synthesis* **2008**, 1979 – 1993; b) L. Tebben, A. Studer, *Angew. Chem.* **2011**, *123*, 5138 – 5174; *Angew. Chem. Int. Ed.* **2011**, *50*, 5034 – 5068.

[10] For examples, see ref. [3d] and: J. Gui, H. Tian, W. Tian, *Org. Lett.* **2013**, *15*, 4802 – 4805.

[11] Theoretically, 1 F mol^{-1} of electricity is required for a one-electron oxidation.

[12] Z. Li, L. Song, C. Li, *J. Am. Chem. Soc.* **2013**, *135*, 4640 – 4643.

[13] Decomposition was observed when the purified **2n** was resubjected to the electrolysis conditions.

[14] M. Newcomb in *Radicals in Organic Synthesis, Vol. 1*(Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, **2001**, pp. 317 – 336.

[15] For examples of TEMPO-mediated electrochemical oxidations, see: a) M. F. Semmelhack, C. R. Schmid, *J. Am. Chem. Soc.* **1983**, *105*, 6732 – 6734; b) M. Schämann, H. J. Schäfer, *Electrochim. Acta* **2005**, *50*, 4956 – 4972; c) M. Kuroboshi, T. Yoshida, J. Oshitani, K. Goto, H. Tanaka, *Tetrahedron* **2009**, *65*, 7177 – 7185; d) C. Li, C.-C. Zeng, L.-M. Hu, F.-L. Yang, S. J. Yoo, R. D. Little, *Electrochim. Acta* **2013**, *114*, 560 – 566.

[16] Potentials were measured by cyclic voltammetry using a glassy carbon working electrode, a Pt wire auxiliary electrode, an Ag/AgCl reference electrode, an electrolyte solution composed of Bu_4NBF_4 (0.1 M) in H_2O/CH_3CN (1:19), one equivalent of Na_2CO_3, a substrate concentration of 0.025 M, and a sweep rate of 50 mV s^{-1}.

[17] J. M. Bobbitt, N. Merbouh, *Org. Synth.* **2005**, *82*, 80 – 86.

[18] CCDC 1006710 (**2h**) and 1006711 (**2q**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

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