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Electrochemically Oxidative C-C Bond Cleavage of Alkylarenes for Anilines Synthesis

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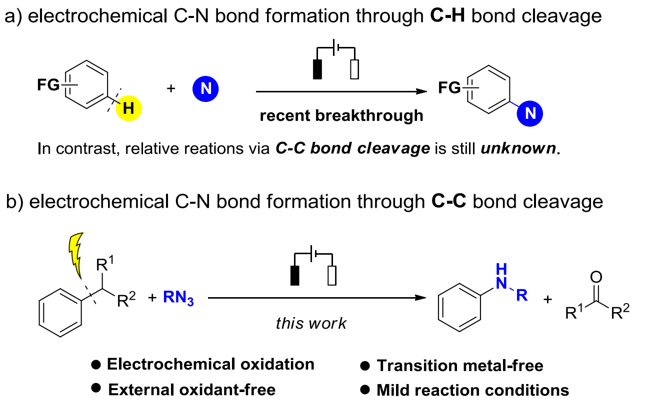
ABSTRACT: In contrast to the recent breakthrough in electrochemical C-H aminations, the electrochemically oxidative C-N bond formation through a C-C bond cleavage is rarely studied. This work describes an electrochemical C-C amination of alkylarenes for the efficient synthesis of versatile anilines, as well as carbonyl compounds. With the cheap and durable graphite plates as electrodes, and in a simple undivided cell, this protocol is much more economical with the consumption of electricity.
Keywords: *electrochemistry • C-C activation • amination • oxidation • rearrangements*

Oxidative processes are ubiquitous in nature as well as in fundamental transformations of chemical synthesis. Recently, the oxidative C-N bond formation through C-H/C-C bond cleavage is of great interest to chemists both in academia and industry due to their importance of *N*-containing compounds in materials and pharmaceuticals.[1,2] Among these oxidative processes, plenty of efficient common oxidants including hypervalent iodine reagents, quinones, peroxides, and metal salts were widely used.[3] However, the stoichiometric loading of these oxidants would cause separation problem and low atom-economy.

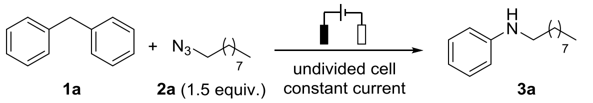
Alternatively, electrochemistry has been convicted powerful in chemicals synthesis,[4-6] and some significant oxidative reactions were achieved by electrochemical oxidation without any external traditional oxidants. Recently, the breakthroughs in electrochemical C-H aminations were remarkably achieved by the consumption of only electricity (Scheme 1a).[7-12] Yoshida and co-workers pioneeringly disclosed an anodic oxidative C-H amination of aromatic substrates with pyridine for the synthesis of arylamines.[7] Xu and co-workers developed an elegant intramolecular C-H amination to afford polycyclic N-heteroaromatic products via nitrogen-centered radicals.[8] Lei's group developed a significant intermolecular dehydrogenative C-H/N-H cross-coupling reaction.[9] More recently, the combination of electrochemistry and transition-metal catalysis for C-H amination of arenes was independently realized by the groups of Lei,[10] Ackermann[11] and Mei.[12] Although great progresses have been made in C-N bonds construction through electrochemically oxidative C-H bonds cleavage, the electrochemically oxidative C-N bond formation through C-C bond cleavage is still undeveloped.



Scheme 1. Different Kinds of Oxidative C-N bond Formation

Kolbe reaction has been developed more than 150 years and widely used for the electrochemical synthesis of alkanes via a decarboxylative process,[13] however, selective electrochemical C-C bond cleavage to synthesize amines is less studied and still a challenge, because the generated amine products are easier oxidized than the parent materials, which would lead to low chemical yield and current efficiency. In addition, it is worthwhile to overcome the chemical bond selectivity for the development of new C-C bond functionalizations. Herein, we describe a novel electrochemical C-C amination of alkylarenes via selective Csp^2-Csp^3 bond cleavage (Scheme 1b). The protocol not only produces arylamines and useful carbonyl compounds simultaneously with high atom economy, but also circumvents the possible over-oxidation of resulting arylamines. On account of trace-less and cheap electrochemical oxidation taking place of toxic and expensive oxidant, this transformation becomes mild, green, sustainable and efficient. Notably, with the cheap and durable graphite plates as electrodes, and in a simple undivided cell, this reaction is much more economical as well. In addition, the transition-metal catalyst free condition eradicates the problem of metal residual in products.

Table 1. Optimization of Reaction Conditions.[a]

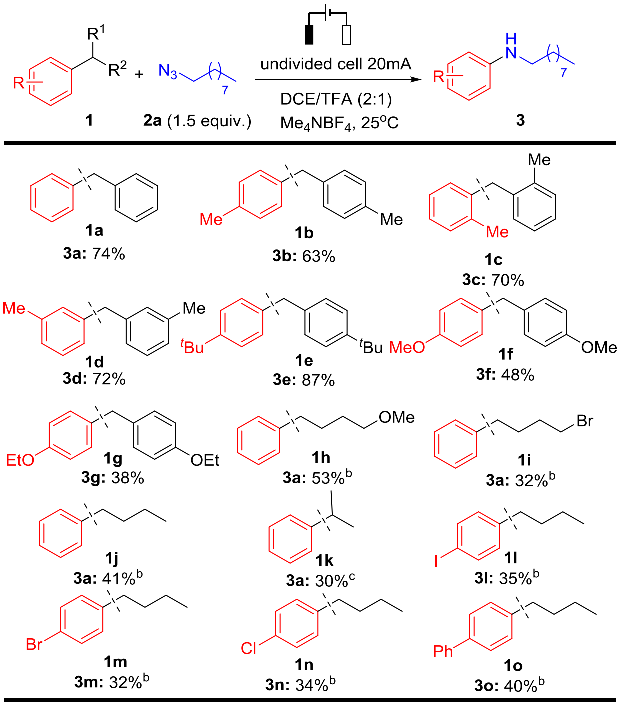


Entry	1a (mmol)	Solvent	Current (mA)	Time (h)	3a yield (%)[b]
1	0.5	TFA	20	2	44[c]
2	0.5	TFA	20	2	56
3	0.5	TFA	0	2	0
4	0.5	DCE/TFA (2:1)	20	2	58
5	0.5	DCE	20	2	0
6	0.5	DCE/HOAc (2:1)	20	2	0
7	0.5	DCE/TFA (2:1)	30	2	52
8	0.5	DCE/TFA (2:1)	10	6	48
9	0.5	DCE/TFA (2:1)	20	2	0[d]
10	0.5	DCE/TFA (2:1)	20	3.5	63
11	**1.0**	**DCE/TFA (2:1)**	**20**	**3.5**	**84(74)**
12	1.0	DCE/TFA (2:1)	20	3.5	69[e]

[a]Reaction conditions: graphite plate anode and cathode (1.5 cm × 1.5 cm × 0.1 cm, J = 8.9 mA/cm^2), Me_4NBF_4 (0.11 M), solvent (9 mL), 25°C, argon. [b]Yields determined by ^{1}H-NMR analysis of the crude reaction mixture using 1,1,2,2-tetrachloroethane as the internal standard. The yield of the isolated product is given within the parentheses. [c]Reaction temperature = 60°C. [d]RVC as electrodes. [e]Bu_4NBF_4 (0.06 M) as the electrolyte.

We previously developed oxidative nitrogenation reactions of simple hydrocarbons with DDQ as the oxidant,[14] which suffers from its toxicity, high cost, and difficulty in the removal of $DDQH_2$ waste. Inspired by the above significant electrochemical C-H amination,[7-12] we therefore tried to investigate the possibility of the electrochemical C-C amination of alkylarenes. This chemistry started by chosing diphenylmethane (**1a**) and 1-azidononane (**2a**) as the model compounds (Table 1). Interestingly, the electrochemical oxidation worked well when graphite plate electrodes were employed as both anode and cathode in the presence of tetramethylammonium tetrafluoroborate (Me_4NBF_4) as the electrolyte, which produced the amination product **3a** in 44-56% (entries 1-2, also see Table S1 in the supporting information). The control experiment without electric current did not afford the product **3a** (entry 3). The reaction using a mixture of 1, 2-dichloroethane (DCE) and trifluoroacetic acid (TFA) as the solvent afforded **3a** in 58% yield (entry 4). The reactions in DCE or DCE/HOAc did not work (entries 5-6). Although the substrate was consumed completely under higher and lower current, the corresponding yields were not improved (52%-48%, entries 7 and 8). No desired product was detected when RVC electrodes were used (entry 9). The yield improved to 84% when the substrate concentration was increased (entry 11). Meanwhile, other electrolytes such as Bu_4NBF_4 did not give better result (69%, entry 12).

Table 2. Electrochemical Oxidative C-C Bond Amination of Alkylarenes.[a]



[a]Standard conditions: see entry 11, Table 1. Yields shown are isolated yields. [b]Bu_4NPF_6 (0.06 M) was used as electrolyte instead of Me_4NBF_4, current density was 25 mA/cm^2. [c]Current density was 30 mA/cm^2.

Then we investigated the protocol using different alkyl benzene substrates under the optimized reaction conditions (Table 2). Diarylmethanes showed good reactivity to afford the corresponding products (**1b-1g**). The aromatic substrates with methyl substitution at different position are competible with this protocol (**1b-1d**). By the selective cleavage of Csp^2-Csp^3 bonds, varieties of diarylmethanes produced different substituted anilines. This transformation also worked well when inert alkyl benzenes were employed as substrates. These substrates afforded the desired N-alkylanilines in moderate to good yields (**1h-1o**). Unfortunately, the current conditions are not efficient to the substrates with strong electron-withdrawing groups.

Interestingly, the chemistry provides a simple approach for ring-opening reactions through selective oxidative C-C bond cleavage at the preferred dibenzylic position. For examples, the substrate dibenzosuberane (**1p**) was efficiently converted into **3p** in 71% yield, which also demonstrated the preferred reactivity in dibenzylic position and the aldehyde by-product of the leaving part of the substrates (Eq. 1). Moreover, **1e** produced the aniline product **3e** in 87% yield with the formation of benzaldehyde **4e** in 71% yield.

Furthermore, the results in Table 3 demonstrate that various alkyl azides were also compatible in this transformation, which make this reaction useful (Table 3). Both primary and secondary azides performed well under the standard conditions (Table 3).

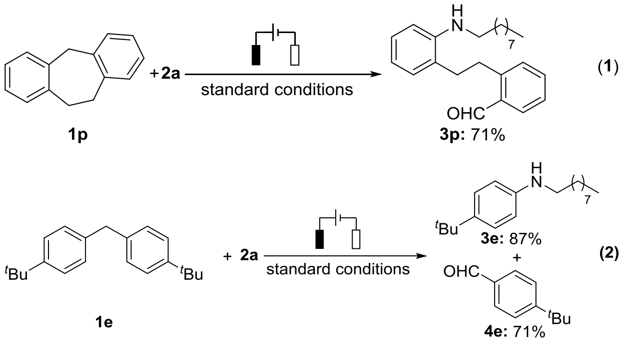
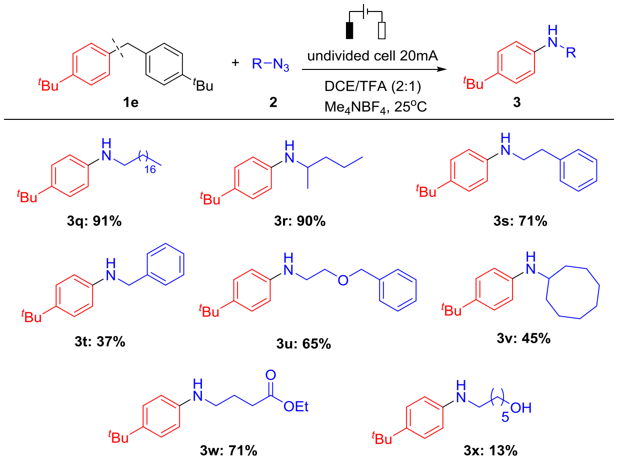


Table 3. Substrate Scope of Different Alkyl Azides [a]



[a]Standard conditions: see entry 11, Table 1. Yields shown are isolated yields.

The results of cyclic voltammetry studies proved that alkyl azide, **2a**, is redox inactive and no obvious oxidative peak was observed with the potential range of 0 to 3.0 V (Figure 1, curve b), whereas, alkyl benzene **1a** exhibits two obvious oxidative peaks at 2.05 V and 2.39 V (*vs* Ag/AgNO$_3$) (Figure 1, curve c), which indicates that **1a** is easier to be oxidized than **2a**. In addition, the irreversible electrochemical behaviour of **1a** discloses that the generated active species from anodic oxidation of **1a** are prone to undergo subsequent chemical reaction(s) (EC process). This is further demonstrated from the CVs of **1a** in the presence of **2a**. For example, the first peak current of **1a** decreased from 19.8 μA to 17.9 μA in the presence of 1 equiv of **2a**.[15] These results demonstrate that the corresponding carbon cation formation with DDQ oxidation could now be replaced by electrochemical oxidation.

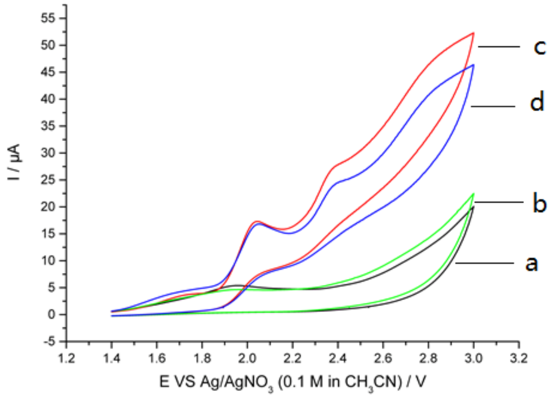
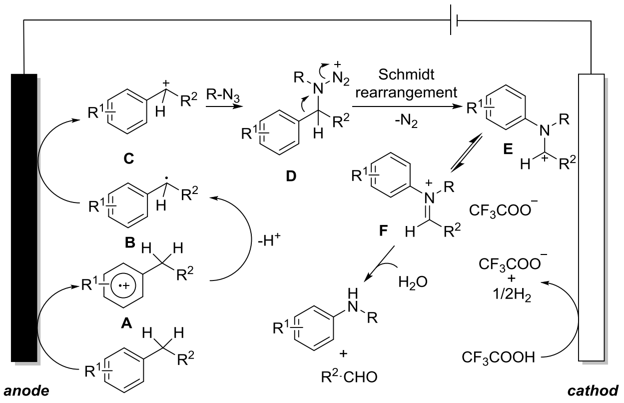


Figure 1. Cyclic voltammograms of **1a** and **2a** in 0.1 M Me$_4$NBF$_4$/DCE:CF$_3$COOH (2:1) using Pt disk working electrode (ϕ 1 mm), Ag wire counter and Ag/AgNO$_3$ (0.1 M in CH$_3$CN) reference electrode at 20 mV/s scan rate. (a) background. (b) **2a** (1 mmol/L). (c) **1a** (1 mmol/L). (d) **1a** + **2a** (1 mmol/L + 1 mmol/L).



Scheme 2. Proposed Mechanism.

On the basis of the cyclic voltammetry studies and the related literature,[16,17] we propose the mechanism of this C-C bond amination process (Scheme 2). First, the substrate is oxidized on the anode, thus generating radical cation **A**. The initially generated radical cation deprotonates to give the benzyl radical **B**, which further undergoes oxidation to form the intermediate cation **C**. Then, the nucleophilic organic azides[18] attack cation **C** to produce the species **D**. Then the intermediate **E** is formed by the Schmidt-type rearrangement[19] of intermediate **D** with the release of dinitrogen gas as the driving force. Next, isomerization and hydrolysis produces *N*-alkylanilines and benzaldehydes.

In summary, we have developed the first electrochemical oxidative C-C amination. The reaction employs a pair of cheap graphite plates as electrodes in an undivided cell without any external catalyst or oxidants. Thus, by avoiding the exogenous stoichiometric oxidants, the protocol is green, sustainable and efficient, and also easy to operate. The anodic generation of carbon cations and their subsequent reactions may be conducive to develop novel electrochemical transformations.

ASSOCIATED CONTENT

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Notes

The authors declare no competing financial interest.

Supporting Information.

Experimental procedures, analytical data for products, NMR spectra of products. The supporting information is available free of charge via the Internet at http://pubs.acs.org.

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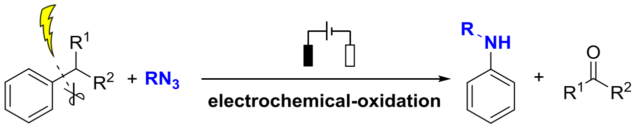

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