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Metal-Free Synthesis

Hydrodehalogenation of Aryl Halides through Direct Electrolysis

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Abstract: A catalyst- and metal-free electrochemical hydrodehalogenation of aryl halides is disclosed. Our reaction by a flexible protocol is operated in an undivided cell equipped with an inexpensive graphite rod anode and cathode. Trialkylamines nBu$_3$N/Et$_3$N behave as effective reductants and hydrogen atom donors for this electrochemical reductive reaction. Various aryl and heteroaryl bromides worked effectively. The typically less reactive aryl chlorides and fluorides can also be smoothly converted. The utility of our method is demonstrated by detoxification of harmful pesticides and hydrodebromination of a dibrominated biphenyl (analogues of flame-retardants) in gram scale.

Hydrodehalogenation of organic halides is an important strategy in functional molecular synthesis.[1] It also allows for detoxification of environmentally hazardous chemicals containing halogen atoms.[2] Numerous methods have been developed for this reductive process that replaces halogen atoms with hydrogen atoms.[3] Representative reductants employed in this process include metals or low-valent metal compounds,[3a] hydrides,[3b–d] hydrogen,[3e] electron-rich organic molecules,[3f] and alcoholate.[3g] These methods, with their own merits and limitations with respect to key measures, such as chemoselectivities and operational costs, are complimentary to each other. There are continuous needs to develop new methods for dehalogenation of organic halides under mild, operationally simple, and cost-effective conditions. Trialkylamines are inexpensive reagents and may behave as effective reductants under suitable activation conditions.[4] For example, Stephenson and König have recently shown that hydrodehalogenation of organic halides can be realized by using trialkylamines as the terminal reductants and hydrogen atom donors (Figure 1 a).[5] In their approaches, metal complexes[5a] or organic sensitizers[5b] are used as the photocatalysts and the radical processes are enabled by visible light.

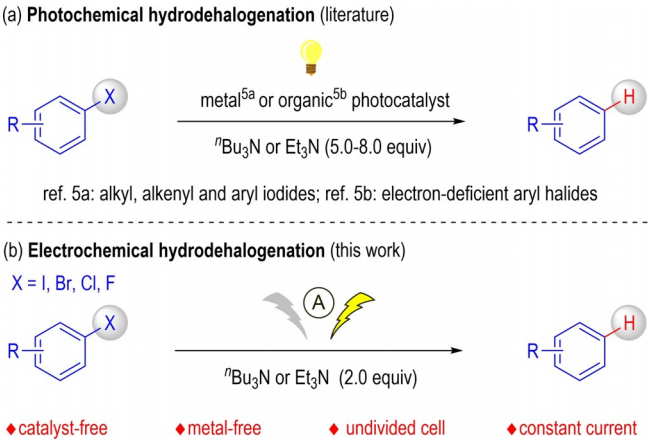

Figure 1. Hydrodehalogenation of aryl halides.

Organic electrosynthesis has been recognized as a versatile and environmentally friendly approach for redox transformations.[6] It has also been well-documented that amines can undergo single-electron-transfer processes and oxidations under electrolysis conditions. This electrochemical oxidation process has been mainly explored to convert amines to iminium intermediates for further addition reactions.[7] Herein we disclose a method for the dehalogenation of organic halides under electrochemical conditions with amines as the terminal reductants and hydrogen atom donors (Figure 1 b). Our reaction is performed in an undivided cell equipped with graphite rod electrodes. Catalysts and metals are not required, and the reductive processes are enabled by electric currents. It is worth noting that in previous electrochemical hydrodehalogenation methods with undivided cells,[8] metals were used as scarified anodes and separate hydrogen atom providers were needed.[9]

The 4-phenoxylbromobenzene **1 a** was chosen as the model substrate to evaluate the reaction conditions for this hydrodehalogenative process (Table 1). We first examined the reaction in an undivided cell equipped with a reticulated vitreous carbon (RVC) anode and cathode. The proposed product **2 a** was not detected when using $LiClO_4$ as the electrolyte and CH_3CN as the solvent under a 10 mA constant current for 3.3 h (Table 1, entry 1). Replacing $LiClO_4$ with Me_4NBF_4 or nBu$_4$NBF$_4$ led to **2 a** with about 10 or 29% yield, respectively (entries 2,3).

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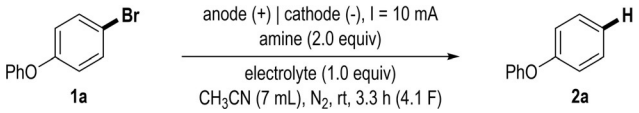
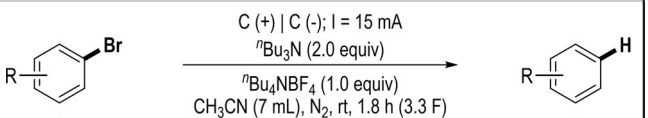
Table 1. Optimization of the reaction conditions.[a]

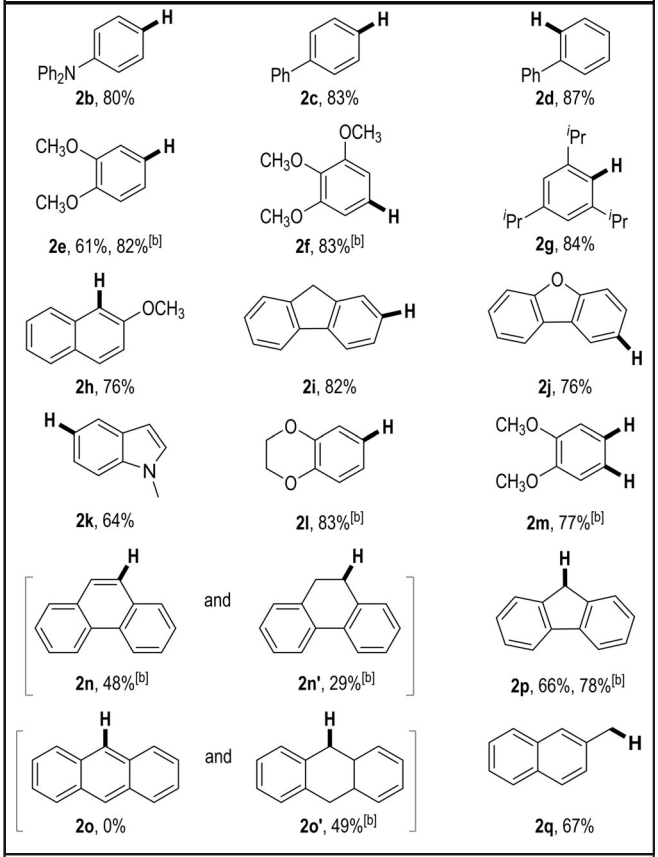


Entry	Amine	Electrolyte	Anode\cathode	**2a** Yield [%][b]
1	none	$LiClO_4$	RVC\RVC	n.d.
2	none	Me_4NBF_4	RVC\RVC	≈10
3	none	nBu_4NBF_4	RVC\RVC	29
4	Et_3N	$LiClO_4$	RVC\RVC	13
5	Et_3N	Me_4NBF_4	RVC\RVC	31
6	Et_3N	nBu_4NBF_4	RVC\RVC	83
7	Et_3N	nBu_4NPF_6	RVC\RVC	83
8	Et_3N	nBu_4NClO_4	RVC\RVC	75
9	Et_3N	nBu_4NBF_4	Pt\Pt	70
10	Et_3N	nBu_4NBF_4	C\C	85
11	nBu_3N	nBu_4NBF_4	C\C	86
12[c]	nBu_3N	nBu_4NBF_4	C\C	90
13[d]	nBu_3N	nBu_4NBF_4	–	n.d.

[a] Reaction conditions: **1a** (0.3 mmol), amine (0.6 mmol, 2.0 equiv), electrolyte (0.3 mmol, 1.0 equiv), CH_3CN (7.0 mL), room temperature, N_2, 3.3 h (4.1 F). [b] Isolated yields. [c] Constant current = 15 mA, 1.8 h (3.3 F). [d] No externally applied current. RVC = Reticulated Vitreous Carbon (1.0 × 1.0 × 1.0 cm), Pt = platinum plate (1.0 × 1.0 × 0.1 cm), C = graphite rod (Φ = 6 mm), n.d. = no detected.

Table 2. Substrate scope of the debromination.[a]





[a] Reaction conditions: Method A: graphite rod anode (Φ = 6 mm), graphite rod cathode (Φ = 6 mm), undivided cell, constant current = 15 mA, **1** (0.3 mmol), nBu_3N (0.6 mmol, 2.0 equiv), nBu_4NBF_4 (0.3 mmol, 1.0 equiv), CH_3CN (7.0 mL), room temperature, N_2, 1.8 h (3.3 F). [b] Method B: RVC anode (1.0 cm × 1.0 cm × 1.0 cm), RVC cathode (1.0 cm × 1.0 cm × 1.0 cm), undivided cell, constant current = 15 mA, **1** (0.3 mmol), Et_3N (0.6 mmol, 2.0 equiv), nBu_4NBF_4 (0.3 mmol, 1.0 equiv), CH_3CN/THF (6.0/1.0 mL), room temperature, N_2, 4.4 h (8.1 F).

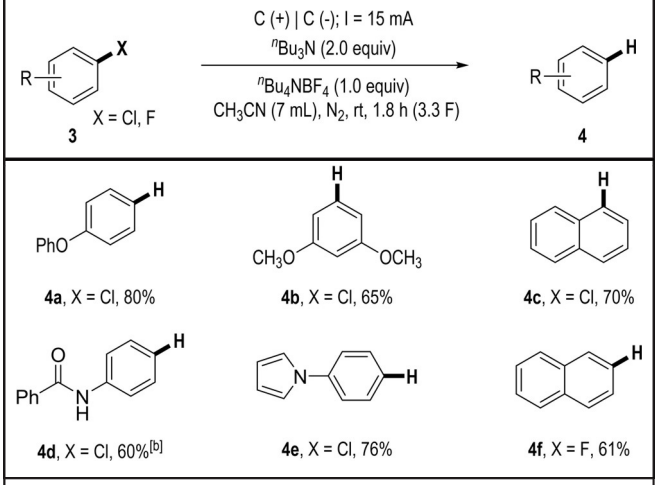
Further optimizations did not lead to obvious improvements on the reaction yields. We suspected that the trace trialkyl amines generated from the ammonium electrolytes under electrolysis[10] might behave as reductants and hydrogen atom providers for the formation of **2a**. We then added Et_3N as a potential reductant to the reaction mixture and found that **2a** was formed in 13% yield with $LiClO_4$ used as the electrolyte (entry 4). In the presence of Et_3N, switching the electrolyte from $LiClO_4$ to Me_4NBF_4 led to **2a** with a significantly improved yield (31% yield, entry 5). The combination of Et_3N as the reductant and nBu_4NBF_4 as the electrolyte led to **2a** with 83% yield (entry 6). Other electrolytes containing different anions have little effect on the formation of the product **2a** (entries 7,8). The yield was decreased to 70% when using platinum plate as the anode and cathode (entry 9), but it could be slightly increased when using the cheap graphite rod as the anode and cathode (entry 10). nBu_3N showed a similar reactivity to that of Et_3N (entry 11), and a slightly increased yield could be obtained under a 15 mA constant current for 1.8 h (entry 12). It is worth to noting that no product **2a** could be detected without application of an external current (entry 13).

With the optimized electrochemical reaction conditions in hand (Table 1, entry 12), we then examined the substrate scope for this transformation using various substituted aryl- or alkyl-bromides (Table 2). Substituents could be installed at each position of the benzene monobromides, with all the products afforded in moderate to good isolated yields (**2b**–**g**,**l**). Strong electron-donating substituents generally give the products in lower yields, but this obstacle could be overcome through a slight modification of the reaction conditions (**2e**,**f**,**l**,**m**). Unfortunately, aryl bromides with electron-deficient substituents (–COOEt, –CN, $-NO_2$) were not compatible under these electrochemical conditions. Only trace products can be detected by GCMS, without any other byproducts and remaining substrates. Multicyclic fused (hetero-) aromatic bromides also work well in this process (**2h**--**k**). Notably, both bromine atoms could be replaced with hydrogen atoms when aryl dibromides were used as the reactants (**2m**). The debromination product could undergo further reductions when using 9-bromophenanthrene (product **2n** and **2n′**) and 9-bromoanthracene (product **2o** and **2o′**) as the substrates. To our delight, substituted benzyl bromides could also undergo the hydrodehalogenative process through this protocol, with the corresponding products afforded in moderate isolated yields (**2p**,**q**).

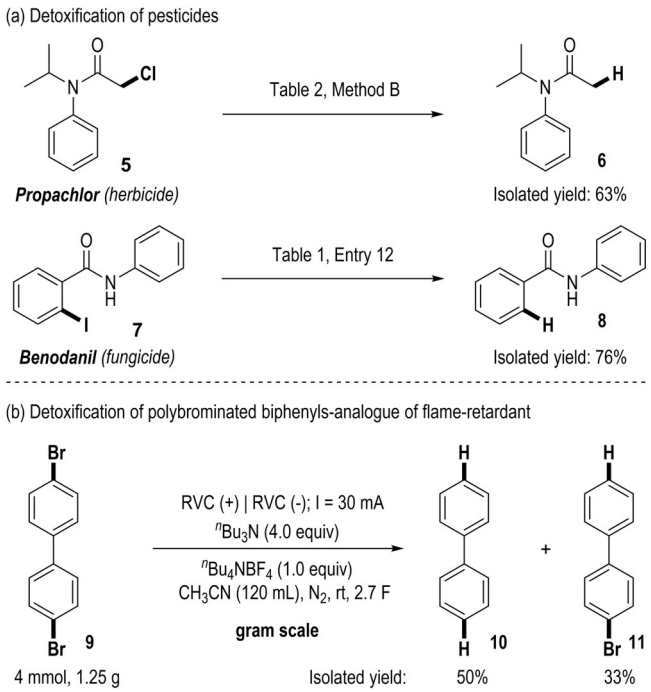
Aryl chlorides and aryl fluorides have been challenging substrates in the hydrodehalogenative reactions. To date, few successful examples have been reported.[3i, 5b, 11] We were delighted

to find that with aryl chlorides or fluorides used as the reaction substrates, this hydrodechlorination process occurred smoothly under the current optimized reaction conditions (Table 3). For example, electron-rich chlorobenzenes bearing various substituents could be effectively reduced to give the substituted benzenes in moderate to good yields (**4a**,**b**,**d**,**e**). Chloro- and fluoro- naphthalenes could also be reduced through this electrochemical transformation, with the naphthalenes (**4c**,**f**) afforded as the final products in moderate yields.

Table 3. Substrate scope of the dechlorination and defluorination.[a]



[a] Reaction conditions: graphite rod anode ($\Phi = 6$ mm), graphite rod cathode ($\Phi = 6$ mm), undivided cell, constant current = 15 mA, **3** (0.3 mmol), nBu$_3$N (0.6 mmol, 2.0 equiv), nBu$_4$NBF$_4$ (0.3 mmol, 1.0 equiv), CH$_3$CN (7.0 mL), room temperature, N$_2$, 1.8 h (3.3 F). [b] Constant current = 20 mA, 3.3 h (8.1 F).



Scheme 1. Applications of our hydrodehalogenation methods.

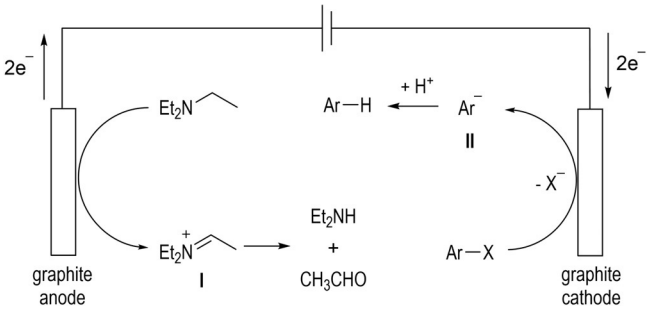


Figure 2. Proposed pathway.

Halogen atoms are widely present in pesticides and chemical materials.[12] These organic halide-containing residuals are toxic, harmful to human health and the ecosystem, and are very difficult to degradate.[13] Dehalogenation of these molecules can reduce their toxicity and accelerate their degradation process. To further demonstrate the potential utilities of this method, we performed hydrodehylogenation reactions with several pesticides and analogues of flame-retardant materials (Scheme 1). For example, Propachlor (herbicide, **5**) and Benodanil (fungicide, **7**) could be smoothly converted to the corresponding non-halogen-containing products through this newly developed electrochemical protocol (Scheme 1 a). 4,4′-Dibromo-1,1′-biphenyl (**9**), an anologue of the polybrominated biphenyls (PBBs) that have been widely used as flame-retardant materials,[14] could also be smoothly reduced through this electrochemical transformation in gram scale, with the fully debrominative product **10** and the single debrominative product **11** afforded in 50 and 33 % yields, respectively (Scheme 1 b).

This catalyst- and metal-free hydrodehalogenative reaction is proposed to go through a two-electron transfer process (Figure 2). A two-electron anodic oxidation of Et$_3$N provides the iminium **I** that may upon hydrolysis lead to diethylamine and acetaldehyde. On the other hand, a two-electron cathodic reduction of aryl halide substrate Ar–X provides the aryl anion **II**, which is then protonated by acetonitrile or trialkylamine to give the desired hydrodehalogenative aryl product (Ar–H).

In summary, we have developed an electrochemical approach for the hydrodehalogenation of organic halides. Our reaction used trialkylamine as the reductant and a hydrogen atom provider under electrochemical conditions. The reaction was carried out in an undivided cell equipped with the inexpensive graphite rod anode and cathode. No catalysts or metals are needed for this transformation. Substituted aryl or alkyl halides bearing different halogen atoms worked well in this hydrodehalogenation process. This method could be used for the detoxification and degradation of harmful organic halides existing in pesticides and flame-retardant materials. The development of efficient and inexpensive electrochemical reactions, including catalytic asymmetric reactions and post-synthetic modification of medicines and pesticides, are currently in progress in our laboratories.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: electrochemistry · hydrodehalogenation · metal-free synthesis · organic halides · trialkylamines

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