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Hydrodehalogenation of Aryl Halides through Direct Electrolysis

Jie Ke,[†] Hongling Wang,[†] Liejin Zhou, Chengli Mou, Jingjie Zhang, Lutai Pan,* and Yonggui Robin Chi*

Abstract: A catalyst- and metal-free electrochemical hydrodehalogenation of aryl halides is disclosed. Our reaction via a flexible protocol is operated in an undivided cell equipped with inexpensive graphite rod anode and cathode. Trialkylamines ^tBu₃N or Et₃N 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 via detoxification of harmful pesticides and hydrodebromination of a dibrominated biphenyl (analogs of flame-retardants) in gram scale.

Hydrodehalogenation of organic halides is an important strategy in functional molecule 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 halogens 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 respects to key measures such as chemo-selectivities 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 1a).^[5] In their approaches, metal complexes^[5a] or organic sensitizers^[5b] are used as the photocatalysts and the radical processes are enabled by visible lights.

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] Here we disclose a method for dehalogenation of organic halides under electrochemical conditions with amines as the terminal

reductants and hydrogen atom donors (Figure 1b). 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 to note that in previous electrochemical hydrodehalogenation methods with undivided cells,^[8] metals were used as sacrificed anodes and separate hydrogen atom providers were needed.^[9]

(a) Photochemical hydrodehalogenation (literature)

(b) Electrochemical hydrodehalogenation (this work)

Figure 1. Hydrodehalogenation of Aryl Halides.

The 4-phenoxybromobenzene **1a** 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 **2a** was not detected when using LiClO₄ as the electrolyte and CH₃CN as the solvent under 10 mA constant current for 3.3 h (entry 1). Replacing LiClO₄ with Me₄NBF₄ or ^tBu₄NBF₄ led to **2a** with about 10% or 29% yield respectively (entries 2-3). 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 Et₃N as a potential reductant to the reaction mixture and found that **2a** was formed in 13% yield with LiClO₄ used as the electrolyte (entry 4). In the presence of Et₃N, switching the electrolyte from LiClO₄ to Me₄NBF₄ led to **2a** with a significantly improved yield (31% yield, entry 5). The combination of Et₃N as the reductant and ^tBu₄NBF₄ as the electrolyte led to **2a** with 83% yield (entry 6). Other electrolytes containing different anion 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). ^tBu₃N showed a similar reactivity as that of Et₃N (entry 11), and a slightly increased yield could be obtained under 15 mA constant current for 1.8 h (entry 12). It is worth to note that no

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product **2a** could be detected without an external current applied (entry 13).

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 ₄ NBF ₄	RVC \ RVC	~10
3	none	ⁿ Bu ₄ NBF ₄	RVC \ RVC	29
4	Et ₃ N	LiClO ₄	RVC \ RVC	13
5	Et ₃ N	Me ₄ NBF ₄	RVC \ RVC	31
6	Et ₃ N	ⁿ Bu ₄ NBF ₄	RVC \ RVC	83
7	Et ₃ N	ⁿ Bu ₄ NPF ₆	RVC \ RVC	83
8	Et ₃ N	ⁿ Bu ₄ NClO ₄	RVC \ RVC	75
9	Et ₃ N	ⁿ Bu ₄ NBF ₄	Pt \ Pt	70
10	Et ₃ N	ⁿ Bu ₄ NBF ₄	C \ C	85
11	ⁿ Bu ₃ N	ⁿ Bu ₄ NBF ₄	C \ C	86
12 ^[c]	ⁿ Bu ₃ N	ⁿ Bu ₄ NBF ₄	C \ C	90
13 ^[d]	ⁿ Bu ₃ N	ⁿ Bu ₄ NBF ₄	—	n.d.

[a] Reaction conditions: **1a** (0.3 mmol), amine (0.6 mmol, 2.0 equiv), electrolyte (0.3 mmol, 1.0 equiv), CH₃CN (7.0 mL), room temperature, N₂, 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 cm × 1.0 cm × 1.0 cm), Pt = Platinum Plate (1.0 cm × 1.0 cm × 0.1 cm), C = Graphite Rod (Φ = 6 mm), n.d. = no detected.

With the optimized electrochemical reaction conditions at 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 on each position of the benzene mono-bromides, with all the products afforded in moderate to good isolated yields (**2b-2g, 2l**). 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, 2f, 2l, 2m**). Unfortunately, aryl bromides with electron-deficient substituents (-COOEt, -CN, -NO₂) were not compatible in this electrochemical condition. Only trace products can be detected by GC-MS, without any other by-products and remaining substrates. Multi-cyclic fused (hetero-) aromatic bromides also work well in this process (**2h-2k**). Notably, both of 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, 2q**).

Table 2. Substrate Scope of the Debromination.^[a]

1		2

[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), ⁿBu₃N (0.6 mmol, 2.0 equiv), ⁿBu₄NBF₄ (0.3 mmol, 1.0 equiv), CH₃CN (7.0 mL), room temperature, N₂, 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), Et₃N (0.6 mmol, 2.0 equiv), ⁿBu₄NBF₄ (0.3 mmol, 1.0 equiv), CH₃CN/THF (6.0 mL/1.0 mL), room temperature, N₂, 4.4 h (8.1 F).

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-4b, 4d-4e**). Chloro- and fluoro- naphthalenes could also be reduced through this

electrochemical transformation, with the naphthalenes (**4c**, **4f**) afforded as the final products in moderate yields.

Table 3. Substrate Scope of the Dechlorination and Defluorination.^[a]

[a] Reaction conditions: graphite rod anode ($\Phi = 6 \text{ mm}$), graphite rod cathode ($\Phi = 6 \text{ mm}$), undivided cell, constant current = 15 mA, **3** (0.3 mmol), $^t\text{Bu}_3\text{N}$ (0.6 mmol, 2.0 equiv), $^t\text{Bu}_4\text{NBF}_4$ (0.3 mmol, 1.0 equiv), CH_3CN (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.

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 degrade.^[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 the hydrodehydrogenation 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 corresponding non-halogen-containing products through this newly developed electrochemical protocol (Scheme 1a). 4,4'-Dibromo-1,1'-biphenyl (**9**), an analogue 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 scales, with the fully debrominative product **10** and the single debrominative product **11** afforded in 50% yield and 33% yield respectively (Scheme 1b).

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_3N 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).

Figure 2. Proposed Pathway.

In summary, we have developed an electrochemical approach for the hydrodehalogenation of organic halides. Our reaction used trialkylamine as the reductant and 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 existed 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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Keywords: electrochemistry • hydrodehalogenation • trialkylamines • organic halides • metal-free

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Layout 2:

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Electrochemical reduction: A catalyst- and metal-free electrochemical hydrodehalogenation of aryl halides is disclosed. Aryl halides with bearing different halogen atoms or different substituents were well tolerated.

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