Visible-Light-Induced, Base-Promoted Transition-Metal-Free Dehalogenation of Aryl Fluorides, Chlorides, Bromides, and Iodides

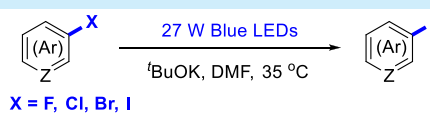Ting-Hui Ding, Jian-Ping Qu,* and Yan-Biao Kang*

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ABSTRACT: We report a simple and efficient visible-light-induced transition-metal-free hydrogenation of aryl halides. The combined visible light and base system is used to initiate the desired radical-mediated hydrogenation. A variety of aryl fluorides, chlorides, bromides, and iodides could be reduced to the corresponding (hetero)arenes with excellent yields under mild conditions. Various functional groups and other heterocyclic compounds are tolerated.
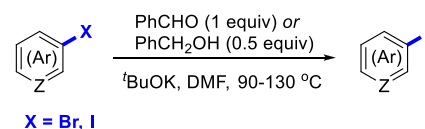
$$(Ar)Z-X \xrightarrow[{}^{t}BuOK, DMF, 35\ ^{o}C]{27\ W\ Blue\ LEDs} (Ar)Z-H$$

X = F, Cl, Br, I

- Visible-light-promoted C-X (X = F, Cl, Br, I) bond cleavage
- Mild conditions • Without the use of extra reducing reagents
- Non-involvement of transition metal or photoredox catalysts
- Readily accessible substrates with broad scopes

Hydrodehalogenation is an important organic reaction[1] that could remove the halogen from organic halides which are not only hazardous to the environment but also health risks.[2] The development of mild and versatile dehalogenation approaches has then attracted considerable interest. Traditional radical processes have been broadly used for dehalogenation, but stoichiometric reagents such as Bu₃SnH and SmI₂, which might cause potential environmental or health risks, are normally involved.[3] Other dehalogenations of aryl halides using transition metal reagents,[4] transition metal photocatalysts,[5] or organic photocatalysts[6] have also been known. Strong base-promoted transition-metal-free dehalogenations of aryl chlorides, bromides, or iodides have been reported albeit with the usage of a large excess of alcohols as hydrogen sources or toxic reagent.[7,8] Considering the environmental sustainability, the development of an efficient and practical expensive transition-metal-free and toxic reagent-free process for dehalogenation is highly desired.
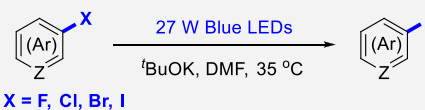
Solar energy holds an enormous potential as a clean and economical energy source, and light excitation could induce chemical reactions which are unavailable by conventional methods. Learning from natural photosynthesis, a variety of artificial photosynthetic processes have been developed.[9] Photoinduced catalyst-free reductions of aryl halides have also been known by using isopropanol, hypophosphorous acid, tristrimethylsilylsilane, borohydrides, or trimethylamine as reducing reagents.[10] Recently, we developed a transition-metal- and catalyst-free dehalogenation of aryl bromides and iodides, in which either BnOH or PhCHO was used as a hydrogen source in the presence of base and DMF, for the first time.[8] A variety of aryl bromides and iodides could be reduced in excellent yields. However, elevated temperature (90−130 °C) is necessary for radical initiation in most cases. In addition, dehalogenations of the corresponding aryl chlorides and fluorides did not occur under the standard reaction conditions. (Scheme 1, top).

Scheme 1. ᵗBuOK-Promoted Dehalogenation of Aryl Halides

Previous Work: TM-free dehalogenation using aldehyde or alcohol as hydrogen source

$$(Ar)Z-X \xrightarrow[{}^{t}BuOK, DMF, 90\text{-}130\ ^{o}C]{PhCHO\ (1\ equiv)\ or\ PhCH_2OH\ (0.5\ equiv)} (Ar)Z-H$$

X = Br, I

This work: Visible-light induced dehalogenation of aryl halides

$$(Ar)Z-X \xrightarrow[{}^{t}BuOK, DMF, 35\ ^{o}C]{27\ W\ Blue\ LEDs} (Ar)Z-H$$

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- Visible-light-promoted C-X (X = F, Cl, Br, I) bond cleavage
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As part of our ongoing research interest in developing practical and efficient dehalogenation of aryl halides, we envisaged that the combination of visible-light irradiation and a base system could be used to initiate the desired radical-mediated hydrogenation of aryl halides, and we found that a variety of aryl fluorides, chlorides, bromides, and iodides could be reduced to the corresponding (hetero)arenes under the

A

irradiation of blue LED with excellent yields under mild conditions without the involvement of any transition metal reagents or organic dyes. Various functional groups and other heterocyclic compounds are tolerated (Scheme 1, bottom). Herein, we report our results on visible-light-induced transition-metal-free dehalogenation of aryl fluorides, chlorides, bromides, and iodides in detail.

First, the reaction conditions were investigated using the dechlorination of 4-chloro-1,1′-biphenyl 1a as a model reaction (Table 1). When the reaction was performed in the presence of

Table 1. Reaction Conditions[a]

| entry	x	light source	T (°C)	time (h)	2a (%)[b]	1a (%)[b]
1	3	blue LED	35	10	43	51
2	3	_[c]	35	10	–	39
3	3	_[c]	90	10	19	16
4	3	blue LED	35	24	60	40
5	4	blue LED	35	24	87	13
6	5	blue LED	35	24	96	–
7[d]	5	blue LED	35	24	–	100

[a]Conditions: 1a (0.5 mmol), [t]BuOK (2.5 mmol), dry DMF (4 mL), 35 °C, under irradiation of blue LED (405 nm, 27 W) under the atmosphere of argon. [b]Yields were determined by ^{1}H NMR analysis of crude products using nitromethane as an internal standard. [c]No light. [d]Tetrahydrofuran, benzonitrile, or octane was used as the solvent.

3 equiv of [t]BuOK in DMF under the irradiation of blue LED (405 nm, 27 W), 43% of dechlorinated product 2a was obtained with 51% of 1a recovered (entry 1). When dechlorination of 1a was performed in the absence of blue LED irradiation, no 2a was generated (entry 2). Elevated temperature without light gave only 19% of 2a (entry 3). Prolonging the reaction time or increasing the amount of [t]BuOK resulted in the improvement in yield of 2a (entries 4–6). Other solvent such as tetrahydrofuran, benzonitrile, or octane was used as the solvent but gave no desired product (entry 7). Reaction in the presence of MeOK instead of [t]BuOK was also investigated, affording 2a in 11% yield with 89% recovery of 1a. These indicate that both [t]BuOK and DMF are necessary for this reaction. The reaction conditions in Table 1 (entry 6) were then selected as the standard conditions.

With the optimized reaction conditions in hand, we first explored the scope of aryl chlorides (Scheme 2). Biphenyl (1a), naphthyl (1b,c), as well as anthracenyl (1d) chlorides reacted smoothly under the standard conditions, providing the corresponding reduction products in 70–97% yields. Moreover, aryl halides bearing either electron-withdrawing (1e–i) or electron-donating (1j–k) groups proved to be competent substrates affording the corresponding arenes in 51–100% yields. Chlorinated heteroarenes such as chlorodibenzofuran (1l), chloroindole (1m–n), chlorocarbazole (1o), chloroquinoline (1p–s), chloroisoquinoline (1t–v), as well as chloromethylquinoline (1w) were also tolerated.

Hydrodefluorination of organic fluorides is not only a useful method for detoxification of environmentally hazardous chemicals containing halogen atoms but also an important strategy for functionalizing molecules especially in drug discovery. Although the development of hydrodefluorination

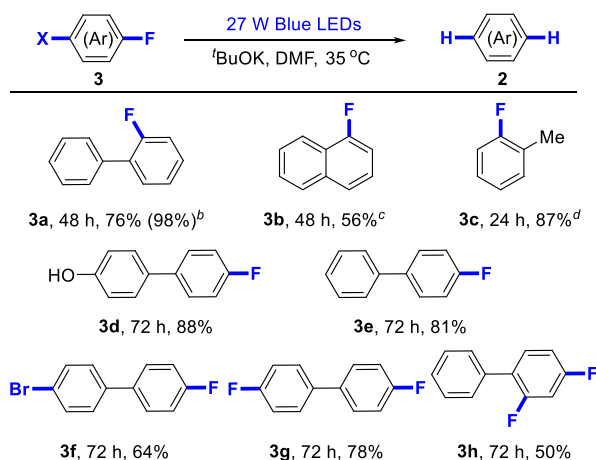**Scheme 2. Reaction Scope of Aryl Chlorides[a]**
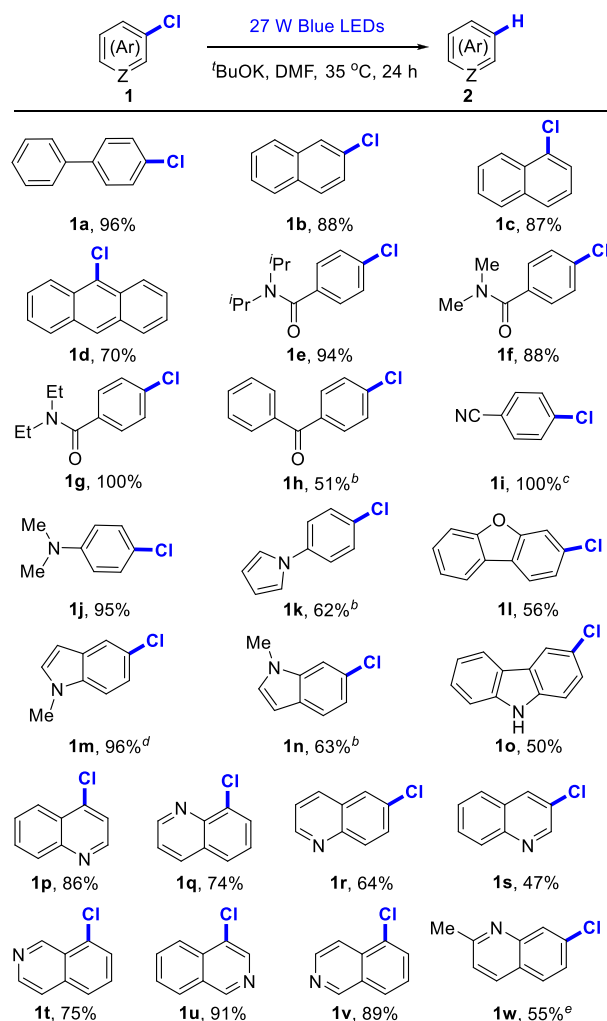
[a]Conditions: 1 (0.5 mmol), [t]BuOK (2.5 mmol), dry DMF (4 mL), 35 °C, under irradiation of blue LED (405 nm, 27 W) under the atmosphere of argon, isolated yields. [b]10 mL of DMF. [c]1.5 mmol of [t]BuOK, 6 mL of DMF. [d]DMSO as a solvent. [e]1.0 mmol of [t]BuOK, 6 mL of DMF.

grows rapidly,[11] light-induced hydrodefluorination of aryl fluoride remains rare. Wu et al. reported UV light-induced reduction of aryl halides with excess trimethylamine, and one example of hydrodefluorination of aryl fluoride is reported with 68% yield.[10a] Fagnoni and co-workers reported that electron-rich aryl fluorides could be converted to the corresponding electron-rich arenes by UV irradiation either in neat isopropanol or in an acetonitrile solution of hypophosphorous acid.[10e] When aryl fluorides 3a–e were subjected to the standard conditions stated in Table 1 (entry 6), hydrodefluorination proceeded smoothly to afford the corresponding arenes in excellent yields (Scheme 3). This result indicates that this method might be useful for both organic synthesis and pharmacy. Hydrodehalogenation of aryl halides bearing two halogens 3f–h was also investigated. To our delight, with prolonged reaction time both halides on the aryl halides could be reduced effectively, yielding the corresponding arenes 2 in good yields. This demonstrated the utility of this method.

To further investigate the scope of this system, aryl halides bearing bromides 4 and iodides 5 were also tested, and the
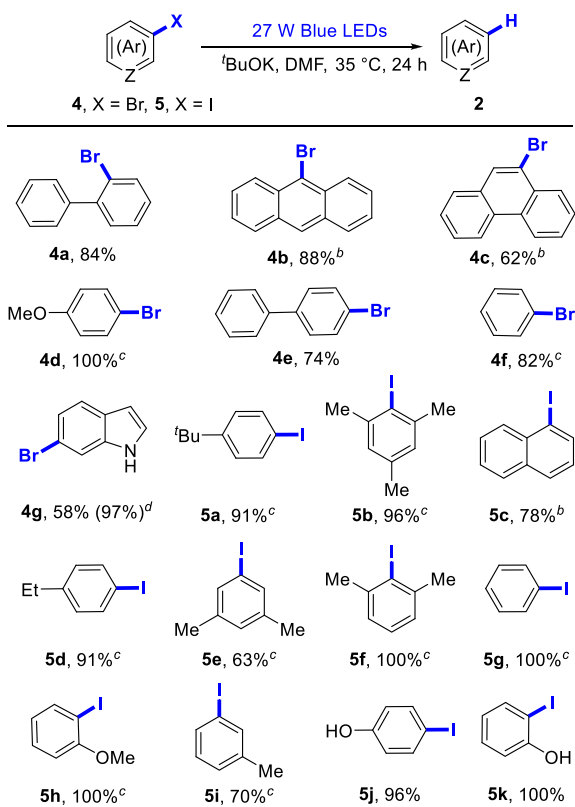
Scheme 3. Reaction Scope of Aryl Fluorides and Aryl Halides Bearing Two Halogens[a]

3a, 48 h, 76% (98%)[b]   3b, 48 h, 56%[c]   3c, 24 h, 87%[d]

3d, 72 h, 88%   3e, 72 h, 81%

3f, 72 h, 64%   3g, 72 h, 78%   3h, 72 h, 50%

[a]Conditions: 3 (0.25 mmol), [t]BuOK (1.25 mmol), dry DMF (5 mL), 35 °C, under irradiation of blue LED (405 nm, 27 W) under the atmosphere of argon, isolated yields. [b]Yield based on the recovered starting materials. [c]A mixture of DMF (2.5 mL) and DMSO (2.5 mL) was used as solvent. [d]Yield was determined by GC analysis.

results were summarized in Scheme 4. To our delight, both aryl bromides 4a−g and aryl iodides 5a−k could be reduced efficiently with excellent yields. This further demonstrated that
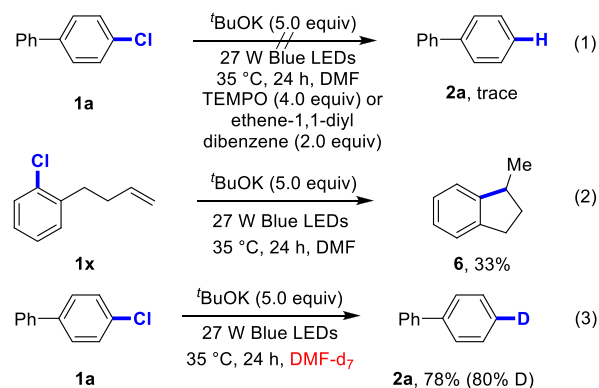
Scheme 4. Reaction Scope of Aryl Bromides and Iodides[a]

4, X = Br, 5, X = I

4a, 84%   4b, 88%[b]   4c, 62%[b]

4d, 100%[c]   4e, 74%   4f, 82%[c]

4g, 58% (97%)[d]   5a, 91%[c]   5b, 96%[c]   5c, 78%[b]

5d, 91%[c]   5e, 63%[c]   5f, 100%[c]   5g, 100%[c]

5h, 100%[c]   5i, 70%[c]   5j, 96%   5k, 100%

[a]Conditions: 4 or 5 (0.5 mmol), [t]BuOK (2.5 mmol), dry DMF (4 mL), 35 °C, under irradiation of blue LED (405 nm, 27 W) under the atmosphere of argon, isolated yields. [b]1.0 mmol of [t]BuOK, 1 mL of DMF, 2 h. [c]Yield was determined by GC. [d]Yield based on the recovered starting materials.

this transition-metal-free and toxic-reagent-free method is an efficient and versatile method for dehalogenation of aryl halides under mild conditions.

To explore the mechanism of this dehalogenation reaction, control experiments have been conducted. Using 1 equiv of a typical radical scavenger TEMPO under the standard conditions lowered the yield of 2a. Increasing the amount of the TEMPO resulted in the decreased yield of 2a, and the reaction was inhibited after the introduction of TEMPO (Scheme 5, eq 1). The radical trapping experiment using 1,1-

Scheme 5. Control and Deuterium-Labeling Experiments

[t]BuOK (5.0 equiv)
27 W Blue LEDs
35 °C, 24 h, DMF
TEMPO (4.0 equiv) or ethene-1,1-diyl dibenzene (2.0 equiv)
2a, trace   (1)

[t]BuOK (5.0 equiv)
27 W Blue LEDs
35 °C, 24 h, DMF
6, 33%   (2)

[t]BuOK (5.0 equiv)
27 W Blue LEDs
35 °C, 24 h, DMF-d[7]
2a, 78% (80% D)   (3)

diphenylethylene under the standard reaction conditions was also performed, and the model reaction was completely inhibited. The radical clock experiment of 1x gave the cyclization product 6 in 33% yield (eq 2). Both radical trapping experiments and the radical clock experiment suggest a possible radical pathway for this dehalogenation reaction. A deuterium-labeling experiment was then performed using DMF-d_7 as solvent. Dehalogenation product 2a was obtained with >80% deuterium incorporation, indicating that DMF is the hydrogen source (eq 3).

On the basis of radical trapping experiments as well as deuteration experiments, a possible reaction mechanism is proposed and demonstrated in Scheme 6. The reaction is initialized by the donation of electron from deprotonated DMF A to aryl halide 1 promoted by visible light, forming radical anion C and radical B. Aryl radical D seizes a hydrogen atom

Scheme 6. Plausible Mechanism
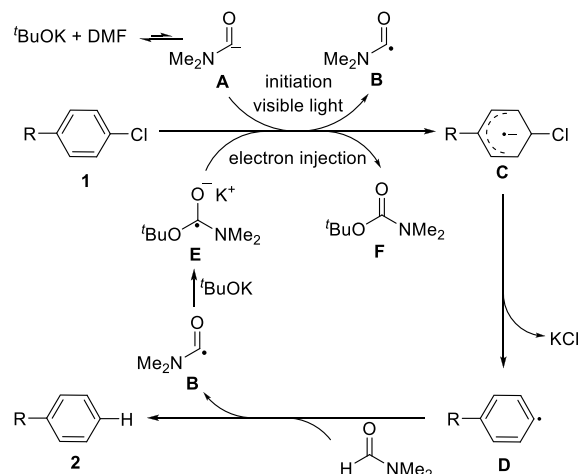
from DMF to afford product **2** with releasing **B**, which is attacked by ^{t}BuOK to afford radical anion **E**. **E** thus becomes the major electron donor for further reaction.

We have developed a simple and efficient visible-induced transition-metal-free hydrogenation of aryl halides. The combined visible light and base system is used to initiate the desired radical-mediated hydrogenation. A variety of aryl fluorides, chlorides, bromides, and iodides could be reduced to the corresponding (hetero)arenes with excellent yields under mild conditions. Various functional groups and other heterocyclic compounds are tolerated.

■ ASSOCIATED CONTENT

ⓈⒾ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c00827.

> Experimental procedures, full analysis data for compounds, and copies of NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

Jian-Ping Qu − *Institute of Advanced Synthesis, School of Chemistry and Molecular Engineering, Nanjing Tech University, Nanjing 211816, China;* ⓞ orcid.org/0000-0002-5002-5594; Email: ias_jpqu@njtech.edu.cn

Yan-Biao Kang − *Department of Chemistry, University of Science and Technology of China, Hefei, Anhui 230026, China;* ⓞ orcid.org/0000-0002-7537-4627; Email: ybkang@ustc.edu.cn

Author

Ting-Hui Ding − *Department of Chemistry, University of Science and Technology of China, Hefei, Anhui 230026, China*

Complete contact information is available at:
https://pubs.acs.org/10.1021/acs.orglett.0c00827

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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