

## Research Article

# Photoinduced C-C Cross-Coupling of Aryl Chlorides and Inert Arenes

Lele Wang, Wenzhao Qiu, Hongge Shao, and Rusheng Yuan

State Key Laboratory of Photocatalysis on Energy and Environment, College of Chemistry, Fuzhou University, Fuzhou 350002, China

Correspondence should be addressed to Rusheng Yuan; [yuanrs@fzu.edu.cn](mailto:yuanrs@fzu.edu.cn)

Received 16 February 2016; Revised 27 March 2016; Accepted 7 April 2016

Academic Editor: Leonardo Palmisano

Copyright © 2016 Lele Wang et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Here we report a facile, efficient, and catalyst-free method to realize C-C cross-coupling of aryl chlorides and inert arenes under UV light irradiation. The aryl radical upon homolytic cleavage of C-Cl bond initiated the nucleophilic substitution reaction with inert arenes to give biaryl products. This mild reaction mode can also be applied to other synthetic reactions, such as the construction of C-N bonds and trifluoromethylated compounds.

## 1. Introduction

The biaryl scaffolds are privileged constituents of natural products, pharmaceuticals, agrochemicals, dyes, and polymers [1]. Transition-metal-catalyzed direct arylation of aromatic C-H bonds has been extensively developed as a valuable and efficient alternative to traditional cross-couplings in the construction of biaryl compounds [2–7]. However, these processes also suffered significant problems such as high economic cost and the presence of transition-metal impurities in the final products. This gives rise to the development of catalyst-free method for constructing biaryls, in which severe experimental conditions must be employed, such as the use of a base and a high temperature [8–15]. In view of the extensive applications of biaryl intermediates in pharmaceuticals, dyestuff, and perfume, the development of efficient and catalyst-free C-C coupling methods will gain more and more attention because most catalytic methods involve the use of toxic/polluting reagents and the residues must be eliminated from the final products.

In the C-C coupling reactions of aryl halide and inert arenes, the cleavage of C-halogen bond is always an essential step; thus there has been growing interest in achieving this by an environmentally friendly and green method [16–19]. In this sense, photochemical reactions are more favorable, because activation can be performed by the absorption of a photon and leaves no residue [20–22]. Kharasch and Nikishin have successfully realized the photolysis of 4-bromobiphenyl

in benzene to synthesize *p*-terphenyl only driven by UV light irradiation. Unfortunately, just more reactive bromobiphenyl or iodobiphenyl can afford coupling products with satisfying yield [23, 24]. For inexpensive aryl chlorides, the activation of C-Cl bond is much more difficult than that of C-Br and C-I bonds, and there were only several literatures about photo-cross-coupling reactions of aryl chlorides [25–27]. Here, we provided an efficient and catalyst-free method to realize C-C cross-coupling of aryl chlorides and inert arenes under UV light excitation. This homolytic radical aromatic substitution (HAS) process gave an extremely facile mode to construct biaryl compounds, and its applicability can be extended to form diverse bonds such as trifluoromethylation and C-N cross-coupling reactions.

## 2. Experimental Section

**2.1. General Procedures for the Direct Cross-Coupling of Aryl Halides with Benzene Derivatives.** All reagents were commercially available and used without further treatment. Anhydrous benzene and predried glassware were used in all reactions. In addition to the contrast experiment under air atmosphere, all other photoexcitation reactions were performed in a 10 mL quartz glass reactor under N<sub>2</sub> atmosphere (balloon pressure) at ambient temperature. In a typical sealed reaction system, 0.1 mmol of 4-chlorotoluene was thoroughly dispersed by magnetic stirring in 1 mL benzene which acts

as solvent and substrate. UV source was provided by 4-W UV lamps with certain wavelengths centered at 254 nm (Philips, TUV 4W/G4 T5). The irradiance spectrum and energy of the light incident on the suspension were measured with a spectroradiometer (International Light Technologies Model ILT950), about  $10 \text{ mW}\cdot\text{cm}^{-2}$ . Generally, after reaction, the mixture was injected into the GC equipped with FID detector (Agilent Technologies, GC 6890N) for analysis. HP-5 5% phenyl methyl siloxane column ( $30 \text{ m} \times 0.32 \text{ mm} \times 0.5 \mu\text{m}$ ) was used. The chemical structures of the products were confirmed by comparison with standard chemicals and GC-MS (Agilent Technologies, GC 6890N, MS 5975). The conversion ratio was described as the ratio of the moles of the generated biaryl compound in the reaction to the initial moles of the corresponding aryl halide.

**2.2. Procedure for Separating Product.** After 24 h of irradiation, the reaction mixture was washed three times with saturated aqueous sodium chloride ( $3 \times 10 \text{ mL}$ ), and the as-obtained aqueous layer in each run was further washed with ethyl acetate (10 mL). Then, all the organic layers were combined, dried over  $\text{Na}_2\text{SO}_4$ , and concentrated under vacuum to afford the corresponding crude products. At last, the crude products were purified by silica gel column chromatography to obtain the corresponding pure products.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR data were obtained on a BRUKER BIOSPIN AVANCE III nuclear resonance spectrometer using tetramethylsilane (TMS) as internal standard and  $\text{CDCl}_3$  as solvent. The NMR spectra of all the isolated cross-coupling products were provided in the Supporting Information in Supplementary Material available online at <http://dx.doi.org/10.1155/2016/5632613>. Silica gel column chromatography was performed using 300–400-mesh silica. Thin-layer chromatography (TLC) was performed on glass-backed plates precoated with silica gel. UV-active compounds were detected at 254 and 365 nm and marked on the TLC plate.

**2.3. Procedure of Competition Reaction between Benzene and  $\text{C}_6\text{D}_6$ .** A 10 mL quartz glass reactor was charged with 4-chlorobenzene (0.4 mmol),  $\text{C}_6\text{D}_6$  (2 mL), and benzene (2 mL) in glove box. Then the tube was removed from the glove box and the resulting mixture was stirred upon UV light for 22 h. The combined organic phase was concentrated under vacuum. The crude product was purified by semipreparative HPLC (80% MeCN) to give the desired product.  $^1\text{H}$  NMR was recorded on a BRUKER BIOSPIN AVANCE III spectrometer using TMS as the internal standard.

**2.4. Detection of Free Radical.** The electron paramagnetic resonance (EPR) measurements were conducted according to the following procedures. A solution containing chlorobenzene (0.1 mmol) and benzene (1 mL) was placed into a quartz cell, and then the quartz cell was sealed. All these procedures were operated in a glove box under  $\text{N}_2$  atmosphere. The quartz cell was then irradiated with UV light, and the spectra were recorded in situ with a Bruker A300 instrument operating in the X-band at room temperature.

TABLE 1: Direct cross-coupling of benzene with 4-chlorotoluene under UV light irradiation<sup>a</sup> (see Scheme 3 and Figure 2).

Entry	Irradiation time [h]	Conversion [%]
1	4	28
2	8	40
3	12	52
4	16	60
5	20	67
6	24	75
7 <sup>b</sup>	24	45
8 <sup>c</sup>	24	0

<sup>a</sup>General reaction conditions: 4-chlorotoluene (0.1 mmol, 1 equiv.), benzene (11.24 mmol, 112.4 equiv.), room temperature (air cooling),  $\text{N}_2$  atmosphere (balloon pressure), and UV light irradiation ( $254 \text{ nm}$ ,  $10 \text{ mW}\cdot\text{cm}^{-2}$ ). <sup>b</sup>Air atmosphere. <sup>c</sup>Conditions changed from irradiating to heating to  $100^\circ\text{C}$ .

### 3. Results and Discussion

Under  $\text{N}_2$  atmosphere, 4-chlorotoluene (0.1 mmol) in benzene (1 mL) was illuminated with UV light for 4 h, affording 28% conversion of 1a into the coupling product 4-phenyltoluene 3a (Table 1, Entry 1). When the irradiation time was prolonged to 24 h, 75% conversion of 1a to 3a was obtained (Table 1, Entry 6). A linear relationship between the conversion of 4-chlorotoluene to 4-phenyltoluene and irradiation time is shown in Table 1. This indicates that the formation of coupling product 3a is directly proportional to the incident photon number. Under air atmosphere, the coupling process was greatly inhibited and showed a much lower conversion of 45% (Table 1, Entry 7), which implied that  $\text{O}_2$  was involved in the reaction processes. In the absence of UV irradiation, no coupling product was obtained even upon heating at elevated temperature (Table 1, Entry 8).

The coupling reactions of other representative aryl halides with benzene were also tested (Table 2). In most cases, the introduction of both electron-donating (Entries 1–4) and electron-withdrawing groups (Entries 5–7) into *p*-substituted aryl halides was beneficial for this cross-coupling reaction and afforded good yields for the desired products. However, 4-chlorobenzonitrile (1h) with electron-withdrawing  $-\text{CN}$  group was not a good substrate for this reaction and showed a decreased reactivity (Entry 8), agreeing well with the results in the thermocatalytic process [12]. Moreover, the cross-coupling reaction was sensitive to steric effects, and the *o*-substituted aryl chlorides exhibited much lower reactivity compared to *p*-substituted aryl chlorides (Entries 1, 12, 4, and 13). For *p*-substituted aryl halides, the cross-coupling reactivity of aryl iodides and aryl bromides was lower than that of aryl chlorides (Entries 1–3). This may be attributed to the fact that the darkening and clouding of the reaction mixture during irradiation hindered the photolysis of aryl iodides and aryl bromides [25]. Similar results were obtained using chlorobenzene, bromobenzene, and iodobenzene as substrates (Entries 9–11). Electron-deficient and electron-rich benzene derivatives such as benzonitrile and anisole could also be utilized to perform the arylation, but the desired products were obtained in inferior yields. Moreover, only

TABLE 2: Direct cross-coupling of benzene with different aryl halides<sup>a</sup> (see Scheme 4).

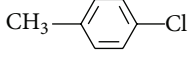
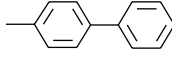
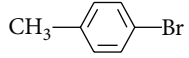
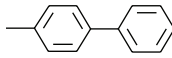
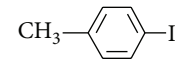
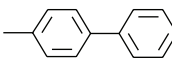
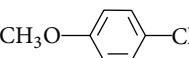
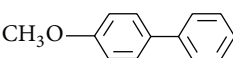
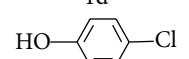
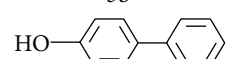
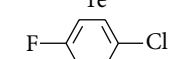
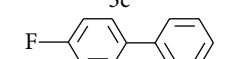
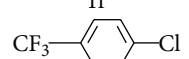
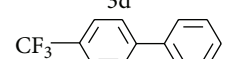
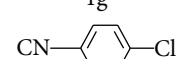
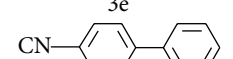
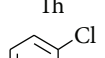
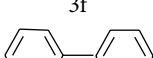
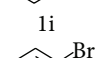
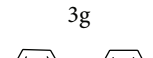
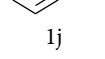
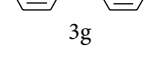
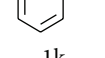
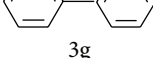
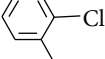
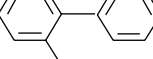
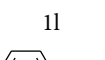
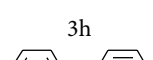
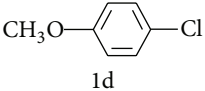
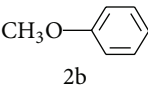
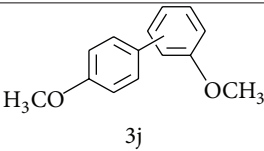
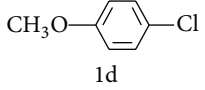
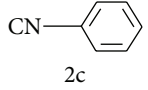
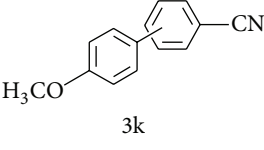
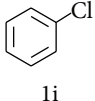
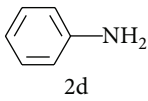
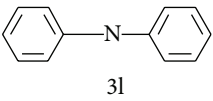
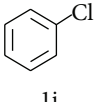
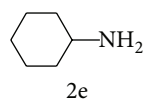
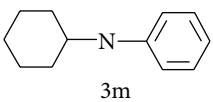
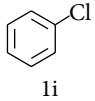
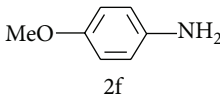
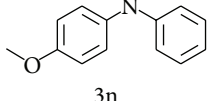
Entry	Substrate 1	Substrate 2	Product	Conversion [%]/isolated yield [%]
1	 1a	2a	 3a	75/47
2	 1b	2a	 3a	47
3	 1c	2a	 3a	65
4	 1d	2a	 3b	93/55
5	 1e	2a	 3c	69/44
6	 1f	2a	 3d	72/45.3
7	 1g	2a	 3e	65/36
8	 1h	2a	 3f	21
9	 1i	2a	 3g	69
10	 1j	2a	 3g	44
11	 1k	2a	 3g	62/37.5
12	 1l	2a	 3h	22
13	 1m	2a	 3i	37
14	 1n	2a	 3i	54/32

TABLE 2: Continued.

Entry	Substrate 1	Substrate 2	Product	Conversion [%]/isolated yield [%]
15 <sup>b</sup>				32 ( <i>o</i> : <i>m</i> : <i>p</i> = 3.1:1.5:1)
16 <sup>b</sup>				60 ( <i>o</i> : <i>m</i> : <i>p</i> = 2.2:1:1.5)
17 <sup>c</sup>				70/44
18 <sup>d</sup>				12
19 <sup>e</sup>				85

<sup>a</sup>General reaction conditions: 4-chlorotoluene (0.1 mmol, 1 equiv.), benzene (11.24 mmol, 112.4 equiv.), room temperature (air cooling), N<sub>2</sub> atmosphere (balloon pressure), and UV light irradiation (254 nm, 10 mW·cm<sup>-2</sup>, 24 h). Isolated yield by silica gel column chromatography. <sup>b</sup>Ratios of the regioisomers were determined by NMR. <sup>c</sup>Aniline (11.0 mmol, 110 equiv.). <sup>d</sup>Cyclohexylamine (8.77 mmol, 87.7 equiv.). <sup>e</sup>Acetonitrile (1 mL), *p*-methoxyaniline (1 mmol, 10 equiv.).

moderate regioselectivity has been observed, and the ratios between the *ortho*-, *meta*-, and *para*-regioisomers in these reactions were 3.1:1.5:1 (Entry 15) and 2.2:1:1.5 (Entry 16), respectively. In addition, this reaction can be extended to the construction of C-N bonds under identical conditions. Under UV light irradiation, the coupling reaction of chlorobenzene with aniline or cyclohexylamine afforded the corresponding products 3l and 3m in the conversion of 70% and 12%, respectively (Entries 17, 18). The *p*-substituted aniline with electron-donating methoxy group exhibited excellent reactivity (Entry 19).

The cross-coupling reaction of aryl halides with benzene proceeded via a free radical process, which was demonstrated by the fact that the addition of PBN (N-tert-butyl- $\alpha$ -phenylnitrone, a typical radical scavenger) to the reaction system led to a significant decrease in the formation of 4-phenyltoluene (Table 3). When four equivalents of PBN were added, the conversion of 4-phenyltoluene was decreased to 2% (Entry 3). The addition of typical ion trapping agent tetrabutylammonium hexafluorophosphate (TBA<sup>+</sup>PF<sub>6</sub><sup>-</sup>) hardly changed the reaction behaviour, suggesting the involvement of radical ions may be ruled out. The possible radical species involved in the reactions were also verified by in situ electron paramagnetic resonance (EPR) spectroscopy (Figure 1). A double-quartet splitting and a large triplet of doublet appeared when the reaction system containing PBN trapping reagent was irradiated by UV light. These peaks can be ascribed to the formation of Cl-PBN• and phenyl-PBN•

TABLE 3: Radical/electron trapping experiments<sup>a</sup> (see Scheme 3).

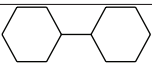
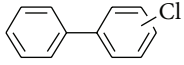
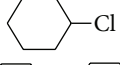
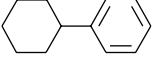
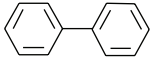
Entry	Trapping agent	Conversion (%)
1	None	<b>28</b>
2	PBN (2 equiv.)	<b>3</b>
3	PBN (4 equiv.)	<b>2</b>
4	TBA <sup>+</sup> PF <sub>6</sub> <sup>-</sup> (2 equiv.)	<b>28</b>

<sup>a</sup>General reaction conditions: 4-chlorotoluene (0.1 mmol, 1 equiv.), benzene (11.24 mmol, 112.4 equiv.), room temperature (air cooling), N<sub>2</sub> atmosphere (balloon pressure), and UV light irradiation (254 nm, 10 mW·cm<sup>-2</sup>, 4 h). TBA<sup>+</sup>PF<sub>6</sub><sup>-</sup> = tetra-n-butylammonium hexafluorophosphate.

adducts [28, 29], which is in good agreement with the theory that UV irradiation of aryl halides can produce halide radical and aryl radical by homolytic cleavage.

In order to further probe more reaction details, the photochemical cross-coupling reaction of chlorobenzene and cyclohexane was tested. The distribution of final products (Table 4 and Figure S1) showed that the direct combination of two aryl radicals was not dominant and the main product was bicyclohexyl (40.9%) (Entry 1). This implies that the cyclohexyl radical should be formed during the reaction process. When cyclohexane was irradiated with UV light, no coupling products were obtained due to its stability. Therefore, the most plausible way to produce cyclohexyl radical is through the hydrogen-abstraction from cyclohexane by reactive chlorine radical although chlorine radical does

TABLE 4: The distribution of the products generated from direct cross-coupling of chlorobenzene with cyclohexane under UV light irradiation<sup>a</sup> (see Scheme 5).

Entry	Product	Distribution (%)
1		40.9
2		18.3
3		18.6
4		15.2
5		7.0

<sup>a</sup>General reaction conditions: chlorobenzene (0.1 mmol, 1 equiv.), cyclohexane (9.26 mmol, 92.6 equiv.), room temperature (air cooling), N<sub>2</sub> atmosphere (balloon pressure), and UV light irradiation (254 nm, 10 mW·cm<sup>-2</sup>, 24 h).

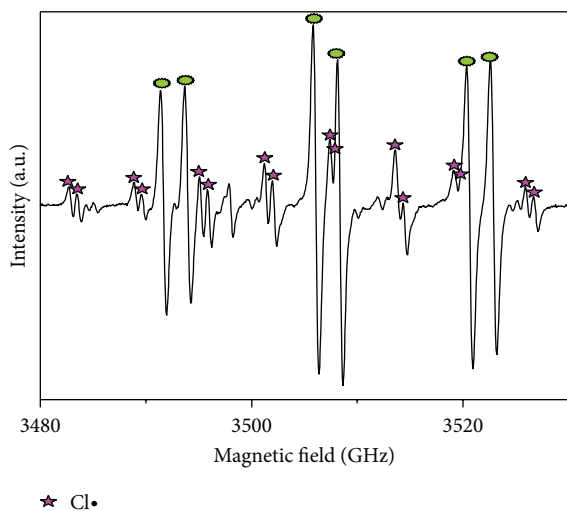


FIGURE 1: EPR spectrum as the evidence for chlorine radicals and phenyl radicals using PBN as trapping agents.

not have the ability to abstract the hydrogen from more stable benzene. The reaction of chlorobenzene with the same amount of benzene and C<sub>6</sub>D<sub>6</sub> gave almost equivalent amount of the products 3a and 3a-d<sub>5</sub> after 22 h under UV light irradiation (Scheme 1 and Figure S2), which indicates that C-H bond cleavage of benzene was not involved in the rate-determining step. Thus, we concluded that the generation of aryl radical from the cleavage of C-halogen bond may be the dominant step.

As shown in Scheme 2, a plausible mechanism for photoinduced cross-coupling of aryl chlorides and benzene was proposed. When irradiating aryl chlorides in benzene with energetic UV light, the weak C-Cl bond undergoes homolytic cleavage to give aryl radical and chlorine radical simultaneously. The aryl radical subsequently combined with inert benzene to form the key transition state of cyclohexadienyl radical (b) via nucleophilic substitution, followed

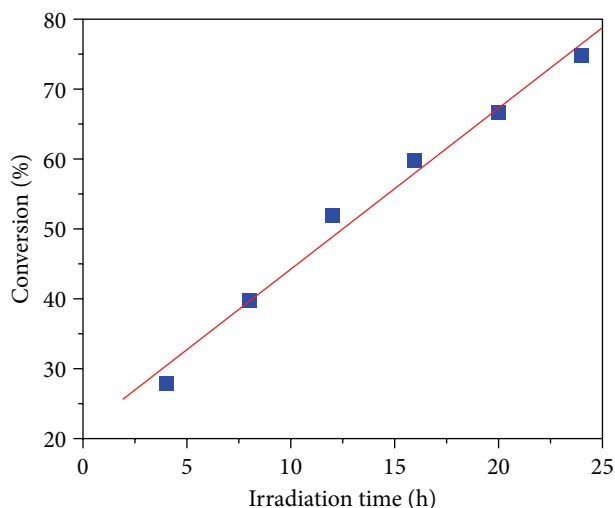


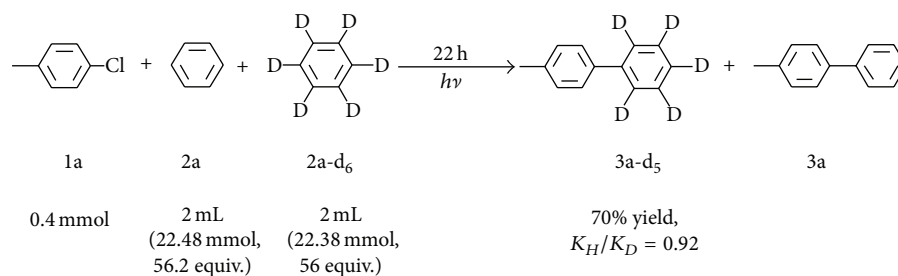
FIGURE 2

by the deprotonation process to afford biaryl product and hydrogen chloride (c). This radical addition process followed by elimination of a hydrogen radical is believed to be one of the most straightforward methods to construct biphenyl frameworks [30, 31]. Among them, the generation of aryl radical is considered to be the crucial and initial step and always be accomplished in the strong alkaline environment during C-C coupling. Direct photolysis of aryl halides with UV light to form aryl radical is simple and effective for propagating the C-C cross-coupling reaction.

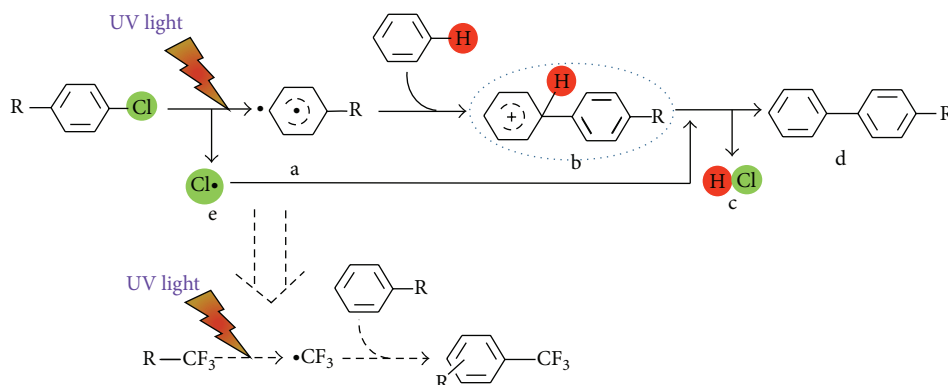
The photoinduced C-C cross-coupling of aryl chlorides and inert arenes is also applied to the trifluoromethylation of aromatic compounds. Direct trifluoromethylation through CF<sub>3</sub> radical-mediated mechanism is one of the most sophisticated strategies [32–36]. Here, we introduced trifluoromethanesulfonyl chloride as CF<sub>3</sub> radical source by photoexcitation (Table 5). UV irradiation resulted in 20% conversion of trifluoromethanesulfonyl chloride to benzotrifluoride in benzene solution (Entry 1). Other substituted benzene derivatives also afforded the corresponding trifluoromethylation products under the same conditions (Entries 2–5). The introduction of electron-donating groups gave higher conversions than that with electron-withdrawing groups (Entries 2–5). Although the conversions for the trifluoromethylation of aromatic compounds were relatively low, the preliminary results demonstrated the feasibility of this photoinduced reaction mode.

## 4. Conclusion

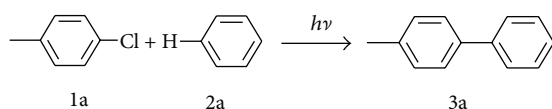
We have developed a facile, efficient, and catalyst-free method to realize direct C-C cross-coupling of aryl chloride and inert arenes under UV light excitation via HAS process. The aryl radical and chlorine radical produced from photoinitiated cleavage of aryl chlorides played a dominant role in the formation of biaryl products. This photoinduced reaction mode can also be applied to other synthetic reactions, such



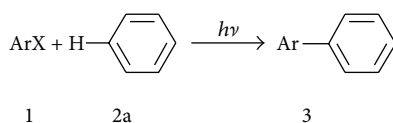
SCHEME 1: KIE experiment.



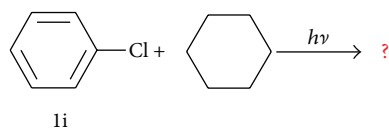
SCHEME 2: Proposed possible mechanism.



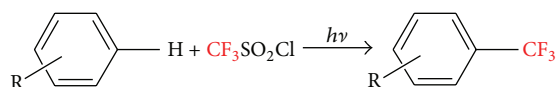
SCHEME 3



SCHEME 4



SCHEME 5



SCHEME 6

TABLE 5: Direct trifluoromethylation of trifluoromethanesulfonyl chloride with benzene derivatives<sup>a</sup> (see Scheme 6).

Entry	R	Product	Conversion (%)
1	H		20
2	I		15 ( $m:p = 1:1$ )
3	Me		40 ( $o:m:p = 3:6:1$ )
4	OMe		30 ( $o:m:p = 2.3:1:1$ )
5	CN		21

<sup>a</sup>General reaction conditions: trifluoromethanesulfonyl chloride (0.1 mmol, 1 equiv.), benzene (11.24 mmol, 112.4 equiv.), iodobenzene (8.93 mmol, 89.3 equiv.), toluene (9.43 mmol, 94.3 equiv.), anisole (9.2 mmol, 92 equiv.), benzonitrile (9.79 mmol, 97.9 equiv.), room temperature (air cooling),  $\text{N}_2$  atmosphere (balloon pressure), and UV light irradiation (254 nm,  $10 \text{ mW}\cdot\text{cm}^{-2}$ , 24 h); conversions were determined by  $^{19}\text{F}$  NMR with benzonitrile as an internal standard.

as the construction of C-N bonds and trifluoromethylated compounds.

## Competing Interests

The authors declare that they have no competing interests.

## Acknowledgments

This work was financially supported by the National Nature Science Foundation of China, 21077023, the National Basic Research Program of China, 2014CB239303, the Natural Science Foundation of Fujian Province of China, 2015J01046, and the Independent Research Project of State Key Laboratory of Photocatalysis on Energy and Environment, 2014B01.

## References

- [1] D. A. Horton, G. T. Bourne, and M. L. Smythe, "The combinatorial synthesis of bicyclic privileged structures or privileged substructures," *Chemical Reviews*, vol. 103, no. 3, pp. 893–930, 2003.
- [2] L.-C. Campeau and K. Fagnou, "Palladium-catalyzed direct arylation of simple arenes in synthesis of biaryl molecules," *Chemical Communications*, no. 12, pp. 1253–1264, 2006.
- [3] V. Hornillos, M. Giannerini, C. Vila, M. Fañanás-Mastral, and B. L. Feringa, "Catalytic direct cross-coupling of organolithium compounds with aryl chlorides," *Organic Letters*, vol. 15, no. 19, pp. 5114–5117, 2013.
- [4] A. W. Lei, W. Liu, C. Liu, and M. Chen, "Arylation of unactivated arenes," *Dalton Transactions*, vol. 39, no. 43, pp. 10352–10361, 2010.
- [5] D. Alberico, M. E. Scott, and M. Lautens, "Aryl-aryl bond formation by transition-metal-catalyzed direct arylation," *Chemical Reviews*, vol. 107, no. 1, pp. 174–238, 2007.
- [6] W. A. Herrmann, C. Brossmer, K. Öfele et al., "Palladacycles as structurally defined catalysts for the heck olefination of chloro- and bromoarenes," *Angewandte Chemie—International Edition*, vol. 34, no. 17, pp. 1844–1848, 1995.
- [7] D. W. Old, J. P. Wolfe, and S. L. Buchwald, "A highly active catalyst for palladium-catalyzed cross-coupling reactions: room-temperature suzuki couplings and amination of unactivated aryl chlorides," *Journal of the American Chemical Society*, vol. 120, no. 37, pp. 9722–9723, 1998.
- [8] E. Shirakawa, K.-I. Itoh, T. Higashino, and T. Hayashi, "Tert-butoxide-mediated arylation of benzene with aryl halides in the presence of a catalytic 1,10-phenanthroline derivative," *Journal of the American Chemical Society*, vol. 132, no. 44, pp. 15537–15539, 2010.
- [9] A. Studer and D. P. Curran, "Organocatalysis and C-H activation meet radical- and electron-transfer reactions," *Angewandte Chemie—International Edition*, vol. 50, no. 22, pp. 5018–5022, 2011.
- [10] W.-C. Chen, Y.-C. Hsu, W.-C. Shih et al., "Metal-free arylation of benzene and pyridine promoted by amino-linked nitrogen heterocyclic carbenes," *Chemical Communications*, vol. 48, no. 53, pp. 6702–6704, 2012.
- [11] S. Yanagisawa, K. Ueda, T. Taniguchi, and K. Itami, "Potassium t-butoxide alone can promote the biaryl coupling of electron-deficient nitrogen heterocycles and haloarenes," *Organic Letters*, vol. 10, no. 20, pp. 4673–4676, 2008.
- [12] C.-L. Sun, H. Li, D.-G. Yu et al., "An efficient organocatalytic method for constructing biaryls through aromatic C–H activation," *Nature Chemistry*, vol. 2, pp. 1044–1049, 2010.
- [13] W. Liu, H. Cao, H. Zhang et al., "Organocatalysis in cross-coupling: DMEDA-catalyzed direct C–H arylation of unactivated benzene," *Journal of the American Chemical Society*, vol. 132, no. 47, pp. 16737–16740, 2010.
- [14] Y. T. Qiu, Y. H. Liu, K. Yang et al., "New ligands that promote cross-coupling reactions between aryl halides and unactivated arenes," *Organic Letters*, vol. 13, no. 14, pp. 3556–3559, 2011.
- [15] Y. J. Zhu, M. Bauer, J. Ploog, and L. Ackermann, "Late-stage diversification of peptides by metal-free C–H arylation," *Chemistry*, vol. 20, no. 41, pp. 13099–13102, 2014.
- [16] P. D. S. José, J. Steffen, and J. T. Nicholas, "Probing the photoreactivity of aryl chlorides with oxygen," *Photochemical & Photobiological Sciences*, vol. 8, no. 2, pp. 210–216, 2009.
- [17] A. F. Littke, L. Schwarz, and G. C. Fu, "Pd/P(*t*-Bu)<sub>3</sub>: a mild and general catalyst for stille reactions of aryl chlorides and aryl bromides," *Journal of the American Chemical Society*, vol. 124, no. 22, pp. 6343–6348, 2002.
- [18] A. F. Littke, C. Dai, and G. C. Fu, "Versatile catalysts for the suzuki cross-coupling of arylboronic acids with aryl and vinyl halides and triflates under mild conditions," *Journal of the American Chemical Society*, vol. 122, no. 17, pp. 4020–4028, 2000.
- [19] N. Kataoka, Q. Shelby, J. P. Stambuli, and J. F. Hartwig, "Air stable, sterically hindered ferrocenyl dialkylphosphines for palladium-catalyzed C–C, C–N, and C–O bond-forming cross-couplings," *Journal of Organic Chemistry*, vol. 67, no. 16, pp. 5553–5566, 2002.
- [20] M. Fagnoni, D. Dondi, D. Ravelli, and A. Albini, "Photocatalysis for the formation of the C–C bond," *Chemical Reviews*, vol. 107, no. 6, pp. 2725–2756, 2007.
- [21] G. Palmisano, V. Augugliaro, M. Pagliaro, and L. Palmisano, "Photocatalysis: a promising route for 21st century organic chemistry," *Chemical Communications*, no. 33, pp. 3425–3437, 2007.
- [22] G. E. Robinson and J. M. Vernon, "Photochemical phenylation of chlorobenzenes," *Journal of the Chemical Society D: Chemical Communications*, no. 17, pp. 977–978, 1969.
- [23] N. Kharasch, R. K. Sharma, and H. B. Lewis, "The photolysis of 4-bromobiphenyl in benzene," *Chemical Communications*, no. 13, pp. 418–419, 1966.
- [24] M. A. Chel'tsova and G. I. Nikishin, "Photolysis of aryl bromides and aryl chlorides in benzene," *Bulletin of the Academy of Sciences of the USSR Division of Chemical Science*, vol. 16, no. 2, pp. 447–448, 1967.
- [25] S. Protti, M. Fagnoni, and A. Albini, "Photo-cross-coupling reaction of electron-rich aryl chlorides and aryl esters with alkynes: a metal-free alkynylation," *Angewandte Chemie—International Edition*, vol. 44, no. 35, pp. 5675–5678, 2005.
- [26] G. E. Robinson and J. M. Vernon, "Photochemical reactions of chlorobenzene derivatives in benzene," *Journal of the Chemical Society C: Organic*, pp. 3363–3367, 1971.
- [27] S. Protti, M. Fagnoni, M. Mella, and A. Albini, "Aryl Cations from aromatic halides. Photogeneration and reactivity of 4-hydroxy(methoxy)phenyl cation," *Journal of Organic Chemistry*, vol. 69, no. 10, pp. 3465–3473, 2004.
- [28] R. S. Yuan, S. L. Fan, H. X. Zhou et al., "Chlorine-radical-mediated photocatalytic activation of C–H bonds with visible light," *Angewandte Chemie*, vol. 125, no. 3, pp. 1069–1073, 2013.
- [29] G. Zhang and I. Hua, "Cavitation chemistry of polychlorinated biphenyls: decomposition mechanisms and rates," *Environmental Science & Technology*, vol. 34, no. 8, pp. 1529–1534, 2000.
- [30] R. Bolton and G. H. Williams, "Homolytic arylation of aromatic and polyfluoroaromatic compounds," *Chemical Society Reviews*, vol. 15, no. 2, pp. 261–289, 1986.

- [31] W. R. Bowman and J. M. Storey, "Synthesis using aromatic homolytic substitution—recent advances," *Chemical Society Reviews*, vol. 36, no. 11, pp. 1803–1822, 2007.
- [32] K. Müller, C. Faeh, and F. Diederich, "Fluorine in pharmaceuticals: looking beyond intuition," *Science*, vol. 317, no. 5846, pp. 1881–1886, 2007.
- [33] A. T. Herrmann, L. L. Smith, and A. Zakarian, "A simple method for asymmetric trifluoromethylation of *N*-acyl oxazolidinones via Ru-catalyzed radical addition to zirconium enolates," *Journal of the American Chemical Society*, vol. 134, no. 16, pp. 6976–6979, 2012.
- [34] A. I. Konovalov, A. Lishchynskyi, and V. V. Grushin, "Mechanism of trifluoromethylation of aryl halides with  $\text{CuCF}_3$  and the ortho effect," *Journal of the American Chemical Society*, vol. 136, no. 38, pp. 13410–13425, 2014.
- [35] E. J. Cho, T. D. Senecal, T. Kinzel, Y. Zhang, D. A. Watson, and S. L. Buchwald, "The palladium-catalyzed trifluoromethylation of aryl chlorides," *Science*, vol. 328, no. 5986, pp. 1679–1681, 2010.
- [36] D. A. Nagib and D. W. C. Macmillan, "Trifluoromethylation of arenes and heteroarenes by means of photoredox catalysis," *Nature*, vol. 480, no. 7376, pp. 224–228, 2011.



