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Visible Light-mediated Direct Arylation of Arenes and Heteroarenes Using Diaryliodonium Salts in the Presence and Absence of a Photocatalyst

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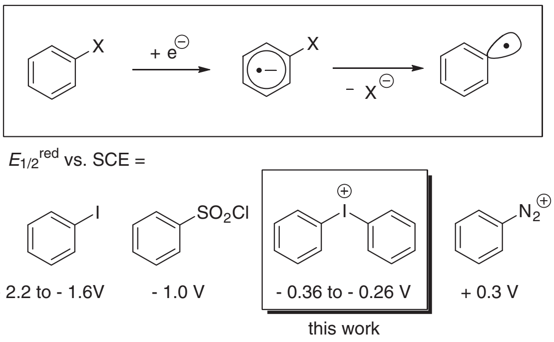
Diaryliodonium salts have been used as aryl radical sources under visible light-mediated photoredox catalysis. Benzene and a range of heteroarenes are arylated with Ar_2I^+ in the presence of $[Ir(ppy)_2(bpy)]PF_6$ upon irradiation with visible light. When pyrroles are used, the arylation proceeds in the absence of a photoredox catalyst. Both processes are initiated by photoinduced single-electron-transfer to Ar_2I^+, generating aryl radicals.

The aryl radical is well known as a highly reactive intermediate capable of participating in a variety of different arylation reactions, including homolytic aromatic substitution.[1] Classically, aryl radicals have been generated according to several different procedures, including thermal decomposition of diaroyl peroxide, the treatment of suitable aromatic precursors with stoichiometric oxidants, reductants, or radical mediators, and the irradiation of suitable precursors with high-energy UV light.[2] Visible light photocatalysis[3,4] has recently emerged as a mild method for the generation of aryl radicals, and therefore represents a powerful strategy for the development of new arylation processes. This approach uses photoexcitation with visible light to initiate a single-electron-transfer (SET) process between a metal catalyst, such as $[Ru(bpy)_3]^{2+}$ or an organic dye, and an aromatic substrate. The most successful acceptor substrates are aryl diazonium salts, which can readily generate aryl radicals via the loss of nitrogen through a photoinduced reductive SET process (Scheme 1).[5] Aryl sulfonyl chlorides[6] and aryl halides,[7] which are both more stable and readily available, have also been shown to be viable precursors, although the application of these precursors is currently limited, partly because of their relatively low reduction potentials.[8] Koike and Akita reported that arylboronates can generate aryl radicals via an oxidative quenching pathway under visible light irradiation.[9] It was envisaged that diaryliodonium salts (Ar_2I^+)[10] could be used as aryl sources in terms of their reduction potentials, stability, and availability. Indeed, it has been proposed that a phenyl radical could be involved in visible light-induced polymerization initiated by Ph_2I^+ and a photocatalyst.[11] Sanford recently reported the use of an aryl radical generated from Ar_2I^+ by visible light photocatalysis as an effective arylating agent in a palladium-catalyzed C–H bond arylation.[12] These reports highlight the need for further investigation into more fundamental reaction systems to fully explore the potential utility of Ar_2I^+ as an aryl source in visible light-induced photoredox reactions. Herein, we describe several different visible light-mediated transformations of Ar_2I^+ in the presence and absence of a photoredox catalyst.

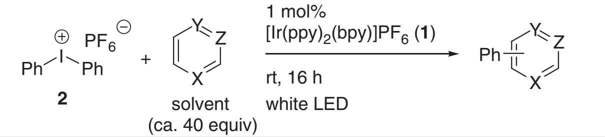


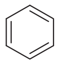
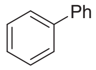
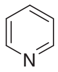
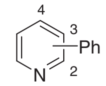
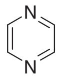
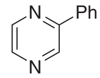
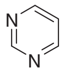
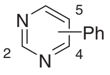
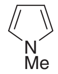
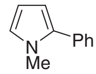
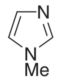
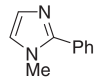
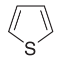
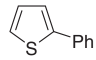
Scheme 1. Generation of an aryl radical via single-electron-transfer and typical reductive quenchers.

After several optimization studies (see SI for details), we found that the aryl radicals could be generated from Ar_2I^+ under irradiation with white LED light ($\lambda = 400$–$750\,nm$) in the presence of $[Ir(ppy)_2(bpy)]PF_6$ (**1**, ppy: 2-phenylpyridine, bpy: 2,2′-bipyridine) and were applicable to homolytic aromatic substitution processes[1,5] (Table 1). When the photolysis of diphenyliodonium **2** was conducted in benzene, biphenyl was obtained in 54% yield (Entry 1). Pyridine was also phenylated under these conditions to give a mixture of regioisomers, suggesting the involvement of a radical substitution process rather than the occurrence of ionic or metal-mediated arylation mechanism (Entry 2).[13] Other electron-deficient *N*-heteroarenes, including pyrazine (Entry 3)[14] and pyrimidine (Entry 4),[13] also participated in this visible light-mediated direct arylation reaction. The phenyl radical generated from **2** was also intercepted by several different five-membered heteroarenes. A particularly successful result was obtained with pyrrole, which delivered the 2-phenylated product exclusively (Entry 5).[15] The application to imidazole and thiophene also resulted in a regioselective phenylation, although the yields were modest (Entries 6 and 7).

During the course of our investigation into the scope of heteroarene acceptors, we noticed that pyrrole behaved differently from other heteroarenes. For example, the arylation of pyridine with iodonium salt **2**, required the presence of the photocatalyst and LED irradiation to efficiently afford the desired product (Table 2). In contrast, pyrrole could be arylated to an appreciable extent under LED irradiation *in the absence of a photocatalyst*, although no arylation occurred in the absence of the LED irradiation. These results appeared to be unusual because pyrrole and iodonium salt **2** do not absorb light in the visible region (400–750 nm). Although several examples of the metal-free direct arylation of (hetero)arenes using Ar_2I^+ salts have been reported in the literature, these reactions usually

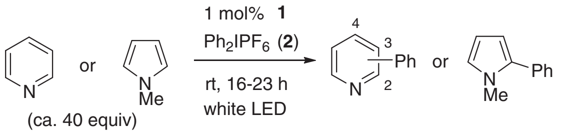
Table 1. Photocatalyzed arylation of (hetero)arenes using **2**[a]



Entry	(Hetero)arene	Product(s)	Yield/%[b]
1[c]			54
2			55 (2-:3-:4- = 56:31:12)
3[d]			33
4			75 (2-:4-:5- = 31:57:12)
5			88
6			36
7			42

[a]Reaction conditions: **2** (0.30 mmol), **1** (3.0 µmol), and degassed (hetero)arene (1.0 mL) in a 10-mL round-bottom flask under irradiation with white LED for 16 h, unless otherwise noted. [b]Isolated yield based on **2**. [c]In degassed benzene (0.90 mL) and EtOH (0.10 mL). [d]**2** (0.30 mmol), **1** (3.0 µmol), pyrazine (12 mmol) in degassed CH_3CN (0.30 mL).

Table 2. Control experiments for photocatalyzed arylation of pyridine and pyrrole using **2**

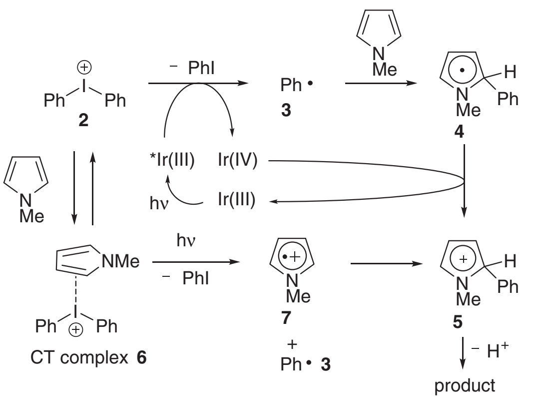


Entry	Variation from the "standard conditions"	Yield with pyridine[a]/%	Yield with pyrrole/%
1	None	57 (54:30:16)	88
2	Without **1**	9 (56:44:0)	54
3	Without LED (in dark)	0	trace
4	Under an atmosphere of air	57 (59:27:14)	75

[a]Ratio of regioisomers in product is shown in parenthesis. 2-:3-:4-position.

require elevated temperatures (100 °C)[16a,16b] or the addition of an acid[16c,16d] or base[16e] to promote the reaction. UV–vis spectroscopic analysis of the reaction mixture revealed the formation of a new absorption band in a visible region when pyrrole and diphenyliodonium **2** were mixed. This new band is attributed to the formation of a colored charge-transfer (CT) complex.[17]

These observations led us to propose that two photochemical pathways are involved in the reaction of iodonium **2** with pyrrole (Scheme 2). One is photoredox catalysis, where a SET from photoexcited *Ir(III) species to **2** would lead to the formation of the phenyl radical **3** and an Ir(IV) complex. Indeed, iodonium **2** decreased the emission intensity of *Ir(III) with a Stern–Volmer constant of $32\,\mathrm{M}^{-1}$, whereas pyrrole did not have any discernible impact on the emission intensity (see SI for details). The subsequent addition of radical **3** to pyrrole forms the dearomatized radical **4**, which is prone to oxidation by Ir(IV), leading to the cationic intermediate **5** and regeneration of the Ir(III) photocatalyst.[18] The second pathway could be initiated by a SET via excitation of the CT complex **6**,[19] which would generate the pyrrole radical cation **7** and phenyl radical **3**. The recombination of **7** and **3** would provide the common cationic intermediate **5**, which leads to a 2-arylated product upon deprotonation. In a separate experiment, we confirmed that when the reaction mixture was placed in the dark following 25 min of irradiation with an LED, it stalled (see SI for details). This observation suggests that the involvement of a radical chain pathway, in which photoirradiation is required only for the initial generation of a radical, is negligible under our catalytic conditions.

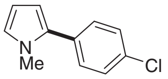
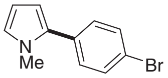
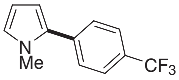
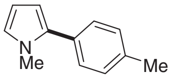
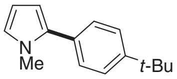
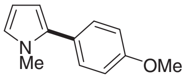
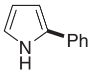
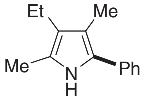


Scheme 2. Two pathways for visible light-mediated arylation of pyrrole with **2**.

The scope of iodonium salts was next investigated in the arylation of pyrroles (Table 3). Several different substituents, including halides (Entries 1 and 2), CF_3 (Entry 3), and alkyl groups (Entries 4 and 5) were found to be well-tolerated and gave the corresponding 2-arylated pyrroles in the presence of photocatalyst **1**. The electron-rich diaryliodonium did not undergo the photoarylation of pyrrole, and this result is consistent with our proposal that the reductive quenching of Ar_2I^+ would initiate the reaction (Entry 6). The electronic effect of the aryl group had a more profound impact on the non-catalyzed pathway. The CF_3-substituted diaryliodonium afforded the corresponding arylated product in 74% yield in the absence of photocatalyst **1**, likely because of the effective formation of a CT complex. It is noteworthy that the unprotected NH-free pyrroles also underwent the photoarylation reaction (Entries 7 and 8).

In summary, we have shown that diaryliodonium salts can be used as aryl radical precursors in the context of visible light-mediated photoredox catalysis. It was demonstrated that an aryl radical generated by the reductive quenching of Ar_2I^+ with an excited *Ir(III) species can participate in a homolytic aromatic substitution reaction with benzene and several heteroarenes at ambient temperature. It is noteworthy that visible light irradi-

Table 3. Photocatalyzed arylation using various Ar_2I^+ [a]

Entry	Ar_2I^+	Product	Isolated yield/%	
			With **1**	Without **1**
1	$(4\text{-}ClC_6H_4)_2IOTf$		75	53
2	$(4\text{-}BrC_6H_4)_2IOTf$		68	41
3	$(4\text{-}CF_3C_6H_4)_2IBF_4$		76	74
4	$(4\text{-}MeC_6H_4)_2IOTf$		60	18
5	$(4\text{-}t\text{-}BuC_6H_4)_2IOTf$		61	13
6	$(4\text{-}MeOC_6H_4)_2IOTf$		trace	trace
7	Ph_2IPF_6		63	32
8	Ph_2IPF_6		48	47

[a]Reaction conditions: iodonium salt (0.30 mmol) and pyrrole derivative (1.0 mL) in a 10-mL round-bottom flask under irradiation with white LED for 16 h, in the presence or absence of **1** (3.0 µmol).

ation can effectively promote the 2-arylation of pyrroles with Ar_2I^+ in the absence of a photoredox catalyst via a CT complex **6**. These results imply that similar noncatalytic pathways could be involved in other known arylation reactions of electron-rich species using Ar_2I^+, in addition to photocatalytic and ionic mechanisms. Further studies toward developing visible light-mediated synthetic methods are currently underway in our laboratory.[20,21]

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