# **ORGANOMETALLICS**

# **Diaryl Ether Formation Merging Photoredox and Nickel Catalysis**

Le Liu and Cristina Nevado\*



aryl halides and phenol derivatives are cross-coupled in the presence of a readily available organic photocatalyst and NiBr<sub>2</sub>(dtbpy). Symmetrical diaryl ethers have also been directly obtained from aryl bromides in the presence of water. Mechanistic investigations support the involvement of Ni(0) species at the

 $R^{1} + or + H_{2}O + R^{2} + H_{2}O + R^{1} + H_{2}O + H_{2}O + R^{1} + H_{2}O + H_{2}O$ 

outset of the reaction and a Ni(II)/Ni(III)-photocatalyzed single electron transfer process preceding the productive  $C(sp^2)$ -OAr reductive elimination.

U llmann couplings rank among the most widely used reactions in organometallic chemistry, providing access to ubiquitous diaryl ether motifs.<sup>1-3</sup> Protocols based on stoichiometric amounts of copper reagents<sup>1a,b</sup> have been replaced by catalytic ones capitalizing on the nature of ligands,<sup>4</sup> bases,<sup>5</sup> and metals<sup>6</sup> (Scheme 1a).<sup>7,8</sup> Alternative methods employing boronic acids<sup>9</sup> or diaryliodonium species<sup>10</sup> have also been developed. Despite significant progress, limitations such as the need for privileged ligands involving multistep preparation, the relatively high reaction temperatures

Scheme 1. Strategies for C(sp<sup>2</sup>)-O Bond Formation a. Conventional Ullmann-type diaryl ether formation



b.Photoredox/Ni dual catalysis to access aryl alkyl ethers and aryl esters



(80–150  $^{\circ}$ C), and the required prefunctionalization of the starting materials still demand further improvements.

The combination of photoredox and transition metal catalysis has recently emerged as a powerful strategy to achieve challenging transformations.<sup>11</sup> Seminal examples by MacMillan's group described the utilization of nickel salts and iridium photocatalysts in the presence of nitrogen-containing additives to forge  $C(sp^2)$ -O bonds:<sup>12</sup> aryl bromides were successfully cross-coupled with primary or secondary alkyl alcohols as well as with carboxylic acids to give alkyl aryl ethers<sup>12a</sup> and aryl esters,<sup>12b</sup> respectively (Scheme 1b). An efficient synthesis of phenols from the corresponding aryl bromides under very similar conditions was also reported.<sup>13</sup> The mechanisms underlying these transformations have been studied in detail, as multiple scenarios can be envisaged to operate under the reaction conditions used.<sup>14</sup> Both electron transfer<sup>12a</sup> and energy transfer<sup>12b</sup> processes have been proposed independently for these reported  $C(sp^2)$ -O bond formations under dual catalytic systems. On the other hand, the direct cross-coupling of aryl halides and phenol derivatives to produce the most useful and widespread diaryl ethers is yet to be reported in this context.<sup>15</sup>

Here we present a dual photoredox/nickel-catalyzed Ullmann-type cross-coupling to access diaryl ethers under mild reaction conditions. The cheap and readily available organic photocatalyst 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicya-nobenzene (4CzIPN) is combined with nickel to couple a broad range of aryl halides and phenol derivatives in high yields. A straightforward route to symmetrical diaryl ethers

Special Issue: Organometallic Solutions to Challenges in Cross-Coupling

Received: January 12, 2021



from aryl bromides and  $H_2O$  has also been devised. Furthermore, we have carried out a detailed mechanistic investigation that supports the involvement of Ni(0) species at the outset of the catalytic cycle and postulate a Ni(II)/Ni(III)photocatalyzed single electron transfer (SET) process that precedes the productive  $C(sp^2)$ –OAr reductive elimination (Scheme 1c).

As shown in Table 1, our efforts to find the optimal conditions focused on the cross-coupling of 1-bromo-4-





"1 (0.15 mmol) and 2 (0.1 mmol) in 1.0 mL of PhCF<sub>3</sub> (0.1 M) irradiated with a 34 W blue LED for 36 h. <sup>b</sup>Yields were determined by <sup>1</sup>H NMR analysis of the crude reaction mixtures using mesitylene as an internal standard. The value in parentheses is the isolated yield after column chromatography. <sup>c</sup>Ir cat stands for  $[Ir{dF(CF_3)-ppy}_2(dtbpy)]PF_6$ . <sup>d</sup><5% indicates that a trace amount of product was observed. <sup>e</sup>Deviation from the reaction conditions in entry 6. <sup>f</sup>NR indicates that no product was detected by <sup>1</sup>H NMR spectroscopy.

(trifluoromethyl)benzene (1) and 1-(4-hydroxyphenyl)ethan-1-one (2). We initiated the reaction screening adopting the same protocol as previously reported for the O-arylation of aliphatic alcohols, which employed  $[Ir{dF(CF_3)}$ ppy}2(dtbpy)]PF6 and NiCl2·glyme (1 and 5 mol %, respectively) along with 4,4'-di-tert-butyl-2,2'-bipyridine (dtbpy) (5 mol %) in the presence of quinuclidine (10 mol %) and base (1.0 equiv of  $K_2CO_3$ ) in acetonitrile as the solvent.<sup>12a</sup> These conditions afforded only traces of the desired product (Table 1, entry 1). Interestingly, when we switched the solvent to PhCF<sub>3</sub> and omitted quinuclidine, which was reported to be the crucial additive for the alcohol cross-coupling reaction,<sup>12a,14</sup> diaryl ether 3 was generated in a promising 32% yield (Table 1, entry 2). Further yield enhancement was achieved by switching the base to K<sub>3</sub>PO<sub>4</sub> (Table 1, entry 3). In order to ensure an effective photocatalytic cycle, we next examined 4CzIPN, which possesses a similar redox potential window but a longer excited-state lifetime  $(5.1 \ \mu s)^{1.6}$  To our delight, 3 was obtained

in an improved 73% yield (Table 1, entry 4). 4CzIPN features a low price (it can be prepared for  $\sim$ \$6 per gram)<sup>17</sup> and thus was selected for further optimization. Increasing the amount of  $K_3PO_4$  to 2.0 equiv led to the formation of 3 in 85% yield (Table 1, entry 5), while no product was observed when the reaction was carried out in its absence (Table 1, entry 8). When preformed NiBr<sub>2</sub>(dtbpy) was used as the catalyst, an excellent 93% yield was obtained for this transformation (Table 1, entry 6). Under the same conditions,  $[Ir(ppy)_3]$ furnished the product only in marginal yields (Table 1, entry 7). (For additional optimization studies, see Tables S1 and S2). Further control experiments demonstrated that the organic photocatalyst, the nickel complex, and light as well as degassed reaction mixtures were critical parameters for a successful outcome (Table 1, entries 9-11). Finally, a gramscale reaction (5 mmol) delivered 3 in 84% yield (Table 1, entry 12), thus highlighting the applicability of this protocol in a preparative context.

With the optimized conditions in hand, we first investigated the scope of the aryl halide component in the reaction (Scheme 2). 1-Chloro-, 1-bromo-, and 1-iodo-4-(trifluoromethyl)benzene were examined in parallel. While

Scheme 2. Reaction Scope for the Synthesis of Nonsymmetrical Diaryl Ethers<sup>a</sup>



"Aryl halide (0.15 mmol), phenol (0.1 mmol), 4-CzIPN (0.02 mmol, 2 mol %), NiBr<sub>2</sub>(dtbpy) (0.05 mmol, 5 mol %), and  $K_3PO_4$  (0.2 mmol, 2.0 equiv) in 1.0 mL of PhCF<sub>3</sub> (0.1 M) irradiated with a 34 W blue LED for 36 h. Isolated yields after column chromatography are shown.

similar yields of the desired product were obtained with the bromide and iodide, only a trace amount of product 3 could be detected with the chloride derivative. Different bromoarenes were examined next. Aromatic rings bearing cyano (4), ester (10), and methylsulfonyl (11) groups were well-tolerated under the mild reaction conditions, delivering the corresponding O-arylation products in high yields. When sterically hindered ortho-substituted aryl bromides (known to be difficult substrates for classical Cu-catalyzed Ullmann coupling reactions<sup>18</sup>) were used as reaction partners, the coupling still proceed smoothly to furnish adducts 9-12. Importantly, both electron-neutral and electron-rich bromobenzenes were also compatible with the optimized conditions, as demonstrated by the efficient formation of diaryl ethers 5-9. Pyridine and quinoline derivatives could also be used as nucleophiles in these reactions to generate the corresponding heteroaryl ether products 13 and 14, respectively.

We then turned our attention to the phenolic component of this etherification process. Phenols with both electronwithdrawing and -donating groups at the para, meta, and ortho positions were efficiently coupled, affording the corresponding products in moderate to good yields (15-21). 2-Naphthol proved to be a good cross-coupling partner, producing diaryl ether 22 in 87% yield. Additionally, a bicyclic flavanone derivative also furnished product 23 in 80% yield. Further expansion of the scope was carried out by combination of electron-neutral and -rich aryl bromides with phenols (24-28). Etherifications of tyrosine and estrone derivatives were also successful (29-32), again highlighting the potential of this method in late-stage functionalization campaigns.<sup>19</sup> In addition, we found that both primary and secondary alcohols are also effectively coupled to generate the corresponding alkyl aryl ethers under these conditions (33, 34), showcasing the generality of this protocol.

Symmetrical diaryl ethers were targeted next. It is wellestablished that water can act as a nucleophile to form phenols from aryl bromides under dual photoredox/nickel catalysis.<sup>13</sup> A fast survey of reaction parameters led to the optimal conditions, which included ([Ir{ $dF(CF_3)ppy$ }\_2(dtbpy)]PF\_6 (1 mol %) and NiBr<sub>2</sub>(dtbpy) (5 mol %) in the presence of K<sub>3</sub>PO<sub>4</sub> and H<sub>2</sub>O (2.0 equiv) in PhCF<sub>3</sub> as the solvent. Bromoarenes bearing both electron-withdrawing and electron-donating substituents delivered the corresponding symmetrical diaryl ethers **35–42** in moderate to excellent yields under the above-mentioned conditions (Scheme 3).<sup>20</sup>



<sup>a</sup>Aryl halide (0.2 mmol),  $H_2O$  (0.2 mmol), 4-CzIPN (0.04 mmol, 2 mol %), NiBr<sub>2</sub>(dtbpy) (0.01 mmol, 5 mol %) and  $K_3PO_4$  (0.4 mmol, 2.0 equiv) in 1.0 mL PhCF<sub>3</sub> (0.2 M) irradiated with 34 W blue LED for 36 h. Isolated yields from column chromatography are shown.

The mechanism underlying the formation of  $C(sp^2)-O$  bonds via dual photoredox/nickel catalysis has been the focus of numerous studies.<sup>12–14</sup> Originally, reactions involving aliphatic alcohols were proposed to proceed via a Ni(I)/Ni(0) SET event at the expense of the photocatalyst.<sup>12a</sup> This mechanism was later revised in order to rationalize the critical role that quinuclidine plays in the reaction. Studies by Nocera et al. showed that a self-sustained Ni(I)/Ni(III) catalytic cycle is likely to operate in these transformations, with the amine additive working both as a base and as a ligand to stabilize dimeric Ni(I) species present in the reaction medium (Scheme 4e, bottom).<sup>14</sup> In contrast, reactions involving carboxylic acids





as oxygen partners<sup>12b</sup> seem to proceed through an excited [ArNi(II)OC(O)R]\* intermediate generated via energy transfer from the photocatalyst, which thereby functions as a sensitizer rather than as an electron shuttle (Scheme 4e, left). Intrigued by how subtle differences in the reaction conditions can affect both the scope and mechanism of these transformations, we designed a number of control experiments to better understand the individual steps operating in this  $C(sp^2)$ -OAr bond-forming process. At the outset, we investigated the reaction of a Ni(0)-dtbpy complex in the presence and absence of the photoredox catalyst. Importantly, in the presence of 4CzIPN, the cross-coupled product 3 was obtained in a yield comparable to that obtained when a Ni(II) precatalyst was used. In contrast, in the absence of the photocatalyst, only trace amounts of the diaryl ether could be detected, even after prolonged heating (Scheme 4a). The high efficiency of the  $C(sp^2)$ -O bond formation in the presence of a Ni(0) complex and 4CzIPN indicated that low-valent nickel species, which can be formed in situ from NiBr<sub>2</sub>(dtbpy) at the expense of the photocatalyst  $(E_{1/2}^{\text{red}}[4\text{CzIPN}^*/[4\text{CzIPN}]^-] =$ +1.35 V vs SCE,  $E_{1/2}^{\text{red}}[\text{Ni}^{\text{II}}/\text{Ni}^{0}] = -1.20$  V vs SCE), are likely

to be involved in the reaction's catalytic cycle. Moreover, the fact that our protocol *proceeds in the absence of nitrogencontaining bases* and the strong dependence of the reaction on light irradiation observed in a light on/off experiment (see Figure S3) further support this notion and disfavor a chainsustained Ni(I)/Ni(III) process.<sup>14</sup>

As to the actual nickel species responsible for the reductive elimination step, the aryl-Ni(II)OAr complex 43 was prepared, and its reactivity was explored in detail. It is important to note that displacement of bromide ligands on Ni(II) with phenols under the reaction conditions is a rather facile process (see Figure S1). After exposure to an LED light source, 43 furnished only negligible amounts of the cross-coupled product, implying that no productive reductive elimination to create the  $C(sp^2)$ -O bond can occur from either this Ni(II) complex or its excited form by direct light irradiation alone. In contrast, in the presence of 4CzIPN, a 35% yield of diaryl ether 9 was obtained after 10 h. While the formation of an excited aryl-alkoxo-Ni(II) complex via energy transfer can be invoked,<sup>12b</sup> several control experiments rule out this possibility. First, the reaction is highly effective with an organic photocatalyst featuring high oxidizing power ( $E_{1/2}^{\text{red}}$ [4CzIPN\*/  $[4CzIPN]^{-}] = +1.35$  V vs SCE) (Table 1, entry 6), while the same reaction in the presence of  $[Ir(ppy)_3]$  featuring a lower oxidation potential  $(E_{1/2}^{\text{red}}[\text{Ir}(\text{III})^*/\text{Ir}(\text{II})] = +0.31 \text{ V vs SCE})$ but high triplet energy (53.6 kcal/mol) furnishes the desired product in only marginal yield (Table 1, entry 7). Second, it has been reported that cerium ammonium nitrate (CAN) can act as a single electron transfer oxidant to oxidize Ni(II) to Ni(III) species.<sup>21</sup> In fact, when CAN was used as the oxidant, diaryl ether 9 could be isolated from complex 43 in 30% yield (Scheme 4b). These results support the generation of transient Ni(III) species via single electron transfer during the reaction as key intermediates for productive  $C(sp^2)-O$  bond formation.<sup>22</sup> Stern-Volmer fluorescence quenching studies showed that the emission intensity of the excited state of 4CzIPN decreased with increasing concentration of 43, following linear Stern-Volmer behavior. In contrast, phenol 2 did not display efficient quenching (Scheme 4d).<sup>23</sup> Cyclic voltammetry of 43 showed an irreversible peak at +0.80 V vs Ag/AgCl in acetonitrile, which is ascribed to the oxidation of Ni(II) to Ni(III) (see Figure S8).<sup>24</sup> These results provide further support for a single electron transfer between Ni(II) and the excited-state photocatalyst, which should be both kinetically and thermodynamically favorable under the reaction conditions  $(E_{1/2}^{\text{red}}[\text{Ni}^{\text{III}}/\text{Ni}^{\text{II}}] = +0.80 \text{ V vs Ag/AgCl}).^{24}$  Finally, complex 43 turned out to be an effective catalyst to mediate the cross-coupling reaction under the standard conditions, which supports the regeneration of the active Ni species with the photocatalyst after reductive elimination  $(E_{1/2}^{red}[Ni^I/Ni^0] =$ -1.10 V vs SCE and  $E_{1/2}^{\text{red}}[4\text{CzIPN}/[4\text{CzIPN}]^{-}] = -1.21$  V vs SCE)<sup>25</sup> (Scheme 4c). To summarize, all of these results favor a mechanism in which oxidation of Ni(II) complex 43 to Ni(III) occurs at the expense of the excited photocatalyst to enable reductive elimination and formation of the new  $C(sp^2)$ -OAr bond. The Ni(I) species produced thereby react with the reduced form of the photocatalyst to produce Ni(0) complexes, thus restarting the catalytic cycle according to the mechanism proposed in Scheme 4e (highlighted in gray).

In summary, here we have demonstrated the power of merging photoredox and nickel catalysis to produce diaryl ethers under mild conditions. This method expands the existing portfolio of  $C(sp^2)$ –OAr bond-forming reactions and

provides a complementary avenue to both symmetrically and nonsymmetrically substituted diaryl ether skeletons. This study also sheds light on the mechanism underlying these transformations. The reactions, carried out in the absence of nitrogen-based additives, proceed via a SET process aided by the photocatalyst in which unreactive ArNi(II)OAr species are transformed into ArNi(III)OAr, prone to undergo reductive elimination to form the new  $C(sp^2)$ –OAr bond.

# ASSOCIATED CONTENT

# Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.organomet.1c00018.

Experimental procedures, characterization of products, and control experiments (PDF)

# AUTHOR INFORMATION

#### **Corresponding Author**

Cristina Nevado – Department of Chemistry, University of Zurich, CH-8057 Zurich, Switzerland; orcid.org/0000-0002-3297-581X; Email: cristina.nevado@chem.uzh.ch

#### Author

Le Liu – Department of Chemistry, University of Zurich, CH-8057 Zurich, Switzerland; orcid.org/0000-0001-8954-9478

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.organomet.1c00018

#### Notes

The authors declare no competing financial interest.

# ACKNOWLEDGMENTS

We thank the Swiss National Science Foundation (SNF 200020\_146853) and the Forschungskredit of the University of Zurich (FK-18-111) for financial support. This publication was created as part of NCCR Catalysis, a National Centre of Competence in Research funded by the Swiss National Science Foundation.

#### REFERENCES

(1) For selected examples, see: (a) Ullmann, F. Ueber 9-Diphenylxanthen. Ber. Dtsch. Chem. Ges. 1904, 37, 853. (b) Lindley, J. Copper Assisted Nucleophilic Substitution of Aryl Halogen. Tetrahedron 1984, 40, 1433. (c) Sambiagio, C.; Marsden, S. P.; Blacker, A. J.; McGowan, P. C. Copper Catalyzed Ullmann Type Chemistry: From Mechanistic Aspects to Modern Development. Chem. Soc. Rev. 2014, 43, 3525. (d) Giri, R.; Brusoe, A.; Troshin, K.; Wang, J. Y.; Font, M.; Hartwig, J. F. Mechanism of the Ullmann Biaryl Ether Synthesis Catalyzed by Complexes of Anionic Ligands: Evidence for the Reaction of Iodoarenes with Ligated Anionic CuI Intermediates. J. Am. Chem. Soc. 2018, 140, 793. (e) Hu, T.; Schulz, T.; Torborg, C.; Chen, X.; Wang, J.; Beller, M.; Huang, J. Efficient Palladium-Catalyzed Coupling Reactions of Aryl Bromides and Chlorides with Phenols. Chem. Commun. 2009, 7330. (f) Monnier, F.; Taillefer, M. Catalytic C-C, C-N, and C-O Ullmann-Type Coupling Reactions. Angew. Chem., Int. Ed. 2009, 48, 6954.

(2) For selected examples, see: (a) Bedos-Belval, F.; Rouch, A.; Vanucci-Bacque, C.; Baltas, M. Diaryl Ether Derivatives as Anticancer Agents – A Review. *MedChemComm* 2012, 3, 1356. (b) Pitsinos, E. N.; Vidali, V. P.; Couladouros, E. A. Diaryl Ether Formation in the Synthesis of Natural Products. *Eur. J. Org. Chem.* 2011, 2011, 1207. (c) Nicolaou, K. C.; Boddy, C. N.; Brase, S.; Winssinger, N. Chemistry, Biology, and Medicine of the Glycopeptide Antibiotics.

Angew. Chem., Int. Ed. **1999**, 38, 2096. (d) Evano, G.; Wang, J.; Nitelet, A. Metal-Mediated C–O Bond Forming Reactions in Natural Product Synthesis. Org. Chem. Front. **2017**, 4, 2480.

(3) For selected examples, see: (a) Ma, D.; Cai, Q. Copper/Amino Acid Catalyzed Cross-Couplings of Aryl and Vinyl Halides with Nucleophiles. *Acc. Chem. Res.* **2008**, *41*, 1450. (b) Thomas, A. W.; Ley, S. V. Modern Synthetic Methods for Copper-Mediated C(aryl)– O, C(aryl)–N, and C(aryl)–S Bond Formation. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400. (c) Luo, F.; Pan, C.; Cheng, J. Recent Advances in Transition-Metal-Catalyzed Esterification. *Synlett* **2012**, *23*, 357. (d) Takise, R.; Isshiki, R.; Muto, K.; Itami, K.; Yamaguchi, J. Decarbonylative Diaryl Ether Synthesis by Pd and Ni Catalysis. *J. Am. Chem. Soc.* **2017**, *139*, 3340.

(4) (a) Fagan, P. J.; Hauptman, E.; Shapiro, R.; Casalnuovo, A. Using Intelligent/Random Library Screening To Design Focused Libraries for the Optimization of Homogeneous Catalysts: Ullmann Ether Formation. J. Am. Chem. Soc. 2000, 122, 5043. (b) Naidu, A. B.; Jaseer, E. A.; Sekar, G. J. General, Mild, and Intermolecular Ullmann-Type Synthesis of Diaryl and Alkyl Aryl Ethers Catalyzed by Diol-Copper(I) Complex. J. Org. Chem. 2009, 74, 3675. (c) Chen, Y.; Chen, H. 1,1,1-Tris(hydroxymethyl)ethane as a New, Efficient, and Versatile Tripod Ligand for Copper-Catalyzed Cross-Coupling Reactions of Aryl Iodides with Amides, Thiols, and Phenols. Org. Lett. 2006, 8, 5609. (d) Mann, G.; Incarvito, C.; Rheingold, A. L.; Hartwig, J. F. Palladium-Catalyzed C-O Coupling Involving Unactivated Aryl Halides. Sterically Induced Reductive Elimination To Form the C-O Bond in Diaryl Ethers. J. Am. Chem. Soc. 1999, 121, 3224. (e) Shelby, Q.; Kataoka, N.; Mann, G.; Hartwig, J. F. Unusual in Situ Ligand Modification to Generate a Catalyst for Room Temperature Aromatic C-O Bond Formation. J. Am. Chem. Soc. 2000, 122, 10718. (f) Zhang, Q.; Wang, D.; Wang, X.; Ding, K. (2-Pyridyl)acetone-Promoted Cu-Catalyzed O-Arylation of Phenols with Aryl Iodides, Bromides, and Chlorides. J. Org. Chem. 2009, 74, 7187. (5) Hosseinzadeh, R.; Tajbakhsh, M.; Mohadjerani, M.; Alikarami,

(S) Hosseinzaden, K.; Tajbakhsh, M.; Monadjerani, M.; Alikarami, M. Copper-Catalyzed Etherification of Aryl Iodides Using KF/Al<sub>2</sub>O<sub>3</sub>: An Improved Protocol. *Synlett* **2005**, 1101.

(6) (a) Lipshutz, B. H.; Unger, J. B.; Taft, B. R. Copper-in-Charcoal (Cu/C) Promoted Diaryl Ether Formation. *Org. Lett.* **2007**, *9*, 1089. (b) Niu, J.; Zhou, H.; Li, Z.; Xu, J.; Hu, S. An Efficient Ullmann-Type C–O Bond Formation Catalyzed by an Air-Stable Copper(I)–Bipyridyl Complex. J. Org. Chem. **2008**, *73*, 7814. (c) Larsson, P.; Correa, A.; Carril, M.; Norrby, P. O.; Bolm, C. Copper-Catalyzed Cross-Couplings with Part-per-Million Catalyst Loadings. *Angew. Chem., Int. Ed.* **2009**, *48*, 5691. (d) Kim, H. J.; Kim, M.; Chang, S. Rhodium(NHC)-Catalyzed O-Arylation of Aryl Bromide. Org. Lett. **2011**, *13*, 2368. (f) Wu, F.; Zhu, K.; Wu, G.; Gao, Y.; Chen, H. Nickel-Catalyzed C-O Cross-Coupling Reaction at Low Catalytic Loading with Weak Base Participation. *Eur. J. Org. Chem.* **2020**, *2020*, 519.

(7) (a) Burgos, C. H.; Barder, T. E.; Huang, X.; Buchwald, S. L. Significantly Improved Method for the Pd-Catalyzed Coupling of Phenols with Aryl Halides: Understanding Ligand Effects. *Angew. Chem., Int. Ed.* **2006**, 45, 4321. (b) Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. Novel Electron-Rich Bulky Phosphine Ligands Facilitate the Palladium-Catalyzed Preparation of Diaryl Ethers. *J. Am. Chem. Soc.* **1999**, *121*, 4369. (c) Maiti, D.; Buchwald, S. L. Cu-Catalyzed Arylation of Phenols: Synthesis of Sterically Hindered and Heteroaryl Diaryl Ethers. *J. Org. Chem.* **2010**, *75*, 1791. (d) Marcoux, J.; Doye, S.; Buchwald, S. L. A General Copper-Catalyzed Synthesis of Diaryl Ethers. *J. Am. Chem. Soc.* **1997**, *119*, 10539.

(8) (a) Fan, M.; Zhou, W.; Jiang, Y.; Ma, D. CuI/Oxalamide Catalyzed Couplings of (Hetero)aryl Chlorides and Phenols for Diaryl Ether Formation. *Angew. Chem., Int. Ed.* 2016, 55, 6211.
(b) Cai, Q.; Zou, B.; Ma, D. Mild Ullmann-Type Biaryl Ether Formation Reaction by Combination of ortho-Substituent and Ligand Effects. *Angew. Chem., Int. Ed.* 2006, 45, 1276. (c) Ma, D.; Cai, Q. N. N-Dimethyl Glycine-Promoted Ullmann Coupling Reaction of Phenols and Aryl Halides. *Org. Lett.* 2003, 5, 3799.

(9) For selected examples, see: (a) Chan, D. M. T; Monaco, K. L; Wang, R.-P.; Winters, M. P New N- and O-Arylations with Phenylboronic Acids and Cupric Acetate. *Tetrahedron Lett.* **1998**, 39, 2933. (b) Chan, D. M. T.; Monaco, K. L.; Wang, R.; Winters, M. P. New N- and O-Arylations with Phenylboronic Acids and Cupric Acetate. *Tetrahedron Lett.* **1998**, 39, 2933. (c) Jung, M. E.; Lazarova, T. I. New Efficient Method for the Total Synthesis of (*S*,*S*)-Isodityrosine from Natural Amino Acids. *J. Org. Chem.* **1999**, 64, 2976. (d) Zhang, J.; Wu, J.; Xiong, Y.; Cao, S. Synthesis of Unsymmetrical Biaryl Ethers Through Nickel-Promoted Coupling of Polyfluoroarenes with Arylboronic Acids and Oxygen. *Chem. Commun.* **2012**, 48, 8553.

(10) (a) Jalalian, N.; Ishikawa, E. E.; Silva, L. F., Jr.; Olofsson, B. Room Temperature, Metal-Free Synthesis of Diaryl Ethers with Use of Diaryliodonium Salts. *Org. Lett.* **2011**, *13*, 1552. (b) Kakinuma, Y.; Moriyama, K.; Togo, H. Facile Preparation of Unsymmetrical Diaryl Ethers from Unsymmetrical Diaryliodonium Tosylates and Phenols with High Regioselectivity. *Synthesis* **2013**, *45*, 183. (c) Gallagher, R. T.; Basu, S.; Stuart, D. R. Trimethoxyphenyl (TMP) as a Useful Auxiliary for *in situ* Formation and Reaction of Aryl (TMP)iodonium Salts: Synthesis of Diaryl Ethers. *Adv. Synth. Catal.* **2020**, *362*, 320.

(11) For selected examples, see: (a) Tellis, J. C.; Kelly, C. B.; Primer, D. N.; Jouffroy, M.; Patel, n. R.; Molander, G. A. Single-Electron Transmetalation via Photoredox/Nickel Dual Catalysis: Unlocking a New Paradigm for sp<sup>3</sup>-sp<sup>2</sup> Cross-Coupling. Acc. Chem. Res. 2016, 49, 1429. (b) Hopkinson, M. H.; Sahoo, B.; Li, J.; Glorius, F. Dual Catalysis Sees the Light: Combining Photoredox with Organo-, Acid, and Transition-Metal Catalysis. Chem. - Eur. J. 2014, 20, 3874. (c) Gui, Y.; Sun, L.; Lu, Z.; Yu, D. Photoredox Sheds New Light on Nickel Catalysis: from Carbon-Carbon to Carbon-Heteroatom Bond Formation. Org. Chem. Front. 2016, 3, 522. (d) Hopkinson, M. N.; Tlahuext-Aca, A.; Glorius, F. Merging Visible Light Photoredox and Gold Catalysis. Acc. Chem. Res. 2016, 49, 2261. (e) Oderinde, M. S.; Frenette, M.; Robbins, D. W.; Aquila, B.; Johannes, J. W. Photoredox Mediated Nickel Catalyzed Cross-Coupling of Thiols With Aryl and Heteroaryl Iodides via Thiyl Radicals. J. Am. Chem. Soc. 2016, 138, 1760. (f) Corcoran, E. B.; Pirnot, M. T.; Lin, S.; Dreher, S. D.; DiRocco, D. A.; Davies, I. W.; Buchwald, S. L.; MacMillan, D. W. C. Aryl Amination Using Ligand-Free Ni(II) Salts and Photoredox Catalysis. Science 2016, 353, 279. (g) Shaw, M. H.; Shurtleff, V. W.; Terrett, J. A.; Cuthbertson, J. D.; MacMillan, D. W. C. Native Functionality in Triple Catalytic Cross-Coupling: sp<sup>3</sup> C-H Bonds as Latent Nucleophiles. Science 2016, 352, 1304. (h) Lin, K.; Wiles, R. J.; Kelly, C. B.; Davies, G. H. M.; Molander, G. A. Haloselective Cross-Coupling via Ni/Photoredox Dual Catalysis. ACS Catal. 2017, 7, 5129. (i) Twilton, J.; Le, C.; Zhang, P.; Shaw, M. H.; Evans, R. W.; MacMillan, D. W. C. The Merger of Transition Metal and Photocatalysis. Nat. Rev. Chem. 2017, 1, 0052.

(12) (a) Terrett, J. A.; Cuthbertson, J. D.; Shurtleff, V. W.; MacMillan, D. W. C. Switching on Elusive Organometallic Mechanisms with Photoredox Catalysis. Nature 2015, 524, 330. (b) Welin, E. R.; Le, C.; Arias-Rotondo, D. M.; McCusker, J. K.; MacMillan, D. W. C. Photosensitized Energy Transfer-Mediated Organometallic Catalysis Through Electronically Excited Nickel(II). Science 2017, 355, 380. For a synthesis of benzylic ethers from  $\alpha$ alkoxymethyltrifluoroborates combining photoredox and Ni catalysis, see: (c) Karakaya, I.; Primer, D. N.; Molander, G. A. Photoredox Cross-Coupling: Ir/Ni Dual Catalysis for the Synthesis of Benzylic Ethers. Org. Lett. 2015, 17, 3294. For a recent example of aryl alkyl ether formation using nickel but not involving photoredox catalysis, see: (d) MacQueen, P. M.; Tassone, J. P.; Diaz, C.; Stradiotto, M. Exploiting Ancillary Ligation To Enable Nickel-Catalyzed C-O Cross-Couplings of Aryl Electrophiles with Aliphatic Alcohols. J. Am. Chem. Soc. 2018, 140, 5023.

(13) Yang, L.; Huang, Z.; Li, G.; Zhang, W.; Cao, R.; Wang, C.; Xiao, J.; Xue, D. Synthesis of Phenols: Organophotoredox/Nickel Dual Catalytic Hydroxylation of Aryl Halides with Water. *Angew. Chem., Int. Ed.* **2018**, *57*, 1968.

(14) (a) Sun, R.; Qin, Y.; Ruccolo, S.; Schnedermann, C.; Costentin, C.; Nocera, D. G. Elucidation of a Redox-Mediated Reaction Cycle for Nickel-Catalyzed Cross Coupling. *J. Am. Chem. Soc.* **2019**, *141*, 89. For a study showing the disproportionation of ArNi(II) species in the presence of light, see: (b) Shields, B. J.; Kudisch, B.; Scholes, G. D.; Doyle, A. G. Long-Lived Charge-Transfer States of Nickel(II) Aryl Halide Complexes Facilitate Bimolecular Photoinduced Electron Transfer. *J. Am. Chem. Soc.* **2018**, *140*, 3035.

(15) During the preparation of this manuscript, Wang and coworkers reported a new protocol for diaryl ether formation from aryl bromides and phenols promoted by visible light. This method works only for aryl bromides with electron-withdrawing groups, and the reaction needs to be carried out at 80 °C. For details, see: Yang, Q.-Q.; Liu, N.; Yan, J.-Y.; Ren, Z.-L.; Wang, L. Visible Light- and Heat-Promoted C–O Coupling Reaction of Phenols and Aryl Halides. *Asian J. Org. Chem.* **2020**, *9*, 116.

(16) (a) Uoyama, H.; Goushi, K.; Shizu, K.; Nomura, H.; Adachi, C. Highly Efficient Organic Light-Emitting Diodes from Delayed Fluorescence. *Nature* 2012, 492, 234. (b) Lowry, M. S.; Goldsmith, J. I.; Slinker, J. D.; Rohl, R.; Pascal, R. A.; Malliaras, G. G.; Bernhard, S. Single-Layer Electroluminescent Devices and Photoinduced Hydrogen Production from an Ionic Iridium(III) Complex. *Chem. Mater.* 2005, 17, 5712.

(17) (a) Wang, X.; Davies, G. H. M.; Koschitzky, A.; Wisniewski, S. R.; Kelly, C. B.; Molander, G. Photoredox Catalysis Enables Access to N-Functionalized 2,1-Borazaronaphthalenes. A. Org. Lett. 2019, 21, 2880. (b) Shu, C.; Mega, R. S.; Andreassen, B. J.; Noble, A.; Aggarwal, V. K. Synthesis of Functionalized Cyclopropanes from Carboxylic Acids by a Radical Addition–Polar Cyclization Cascade. Angew. Chem., Int. Ed. 2018, 57, 15430. (c) Shang, T.; Lu, L.; Cao, Z.; Liu, Y.; He, W.; Yu, B. Recent Avances of 1,2,3,5-Tetrakis(carbazol-9-yl)-4,6-dicyanobenzene (4CzIPN) in Photocatalytic Transformations. Chem. Commun. 2019, 55, 5408.

(18) (a) Altman, R. A.; Buchwald, S. L. Cu-Catalyzed N- and O-Arylation of 2-, 3-, and 4-Hydroxypyridines and Hydroxyquinolines. *Org. Lett.* **2007**, *9*, 643. (b) Zhai, Y.; Chen, X.; Zhou, W.; Fan, M.; Lai, Y.; Ma, D. Copper-Catalyzed Diaryl Ether Formation from (Hetero)-aryl Halides at Low Catalytic Loadings. J. Org. Chem. **2017**, *82*, 4964.

(19) Lee, H.; Boyer, N. C.; Deng, Q.; Kim, H.; Sawyer, T. K.; Sciammetta, N. Photoredox Ni-Catalyzed Peptide  $C(sp^2)$ –O Cross-Coupling: From Intermolecular Reactions to Side Chain-to-Tail Macrocyclization. *Chem. Sci.* **2019**, *10*, 5073.

(20) For examples of the direct transformation of aryl halides into symmetrical diaryl ethers, see: Tlili, A.; Monnier, F.; Taillefer, M. Selective One-Pot Access to Symmetrical or Unsymmetrical Diaryl Ethers by Copper-Catalyzed Double Arylation of a Simple Oxygen Source. *Chem. - Eur. J.* **2010**, *16*, 12299.

(21) Pirovano, P.; Farquhar, E. R.; Swart, M.; McDonald, A. R. Tuning the Reactivity of Terminal Nickel(III)–Oxygen Adducts for C–H Bond Activation. J. Am. Chem. Soc. **2016**, *138*, 14362.

(22) (a) Matsunaga, P. T.; Hillhouse, G. L.; Rheingold, A. L. Oxygen-Atom Transfer from Nitrous Oxide to a Nickel Metallacycle. Synthesis, Structure, and Reactions of [cyclic] (2,2'-bipyridine)Ni-(OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>). J. Am. Chem. Soc. **1993**, 115, 2075. (b) Han, R.; Hillhouse, G. L. Carbon–Oxygen Reductive-Elimination from Nickel(II) Oxametallacycles and Factors That Control Formation of Ether, Aldehyde, Alcohol, or Ester Products. J. Am. Chem. Soc. **1997**, 119, 8135.

(23) Since base proved to be critical to the transformation, fluorescence quenching with the corresponding phenolate of 2 in DMF was also carried out. The quenching rate of Ni(II) species 43 is much higher than that of the phenolate. For details, see the Supporting Information.

(24) The data are in agreement with reported data for oxidation of Ni(II) to Ni(III). See: Klein, A.; Kaiser, A.; Wielandt, W.; Belaj, F.; Wendel, E.; Bertagnolli, H.; Zalis, S. Halide Ligands—More Than Just  $\sigma$ -Donors? A Structural and Spectroscopic Study of Homologous Organonickel Complexes. *Inorg. Chem.* **2008**, 47, 11324. Also see ref 12.

(25) (a) Luo, J.; Zhang, J. Donor–Acceptor Fluorophores for Visible-Light-Promoted Organic Synthesis: Photoredox/Ni Dual Catalytic  $C(sp^3)-C(sp^2)$  Cross-Coupling. ACS Catal. **2016**, 6, 873. (b) Le Vaillant, F.; Garreau, M.; Nicolai, S.; Gryn'ova, G.; Corminboeuf, C.; Waser, J. Donor–Acceptor Fluorophores for Visible-Light-Promoted Organic Synthesis: Photoredox/Ni Dual Catalytic  $C(sp^3)-C(sp^2)$  Cross-Coupling. Chem. Sci. **2018**, 9, 5883.