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Effects of Molecular Oxygen, Solvent, and Light on Iridium-Photoredox/Nickel Dual-Catalyzed Cross-Coupling Reactions

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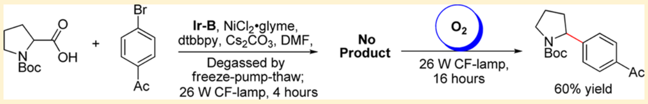
Ⓢ *Supporting Information*

ABSTRACT: In order to achieve reproducibility during iridium-photoredox and nickel dual-catalyzed sp^3−sp^2 carbon−carbon bond-forming reactions, we investigated the role that molecular oxygen (O$_2$), solvent and light-source (CF lamp or blue LED) play in a variety of Ir-photoredox mediated transformations. The presence of O$_2$ was discovered to be important for catalyst activation when air-stable Ni(II) precatalysts were used in DMF under CF lamp irradiation; however, O$_2$ was not required for catalysis when conducted with Ni(COD)$_2$ in the same reaction system. O$_2$ is believed to promote rapid reduction of the Ni(II) precatalyst by Ir(II) to Ni(0). In addition to O$_2$, the effects that solvent and light-source have on the dual-catalyzed decarboxylative cross-coupling reactions will be discussed. These findings have enabled us to develop a more robust dual-catalyzed decarboxylative cross-coupling protocol.

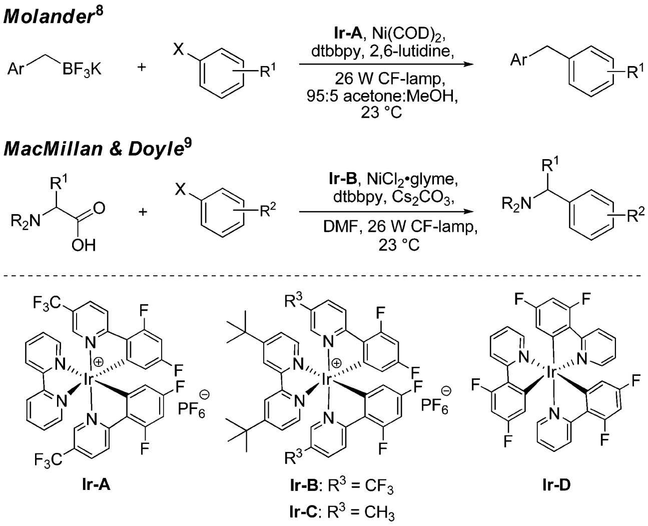


■ INTRODUCTION

Recent progress in photoredox chemistry has expanded the toolbox for carbon−carbon bond-forming reactions. The ability of photoredox transition-metal complexes to engage in single-electron transfer (SET) processes upon excitation by visible light with both electron-releasing and electron-accepting organic and organometallic compounds under mild conditions to generate reactive radical species make them powerful synthetic tools.[1−5] During the past decade, nickel catalysis has enabled the construction of various carbon−carbon bonds via the cross-coupling of organometallic nucleophiles with various electrophiles including aryl, vinyl, and alkyl halides.[6] The easy accessibility of Ni(I) and Ni(III) oxidation states in nickel catalysis also allows different modes of reactivity relative to the reactivity patterns of the well-known palladium catalytic cycle.[7]

Molander[8] and MacMillan and Doyle[9] recently reported their pioneering findings of Ir-photoredox/nickel dual catalysis in sp^3−sp^2 carbon−carbon bond formation (Scheme 1). While Molander showed the cross-coupling of potassium benzyltrifluoroborates with aryl halides,[8] MacMillan and Doyle demonstrated the decarboxylative cross-coupling of α-amino acids with aryl halides.[9] In the context of medicinal chemistry, the construction of strategic bonds between readily accessible α-amino acids or potassium benzyltrifluoroborates and aryl halides attracted our attention to these two protocols. In addition, we were intrigued by the use of air-stable NiCl$_2$·glyme as the precatalyst for the cross-coupling reactions. Our interest in the application of both protocols led us to discover that O$_2$ can play an important role in the decarboxylative cross-coupling reactions under Ir-photoredox/Ni dual catalysis. Specifically, we discovered that exposure of the reaction to O$_2$ is crucial for the activation of the Ni(II) precatalyst and the reproducibility of the reaction under certain conditions. Because of this discovery, more thorough experimental and mechanistic investigations of the Ir-photoredox/Ni dual catalysis as well as studies of the O$_2$ effect on other Ir-photoredox carbon−carbon bond-forming reactions were initiated.

Scheme 1. Reported Dual-Catalyzed sp^3−sp^2 Cross-Coupling Reactions[8,9]



Herein, we report on the effects of molecular oxygen (O$_2$), solvents, and light on the Ir-photoredox and nickel dual-catalyzed cross-coupling reactions.

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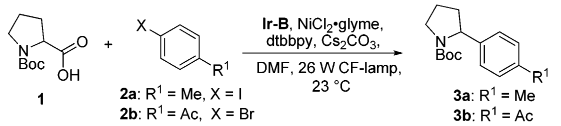
■ RESULTS AND DISCUSSION

We began our investigations by conducting the decarboxylative cross-coupling reaction of Boc-Pro-OH (**1**) and 4-iodotoluene (**2a**) following the reported protocol with the in situ generated $NiCl_2$·dtbbpy complex and photoredox catalyst **Ir–B** with the rigorous exclusion of O_2 (Table 1).[9] Surprisingly, no cross-coupled product (**3a**) was formed, and the 4-iodotoluene (**2a**) was quantitatively recovered (Table 1, entry 1). Likewise, no product was obtained when the reaction was conducted with a DMF/H_2O (99:1) solvent mixture in the absence of O_2, suggesting that H_2O does not initiate catalysis (entry 2). Based on these observations, we suspected that O_2 could be required for the catalysis to proceed.[10,11] Gratifyingly, the expected cross-coupled product (**3a**) was obtained in 69% yield when the reaction mixture was not degassed (entry 3). Similarly, the decarboxylative cross-coupling of Boc-Pro-OH (**1**) and 4-bromoacetophenone (**2b**), which did not proceed under rigorously degassed conditions (entry 4), proceeded to give **3b** in 95% yield when the reaction mixture was not degassed (entry 5). The rate studies of this particular reaction showed 60% conversion to **3b** in 5 h (see the Supporting Information for the rate curve). In contrast to **Ir-B**, the following yields were obtained for **3b** when the reaction was carried out with other photoredox catalysts and $NiCl_2$·dtbbpy under 26 W CF lamp irradiation: **Ir-A** (with O_2 = 17%, without O_2 = 0%), **Ir-C** (with O_2 = 82%, without O_2 = 14%), and **Ir-D** (with and without O_2 = 0%). After further optimization studies with **Ir-B** and $NiCl_2$·dtbbpy, the reaction concentration was increased to 0.04 M from 0.02 M, and the reaction time was significantly reduced from 72 h to less than 20 h (see Table S1 in the Supporting Information for 12 substrate examples).

Table 1. O_2 Effect on the Ir-Photoredox/Nickel Dual-Catalyzed Decarboxylative Cross-Coupling Reaction[a]



entry	X	R[1]	conditions[b]	reaction mixture	% yield[c]
1	I	CH_3	none	degassed	0
2	I	CH_3	H_2O[d]	degassed	0
3	I	CH_3	none	not degassed[e]	69
4	Br	$COCH_3$	none	degassed	0
5	Br	$COCH_3$	none	not degassed[e]	>95
6	Br	$COCH_3$	NiI_2[f]	degassed	0
7	Br	$COCH_3$	$Ni(OTf)_2$[f]	degassed	0
8	Br	$COCH_3$	NiI_2[f]	not degassed[e]	30
9	Br	$COCH_3$	$Ni(OTf)_2$[f]	not degassed[e]	50
10	Br	$COCH_3$	$Ni(COD)_2$[f]	degassed	>95
11	Br	$COCH_3$	$Ni(COD)_2$[f]	not degassed[e]	>95

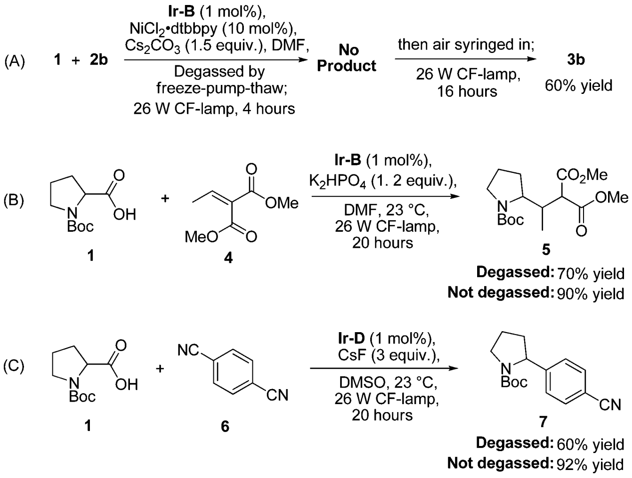
[a] Unless otherwise indicated, reactions were carried out with Boc-Pro-OH (**1**) (0.6 mmol), aryl halide (**2**) (0.4 mmol), **Ir-B** (1 mol %), $NiCl_2$·glyme (10 mol %), dtbbpy (15 mol %), DMF (10 mL), and Cs_2CO_3 (0.6 mmol) and irradiated with one 26 W CF lamp at room temperature for 20 h; the reaction mixture was degassed either by sparging with an argon or a nitrogen stream for at least 20 min or by three freeze−pump−thaw cycles before irradiation. [b] Variation from standard conditions *a*. [c] Each reaction was repeated multiple times. [d] DMF/H_2O (99:1) mixture was used. [e] The headspace was purged with N_2 for 10 s to remove excess O_2. [f] NiX_2 (10 mol %) and dtbbpy (15 mol %) were used.

To ensure that the O_2 effect on this catalysis is not limited to the use of $NiCl_2$·dtbbpy, we carried out the reaction of **1** and **2b** with in situ generated NiI_2·dtbbpy and $Ni(OTf)_2$·dtbbpy. Similar to $NiCl_2$·dtbbpy, no cross-coupled product was obtained with either Ni(II) complex in the absence of oxygen (Table 1, entries 6 and 7). Conversely, the cross-coupled product (**3b**) was obtained in 30% and 50% yield, respectively, when neither reaction mixture was degassed (Table 1, entries 8 and 9).

To this end, the quantitative recovery of the aryl halides (**2a** and **2b**) in the absence of O_2 led us to think that the presence of O_2 may be crucial for the activation of the Ni(II) precatalyst to give an active Ni species (Ni(I) or Ni(0)), which initiates the Ni cycle. In such a case, a reaction with a Ni(0) precatalyst should proceed in the absence of O_2. Indeed, the cross-coupling reaction of **1** and **2b** proceeded to give **3b** in quantitative yield when $Ni(COD)_2$ was used under O_2-free conditions (all reagents were added inside an N_2-filled glovebox, Table 1, entry 10). Remarkably, when $Ni(COD)_2$ was weighed out in air and used in the cross-coupling reaction of **1** and **2b** that was not degassed prior to irradiation, the reaction still proceeded to give **3b** in quantitative yield (Table 1, entry 11). The ability to carry out this dual catalysis with $Ni(COD)_2$ in the presence of O_2 shows the high tolerance of this catalysis to O_2.

To better understand the role that O_2 plays in this dual catalysis, additional control reactions were conducted. Hence, the reaction of **1** and **2b** under O_2-free conditions that did not show any cross-coupled product after 4 h was initiated by introducing air into the reaction mixture with a syringe. Further irradiation of the same reaction resulted in the formation of **3b** in 60% yield (Scheme 2a). This shows that O_2 is indeed required to promote the catalysis under these reaction conditions. In addition, when the Ir-photoredox-mediated decarboxylative conjugate addition reaction of Boc-Pro-OH (**1**) to malonate **4** was conducted in the absence of O_2, a diastereomeric mixture of **5** was obtained in 70% yield (Scheme 2b).[12a] Similarly, the Ir-photoredox-mediated decarboxylative arylation of Boc-Pro-OH (**1**) with 1,4-dicyanobenzene (**6**) gave **7** in 60% yield in the absence of O_2 (Scheme 2c).[12b] However, the yields of compounds **5** and **7** both increased to 90% and 92%, respectively, when their reactions (parts b and c of Scheme 2), were carried out in the presence of O_2. To the best

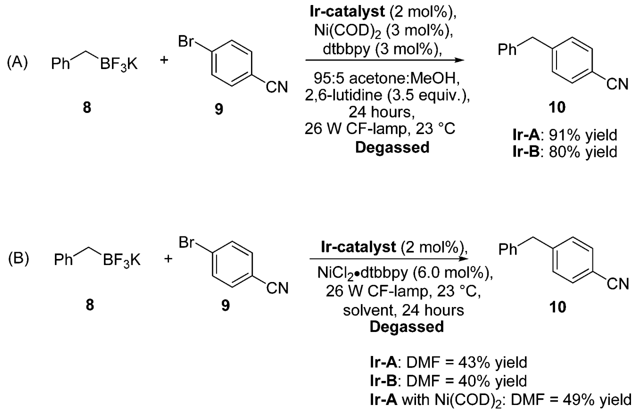
Scheme 2. Control Experiments To Demonstrate O_2 Effect on Ir Photocatalysis



of our knowledge, this is also the first report of O_2 effects and tolerance in both of these synthetically useful reactions.

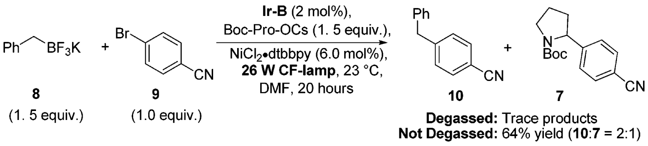
To investigate whether O_2 plays a role in other Ir-photoredox/Ni dual catalysis, we turned our attention to the reported dual-catalyzed cross-coupling protocol of potassium benzyltrifluoroborate (**8**) and 4-bromobenzonitrile (**9**) with $Ni(COD)_2$ as the precatalyst in acetone−methanol−2,6-lutidine solvents system.[8a] The cross-coupling of potassium benzyltrifluoroborate (**8**) and 4-bromobenzonitrile (**9**) under O_2-free conditions (an N_2-filled glovebox was used) gave the cross-coupled product (**10**) in 80−91% yield with either **Ir-A** or **Ir-B** and $Ni(COD)_2$ dual catalyst (Scheme 3a).[8a] In order to gain a better understanding of the dual catalysis, and in particular the catalysis with Ni(II) precatalyst, we studied this reaction in DMF. When the dual-catalyzed cross-coupling of **8** and **9** was carried out in DMF with the rigorous exclusion of O_2 with **Ir-A** and $NiCl_2{\cdot}dtbbpy$ precatalyst, the reaction proceeded to give product **10** in 43% yield while the mass balance was the unreacted 4-bromobenzonitrile (**9**) (Scheme 3b). Notably, the yield of **10** was not impacted in any significant way when either photoredox catalyst **Ir-B** or $Ni(COD)_2$ precatalyst was used in the absence of O_2 (Scheme 3b).[13] These results imply that the $NiCl_2{\cdot}dtbbpy$ precatalyst can be reduced by Ir(II) to the active Ni(0)·dtbbpy under this dual catalysis and in the absence of O_2. Nonetheless, we considered the possibility of potassium benzyltrifluoroborate (**8**) activating the $NiCl_2{\cdot}dtbbpy$ to the Ni(0)·dtbbpy via a double-transmetalation/reductive elimination mechanism.[6,7] This alternate activation mechanism was, however, ruled out after a reaction mixture of 20 mol % of **8** and 10 mol % $NiCl_2{\cdot}dtbbpy$ failed to initiate the decarboxylative cross-coupling reaction of **1** and **2b** in the absence of O_2.

Scheme 3. Dual-Catalyzed Cross-Coupling Reaction of Potassium Benzyltrifluoroborate and 4-Bromobenzontrile in the Absence of O_2



To explain the drastically different oxygen dependencies of these two closely related catalytic systems, we suspected that in the case of the decarboxylative cross-coupling reaction the carboxylate salt could be reacting rapidly with the $NiX_2{\cdot}dtbbpy$ to form a new Ni(II) complex, which is not being reduced by Ir(II). In this regard, experiments to examine the effects of Boc-Pro-OCs on the cross-coupling reaction of potassium benzyltrifluoroborate (**8**) and 4-bromobenzonitrile (**9**) were carried out. When the cross-coupling reaction of potassium benzyltrifluoroborate (**8**) and 4-bromobenzonitrile (**9**) was performed in the presence of in situ generated Boc-Pro-OCs (1.5:1.5:1.0 ratio of Boc-Pro-OCs:**8**:**9**) and $NiCl_2{\cdot}dtbbpy$ precatalyst with the rigorous exclusion of O_2, only trace cross-coupled products were observed (Scheme 4). Conversely, when the same reaction was carried out in the presence of O_2, catalysis occurred to give products **10** and **7** in combined 64% yield (**10**:**7** = 2:1). These control reactions show that the presence of Boc-Pro-OCs prevents catalysis with $NiCl_2{\cdot}dtbbpy$ precatalyst from occurring in the absence of O_2.

Scheme 4. Effects of Boc-Pro-OCs on the Cross-Coupling Reaction of Potassium Benzyltrifluoroborate and 4-Bromobenzontrile



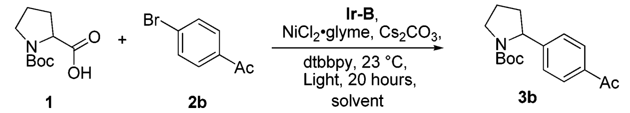
In fact, there is a ligand exchange reaction between $NiCl_2{\cdot}$dtbbpy (1.0 equiv) and Boc-Pro-OCs (15 equiv) in DMF at room temperature to give what is believed to be (Boc-Pro-O)NiCl·dtbbpy (**11**) as indicated by in situ mass spectroscopic analysis (m/z $[M - Cl]^+$ = 540.20 and 542.20 in 3:1 isotopic ratio, indicating the presence of one Cl atom in the complex). The same mass peaks were also observed in reaction mixtures that did not proceed in the absence of O_2. Unfortunately, the full characterization of complex **11** by other spectroscopic methods has so far been unsuccessful due to decomposition during isolation.

We recognized that $O_2^{\bullet -}$ is known to be generated in situ from the reduction of O_2 in Ir-photoredox catalyzed reactions;[11] hence, we examined if $O_2^{\bullet -}$ activates the Ni(II) complex by reducing it via a SET process to give Ni(0) species and O_2. However, no oxidative addition product was observed when 2 equiv of KO_2 was stirred with a mixture of $NiCl_2{\cdot}$dtbbpy, Boc-Pro-OCs, and **2a** in DMF. Therefore, the inability to detect any oxidative addition product suggests that $O_2^{\bullet -}$ is not reducing the Ni(II) complex to an active Ni species (see the Supporting Information). Exploration of the literature revealed that molecular oxygen enhances the intersystem crossing (ISC) processes of organic molecules (assisted intersystem crossing).[14,15] We believe that the presence of O_2 in all these photoredox reactions enhanced the intersystem crossing (ISC) process of the excited singlet state of *Ir(III) to its excited triplet state, which has a longer lifetime.[1,14,15] An enhancement of the ISC process will result in a more efficient formation of the excited triplet state of *Ir(III) and a faster reductive quenching of *Ir(III) by the carboxylate salt to give Ir(II) and carboxyl radical. In other words, the reductant Ir(II) will be formed at a faster rate when the ISC process is enhanced. Therefore, the rate of reduction of $NiCl_2{\cdot}dtbbpy$ by Ir(II) to Ni(0)·dtbbpy must be faster than the rate of the ligand exchange reaction for the cross-coupling reaction to have proceeded.

Based on this hypothesis, we screened several ligands and solvents in search of a reaction protocol that tolerates O_2 but does not depend on O_2 for catalyst activation when Ni(II) precatalyst is used (see Table S2 in the Supporting Information).

Gratifyingly, we found that by simply carrying out the reaction in MeCN instead of DMF the decarboxylative cross-coupling reaction of **1** and **2b** with $NiCl_2{\cdot}dtbbpy$ proceeded in the absence of O_2 to give **3b** in 68% yield (Table 2, entry 2).

Table 2. Solvents and Light Effects on the Ir-Photoredox/Nickel Dual-Catalyzed Decarboxylative Cross-Coupling Reaction[a]



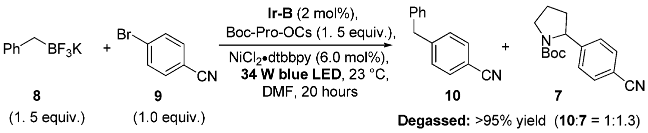
entry	light source	solvent	reaction mixture	% yield[b,c]
1	26 W CF lamp	DMF	degassed	0
2	26 W CF lamp	MeCN	degassed	68
3	26 W CF lamp	MeCN/DMF (4:1)	degassed	90
4	34 W blue LEDs	DMF	degassed	>95[d]

[a] Unless otherwise indicated, reactions were carried out with Boc-Pro-OH (**1**) (0.6 mmol), aryl halide (**2**) (0.4 mmol), **Ir-B** (1 mol %), $NiCl_2$·glyme (10 mol %), dtbbpy (15 mol %), solvent (10 mL), and Cs_2CO_3 (0.6 mmol) at room temperature for 20 h; the reaction mixture was degassed by sparging with a nitrogen stream for at least 20 min. [b] Each reaction was repeated multiple times. [c] >95% yield was obtained when the reaction mixture was not degassed. [d] This reaction went to completion within 5 h.

Unlike in DMF, the ligand-exchange reaction between $NiCl_2$·dtbbpy and carboxylate salt is very slow in MeCN due to the poor solubility of the carboxylate salt. The lower yield of the product in MeCN can also be attributed to the poor solubility of the carboxylate salt. Upon further optimization studies, the use of a 4:1 MeCN/DMF solvent mixture was found to be the ideal solvent combination for the reaction and gave **3b** in 90−95% yield with and without O_2 (Table 2, entry 3).

Interestingly, when the cross-coupling reaction of **1** and **2b** was carried out with $NiCl_2$·dtbbpy in DMF with the rigorous exclusion of O_2 and irradiated with blue LEDs instead of CF lamp, the cross-coupled product **3b** was obtained in quantitative yield in less than 5 h (Table 2, entry 1 versus 4). In addition, when the cross-coupling reaction of potassium benzyltrifluoroborate (**8**) and 4-bromobenzonitrile (**9**) in the presence of in situ generated Boc-Pro-OCs (1.5:1.5:1.0 ratio of Boc-Pro-OCs/**8**/**9**) and $NiCl_2$·dtbbpy precatalyst with the rigorous exclusion of O_2 was repeated under blue LEDs irradiation, the aryl bromide (**9**) was quantitatively converted to the cross-coupled products **10** and **7** (Scheme 5). Under this condition, the amount of **7** observed in the products mixture was also higher than **10** (**10**:**7** = 1:1.3), which is in contrast to the result obtained under the CF-lamp irradiation (Scheme 4 versus Scheme 5). In metal-photoredox-catalyzed reactions, the irradiation with a monochromatic blue LED has been reported to be more efficient and produce reactions with faster rates than those irradiated with a broad-spectrum white CF lamp.[16] Therefore, similar to our explanation of the molecular oxygen effect, we believe that the photoinduced formation of the excited triplet state of *Ir(III) is more efficient (longer lifetime and higher quantum yield)[17] under blue-LED irradiation than CF-lamp irradiation. Consequently, the SET quenching of the *Ir(III) by the carboxylate salt to give the reductant Ir(II) and the carboxyl radical as well as the reduction processes of both the Ni(II) and Ni(I) species by Ir(II) to their corresponding Ni(I) and Ni(0) species are much faster under blue-LED irradiation. The use of blue LEDs in this dual-catalytic process delivers a more efficient reaction than the use of CF lamps and molecular oxygen. It is important to note that we examined and ruled out reaction temperature as the source of the difference in the outcome of the reactions performed in the absence of O_2 under blue LEDs and CF-lamp irradiations.

Scheme 5. Effects of Boc-Pro-OCs on the Cross-Coupling Reaction of Potassium Benzyltrifluoroborate (8) and 4-Bromobenzontrile (9)



That said, another notable aspect of the reaction in Scheme 5 is that both the α-amino and benzyl radicals are being generated in the same reaction, yet the reaction favors the Ni-catalyzed cross-coupling rather than a combination reaction between these two different radicals. Studies on the effects of 2,2,6,6-tetramethyl-1-piperidinyloxy, free radical (TEMPO) on these reactions, showed that both the α-amino and benzyl radicals are indeed being generated and were trapped by TEMPO (Scheme 6). Hence, this observation is a clear manifestation of persistent radical effect.[18] In this catalytic reaction, the high energy fleeting carbon-centered radicals react selectively with the nickel species, which are the persistent radicals and are also present in a higher concentration than any carbon-centered radical whose concentration cannot be higher than that of the iridium catalyst.

A plausible mechanism for the **Ir-B** and Ni-complex dual-catalyzed decarboxylative cross-coupling reaction is shown in Figure 1. The visible-light induced photoexcitation of the singlet ground state Ir(III) gives an excited triplet state *Ir(III).[1] The *Ir(III) ($E_{1/2}^{red}$ [$*Ir^{(III)}/Ir^{(II)}$] = +1.21 V vs SCE in MeCN)[17] then accepts a single electron from an α-amino carboxylate salt ($E_{1/2}^{red}$ [Boc-Pro- OCs] = +0.95 V vs SCE in MeCN)[12b] to give the Ir(II) (reductive quenching) and a carboxyl radical.

This carboxyl radical spontaneously loses CO_2 to give an α-amino radical. Under ideal reaction conditions as discussed above and based on the known reduction potentials of the Ir(II)-complex ($E_{1/2}^{red}$ [$Ir^{(III)}/Ir^{(II)}$] = −1.37 V vs SCE in MeCN)[17] and Ni(II)halides ($E_{1/2}^{red}$ [$Ni^{(II)}/Ni^{(0)}$] = −1.20 V vs SCE in DMF),[19] a two-electron reduction of Ni(II) by Ir(II) to give Ni(0) via Ni(I) is a thermodynamically favorable process. From Ni(0)·dtbbpy (**13**), there are two possible ways by which the reaction can proceed. Ni(0)·dtbbpy (**13**) can either undergo oxidative addition to the aryl halide[9] or it can be trapped by an α-amino radical to give Ni(I)−alkyl complex **14**.[8b,c,20] The alkyl radical trap of the Ni(0)·dtbbpy (**13**) to give Ni(I)−alkyl complex **14** appears to occur more rapidly and may also explain why the reaction proceeded effectively with $Ni(COD)_2$/dtbbpy precatalyst in the presence of O_2. The Ni(I)−alkyl complex **14** will then undergo oxidative addition to aryl halide to give Ni(III) complex **15**. The Ni(III) complex **15** will undergo reductive elimination to deliver the product (Ar-R) and regenerates the Ni(I)X complex **12**, which turns over the Ni cycle.[8b,c,20] An alternate mechanistic pathway wherein Ni(I)X·dtbbpy (**12**) is first trapped by an α-amino radical to give the corresponding Ni(II) species followed by its SET reduction by Ir(II) to deliver the Ni(I)−alkyl complex **14** and Ir(III) cannot be ruled out.[20]

■ CONCLUSION

In conclusion, we have demonstrated the effect of O_2 on a variety of Ir-photoredox-mediated reactions. In order to render

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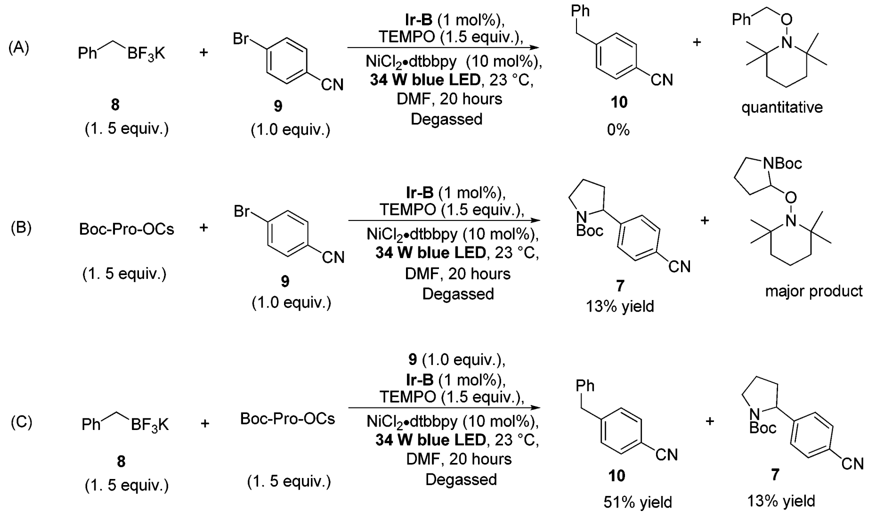
Scheme 6. TEMPO as a Free-Radical Trap of α-Amino and Benzyl Radicals



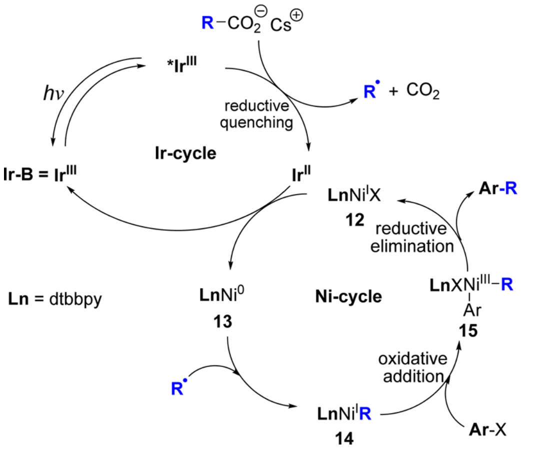


Figure 1. Proposed mechanism of Ir-photoredox/Ni dual-catalyzed decarboxylative cross-coupling reaction.

the decarboxylative cross-coupling reactions more practical and reproducible, we studied the effects of O_2 on the Ir-photoredox and nickel dual-catalyzed cross-coupling reactions. In our hands, no reaction was observed in the absence of O_2 when Ni(II) precatalyst and a CF lamp were employed in the decarboxylative cross-coupling reactions in DMF. This observation was attributed to the lack of formation of an active Ni(I) or Ni(0) species under these reaction conditions since reaction occurred with Ni(0) precatalyst in the absence of O_2. The SET reduction of Ni(II) precatalyst by Ir(II) is a thermodynamically favorable process as demonstrated by control experiments. However, reaction may not proceed if the reductant Ir(II) is being produced at a rate that is slower than the undesired ligand-exchange reaction between the substrate/reagent and the Ni(II)-precatalyst, which produces a new Ni(II)-complex with a different reduction potential. Therefore, the presence of O_2 in the reaction or the use of blue LEDs for the irradiation can impact the catalysis by enhancing the photoexcited *Ir(III) ISC process, which leads to a more rapid formation of the reductant Ir(II). Most importantly, the presence of O_2, type of solvent, and light used for the Ir-photoredox reactions have more of an impact on the catalysis than the feasibility of electron transfer. Finally, the decarboxylative cross-coupling reaction with $Ni(COD)_2$ precatalyst can be carried out with high efficiency in the presence of O_2. We hope that the new insights presented in this work regarding the effects of O_2 and blue LEDs will enable further exploitation and development of these highly valued photocatalytic carbon−carbon bond-forming reactions for the easy access of pharmacophores in both academic and industrial settings.

EXPERIMENTAL SECTION

General Methods. Reagents were purchased from commercial sources and were used as received unless otherwise stated. Ir complexes (**Ir-A**, **Ir-B**, and **Ir-C**) were synthesized following literature procedures.[17] Reactions were monitored by reversed-phase UPLC−MS. All reactions were performed using borosilicate glass vials of appropriate sizes. ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded on 400 and 500 MHz spectrometers and were internally referenced to residual protio solvent signals ($CDCl_3$ referenced at 7.26 and 77.0 ppm respectively, and $CO(CD_3)_2$ referenced at 2.05 and 29.9 ppm respectively). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad), integration, and coupling constant (Hz). Data for ^{13}C{^{1}H} NMR are reported in terms of chemical shift, and no special nomenclature is used for equivalent carbons. The HRMS were obtained using a hybrid quadrupole time-of-flight mass spectrometer in ESI$^+$ mode.

[Ir(dF(CF$_3$)ppy)$_2$(bpy)]PF$_6$ (Ir-A). A mixture of bis(μ)-chlorotetrakis-(2-(4,6-difluoromethylphenyl)pyridinato-C^2,N)diiridium(III)[17] (300 mg, 0.20 mmol, 1.0 equiv) and 2,2′-bipyridine (79 mg, 0.50 mmol, 2.5 equiv) in ethylene glycol (14 mL) was stirred and heated to reflux (150 °C) under gentle nitrogen flow for 18 h. After being cooled to room temperature, the mixture was transferred to a separatory funnel with water (100 mL) and washed with hexanes (3 × 100 mL). The yellow aqueous bottom phase was drained into an Erlenmeyer flask equipped with a magnetic bar and placed in an oil bath that had been preheated to 85 °C and stirred at the same temperature for 15 min. The flask was then immersed in an ice bath, and 20 mL of aqueous NH_4PF_6 solution (2.0 g in 20 mL of water) was added to the reaction mixture, producing a yellowish precipitate. After cooling for 20 min in the ice bath, the yellow product was collected by vacuum filtration, washed copiously with water followed by hexanes, and dried under vacuum. **Ir-A** was obtained as a bright yellow solid in 389 mg (95% yield) and confirmed pure by UPLC−MS and ^{1}H NMR. ^{1}H NMR (400 MHz, acetone-d_6): δ 8.90 (d, J = 8 Hz, 2H), 8.62 (dd, J = 8 Hz, 3 Hz, 2H), 8.41 (m, 4H), 8.31 (d, J = 6 Hz, 2H), 7.97 (s, 2H), 7.81 (t, J = 6 Hz, 2H), 6.86 (ddd, J = 13 Hz, 9 Hz, 2 Hz, 2H), 5.97 (dd, J = 9 Hz, 2 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, acetone-d_6): δ 168.7, 166.8, 164.5, 162.1, 156.9, 156.0, 152.5, 147.0, 141.6, 138.2, 130.1, 126.3,

124.9, 124.4, 121.7, 115.4, 100.3. ^{19}F-NMR (282 MHz, acetone-d_6): δ 113.9, 106.1, 103.6, 72.8, 72.7, 69.6, 69.5 ppm. HRMS (ESI): *m/z* calcd for $C_{34}H_{18}F_{10}IrN_4$ [M^+] 865.0996, found 865.1033.

*[Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ (**Ir-B**).* A mixture of bis(μ)-chlorotetrakis(2-(4,6-difluoromethylphenyl)pyridinato-C^2,N) diiridium(III)[17] (850 mg, 0.57 mmol, 1.0 equiv) and 4,4′-di-*tert*-butyl-2,2′-bipyridine (337 mg, 1.26 mmol, 2.2 equiv) in ethylene glycol (40 mL) was stirred and heated to reflux (150 °C) under nitrogen for 18 h. After being cooled to room temperature, the mixture was transferred to a separatory funnel with water (300 mL) and washed with hexanes (3 × 200 mL). The yellow aqueous bottom phase was drained into an Erlenmeyer flask equipped with a magnetic bar and placed in an oil bath taht had been preheated to 85 °C and stirred at same temperature for 15 min. The flask was then immersed an ice bath, and 20 mL of aqueous NH_4PF_6 solution (15.0 g in 150 mL of water) was added to the reaction mixture, producing a yellowish precipitate. After being cooled for 20 min in the ice bath, the yellow product was collected by vacuum filtration, washed copiously with water followed by hexanes, and dried under vacuum. **Ir-B** was obtained as a bright yellow solid in 1.24 g (96% yield) and confirmed pure by UPLC-MS and ^{1}H NMR. ^{1}H NMR (400 MHz, acetone-d_6): δ 8.93 (d, *J* = 8 Hz, 2H), 8.61 (dd, *J* = 9 Hz, 3 Hz, 2H), 8.40 (dd, *J* = 9 Hz, 2 Hz, 2H), 8.20 (d, *J* = 6 Hz, 2H), 7.76−7.86 (m, 4H), 6.89 (ddd, *J* = 13 Hz, 9 Hz, 2 Hz, 2H), 5.97 (dd, *J* = 9 Hz, 2 Hz, 2H), 1.43 (s, 18H). ^{13}C{^{1}H} NMR (100 MHz, acetone-d_6): δ 168.9, 166.5, 164.6, 162.2, 157.1, 156.8, 152.1, 146.8, 138.2, 127.9, 127.1, 125.1, 125.0, 123.6, 121.8, 115.6, 115.4, 100.3, 36.7. ^{19}F-NMR (282 MHz, acetone-d_6): δ 113.8, 106.1, 103.6, 72.8, 72.7, 69.5, 69.4. HRMS (ESI): *m/z* calcd for $C_{42}H_{34}F_{10}IrN_4$ [M^+] 977.2248, found 977.2271. Characterization data for this compound matched that reported in the literature.[17]

General Experimental Procedures. *Procedure A.* A 20 mL vial was charged with Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ (**Ir-B**) (4.5 mg, 4.00 μmol, 0.01 equiv), $NiCl_2$·glyme (8.76 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (**2b**) (79.6 mg, 0.40 mmol, 1.0 equiv), Cs_2CO_3 (195.0 mg, 0.60 mmol, 1.5 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), a magnetic stirring bar, and DMF (10 mL). The headspace of the reaction mixture was purged with nitrogen for 10 s according to Figure S3, sealed, and wrapped with parafilm. The reaction mixture was then irradiated for 20 h with a 26 W CF lamp clamped at approximately 2 cm away from the reaction vial. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (10 mL) and extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with water (3 × 25 mL) and brine (50 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash chromatography on silica gel, eluting with EtOAc and hexanes gradient, afforded the desired product.

Procedure B. A 20 mL vial was charged with Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ (**Ir-B**) (4.5 mg, 4.00 μmol, 0.01 equiv), Ni(COD)$_2$ (11.0 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (**2b**) (79.6 mg, 0.40 mmol, 1.0 equiv), Cs_2CO_3 (195.0 mg, 0.60 mmol, 1.5 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), a magnetic stirring bar, and DMF (10 mL). The headspace of the reaction mixture was purged with nitrogen for 10 s according to Figure S3, sealed, and wrapped with parafilm. (*Note: this procedure gave product with similar yield when conducted in the absence of molecular oxygen.*) The reaction mixture was then irradiated for 20 h with a 26 W CF lamp clamped at approximately 2 cm away from the reaction vial. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (10 mL), extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with water (3 × 25 mL) and brine (50 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash chromatography on silica gel, eluting with EtOAc and hexanes gradient, afforded the desired product.

Procedure C. A 20 mL vial was charged with Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ (**Ir-B**) (4.5 mg, 4.00 μmol, 0.01 equiv), $NiCl_2$·glyme (8.76 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (**2b**) (79.6 mg, 0.40 mmol, 1.0 equiv), Cs_2CO_3 (195.0 mg, 0.60 mmol, 1.5 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), a magnetic stirring bar, and MeCN/DMF (8 mL:2 mL). The headspace of the reaction mixture was purged with nitrogen for 10 s according to Figure S3, sealed, and wrapped with parafilm. (*Note: this procedure gave product in good yield when conducted in the absence of molecular oxygen.*) The reaction mixture was then irradiated for 20 h with a 26 W CF lamp clamped at approximately 2 cm away from the reaction vial. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (10 mL), extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with water (3 × 25 mL) and brine (50 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash chromatography on silica gel, eluting with EtOAc and hexanes gradient, afforded the desired product.

Procedure D. A 40 mL vial was charged with Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ (**Ir-B**) (4.5 mg, 4.00 μmol, 0.01 equiv), $NiCl_2$·glyme (8.76 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (**2b**) (79.6 mg, 0.40 mmol, 1.0 equiv), Cs_2CO_3 (195.0 mg, 0.60 mmol, 1.5 equiv), Boc-Pro-OH (**1**) (129 mg, 0.60 mmol, 1.5 equiv), a magnetic stirring bar, and DMF (10 mL). The reaction mixture was degassed either by sparging with nitrogen/argon stream for 20−30 min according to Figure S1 or by a freeze−pump−thaw technique according to Figure S2. (*Note: the reaction proceeded with high efficiency without degassing; hence, degassing is unnecessary and a simple headspace purge is sufficient.*) The reaction mixture was then irradiated for 5−20 h with 34 W blue LEDs as shown in Figure S5. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (10 mL) and extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with water (3 × 25 mL) and brine (50 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash chromatography on silica gel, eluting with EtOAc and hexanes gradient, afforded the desired product.

*tert-Butyl 2-p-Tolylpyrrolidine-1-carboxylate (**3a**).* A 20 mL vial was charged with Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ (**Ir-B**) (4.5 mg, 4.00 μmol, 0.01 equiv), $NiCl_2$·glyme (8.76 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-iodotoluene (**2a**) (89.0 mg, 0.40 mmol, 1.0 equiv), Cs_2CO_3 (195.0 mg, 0.60 mmol, 1.5 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), a magnetic stirring bar, and DMF (10 mL). The headspace of the reaction mixture was purged with nitrogen for 10 s according to Figure S3, sealed, and wrapped with parafilm. The reaction mixture was then irradiated for 20 h with a 26 W CF lamp clamped at approximately 2 cm away from the reaction vial. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ solution (10 mL) and extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with water (3 × 25 mL) and brine (50 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash chromatography on silica gel, eluting with 15% EtOAc and 85% hexanes, gave **3a** as a colorless oil (89 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) rotameric mixture: δ 7.10−7.03 (m, 4H), 4.79 (br, 1H), 3.60−3.52 (m, 2H), 2.33−2.25 (m, 4H), 1.91−1.79 (m, 3H), 1.24 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) rotameric mixture, resonances for minor rotamer are enclosed in parentheses: δ 154.7, 142.1 (141.1), 135.9, (129.0) 128.8, 125.4, 79.1, 61.0 (60.5), (47.3) 47.0, 36.0 (34.9), (28.6) 28.2, (23.4) 23.1, 21.0. HRMS (ESI): *m/z* calcd for $C_{16}H_{24}NO_2$ [$(M + H)^+$] 262.1802, found 262.1809. Characterization data matched that reported in the literature.[9a]

*tert-Butyl 2-(4-Acetylphenyl)pyrrolidine-1-carboxylate (**3b**).* A 20 mL vial was charged with Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ (**Ir-B**) (4.5 mg, 4.00 μmol, 0.01 equiv), $NiCl_2$·glyme (8.76 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (**2b**) (79.6 mg, 0.40 mmol, 1.0 equiv), Cs_2CO_3 (195.0 mg, 0.60 mmol, 1.5 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), a magnetic stirring bar, and DMF (10 mL). The headspace of the reaction mixture was purged with nitrogen for 10 s according to Figure S3, sealed, and wrapped with parafilm. The reaction mixture was then irradiated for 20 h with a 26 W CF lamp clamped at approximately 2 cm away from the reaction vial. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ solution (10 mL), extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with water (3 × 25 mL) and brine (50 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash chromatography on silica gel, eluting with 20% EtOAc and 80% hexanes gradient, gave **3b** as a colorless oil (110 mg, 95%). ^1H NMR (400 MHz, $CDCl_3$) rotameric mixture: δ 7.91 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 4.97 and 4.82 (2 brs, 1H, rotamer), 3.70–3.51 (m, 2H), 2.60 (s, 3H), 2.38–2.32 (m, 1H), 1.94–1.76 (m, 3H), 1.46 (s, 3H), 1.19 (s, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) rotameric mixture, resonances for minor rotamer are enclosed in parentheses: δ 197.7, 154.4, 150.8 (149.8), 135.7, 128.4, 125.6, 79.5, 61.1 (60.7), 47.1, 35.9 (34.8), (28.4) 28.2, 26.6, (23.6) 23.3. HRMS (ESI) m/z calcd for $C_{17}H_{24}NO_3$ [$(M + H)^+$] 290.1751, found 290.1759. Characterization data matched that reported in the literature.[9a]

*Dimethyl 2-(1-(1-(tert-Butoxycarbonyl)pyrrolidin-2-yl)ethyl)-malonate (**5**).* Into a 10 mL glass vial were added Ir[dF(CF_3)-ppy)]$_2$(dtbbpy)PF_6 (**Ir-B**) (11.2 mg, 10.0 μmol, 0.01 equiv), Boc-Pro-OH (**1**) (215 mg, 1.00 mmol, 1.0 equiv), dimethyl ethylidenemalonate (**4**) (158 mg, 1.00 mmol, 1.0 equiv), K_2HPO_4 (209 mg, 1.20 mmol, 1.2 equiv), and 2.5 mL of DMF. The reaction mixture was degassed by a freeze–pump–thaw technique according to Figure S2. The mixture was then irradiated for 20 h with a 26 W fluorescent lamp clamped at approximately 2 cm away from the reaction vial. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ solution (5 mL), extracted with Et_2O (3 × 50 mL). The combined organic extracts was washed with water (30 mL) and brine (30 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash chromatography on silica gel, eluting with 20% EtOAc and 80% hexanes gradient, gave **5** as a pale yellow oil (231 mg, 70%). ^1H NMR (400 MHz, $CDCl_3$) mixture of diastereomers (1:1) and rotamers, hence see spectra below: δ 3.98–3.80 (m, 0.38H), 3.73–3.71 (s,s,s, 6H), 3.67–3.27 (m, 2H), 3.16–3.00 (m, 1H), 2.86–2.77 (m, 0.53H), 2.75–2.60 (br, 0.21H), 2.59–2.50 (br, 0.18H), 2.01–1.90 (m, 0.78H), 1.88–1.63 (m, 3H), 1.48 (s, 9H), 1.38 (d, J = 6 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) mixture of diastereomers and rotamers: δ 168.9, 168.5, 155.0, 154.6, 79.6, 79.0, 77.3, 77.2, 77.0, 76.7, 61.0, 60.5, 60.1, 55.0, 54.2, 53.7, 52.2, 52.1, 52.0, 47.6, 47.1, 46.6, 37.8, 37.1, 36.9, 36.7, 28.4, 28.2, 24.1, 23.4, 23.0, 14.5, 14.2, 13.9, 13.6. HRMS (ESI) m/z calcd for $C_{16}H_{28}NO_6$ [$(M + H)^+$] 330.1911, found 330.1906.

*tert-Butyl 2-(4-Cyanophenyl)pyrrolidine-1-carboxylate (**7**).* A 40 mL vial was charged with Ir(dFppy)$_3$ (**Ir-D**) (6.19 mg, 8.12 μmol, 0.02 equiv), CsF (185 mg, 1.22 mmol, 3.0 equiv), terephthalonitrile (**6**) (52 mg, 0.41 mmol, 1.0 equiv), Boc-Pro-OH (**1**) (264 mg, 1.22 mmol, 3.0 equiv), and anhydrous DMSO (20 mL). The reaction mixture was degassed by a freeze–pump–thaw technique according to Figure S2. The mixture was then irradiated for 20 h with a 26 W fluorescent lamp clamped at approximately 2 cm away from the reaction vial. Then, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ solution (10 mL) and extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with water (3 × 25 mL) and brine (50 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash chromatography on silica gel, eluting with 15% EtOAc and 85% hexanes solvent gradient gave **7** as a colorless oil (67 mg, 60%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 4.94, 4.78 (2 brs, 1H, rotamer), 3.64–3.60 (m, 2H), 2.38–2.36 (m, 1H), 1.89–1.87 (m, 2H), 1.77–1.75 (m, 1H), 1.45 (s, 4H), 1.17 (s, 5H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 154.2, 150.9, (149.7), 132.1, 126.2, 118.9, 110.4, 79.7, 61.3 (60.6), 47.6, 35.9, (34.7), (28.4), 28.1 (23.6), 23.2. HRMS (ESI): m/z calcd for $C_{16}N_2O_2H_{21}$ [$(M + H)^+$] 273.1598, found 273.1597. Characterization data matched that reported in the literature.[12b]

By Ir/Ni-Dual Catalysis. A 20 mL vial was charged with Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**Ir-B**) (4.5 mg, 4.00 μmol, 0.01 equiv), $NiCl_2$·glyme (8.76 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromobenzonitrile (**9**) (72.8 mg, 0.40 mmol, 1.0 equiv), Cs_2CO_3 (195.0 mg, 0.60 mmol, 1.5 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), a magnetic stirring bar, and DMF (10 mL). The headspace of the reaction mixture was purged with nitrogen for 10 s according to Figure S3, sealed, and wrapped with parafilm. The reaction mixture was then irradiated for 20 h with a 26 W CF lamp clamped at approximately 2 cm away from the reaction vial. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ solution (10 mL) and extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with water (3 × 25 mL) and brine (50 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash chromatography on silica gel, eluting with 25% EtOAc and 75% hexanes solvent gradient gave **7** as a colorless oil (104.6 mg, 96%).

*4-Benzylbenzonitrile (**10**).* A 10 mL vial inside a nitrogen-filled glovebox was charged with Ni(COD)$_2$ (4.13 mg, 0.015 mmol, 0.03 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (4.03 mg, 0.015 mmol, 0.03 equiv), [Ir(dF(CF_3)ppy)$_2$(bpy)]PF_6 (**Ir-A**) (10.10 mg, 10.00 μmol, 0.02 equiv), 4-bromobenzonitrile (**9**) (91.0 mg, 0.50 mmol, 1.0 equiv), $BnBF_3K$ (**8**) (119.0 mg, 0.60 mmol, 1.2 equiv), a magnetic stirrer, 4.75 mL of acetone, 0.25 mL of MeOH, and 2,6-dimethylpyridine (202 μL, 1.75 mmol, 3.5 equiv). The vial was sealed, wrapped with parafilm and black tape, and then removed from the glovebox. The reaction mixture was then irradiated for 24 h with one 26 W fluorescent lamp clamped at approximately 2 cm away from the reaction vial. UPLC-MS and ^1H NMR analysis of the crude reaction after 24 h showed 95% conversion to product. The crude mixture was filtered through a plug of Celite, washed with EtOAc, concentrated in vacuo, and then purified by flash chromatography on silica gel, eluting with 20% EtOAc and 80% hexanes gradient to give **10** as a colorless oil (88 mg, 91%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 8.0 Hz, 2H), 7.25–7.34 (m, 5H), 7.17 (d, J = 8.0 Hz, 2H), 4.04 (s, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 146.7, 139.3. 132.2, 129.6, 128.9, 128.7, 126.6, 118.9, 110.1, 41.9. HRMS (ESI): m/z calcd for $C_{14}NH_{12}$ [$(M + H)^+$] 194.0964, found 194.0958. Characterization data matched that reported in the literature.[8a]

*Procedures for 4-Benzylbenzonitrile (**10**) in Scheme 3B: With $NiCl_2$·glyme.* A 10 mL vial was charged with $NiCl_2$·glyme (6.60 mg, 0.03 mmol, 0.06 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (9.7 mg, 0.04 mmol, 0.072 equiv), [Ir(dF(CF_3)ppy)$_2$(bpy)]PF_6 (**Ir-A**) (10.0 mg, 10.00 μmol, 0.02 equiv), 4-bromobenzonitrile (**9**) (91.0 mg, 0.50 mmol, 1.0 equiv), $BnBF_3K$ (**8**) (149.0 mg, 0.75 mmol, 1.5 equiv), a magnetic stirrer, and DMF (5 mL). The vial was sealed, wrapped with parafilm, and sparged with nitrogen for 20 min according to Figure S1. The vial was again wrapped twice with parafilm and white tape to prevent any air leakage into the reaction during irradiation. The reaction mixture was then irradiated for 24 h with a 26 W CF lamp clamped at approximately 2 cm away from the reaction vial. UPLC–MS analysis before workup and ^1H NMR analysis of the crude reaction after workup both showed 43% conversion to product **10**.

With Ni(COD)$_2$. A 10 mL vial was charged with [Ir(dF(CF_3)-ppy)$_2$(bpy)]PF_6 (**Ir-A**) (10.1 mg, 10.00 μmol, 0.02 equiv), 4-bromobenzonitrile (**9**) (91.0 mg, 0.50 mmol, 1.0 equiv), $BnBF_3K$ (**8**) (149.0 mg, 0.75 mmol, 1.5 equiv), a magnetic stirrer, and DMF (5 mL). The vial was sealed, wrapped with parafilm, and sparged with nitrogen for 15 min according to Figure S1. Then a mixture of Ni(COD)$_2$ (8.25 mg, 0.03 mmol, 0.060 equiv) and 4,4′-di-*tert*-butyl-2,2′-bipyridine (9.7 mg, 0.04 mmol, 0.072 equiv) was added under argon atmosphere in one shot. The vial was sealed, wrapped with parafilm, and sparged for with nitrogen for another 10 min according to Figure S1. The vial was again wrapped twice with parafilm and white tape to prevent any air leakage into the reaction during irradiation. The reaction mixture was then irradiated for 24 h with a 26 W CF lamp clamped at approximately 2 cm away from the reaction vial. UPLC–MS analysis before workup and ^1H NMR analysis of the crude reaction after workup both showed 49% conversion to product (**10**).

*tert-Butyl 2-(4-Methoxyphenyl)pyrrolidine-1-carboxylate (**17b**).* According to the general procedure A, Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**Ir-B**) (4.5 mg, 4.0 μmol, 0.01 equiv), $NiCl_2$·glyme (8.8 mg, 0.04 mmol, 0.10 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-iodoanisole (96.0 mg, 0.40 mmol, 1.0 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), Cs_2CO_3 (195.6 mg, 0.60 mmol, 1.5 equiv), and 10 mL of DMF were used. Purification by flash chromatography on silica gel, eluting with 15% EtOAc and 85% hexanes gradient, gave **17b** as a colorless oil (83 mg, 75%). ^1H NMR (400 MHz, $CDCl_3$) rotameric mixture: δ 7.09 (d, J = 8.0 Hz, 2H), 6.84 (d, J = 8.0 Hz, 2H), 4.90 and 4.74 (2 brs, 1H, rotamer), 3.80 (s, 3H), 3.61−3.51 (m, 2H), 2.28 (br, 1H), 1.92−1.78 (m, 3H), 1.47 (s, 3H), 1.21 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) rotameric mixture, resonances for minor rotamer are enclosed in parentheses: δ 158.3, 154.7, 137.3, 126.6, (113.8) 113.5, 79.1, 60.7 (60.1), 55.3, (47.3) 47.0, 36.1 (34.9), 30.6, (28.5), (23.5) 23.2. HRMS (ESI): m/z calcd for $C_{16}H_{24}NO_3$ [(M + H)$^+$] 278.1751, found 278.1764. Characterization data matched that reported in the literature.[9a]

*tert-Butyl 2-(4-(Methoxycarbonyl)phenyl)pyrrolidine-1-carboxylate (**17c**).* According to the general procedure A, Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**Ir-B**) (4.5 mg, 4.0 μmol, 0.01 equiv), $NiCl_2$·glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), methyl-4-iodobenzoate (88.0 mg, 0.40 mmol, 1.0 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), Cs_2CO_3 (195.6 mg, 0.60 mmol, 1.5 equiv), and 10 mL of DMF were used. Purification by flash chromatography on silica gel, eluting with 25% EtOAc and 75% hexanes gradient, gave **17c** as a colorless oil (102.6 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) rotameric mixture: δ 7.97 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 4.97 and 4.80 (2 brs, 1H, rotamer), 3.92 (s, 3H), 3.65−3.52 (m, 2H), 2.37−2.31 (m, 1H), 1.92−1.77 (m, 3H), 1.47 (s, 3H), 1.16 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) rotameric mixture, resonances for minor rotamer are enclosed in parentheses: δ 166.9, 154.4, 150.6 (149.5), (129.8) 129.6, 128.5, 125.5, 79.5 (65.8), 61.2 (60.6), 51.9, (47.4) 47.1, 35.9 (34.7), (29.8), (28.4) 28.1, (23.6) 23.3. HRMS (ESI): m/z calcd for $C_{17}H_{24}NO_4$ [(M + H)$^+$] 306.1700, found 306.1708. Characterization data matched that reported in the literature.[9a]

*tert-Butyl 2-(4-Cyano-3-fluorophenyl)pyrrolidine-1-carboxylate (**17d**).* According to the general procedure A, Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**Ir-B**) (4.5 mg, 4.0 μmol, 0.01 equiv), $NiCl_2$·glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromo-2-fluorobenzonitrile (82.0 mg, 0.40 mmol, 1.0 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), Cs_2CO_3 (195.6 mg, 0.6 mmol, 1.5 equiv), and 10 mL of DMF were used. Purification by flash chromatography on silica gel, eluting with 30% EtOAc and 70% hexanes solvent gradient gave **17d** as a colorless oil (112.6 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) rotameric mixture: δ 7.57 (t, J = 8.0 Hz, 1H), 7.09 (d, J = 8.0 Hz, 1H), 7.04 (d, J = 8.0 Hz, 1H), 4.93 and 4.79 (2 brs, 1H, rotamer), 3.66−3.55 (m, 2H), 2.40−2.32 (m, 1H), 1.93−1.87 (m, 2H), 1.82−1.75 (m, 1H), 1.46 (s, 4H), 1.22 (s, 5H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) rotameric mixture, resonances for minor rotamer are enclosed in parentheses: δ (164.4) 162.3, (154.5) 154.37, 154.4 (153.5), 134.4, (133.5) 133.4, 121.9, (114.1) 114.0, 113.4 (99.4), (80.0), 79.9 (65.8), 60.9 (60.5), (47.5) 47.2, 35.8 (34.6), (28.4) 28.1, (23.7) 23.3. ^{19}F-NMR (282 MHz, $CDCl_3$): δ −106.6. HRMS (ESI): m/z calcd for $C_{16}H_{20}FN_2O_2$ [(M + H)$^+$] 291.1503, found 291.1522. Characterization data matched that reported in the literature.[9a]

*tert-Butyl 2-(3,5-Bis(trifluoromethyl)phenyl)pyrrolidine-1-carboxylate (**17e**).* According to the general procedure A, Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**Ir-B**) (4.5 mg, 4.0 μmol, 0.01 equiv), $NiCl_2$·glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 1,3-bis(trifluoromethyl)-5-bromobenzene (118.0 mg, 0.40 mmol, 1.0 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), Cs_2CO_3 (195.6 mg, 0.60 mmol, 1.5 equiv), and 10 mL of DMF were used. Purification by flash chromatography on silica gel, eluting with 30% EtOAc and 70% hexanes solvent gradient, gave **17e** as a colorless oil (141 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) rotameric mixture: δ 7.76 (s, 1H), 7.63 (s, 2H), 5.01 and 4.84 (2 brs, 1H, rotamer), 3.69−3.54 (m, 2H), 2.44−2.40 (m, 1H), 1.94−1.83 (m, 3H), 1.46 (s, 3H), 1.16 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) rotameric mixture, resonances for minor rotamer are enclosed in parentheses: δ (158.2), (154.5) 154.2, 147.9 (146.8), 131.6 (q, J = 33.8 Hz), 125.9 (125.6), 123.3 (q, J = 271.3 Hz), (120.7) 120.6, (80.1) 80.0, 60.9 (60.3), (47.4) 47.3, 36.1 (34.8), (28.3) 27.9, 23.5 (22.7). ^{19}F-NMR (282 MHz, $CDCl_3$): δ −62.9. HRMS (ESI): m/z calcd for $C_{17}NO_2F_6H_{20}$ [(M + H)$^+$] 384.1393, found 384.1411. Characterization data matched that reported in the literature.[9a]

*tert-Butyl 2-(Benzo[β]thiophen-3-yl)pyrrolidine-1-carboxylate (**17f**).* According to the general procedure A, Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**Ir-B**) (4.5 mg, 4.0 μmol, 0.01 equiv), $NiCl_2$·glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 3-bromobenzo[β]thiophene (85 mg, 0.40 mmol, 1.0 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), Cs_2CO_3 (195.6 mg, 0.60 mmol, 1.5 equiv), and 10 mL of DMF were used. Purification by flash chromatography on silica gel, eluting with 20% EtOAc and 80% hexanes solvent gradient, gave **17f** as a pale yellow oil (94 mg, 78%). Note: This compound contains inseparable *N*-Boc-pyrrolidine side-product (see the ^{1}H NMR spectrum). ^{1}H NMR (400 MHz, $CDCl_3$) rotameric mixture: δ 7.77 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.37−7.27 (m, 2H), 7.07 (br, s, 1H), 5.16 and 5.27 (2 brs, 1H, rotamer), 3.63−3.45 (m, 1H), 3.37−3.28 (m, 1H), 2.39−2.23 (m, 1H), 2.14−2.02 (m, 1H), 2.00−1.88 (m, 2H), 1.47 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) rotameric mixture, resonances for minor rotamer are enclosed in parentheses: δ (154.65) 154.4, 149.7 (149.1), 139.7, 138.9, 124.1, 123.6, 123.0, 122.2, (119.5) 119.3, 79.7 (78.0), 57.4 (57.0), (46.7) 46.3, 35.2 (34.2), (30.4), 28.5 (28.3), (23.9) 23.2. HRMS (ESI): m/z calcd for $C_{17}H_{22}NO_2S$ [(M + H)$^+$] 304.1366, found 304.1381.

*tert-Butyl 2-(4-(Trifluoromethyl)pyridin-2-yl)pyrrolidine-1-carboxylate (**17g**).* According to the general procedure A, Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**Ir-B**) (4.5 mg, 4.0 μmol, 0.01 equiv), $NiCl_2$·glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 2-chloro-4-(trifluoromethyl)pyridine (72.6 mg, 0.40 mmol, 1.0 equiv), Boc-Pro-OH (**1**) (129.0 mg, 0.60 mmol, 1.5 equiv), Cs_2CO_3 (195.6 mg, 0.60 mmol, 1.5 equiv), and 10 mL of DMF were used. Purification by flash chromatography on silica gel, eluting with 30% EtOAc and 70% hexanes solvent gradient, gave **17g** as a pale yellow oil (114 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) rotameric mixture: δ 8.73 (d, J = 8.0 Hz, 1 H), 7.34−7.19 (br, s, 2H), 5.06 and 4.92 (2 brs, 1H, rotamer), 3.71−3.62 (m, 2H), 2.52−2.28 (m, 2H), 2.09−1.96 (m, 2H), 1.47 (s, 3H), 1.20 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) rotameric mixture, resonances for minor rotamer are enclosed in parentheses: δ 165.5 (164.5), (154.6) 154.3, (150.2) 150.1, 138.6, 122.5, (117.3) 117.1, 115.7, (79.7) 79.7, 62.7 (62.1), (47.4) 47.2, 34.2 (33.0), 29.7, 28.4, 28.0, (23.8) 23.4. ^{19}F-NMR (282 MHz, $CDCl_3$): δ −64.9. HRMS (ESI): m/z calcd for $C_{15}H_{20}F_3N_2O_2$ [(M + H)$^+$] 317.1471, found 317.1459.

*tert-Butyl 2-(4-Acetylphenyl)piperidine-1-carboxylate (**19a**).* According to the general procedure D with headspace purge, Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**Ir-B**) (4.5 mg, 4.0 μmol, 0.01 equiv), $NiCl_2$·glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (79.6 mg, 0.40 mmol, 1.0 equiv), Boc-Pip-OH (**18a**) (138 mg, 0.60 mmol, 1.5 equiv), Cs_2CO_3 (195 mg, 0.6 mmol, 1.5 equiv), and 10 mL of DMF were used. The mixture was irradiated for 20 h with 34 W blue LED lights and fanned to reduce the temperature from the heat generated as shown in Figure S5. Purification by flash chromatography on silica gel, eluting with 20% EtOAc and 80% hexanes solvent gradient, gave **19a** as a colorless oil (97 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 5.44 (s, 1H), 4.08 (d, J = 12.0 Hz, 1H), 2.76 (td, J = 12.0 Hz, J = 3.5 Hz, 1H), 2.61 (s, 3H), 2.32−2.29 (m, 1H), 1.96−1.89 (m, 1H), 1.65−1.52 (m, 3H), 1.47 (s, 9H), 1.39−1.33 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, CDCl3) δ 197.5, 155.4, 146.3, 135.3, 128.5, 126.5, 79.7, 53.3, 40.2, 28.3, 28.3, 26.5, 25.1, 19.2. HRMS (ESI) m/z calcd for $C_{18}NO_3H_{26}$ [(M + H)$^+$] 304.1907, found 304.1917. Characterization data matched that reported in the literature.[9a]

*tert-Butyl 3-(4-Acetylphenyl)morpholine-4-carboxylate (**19b**).* According to the general procedure D with headspace purge, Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**Ir-B**) (4.5 mg, 4.0 μmol, 0.01 equiv), $NiCl_2$·glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (79.6 mg, 0.40 mmol, 1.0 equiv), Boc-Morph−OH (**18b**) (139 mg, 0.60 mmol, 1.5 equiv), Cs_2CO_3 (195 mg, 0.60 mmol, 1.5 equiv), and 10 mL of DMF were used. The mixture was irradiated for 20 h with 34 W blue LED lights and fanned to reduce the temperature from the heat generated as shown in Figure S5. Purification by flash chromatography on silica gel, eluting with 20% EtOAc and 80% hexanes solvent gradient, gave **19b** as a colorless oil (86 mg, 70%). ^{1}H

NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 5.12 (br, 1H), 4.35 (d, *J* = 7.0 Hz, 1H), 3.91−3.87 (m, 2H), 3.83−3.80 (m, 1H), 3.61 (td, *J* = 12.0 Hz, *J* = 3.5 Hz, 1H), 3.11 (td, *J* = 12.0 Hz, *J* = 3.5 Hz, 1H), 2.60 (s, 3H), 1.47 (s, 9H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 197.7, 154.8, 144.9, 136.0, 128.5, 127.8, 80.6, 68.9, 66.9, 53.3, 39.9, 28.4, 26.6. HRMS: (ESI) *m*/*z* calcd for $C_{17}NO_4H_{24}$ [$(M + H)^+$] 306.1700, found 306.1714. Characterization data matched that reported in the literature.[9a]

1-(4-(Tetrahydrofuran-2-yl)phenyl)ethan-1-one (**19c**). According to the general procedure D with headspace purge, Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**Ir-B**) (4.5 mg, 4.0 μmol, 0.01 equiv), $NiCl_2$·glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromoacetophenone (79.6 mg, 0.40 mmol, 1.0 equiv), tetrahydro-2-furoic acid (**18c**) (69.7 mg, 0.60 mmol, 1.5 equiv), Cs_2CO_3 (195 mg, 0.60 mmol, 1.5 equiv), and 10 mL of DMF were used. The mixture was irradiated for 20 h with 34 W blue LED lights and fanned to reduce the temperature from the heat generated as shown in Figure S5. Purification by flash chromatography on silica gel, eluting with 20% EtOAc and 80% hexanes solvent gradient, gave **19c** as a colorless oil (74 mg, 97%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 4.95 (t, *J* = 8.0 Hz, 1H), 4.11 (q, *J* = 8.0 Hz, 1H), 3.97 (q, *J* = 8.0 Hz, 1H), 2.60 (s, 3H), 2.40−2.34 (m, 1H), 2.04−1.99 (m, 2H), 1.81−1.74 (m, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 197.7, 149.2, 136.0, 128.4, 125.6, 80.1, 68.8, 34.7, 26.6, 25.9. HRMS (ESI) *m*/*z* calcd for $C_{12}H_{15}O_2$ [$(M + H)^+$] 191.1067, found 191.1048. Characterization data matched that reported in the literature.[9a]

4-(Tetrahydrofuran-2-yl)benzonitrile (**19d**). According to the general procedure D with headspace purge, Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**Ir-B**) (4.5 mg, 4.0 μmol, 0.01 equiv), $NiCl_2$·glyme (8.8 mg, 0.04 mmol, 0.1 equiv), 4,4′-di-*tert*-butyl-2,2′-bipyridine (16.1 mg, 0.06 mmol, 0.15 equiv), 4-bromobenzonitrile (72.8 mg, 0.40 mmol, 1.0 equiv), tetrahydro-2-furoic acid (**18c**) (69.7 mg, 0.60 mmol, 1.5 equiv), Cs_2CO_3 (195 mg, 0.60 mmol, 1.5 equiv), and 10 mL of DMF were used. The mixture was irradiated for 20 h with 34 W blue LED lights and fanned to reduce the temperature from the heat generated as shown in Figure S5. Purification by flash chromatography on silica gel, eluting with 15% EtOAc and 85% hexanes solvent gradient, gave **19d** as a colorless oil (62.4 mg, 90%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 4.94 (t, *J* = 8.0 Hz, 1H), 4.13 (dd, *J* = 15.0, 8.0 Hz, 1H), 3.98 (dd, *J* = 15.0, 8.0 Hz, 1H), 2.45−2.35 (m, 1H), 2.08−1.98 (m, 2H), 1.83−1.71 (m, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 149.2, 132.2, 126.2, 118.9, 110.9, 79.8, 68.9, 34.7, 25.9. HRMS (ESI) *m*/*z* calcd for $C_{11}H_{12}NO$ [$(M + H)^+$] 174.0913, found 174.0935. Characterization data matched that reported in the literature.[12b]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Expanded general materials and methods, additional experimental procedures for control reactions, additional tables and graphs, expanded discussions of peripheral findings, and copies of ^1H and $^{13}C\{^1H\}$ NMR spectra. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01193.

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Notes

The authors declare no competing financial interest.

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(10) The Cs_2CO_3 used for these studies was purchased from Strem Chemicals, Inc. However, when we used Cs_2CO_3 purchased from Sigma-Aldrich, some decarboxylative cross-coupling reactions proceeded with $NiCl_2$·dtbbpy in the absence of O_2. Those catalysis that were performed with Cs_2CO_3 from Sigma-Aldrich required longer reaction time (72 h) and were not reproducible in the absence of O_2. The reagent(s) in the Cs_2CO_3 from Sigma-Aldrich that promoted the reaction albeit at a slower rate remains unknown.

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(20) We conducted our own DFT studies using similar methods (functionals and basis sets) as Molander and Kozlowski (see ref 8c). We found that the α-amino radical trap Ni(I)X complex **12** and Ni(0) complex **13** to give their corresponding Ni(II) and Ni(I) species, respectively, and the processes are highly exergonic. The transition state of Ni(I)-alkyl (**14**) oxidative addition to 4-iodotoluene was also located. Also see:. Cornella, J.; Gómez-Bengoa, E.; Martin, R. *J. Am. Chem. Soc.* **2013**, *135*, 1997−2009.