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### Recent Advances in Transition Metal - Visible Light Photoredox Dual Catalysis

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## Recent Advances in Transition Metal - Visible Light Photoredox Dual Catalysis

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### ABSTRACT

In this Digest article we collected and shortly summarized the recently developed dual transition metal – visible light photoredox catalytic processes including arylation, alkynylation, alkenylation, allylation, alkylation, fluoroalkylation, benzylation, acylation and cyclization reactions. The utilization of multimetallic catalytic systems provide new synthetic strategies for the synthesis and functionalization of versatile and novel organic compounds.

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### 1. Introduction

The transition metal catalyzed cross-coupling reactions,<sup>1</sup> C-H bond activation<sup>2</sup> and the photoredox catalysis<sup>3</sup> separately have been well investigated. In the last decade, the photocatalysis is experiencing a renaissance, considering the number of recent publications. The conversion of visible light into chemical redox energy is beneficial and contribute to the development of milder reaction conditions and more energy-efficient transformations. Radicals are formed by the photo-triggered single electron transfer (SET), which provides reactivity as driving force. On the other hand, the expandable regioselectivity generally remained unresolved. Thus, the exploitation of the possibilities in the integration of photolytically generated radicals into transition metal catalysis has been initiated. Reasonably, in a co-operative photoredox and transition metal catalyzed coupling, the opportunity to modulate the oxidation state of transition metal species opens new pathways for efficient syntheses.<sup>4</sup>

In these processes, the reactivity and the selectivity are ensured at the same time by the two catalytic cycles. Herein, we intend to summarize recent solutions for combined, 'dual' photoredox-transition metal catalyzed syntheses. On theoretical grounds, the term of "dual catalysis" can include two main types of mechanisms. First, the two catalytic cycles can work separately and a) the produced fragments react with each other, b) the produced intermediate consecutively consumed by the other cycle. Second, the two catalytic cycles are synergistically coupled, the catalysts must collide to push forward the reaction. Alternatively, in borderline case these two roles can be played simultaneously by one bifunctional catalyst, but now these are not discussed here.

Dual catalysis is a very hot topic in organic chemistry regarding to its history no more than 10 years old and in last 2 years, the number of papers increased almost fourfold.

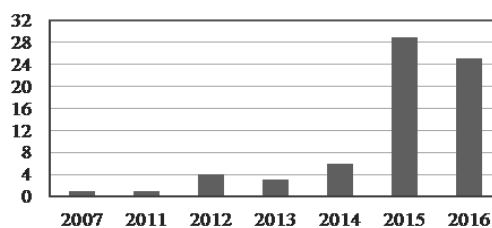


Figure 1. The evolution of photoredox-transition metal catalysis: Number of publications versus year (until 2016 April).

At a closer inspection of these dual systems, we can conclude that, on the side of photoredox catalysts primarily the widely used but extremely expensive Ir complexes are prevalent. Nevertheless, we can find abundantly examples for application of Ru(bpy)<sub>3</sub><sup>2+</sup> catalysts. Exploitation of organic dyes in this field of visible light induced photocatalysis is in early stage. In view of the transitional metals utilized in the catalytic cycle of the coupling Ni complexes are most widespread, although Pd, Au and Cu species are also extensively applied. Considering the type of the transformations C-C and C-X (X = N, O, S, P) bond formations can be highlighted, including arylation, alkynylation, alkenylation, allylation, alkylation, fluoroalkylation, benzylation, acylation and cyclization reactions. As shown, the opportunity is

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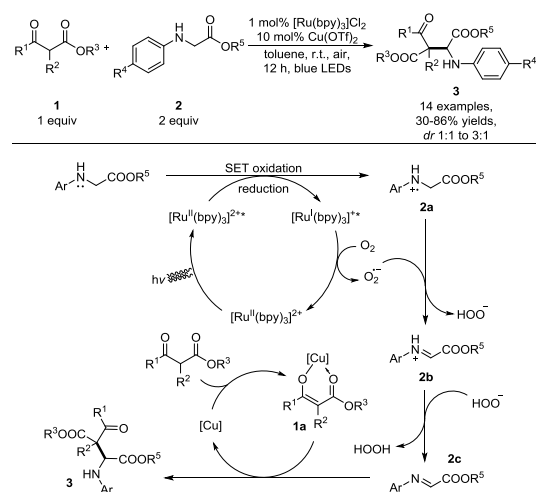
given to introduce several functional groups into substrates like (hetero)aromatic, saturated heterocyclic, (un)saturated aliphatic systems. Therefore, the reagents can be diverse, but trends are outlined in application of aryl iodides and bromides,  $\alpha$ -CH<sub>2</sub>-amines, carboxylic acids and their derivatives, diazonium salts, potassium trifluoroborate salts or hypervalent silicones.

## 2. Lewis acid supported photocatalysis

In these transformations, the transition metal catalysts serve as Lewis acids and the reactive electrophiles are generated in the photocatalytic cycle.

In 2012, Rueping and Zhu presented a mild functionalization and arylation of glycine derivatives.<sup>8</sup> In their work indoles in position C2 were successfully coupled with alkyl 2-(arylamino)acetates in the presence of Lewis acidic Zn(OAc)<sub>2</sub> and 1 mol% [Ir(ppy)<sub>3</sub>]PF<sub>6</sub> photocatalyst.

Similarly, in 2013 Wu's group reported an alkylation reaction of secondary amines (**Figure 2**).<sup>9</sup> For the C-N bond formation 10 mol% of copper(II) triflate was used as Lewis acid, and the photocatalytic cycle was driven by 1 mol% of [Ru(bpy)<sub>3</sub>]Cl<sub>2</sub> photocatalyst under blue light irradiation.



**Figure 2.** Combining visible-light catalysis and transition metal catalysis for the alkylation of secondary amines.

The proposed mechanism of this reaction is based on a separated dual catalytic system. First, the alkyl-aryl amine is oxidized in the photocatalytic cycle to form a radical cation (**2a**), which loses the  $\alpha$ -hydrogen atom by interaction with a superoxide radical anion to form the highly reactive iminium cation (**2b**). An additional deprotonation provides the electrophile *N*-aryl imine (**2c**), which can be attacked by the nucleophilic Cu chelated  $\beta$ -keto esters (**1a**) to give the desired product.

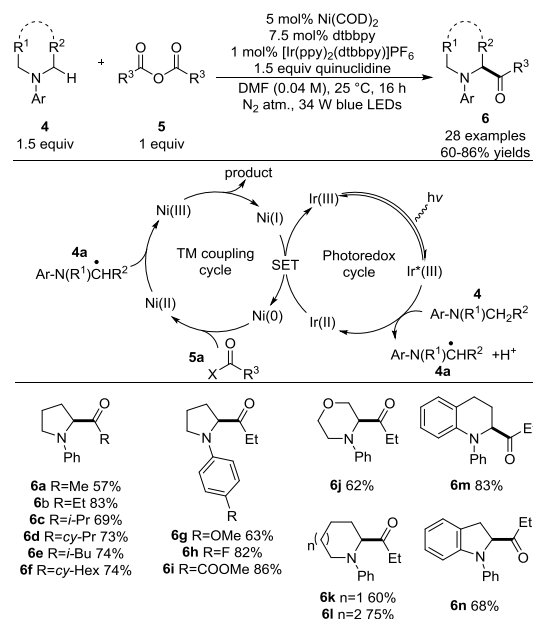
In 2016 M. Xiang et. al. reported a C-C bond forming reaction of Cu chelated  $\beta$ -keto esters and isochromans in the visible light driven catalytic transformation of two different C-H bonds. The applicability of the developed transformation was demonstrated with 16 examples, and the appropriate C-alkylated isochroman derivatives were isolated in 28-83% yields.<sup>10</sup> They utilized Cu(OTf)<sub>2</sub> as Lewis acid and organic photocatalyst for the coupling reaction (10 mol% of Fukuzumi's catalyst, 9-mesityl-10-methylacridinium perchlorate, (NMeAc<sup>+</sup>-Mes)ClO<sub>4</sub>). The

reaction mixture which was irradiated with blue light to generate the electrophilic 3,4-dihydroisochromenylum intermediate. This oxonium species react with the ketoester activated by the copper based Lewis acid to form the desired C-C bond.

## 3. Cross-coupling-like dual catalysis

This chapter covers a truly diverse and spacious field of dual transition metal and photoredox catalysis. As initial trials the ruthenium photocatalyzed copper-free Sonogashira coupling of aryl bromides was reported by Akita.<sup>11</sup> Recently, the cross-coupling reaction of aryl diazonium tetrafluoroborate salts with acetylenes<sup>12</sup> and trimethylsilylacetylenes<sup>10</sup> were investigated utilizing a synergistic Au-Ru (TM-PC) dual catalytic system. Additionally, Cu-Ru(bpy)<sub>3</sub><sup>2+</sup> (TM-PC) catalyzed trifluoromethylation of boronic acids with CF<sub>3</sub>I was described by Sanford.<sup>13</sup>

In 2016, Doyle and Joe introduced a method for direct C-acylation of tertiary amines (**4**) in the  $\alpha$ -C(*sp*<sup>3</sup>) position at room temperature (**Figure 3**).<sup>14</sup> The  $\alpha$ -amino radicals (**4a**) generated by the excited Ir(III) complex in the photoredox cycle from the tertiary amine. The radical species enters into the transition metal driven cycle, and interacts with the Ni(II) coupling catalyst to form a Ni(III) species. After a reductive elimination step the desired C-C(*sp*<sup>3</sup>) coupled saturated heterocycles were obtained. The photoredox and the TM coupling cycles are coupled as the Ir photocatalyst reduces the Ni(I) species in a single electron transfer step to turn over the process. This synthetic method enables the access of broad range of  $\alpha$ -amino ketones with good functional group tolerance in moderate to very good yields.



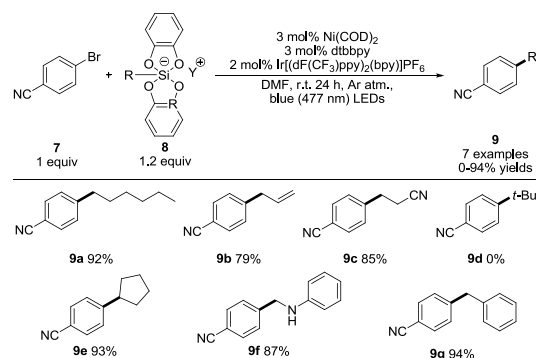
**Figure 3.** The outline of Ni-Ir dual catalytic mechanism and scope of the direct acylation of *N*-aryl amines.

### 3.1. Application of hypervalent silicon reagents in dual catalysis

Hypercoordinate alkyl silicates became novel and readily available precursors for transferring alkyl radicals under very mild photocatalytic reaction conditions. Due to their low oxidation potentials the catalytic photooxidation is broadly

feasible. Hypervalent alkyl silicon compounds represent attractive reagents regarding to high stability, solubility and harmless user-friendly side products, respectively.

In 2015, groups of Fensterbank and Goddard achieved the Ni-Ir dual catalytic alkylation of 4-bromobenzonitrile (**7**) (**Figure 4**).<sup>15</sup> To ensure modularity a wide variety of hypervalent alkyl silicates (**8**) were prepared as coupling partners. The silicon reagents readily provided the highly reactive primary alkyl radicals via Ir photocatalysis, which were captured by nickel complex. In this transformation, *t*-Bu radical could not be involved, but secondary, allyl and benzyl or even the unstabilized primary alkyl radicals were coupled efficiently with the 4-bromobenzonitrile.



**Figure 4.** Ni-Ir dual catalysis utilizing hypervalent silicates as radical alkylating agents.

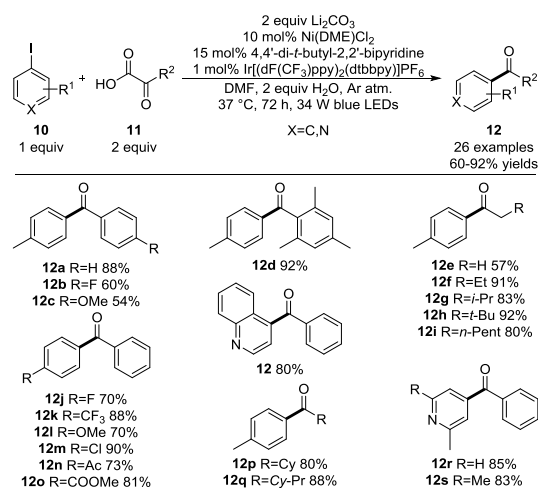
Very recently, the Molander research group widened the synthetic application of hypervalent silicon reagents in dual photoredox-transition metal catalyzed couplings. Notably, these developments are also based on the involvement of the photocatalytically generated alkyl radicals in nickel catalyzed cross-coupling reactions. For the successful couplings 5 mol% of Ni(DME)Cl<sub>2</sub> catalyst was used in the presence of 5 mol% 4,4'-di-*tert*-butyl-2,2'-bipyridine (dtbbpy) ligand besides the illumination of 2 mol% Ru(bpy)<sub>3</sub>(PF<sub>6</sub>)<sub>2</sub> photocatalyst. Remarkably, the alkylation of (hetero)aromatic bromides,<sup>14</sup> alkenyl iodides and bromides,<sup>15</sup> 2,1-borazaronaphthalene bromide compounds<sup>16</sup> and thioetherification of aryl bromides<sup>17</sup> were implemented.

### 3.2. Decarboxylative photoredox cross-coupling reactions

Carboxylic acid derivatives can serve as radical sources via a photocatalytic oxidation step followed by CO<sub>2</sub> extrusion. The formed organic radicals can react with the transition metal catalyst (palladium or more often nickel) in a radical oxidative addition step. Two early examples described CO<sub>2</sub> extrusion-recombination reaction by dual catalysis. In the first synthetic approach *in situ* generated mixed anhydrides from carboxylic acids and acyl chlorides were converted to ketones via Ni-Ir dual system with high efficiency.<sup>18</sup> Furthermore, in Pd-Ir dual catalytic setup, *N*-protected  $\alpha$ -allyl ester compounds gave *N*-protected homoallyl amines in a fast reaction.<sup>19b</sup>

Recently, the groups of MacMillan, Doyle and Fu presented a unique method for decarboxylative nickel mediated iridium photoredox cross-coupling of amino acids and aryl halides to form benzylic amines.<sup>20</sup> In the following year, the scope was expanded to the coupling of  $\alpha$ -oxo acids and alkyl acids with vinyl halides,<sup>21</sup> and subsequently a new reaction was described for enantioselective arylation of  $\alpha$ -amino acids.<sup>22</sup>

In 2015, MacMillan presented a Ni-Ir dual setup for decarboxylative coupling of aryl halides (**10**: I, Br) with 2 equivalents of ketocarboxylic acids (**11**) (**Figure 5**).<sup>23</sup> Similarly to the previously mentioned synergistic dual catalytic mechanism, photo-generated acyl radical adds to the Ni(0) complex. The extensibility of the reaction was studied on the side of (hetero)aryl iodides as well as the aryl ketocarboxylic acids. In general, the developed methodology provides the appropriate products with good functional group tolerance in good isolated yields (26 examples, 60-92% yields).



**Figure 5.** Dual catalytic approach for synthesis of ketones by decarboxylative arylation of keto acids.

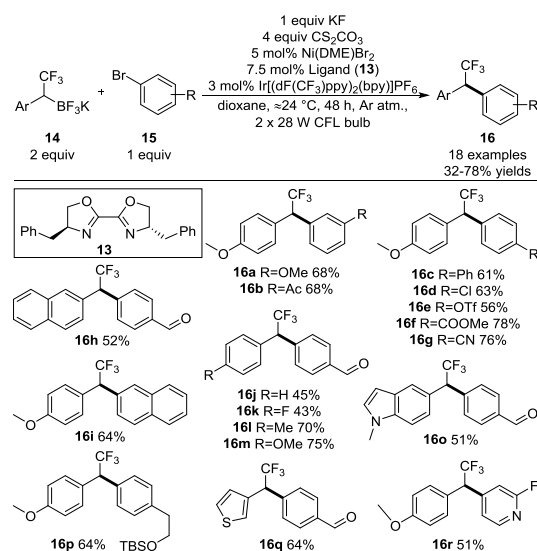
Further comprehensive optimization studies have been performed regarding the effect of molecular oxygen, solvent and light on Ni-Ir dual catalytic systems.<sup>24</sup> Oderinde and co-workers 2-arylated-*N*-Boc pyrrolidines in the decarboxylative coupling of proline and aryl halides in Ir-Ni dual photoredox-coupling systems. Additionally, Zhang and Luo developed similar coupling reaction. They developed new carbazolyl dicyanobenzene-based fluorophores, and successfully applied as transition metal free photoredox catalyst along with nickel coupling catalyst for the decarboxylative coupling of Boc protected proline and aryl iodides.<sup>25</sup>

### 3.3. Alkylations with RBF<sub>3</sub>K salts by photoredox cross-coupling

The chemistry of alkyl trifluoroborate salts and dual photoredox catalysis was combined together first by Molander's group.<sup>26</sup> Compared to boronic acids or esters the RBF<sub>3</sub><sup>-</sup> salts have lower energy barrier against one electron oxidation. Due to their high stability and storability wide application was achieved.<sup>27</sup> In a Ni transition metal merged Ir photocatalyzed coupled system, a wide variety of (hetero)aryl bromides were coupled with substituted benzyl BF<sub>3</sub>K salts,<sup>26, 28</sup> secondary alkyl trifluoroborates,<sup>29</sup>  $\alpha$ -alkoxymethyltrifluoroborates,<sup>30</sup> Boc-protected *N*-trifluoroboratomethyl amino acids<sup>31</sup> and aryl or aralkyl acyl chlorides with  $\alpha$ -alkoxymethyltrifluoroborates.<sup>32</sup>

In 2016, the synthesis of 1,1-diaryl-2,2,2-trifluoroethanes (**16**) were investigated by Molander and his co-workers (**Figure 6**).<sup>33</sup> In their methodology excess of benzylic  $\alpha$ -trifluoromethylated alkylboron reagents (**14**) were coupled with (hetero)aryl bromides (**15**) via Ni-Ir dual photoredox catalysis. The reaction tolerates halides like F, Cl, and various electron donating groups

(**16a** OMe, **16p** TBSO) or even electron withdrawing CN (**16g**), COOMe (**16f**) and OTf (**16e**) functional groups. Demonstrating the power of the developed transformation the desired C-C bond formation also took place in case of indole and thiophene derivatives providing the appropriate functionalized heterocyclic systems.

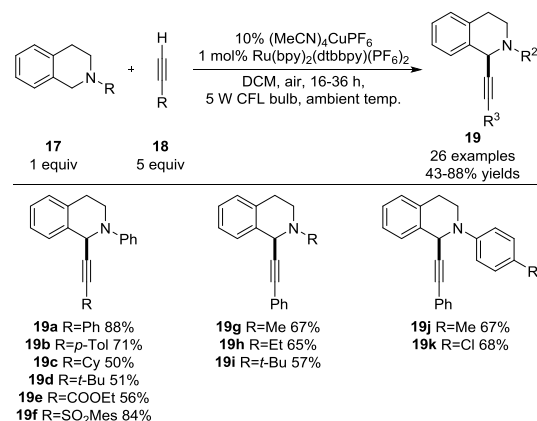


**Figure 6.** Synthesis of 1,1-diaryl-2,2,2-trifluoroethanes via Ir photoredox Ni dual catalytic cross-coupling.

The mechanism and the stereoinduction of Ni-Ir photoredox dual cross-coupling between secondary alkyl trifluoroborate salts and aryl bromides have been scrutinized by Molander and Kozlowski involving dynamic kinetic resolution and theoretical chemical calculations.<sup>34</sup>

### 3.4. Alkynylation, allylation and arylation reactions

As it has already been demonstrated, the Sonogashira-type photoredox transformations allow introduction of alkynyl moieties into arenes.<sup>8</sup> Alternatively, acetylenes can be coupled with tetrahydroisoquinolines (THIQ) by photoredox-transition metal dual catalysis.

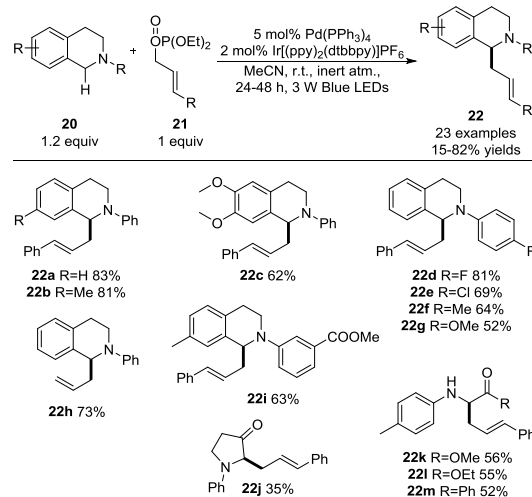


**Figure 7.** Cu-Ru dual photoredox catalytic approach for synthesis of alkyne-alkylated tetrahydroisoquinolines.

In 2012, Rueping and his co-workers published a copper mediated ruthenium based photocatalyzed  $C(sp^3)$ - $C(sp)$  bond formation reaction (**Figure 7**).<sup>35</sup> In this dual setup, the two catalytic cycles are operating separately. As a well-known model substrate, *N*-protected THIQ (**17**) provides a reactive iminium cation via photocatalytic oxidation, which can be attacked by copper acetylide. However, in order to achieve a successful coupling 5 equivalent of alkyne (**18**) was necessary. The authors demonstrated the applicability of the developed conditions on 26 examples (**19**) to show the wide functional group tolerance of the transformation.

In the same year, Xu and co-workers presented an alternative photocatalytic solution, which ensures the direct alkylation of the heterocyclic frame with terminal alkynes in the presence of 5 mol% Rose Bengal organic dye as photocatalyst together with 10 mol% of CuI.<sup>36</sup>

Recently, efficient  $\alpha$ -allylation of tetrahydroisoquinolines (**20**) and other amines was realized by Lu and Xiao (**Figure 8**).<sup>37</sup> In this synergistic Pd-Ir dual catalysis, the THIQ is oxidized to form  $\alpha$ -amino alkyl radical by the photocycle and after the one electron reduction of  $\pi$ -allylpalladium complex the separately formed radicals are recombined by a radical cross-coupling step, which provides the corresponding product. 5 mol% of Pd(PPh<sub>3</sub>)<sub>4</sub> and 2 mol% Ir[(ppy)<sub>2</sub>(dtbbpy)]PF<sub>6</sub> was used as catalysts. The reaction was carried out in acetonitrile at room temperature under inert atmosphere. The reaction mixture was irradiated with blue LEDs for 24-48 hours. Unsubstituted 7-methyl (**22b**) and dimethoxy (**22c**) *N*-phenyl tetrahydroisoquinoline underwent smoothly with cinnamyl diethyl phosphate (**22** R=Ph). In this  $\alpha$ -allylation process, the desired products were obtained in 62-83% yields. On the *N*-aryl part, F, Cl, Me and MeO groups (**22d-g**) are well-tolerated. Moreover,  $\alpha$ -arylamino esters (**22k-m**) and 1-phenylpyrrolidin-3-one (**22j**) were also suitable for this transformation.

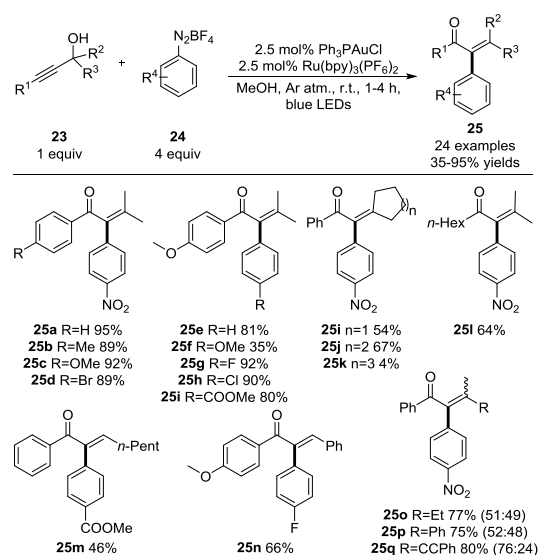


**Figure 8.** Combining Pd catalysis with Ir photoredox catalysis to synthesize  $\alpha$ -allylated tetrahydroquinolines.

Aryl diazonium compounds have been utilized extensively as arylating agents in numerous cases regarding their approximately 0 V reduction potential. Consequently, aryl radicals can be formed readily by using wide variety of photoredox catalyst and visible light. In dual catalysis this possibility was also exploited

in many ways. Toste and co-workers developed a gold-ruthenium catalyzed arylation procedure for the synthesis of functionalized cyclic ketones from aryldiazonium salts and allenyl cycloalkanol.<sup>38</sup> Shin and co-workers described the arylation ring closure reaction of catalytically generated vinyl gold intermediates from *tert*-butyl allenates and aryldiazonium salts under visible light photoredox condition.<sup>39</sup>

Nowadays, Um et al. introduced an Au-Ru dual photoredox catalyzed process for arylation of Meyer-Schuster intermediates (**Figure 9**).<sup>40</sup> The photogenerated aryl radical adds to the Au(I) catalyst to form Au(II), then one electron oxidation results an Au(III) highly active species. By  $\pi$ -bond coordination to the Au(III) catalyst, a Meyer-Schuster rearrangement takes place and the propargylic alcohols turn into  $\alpha,\beta$ -arylated unsaturated carbonyl compounds (**25**). The arylation reaction underwent in methanol, under argon atmosphere by irradiation of blue light. This mild transformation enables the isolation of the products in up to 95% yield with good functional group tolerance.



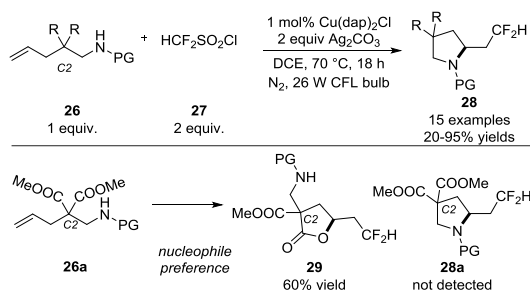
**Figure 9.** Au-Ru dual catalytic setup to synthesize  $\alpha$ -arylated enones from substituted propargylic alcohols.

### 3.5. C-Heteroatom bond formation: N, O, S, P-functionalization

Alkene cyclizations are also known reaction types in photoredox chemistry. Zhang's method is an excellent example for the intramolecular version of these transformations. The reaction involves a C-N bond forming step which is the result of the interaction of the unsaturated C=C bond and the difluoromethyl radical generated from  $\text{HCF}_2\text{SO}_2\text{Cl}$  by copper based  $\text{Cu}(\text{dap})_2\text{Cl}$  photocatalyst and visible light (**Figure 10**).<sup>41</sup> Alkenes (**26**), having tosylated terminal amino-function are converted into 2-difluoroethyl-pyrrolidines (**28**), except those bearing better nucleophiles, such as carboxylate-substituents which afforded the corresponding lactones.

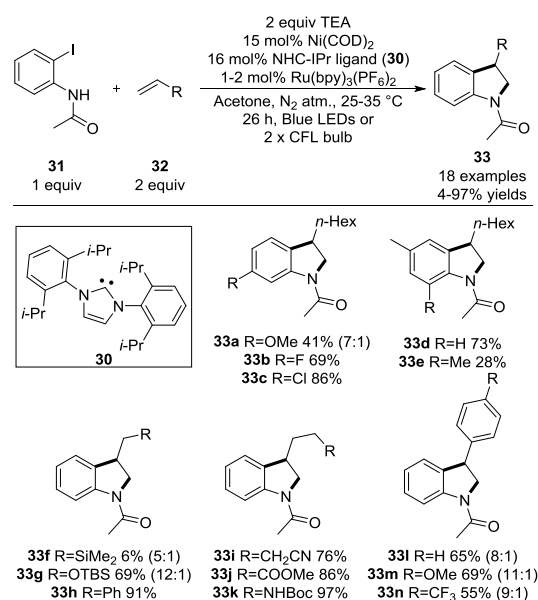
Kobayashi and co-workers reported a visible light mediated oxidative Chan-Lam type coupling of aniline and boronic acid derivatives. The developed reaction conditions enable the *N*-arylation of aniline compounds under mild reaction conditions.<sup>42</sup> This procedure is based on the combination of Cu-Ir metals as coupling and photoredox catalysts. The open air reaction in

MeCN/toluene solvent mixture provide the *N*-arylated products in good yields at 35°C.



**Figure 10.** Ag-Cu photocatalyzed difluoromethylation.

In 2015, Jamison and Tasker presented a Ni-Ru dual photoredox catalyzed solution for regioselective synthesis of 3-alkylated and arylated indoline derivatives (**Figure 11**).<sup>43</sup>

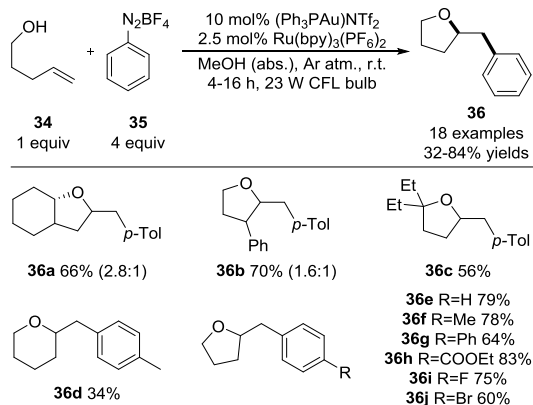


**Figure 11.** Ni-Ru dual setup for cyclize 2-iodoacetanilides with alkenes.

Practically, 2-iodoacetanilides (**31**) cyclized with alkenes (**32**) under the irradiation of blue light, at ambient temperature. The mechanism is very similar to the previously mentioned reactions. The nickel catalyst in zero oxidation state takes part in the oxidative addition step, while the photocatalytic cycle enables the oxidation of Ni(II) to Ni(III). The reductive elimination from Ni(III) complex is more facile, and results the desired C-N bond formation. Electron donating groups like OMe (**33a**) or OTBS (**33g**) are well tolerated but in the presence of  $\text{SiMe}_2$  (**33f**) only poor yield was achieved. Coupling with alkenes bearing electron-withdrawing groups like  $\text{CF}_3$  (**33n**), COOMe (**33j**) gave the appropriate products in 55% and 86% yield.

As it was earlier mentioned, the diazonium salts have widespread application in photoredox chemistry, while these reagents are excellent coupling partners in C-C bond forming reactions. Glorius et al. also used aryl diazonium salts for the

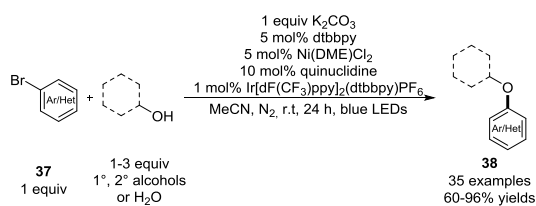
generation of aryl radicals by ruthenium based photocatalysis. The aryl radical acts as one electron oxidant on the alkylgold species formed from the  $\text{Ph}_3\text{AuNTf}_2$  catalyzed cyclization of various 4-penten-1-ol and 5-hexen-1-ol derivatives (**Figure 12**).<sup>44</sup>



**Figure 12.** Oxyarylation of alkenes by Au-Ru dual catalysis.

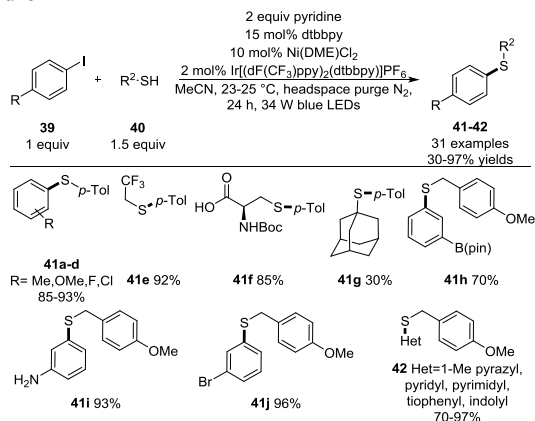
By the intramolecular cyclization and arylation of the C=C double bonds of the alkenes, 2-arylated tetrahydrofurans (**36**) and tetrahydropyrans (**36d**) are afforded. The mechanism of this oxyarylation has been investigated using DFT calculations.<sup>45</sup>

For the transition metal catalyzed formation of aryl-alkyl ethers, having synthetically potent and desirable structure, palladium and copper catalysis is usually employed, as the reductive elimination from the corresponding organo-TM(II) species is favorable (exothermic). Instead of Ni(II), Ni(III)-alkoxides are required for C-O bond formation via reductive elimination. MacMillan et al. used the photoexcited \*Ir(III) photosensitizer to oxidize the Ni(II)-arylalkoxide, originating from the oxidative addition of the substrates onto the catalyst, and after reductive elimination of the product (**Figure 13**).<sup>46</sup> Alkyl-aryl ethers are prepared from aryl-bromides and the corresponding alcohols at room temperature with blue light irradiation. Replacing alcohols with water afforded the appropriate phenol derivatives.



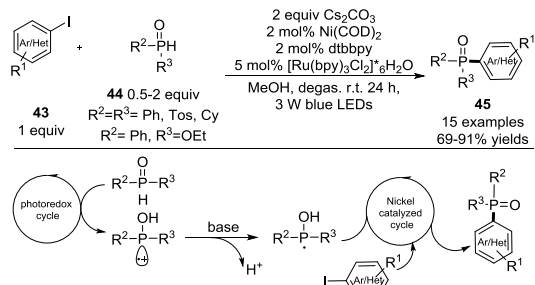
**Figure 13.** Ni-Ir catalyzed direct esterification using alcohols.

The same catalytic system was used by Oderinde and Johannes to synthesize the thio-analogues of aryl-alkyl ethers from aryl-iodides and thiols (**Figure 14**).<sup>47</sup> Thiol radical cation is generated by the excited \*Ir(III) photocatalyst and deprotonated by pyridine additive to afford thiyl radical to be intercepted by Ni(I). SET with the photocatalyst and oxidative addition of the aryl-iodide gives the organonickel(III) species, which straightforwardly undergo reductive elimination step and provide the appropriate thioethers. Noteworthy, the bromo-function on the aryl-halide remains intact in the reaction.



**Figure 14.** Ni-Ir dual system for C-S bond formation using thiols.

Carbon-phosphorous bond formation was also achieved via nickel-photoredox dual catalysis, as reported by Xiao and Lu using ruthenium photocatalyst for the coupling of triaryl-phosphine oxides (**44**) with aryl iodides (**Figure 15**).<sup>48</sup> The generation of the necessary phosphorous centered radical from phosphinous acid is analogous to that of the mentioned thiyl radical cation. In the hypothesized mechanism of the catalytic cycle suggested by the authors, the first step is the oxidative addition of the aryl-halide to the Ni(0) catalyst. This step was followed by the interception of the phosphorous radical generates the organo-Ni(III) species for reductive elimination. Aryl, pyridyl, indolyl iodides are functionalized with triaryl phosphine oxides.



**Figure 15.** Ni-Ir dual system for C-P bond formation using phosphinous acid.

The Toste research group also presented a gold-ruthenium based combined catalytic approach for the carbon-phosphorous bond formation.<sup>49</sup>

#### 4. C-H Activation and photoredox dual catalysis

The aid of directing groups in the aromatic core allowed the *ortho*-selective C-H bond breaking and thereby selective functionalization of arenes. For achieving the desired reactivity, generally, harsh conditions are required, nevertheless the energetics of the coupling reactants permit the utilization of mild conditions and room temperature. Photochemical methods and the application of resulting radical intermediates in dual catalytic fashion are an attractive alternative reaction path to form in a shortened synthesis the wide variety of structures.

The research in this field started after 2010, thereby only few publications have been released. However, the transformations allowed multifarious reactions such as arylation, alkenylation, acylation and cyclization.

First, in a Pd(OAc)<sub>2</sub>-Ru(bpy)<sub>3</sub><sup>2+</sup> dual catalytic system aryl-2-pyridines and *N*-arylpiperidin-2-ones were arylated selectively in the *ortho* position by the Sanford's group via palladium catalyzed *ortho* C-H activation.<sup>50</sup> The photocatalytically generated aryl radicals from aryl diazonium salts served react with the cyclopalladated species. The final, reductive elimination step of the catalytic cycle ensures the carbon-carbon bond forming step and release the arylated product. Various *N*-heterocyclic systems were arylated under the mild dual catalytic conditions, and the products were isolated in 44-87% yield.

*Ortho*-C-H acylation of acetanilides has been developed via Pd - Eosin Y dual catalytic system by Wang and co-workers.<sup>51</sup> At room temperature in this organic dye photocatalyzed setup,  $\alpha$ -oxocarboxylic acids decarboxylatively generated the acyl radicals, which added to the palladium center. In 2016, the same research group continued the development of the organic dye photocatalyzed decarboxylative C-H bond activation reactions (Figure 16).<sup>52</sup>

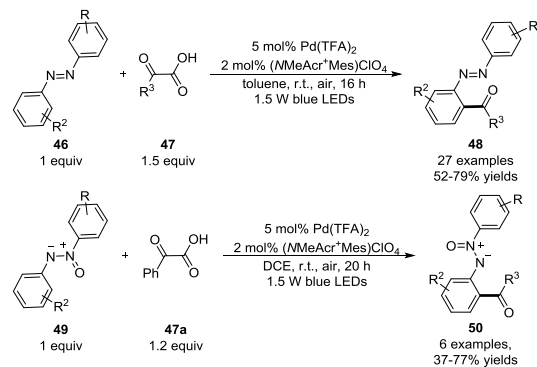


Figure 16. Acylation of azo- and azoxybenzenes by Pd- Fukuzumi's catalyst system.

Azo- (46) and azoxybenzenes (49) were acylated efficiently in *ortho* position. Similarly, the acyl radical formed from  $\alpha$ -oxocarboxylic acid derivatives. 5 mol% palladium(II) trifluoroacetate was used as catalyst for the C-H activation, and the 9-mesityl-10- methylacridinium perchlorate (Fukuzumi's catalyst) worked as photocatalyst in this synergistic dual system.

In 2014, the Rueping research group combined the rhodium catalyzed *ortho* C-H activation with ruthenium driven photoredox catalysis (Figure 17).<sup>53</sup> Benzamide derivatives (51) were alkenylated directly using the alkenes. In the proposed mechanism, the role of stoichiometric amount of oxidating agent deputized by Ru photocatalytic cycle. The silver hexafluoroantimonate salt is intend to remove the Cl<sup>-</sup> anion, and facilitate the formation of the active rhodium catalyst. One year later, this group published a similar method for alkenylation of phenols.<sup>54</sup> The directed *ortho* C-H activation of phenols were allowed by Ru/Ag catalyst mixture, while Ir visible-light-photoredox catalysis functionalized as electron transfer system.

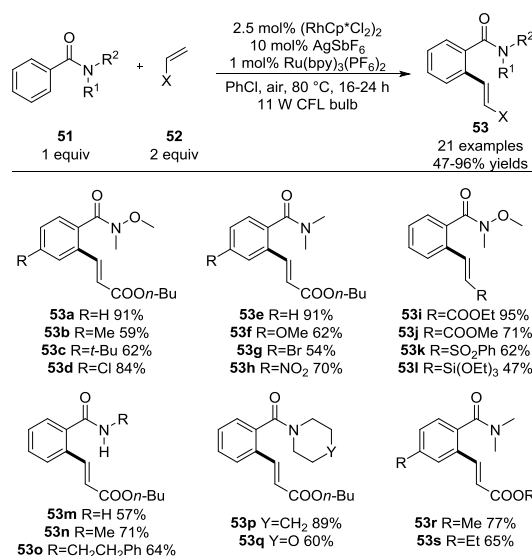


Figure 17. C-H photoredox *ortho*-alkenylation of benzamide derivatives.

The C-H activation-photoredox dual catalyzed cyclization reactions are providing prominent opportunity to prepare complex molecules exclusively. In 2015, Cho's group published a ring closure reaction to form carbazole derivatives (55), used Pd-Ir dual system.<sup>55</sup> The 2-amino-biphenyls (54) underwent in C-N bond formation and the desired products were isolated good to excellent yields. In the same year, the Lei group presented a mild and elegant way to cyclize *N*-arythioamides (56) by a Co-Ru dual catalysis.<sup>56</sup> Interestingly, as side product gaseous hydrogen was formed.

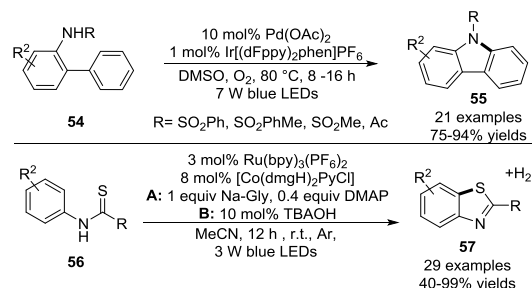


Figure 18. C-H activation combined photoredox dual catalyzed cyclizations.

## 5. Conclusion

The transition metal mediated photoredox dual catalysis has been developed in the last 10 years and it is undergoing explosive growth since 2015. In these reactions the advantages of the two catalytic methods are merged to achieve new synthetic transformations. Reactive radicals could be formed under mild conditions via application of photoredox catalysts with visible light irradiation. On the other hand, the transitional metal catalysts enable the generation of reactive organometallic intermediates by the interaction of transition metal catalysts and the organic substrates. The application of dual catalysis enables the formation of reactive species in the same reaction mixture,



and their interaction and reaction enables the formation of new chemical substances, design of new molecular frames and motifs. The dual catalysis provide opportunity to the easier access of target molecules under simpler and energetically more benign reaction conditions. We believe these pioneering discoveries and developments could serve as solid base for future investments in this field of organic transformations, and exploitation of the concept of dual transition metal-photocatalysis will significantly contribute to the evolution of organic synthesis.

## 6. Acknowledgments

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