

REVIEW ARTICLE

Constructing Heterocycles by Visible Light Photocatalysis

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Abstract: Heterocycles are widely spread in natural products and in many bioactive compounds, as well as in a variety of fine chemicals. Synthesis through catalysis is always an advantageous strategy and today it is difficult to consider an approach to a target molecule without the inclusion of a catalytic step. Moreover, it is indeed almost a required characteristic for all the synthetic transformations in line with the principles of green chemistry and sustainable processes.

Chemical transformations via visible light photocatalysis are emerging strategies that meet the increasing demand for more sustainable chemical processes. Up to date, several visible light approaches have been successfully applied to various organic transformations. Moreover, potential advantages are envisaged in this highly active new field.

This review gives a brief overview of methods based on visible-light photoredox catalysis that have been developed for the synthesis of heterocycles using transition metal catalysts and organic catalysts. Only works in which at least one heterocycle is constructed are included, leaving the vast area of functionalization of heterocycles for other reviews.



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1. INTRODUCTION

The synthesis of heterocycles has considerably expanded because of the pharmacological, agricultural, and industrial importance of most heterocyclic compounds. The contribution of heterocyclic chemistry to several areas is unquestionable. Heterocycles are the basic moieties of many natural organic compounds; they are widely used in industrial chemistry, such as in agrochemicals, colorants, plastics, perfumes and antioxidants. Moreover, heterocycles compounds have many pharmacological activities. In the Comprehensive Medicinal Chemistry database, more than 67% of the compounds listed contain heterocyclic rings [1]. A large number of combinations of carbon, hydrogen and heteroatoms can be designed, thereby providing compounds with the most diverse physical, chemical and biological properties. Approximately 70% of all agrochemicals that have been introduced into the market within the last 20 years bear, at least, one heterocyclic ring [2]. Because of this, the synthesis of heterocycles is of remarkable value, leading to a growing interest in new and more effective methods.

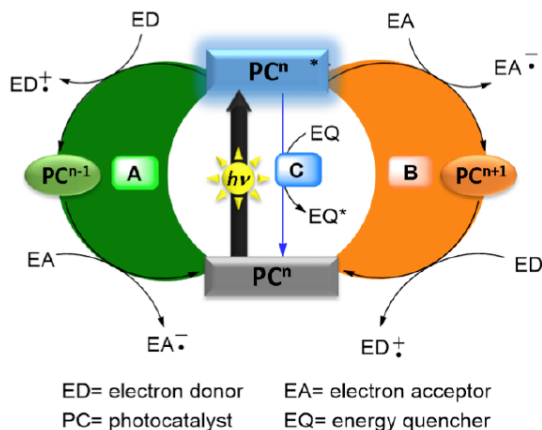
Synthesis through catalysis is always an advantageous strategy and today it is difficult to consider an approach to a target molecule without the inclusion of a catalytic step. Moreover, it is actually almost a required characteristic for any synthetic transformation in line with the principles of green chemistry and sustainable processes. This last characteristic is particularly important, not only in organic chemistry, but also in terms of a broad social acceptance of chemical transformations at an industrial scale.

Likewise, the processes promoted by visible light are important in response to the energy problem facing humanity, and its use is encouraged not only in chemistry but in all fields of science in order to arrive at an ideal source of energy: the sun. In particular, the synthesis via visible light photocatalysis is one of the emerging strategies to meet the increasing demand for more sustainable chemical processes. Access to electronically excited organic molecules using visible light suggests a much wider diversity of reactions than processes traditionally conducted with high-energy UV light. In addition, we could expect more operationally accessible and tolerant methods to access complex functionality using visible light photocatalysts.

Based on the stronger reduction or oxidation capability of the excited state than that of the corresponding ground state, photocatalyzed electron transfer (ET) is one of the most used photocatalysis. The mechanism of a photoredox catalysis (PRC) starts with irradiation of a photocatalyst (PCn) to produce an excited state (PCn)*, which can be either reduced (Scheme 1, Path A) or oxidized (Scheme 1, Path B) by single electron transfer (SET). The terms 'reductive quenching' and 'oxidative quenching' are used to describe the two distinctive pathways. Thus, the reductive quencher or electron donor (ED) reduces the excited-state catalyst to the corresponding low-oxidation state species, while the oxidative quencher or electron acceptor (EA) oxidizes the excited state catalyst to the corresponding high oxidation state species. Radical ion intermediates (ED⁺ and EA⁻) are formed from a SET step through either oxidative quenching or reductive quenching. Significantly, most radical ions subsequently undergo a second chemical step to be transformed into either radicals or ions, serving as the real key reactive species to react with other molecules. However, some radical ions still remain as key species directly participating in some

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chemical reactions. Overall, photoredox catalytic reactions typically involve a radical ion, a radical or an ion as the key reactive intermediate. Independently if oxidative or reductive quenching is taking place, a pair of radical ions (anion and cation) is produced and the final product could be the same. Moreover, in several cases the real mechanism is unclear due to the poor thermodynamic and kinetic information of the elementary steps involved.



Scheme 1. Three types of catalytic cycles involved in visible-light-promoted photocatalytic processes. A) Reductive quenching. B) Oxidative quenching. C) Energy transfer.

In addition, the photoexcited states of photocatalysts can serve as energy donors, activating organic substrates through an energy transfer process (Scheme 1, Path C). This strategy, although less explored, could open the possibility for obtaining different products not accessible through a PRC. Although energy transfer photocatalysis (EP) is mechanistically less complicated, a successful transformation is usually more difficult due to competing process such as ET.

For almost the last decade, photoredox catalysis has received much attention from the organic synthetic community since the independent seminal reports from the MacMillan's, Yoon's, and Stephenson's groups. Up to date, this approach has been successfully applied to various organic transformations, including aza-Henry reactions, asymmetric alkylations, cycloadditions, Diels-Alder reactions, reductive dehalogenations, oxidations, among others [3-9]. Moreover, potential advantages are envisaged in this highly active new field.

Among the photocatalysts used, two groups could be defined: complex of transition metals (Ru, Ir, etc) and pure organic dyes. Reactions promoted by Ru-based photocatalysts can be considered as significant for development of visible light photocatalysis. Many years before the development of this field, the photophysical and photochemical properties of tris(bipyridine)ruthenium(II) chloride was studied in detail and some examples showed that these properties were suitable for photocatalysis, namely long life time of excited state and high photo stability. Seminal works using this Ru catalyst aroused synthetic interest, allowing useful synthesis by visible light photocatalysis [6]. Therefore, it is not surprising that most of the following examples use Ru and Ir complexes to produce various chemical transformations. However, similar to what happens in other catalysis, the cost and potential toxicity of transition metal direct the attention to dyes as photocatalysts. Underestimated in the first years of development, organic photocatalysts has shown to be a good alternative in many reactions driven by metals complexes [7, 8]. In general, organic photocatalysts have less photostability and a shorter life-time of the excited state than metal photocatalysts. Consequently, higher catalyst loading and longer reaction times are usually required. However, most organic dyes are cheaper and much more available than metal ones. In addition, little effort

has been put in the development of organic photocatalysts with enhanced properties. If we compare the effort devoted to metal-based catalysts, we can expect a higher performance of organic dyes, when more development appears in the context of visible light photocatalysis. As part of the previous comparison, it is important to note that many studies that claim a better performance of metal complexes compare optimized with not optimized conditions and usually put no effort into the screening of organic dyes.

In this review, we will describe the synthesis of the heterocyclic moiety by visible light photocatalysis. We include works in which at least one heterocycle is formed, leaving the vast area of functionalization of heterocycles for a comprehensive review. The synthesis has been organized in terms of the type of catalyst used: 1) transition metal catalysts and 2) organic (transition metal-free) catalysts. Each section is divided into intramolecular and intermolecular processes from simpler to more complex synthetic strategies.

2. TRANSITION METAL CATALYST

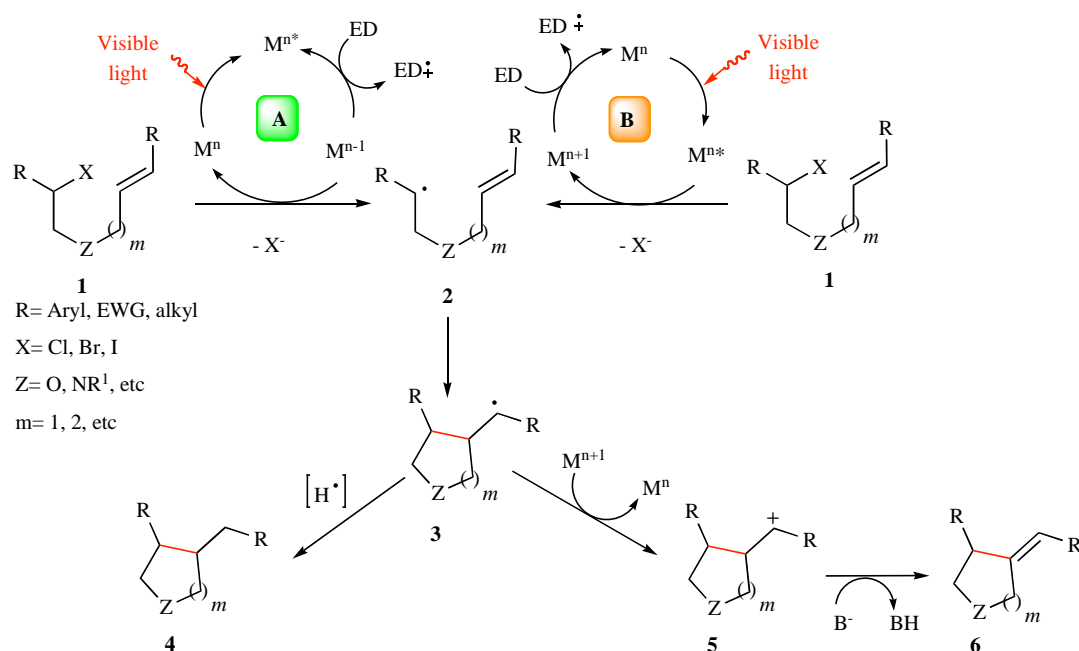
Photoredox catalysis by a well-known method, and ruthenium(II) and iridium(III) polypyridine complexes, has become a powerful tool for redox reactions in synthetic organic chemistry, since they can effectively catalyze SET processes by irradiation with visible light. Remarkably, since 2008, this photocatalytic system has gained importance in radical reactions for being not only a useful and selective protocol but also for adhering to the principles of green chemistry [9].

2.1. Intramolecular Processes

The ability of photoredox catalysts to reduce chemoselectively suitable activated carbon-halogen bonds under mild conditions and irradiation by visible light represents in advance in the both fields: free radical and photochemistry applied to organic synthesis. Furthermore, the use of visible light to induce these reactions is of particular significance for the more environmentally conscious chemical community, since it allows for the generation of free radicals without using highly toxic, environmentally hazardous or explosive reagents (alkyl stannanes, boranes, AIBN, etc) and avoidance of specialized and expensive reaction equipment. Progress made in the application of visible light photoredox catalysts in a free radical reaction includes cyclization onto unactivated π -systems.

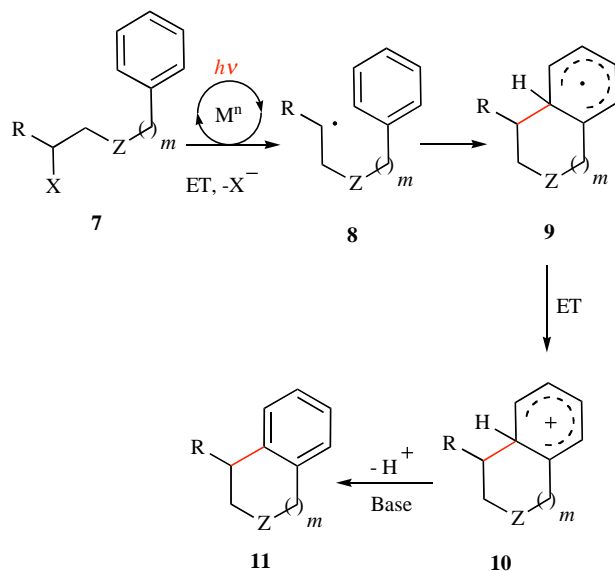
Photoactive metal-catalysts, M^n , undergo a visible light induced excitation to afford an excited state, M^{n*} (Scheme 2). This excited state can then be reductively quenched by a sacrificial electron source (in general trialkyl amines are particularly effective in this regard) to afford a powerful single electron reductant M^{n-1} (Scheme 2, Path A). The species M^{n-1} has a reduction potential higher enough to reduce alkyl halides **1** and afford radical **2** and regenerate the photoactive catalysts M^{n+} . Alternatively, depending on redox potential of photocatalysts and RX, radical **2** could be generated from **1** by oxidative quenching (Scheme 2, Path B). In this case, the excited state M^{n*} reacts directly with RX to afford radical **2** and M^{n+1} . Both strategies (reductive or oxidative quenching) lead to the formation of the same reactive intermediate **2**, they could also be used for constructing several heterocyclic in intermolecular approaches (see section 2.2).

Then, the alkyl radical can be trapped by the double (or triple) bond in an *exo* (or *endo* not drawn in Scheme 2) ring closure mode to give radical **3**, which, depending on reaction conditions, can take two different pathways. In the presence of sacrificial reducing agent, heterocycle **4** could be obtained and the overall process gives the addition-reduction product. On the other hand, oxidation of radical **3** followed by deprotonation gives the corresponding substitution product **6**. In this case, extra sacrificial donor is not needed (neutral reactions) and radical **3** is used as an electron donor forming cation **5**.



Scheme 2. Synthesis of heterocycles from RX (reductive and oxidative quenching).

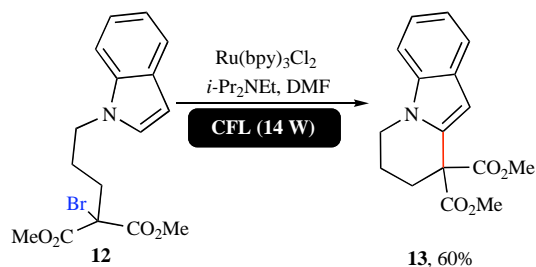
Another general procedure for heterocyclic synthesis involves the cyclization of substrate **7**, in an intramolecular homolytic aromatic substitution or HAS (Scheme 3).



Scheme 3. Synthesis of fused heterocycles by HAS.

Once radical **8** is generated (by oxidative or reductive quenching), it adds to the arene moiety to give cyclohexadienyl radical **9**, which after oxidation-deprotonation reactions, gives the fused heterocycle **11**. If this reaction proceeds by oxidative quenching (neutral reactions), a catalytic amount of external sacrificial donor is enough; however, in many systems they are added in a stoichiometric amount due to kinetic issues.

Thus, Stephenson demonstrated that a radical formed from activated α -bromodicarbonyl compounds (**12**) reacts with indoles and pyrroles by Ru(bpy)₃Cl₂ (bpy=2,2'-bipyridine) photoredox catalysis in the presence of amines (reductive quenching). For instance, the reaction of **12** afforded heterocycle **13** in good yields (Scheme 4) [10].



Scheme 4. Synthesis of indole dicarboxylate **13**.

Both six- and five-membered fused rings are possible, although five-member rings are more difficult to form and generally require a substituent at C-3 to stabilize the tertiary radical resulting from cyclization. Selected examples (**14-19**) of this reaction are shown in Figure 1.

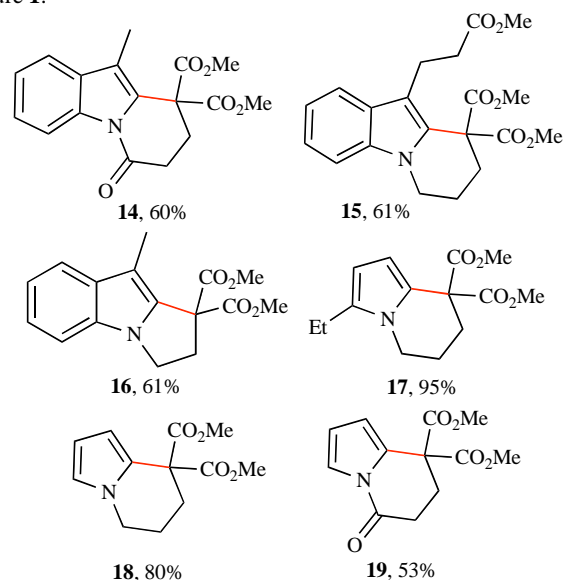
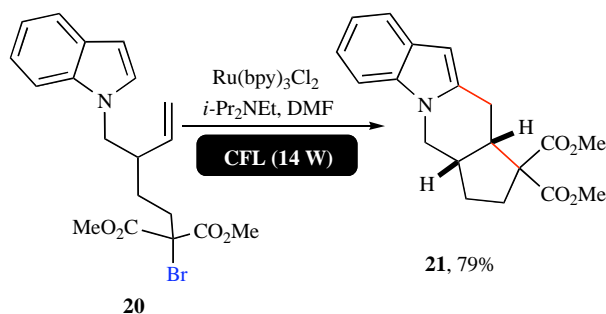


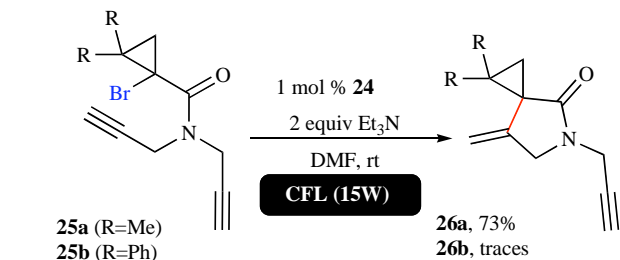
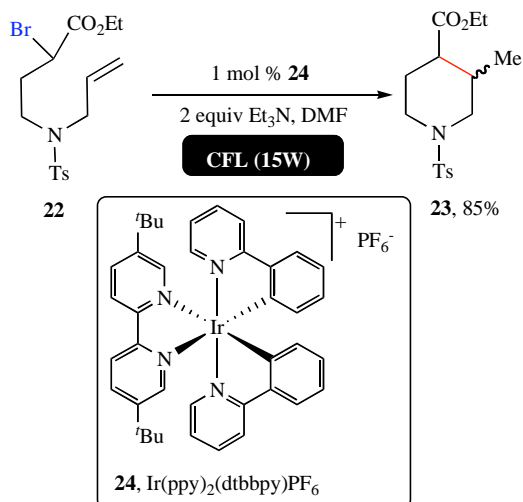
Fig. (1). Photoredox-catalyzed HAS of α -dicarbonyl radical onto indoles and pyrroles.

Another example of photoredox-mediated radical generation is the cascade radical cyclization of substrate **20** to afford product **21** in good yield (Scheme 5) [10].



Scheme 5. Tandem synthesis to obtain **21**.

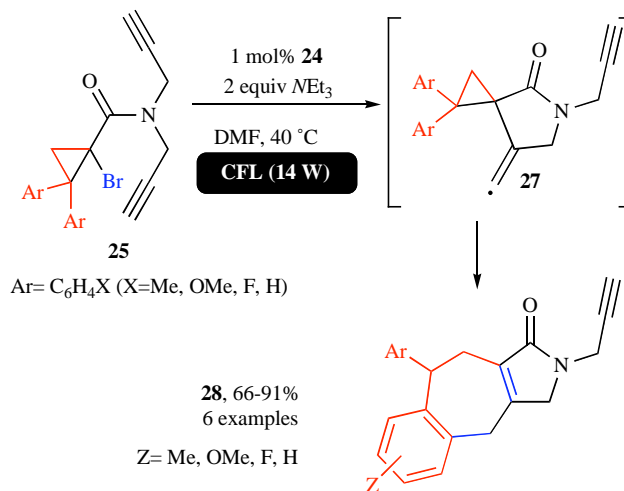
However, the treatment of α -monocarbonyl substrates **22** (Scheme 6) using $\text{Ru}(\text{bpy})_3\text{Cl}_2$ -mediated cyclization conditions presented in Scheme 5, resulted in recovery of the starting material. Hence, a more powerful reducing agent was needed to initiate this transformation. One of the advantages of photoredox using transition-metal catalysis is the possibility of modulating the reactivity with the choice of metal and ligand. Indeed, changing from $\text{Ru}(\text{bpy})_3\text{Cl}_2$ catalyst to $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (**24**, ppy =2-phenylpyridine; dtbbpy =4,4'-di-*tert*-butyl-2,2'-bipyridine) catalyst caused the increase required in the reduction potential (-1.51 V *vs* SCE) for **24** -1.31 V for $\text{Ru}(\text{bpy})_3\text{Cl}_2$), now giving the reactions that previously failed. Accordingly, α -bromo ester **22** and α -bromo amide **25a** ($\text{R}=\text{Me}$), efficiently underwent cyclization under irradiation with condensed fluorescent light (CFL) to afford *N*-tosyl piperidine **23** and spiro-cyclopropane pyrrolidinone **26a** ($\text{R}=\text{Me}$), respectively, under Ir-mediated photoredox conditions (Scheme 6) [11].



Scheme 6. Phoredox reactions using Ir complex **24**.

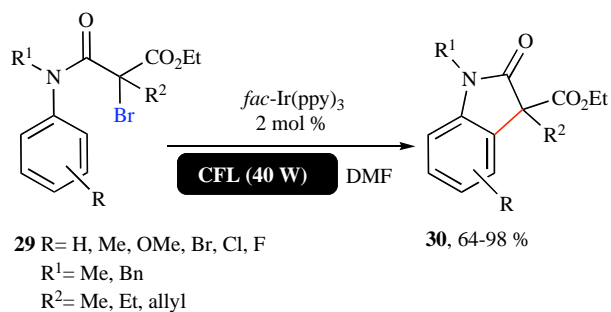
When the aryl analog α -bromo amide **25b** ($\text{R}=\text{Ph}$) was subjected to Ir-mediated cyclization conditions at rt, only traces

amounts of the corresponding **26b** were observed (Scheme 6). Instead, the fused tricyclic pyrrolidinone **28** was generated as the major product in 69% yield, after 12 h at 40°C (Scheme 7) [12]. This strategy was applied to several diaryl substituted bromocyclopropanes **25** and tricyclic pyrrolidinones **28** were isolated in very good yields. Two mechanisms were proposed, sharing an initial cyclization via vinylcyclopropane intermediate **27** followed by a second cyclization onto one aromatic system (HAS reaction) or a reduction to **26** followed by a Claisen rearrangement.



Scheme 7. Tandem synthesis to obtain **28**.

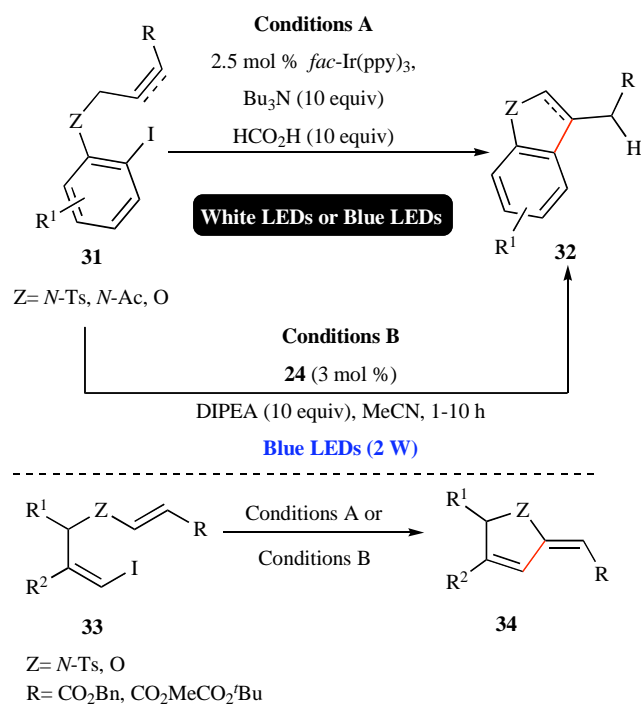
The synthesis of 3,3-disubstituted oxindoles **30** from 2-bromoanilides **29** by an intramolecular HAS using *fac*- $\text{Ir}(\text{ppy})_3$ was reported (Scheme 8) [13]. Other commonly used transition metal photo-catalysts such as $\text{Ru}(\text{bpy})_3\text{Cl}_2$ and **24** were examined, and the reactions proceeded with lower yields, requiring tertiary amines as sacrificial reductants. In this case an oxidative quenching mechanism is taken place, following the mechanisms shown in Scheme 3.



Scheme 8. Synthesis of 3,3-disubstituted oxindoles derivatives **30**.

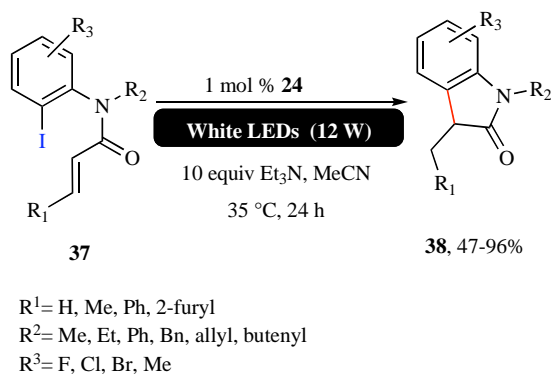
Although the photoinduced cyclization of organobromides shown before has several advantageous features in terms of ability to form complex ring systems, the strategy needs to use bromides adjacent to a π system (α -carbonyl, benzyl) or heteroatom. Stephenson *et al.* and Lee *et al.*, independently, reported the reductive transformations of unactivated aryl **31**, alkenyl **33** and alkyl **35** iodides based on iridium(III) photocatalysts (Conditions A or B, Scheme 9) [14, 15]. The mechanisms proposed are under discussion since Lee's group indicates that reductive quenching is operating while Stephenson's group indicates that oxidative quenching is taking place.

The examples shown in Scheme 9 involve intramolecular radical cyclization via a radical addition onto β -position (Michael-type addition) of α,β -unsaturated esters and amides. Recently, the radical cyclization reaction of *o*-iodophenylacrylamides **37** through an "anti-Michael" type addition gave the corresponding indolin-2-ones



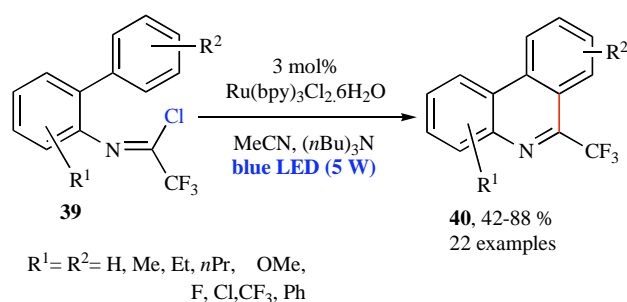
Scheme 9. Synthesis of heterocycles from aryl, vinyl and alkyl iodides using iridium(III) catalysts.

38 in good yields using [Ir(ppy)₂(dtb-bpy)]PF₆ (**24**) in MeCN (Scheme 10) [16].

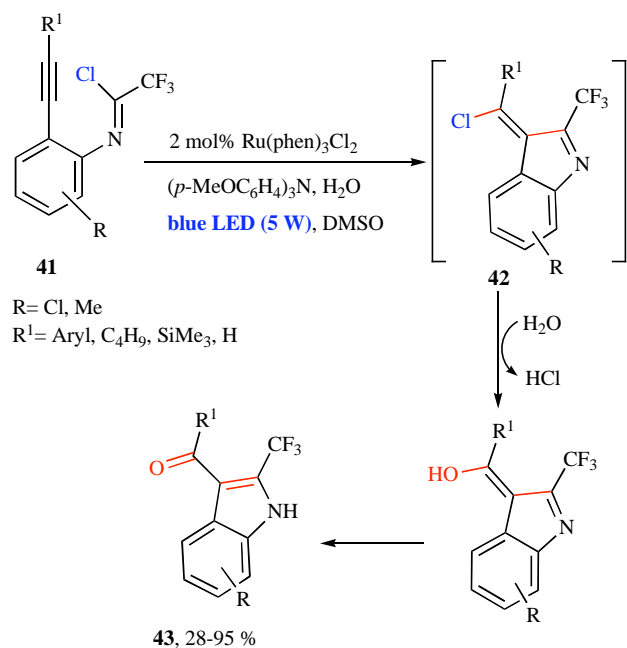


Scheme 10. Synthesis of substituted indolin-2-ones **38**.

Fu and co-workers developed an intramolecular HAS of trifluoroacetimidoyl chlorides **39** for the synthesis of 6-(trifluoromethyl)phenanthridine derivatives **40** based on the activation of C(sp²)-Cl bond under visible-light irradiation (Scheme 11) [17]. As a continuation of this work, the synthesis of 2-trifluoromethyl-3-acyl indoles **43** from *N*-[2-(alkynyl)phenyl]trifluoroacetimidoyl chlorides **41** was investigated using a Ru-catalyst and blue LEDs (Scheme 12) [18]. In this case, the photoreaction was initiated by reductive quenching using triaryl amines as sacrificial ED in a radical chain propagation process. Vinyl chloride **42** was proposed as an intermediate, which, by hydrolysis finally gave acylindoles **43**.



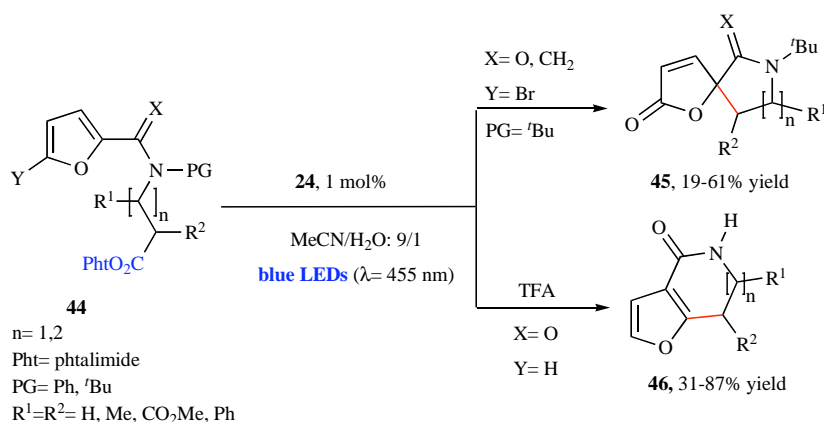
Scheme 11. Synthesis of substituted 6-(trifluoromethyl)-phenanthridines **40**.



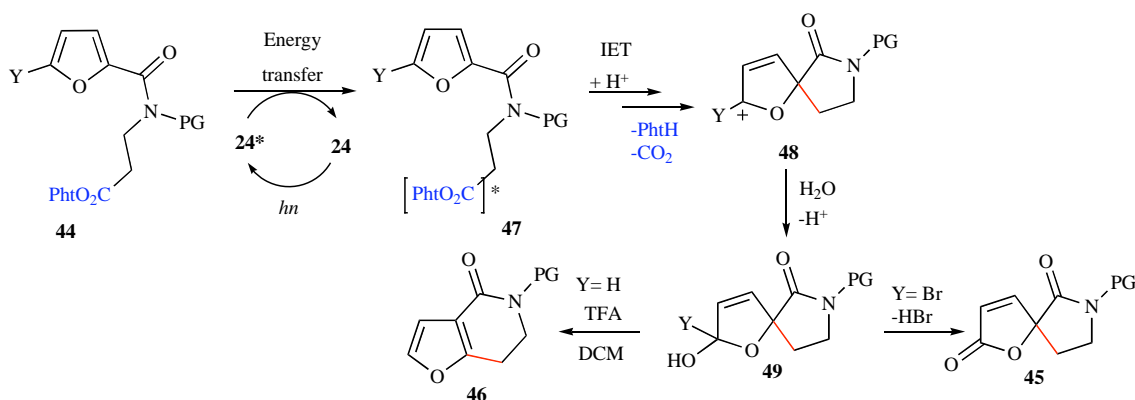
Scheme 12. Synthesis of 2-trifluoromethyl-3-acyl indoles **43**.

Visible light-mediated decarboxylation using *N*-acyloxyphthalimides **44** as the source for carbon-centered radicals was applied for the synthesis of spirobutenolides **45** and 2,3-annellated furans **46** using iridium catalysts **24** (Scheme 13) [19]. Analyzing the redox potential of **24** and *N*-acyloxyphthalimides **44** reveals that an oxidative quenching cycle is not favored thermodynamically. Moreover, due to the absence of a suitable electron donor that could act as a reductant for these catalysts, a reductive quenching cycle is also ruled out. However, the fluorescence of **24** is quenched by **44** and, since the redox pathway is discarded, the authors have proposed that **24** acts as a sensitizer, transferring energy from its excited state to the phthalimide moiety in **44**, generating its triplet state **47** with higher redox potential (Scheme 14). Intramolecular electron transfer (IET), protonation, decarboxylation and radical recombination sequence give spirocations **48**. Water present in the reaction media attacks cation **48** and gives hydroxyl-spiro **49**, which depending of the nature of Y moiety, follows two different routes. If Y=Br, direct elimination of HBr provides butenolide **45**. Alternatively, if Y=H, cation **49** via acid-catalyzed vinylogous semipinacol rearrangement is transformed into 2,3-annellated furans **46**.

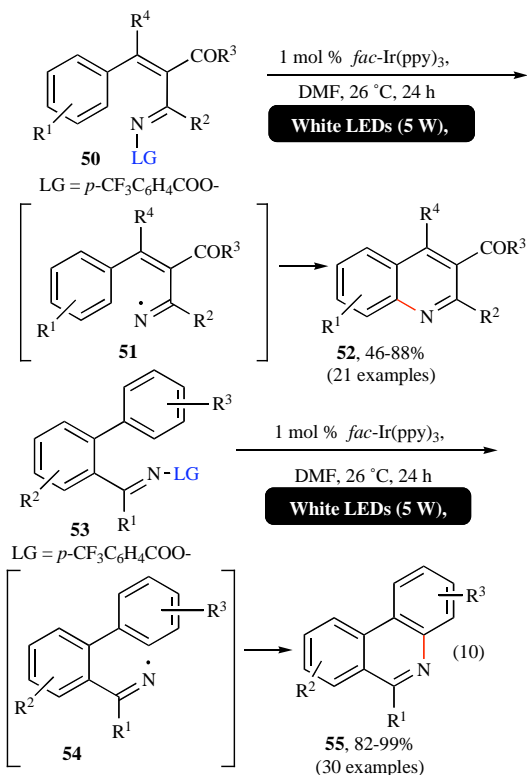
In general, nitrogen-centered radical are generated by nitrogen-leaving group (N-LG) homolysis. Acyl oximes are versatile building blocks for the synthesis of structurally diverse and biologically active *N*-heterocycles through N-O bond cleavage and C-N bond



Scheme 13. Synthesis of spirobutenolides **45** and 2,3-annellated furans **46**.



Scheme 14. Mechanisms proposed for energy transfer to **44**.



Scheme 15. Synthesis of substituted quinolines **52** and phenanthridines **55**.

formation via iminyl-radical formation [20]. Using *fac*-[Ir(ppy)₃] as a photoredox catalyst, acyl oximes **50** and **53** were converted by

one electron reduction into iminyl radical intermediates **51** and **54**, which subsequently underwent intramolecular HAS to give quinolines **52** and phenanthridines **55** (Scheme 15).

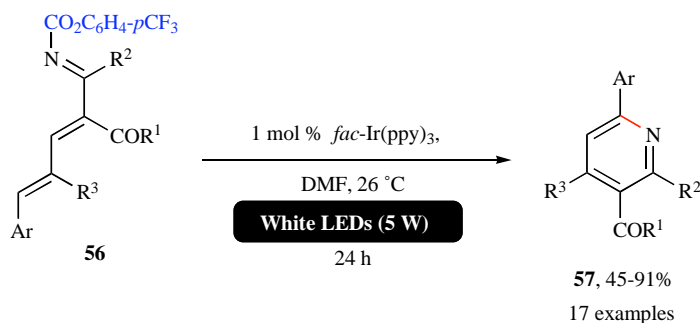
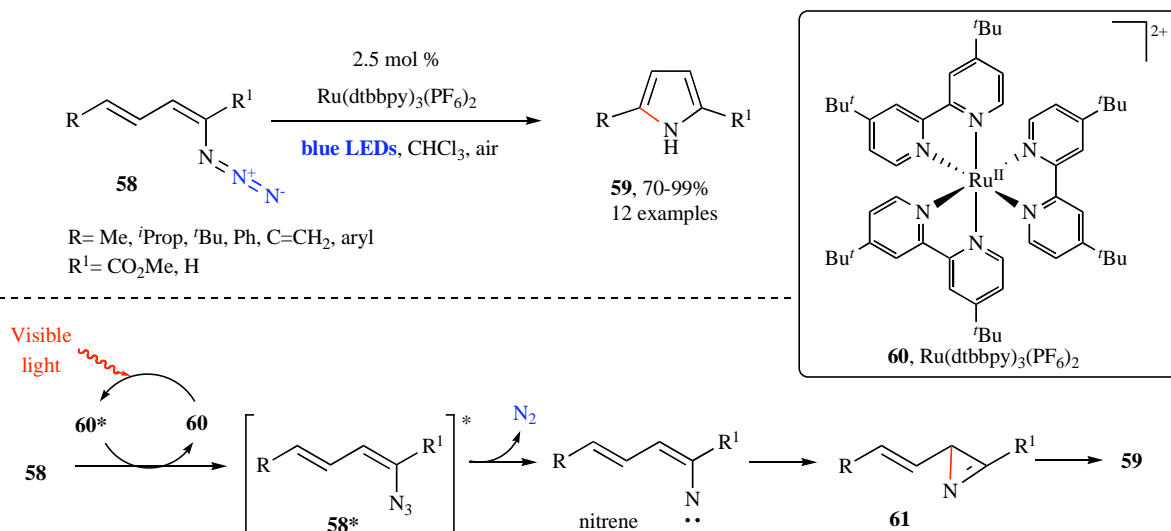
Moreover, tri- and tetra-substituted pyridines **57** can also be accessed by this strategy from acyl oximes **56** in good yields (Scheme 16) [21].

Irradiation of dieny azides **58** in the presence of Ru photocatalyst (**60**) results in the formation of reactive azirine **61** (via nitrene), affording pyrroles **59** (Scheme 17) [22]. The mechanism proposed involves energy transfer. Irradiation of Ru(dtbbpy)₂²⁺ with visible light produces its long-lived excited state; exergonic energy transfer to dieny azide **58** produces triplet **58***, which expels dinitrogen to produce a nitrene intermediate. Ring-closure affords azirine **61**, which undergoes slow but high-yielding rearrangement to pyrrole **59**.

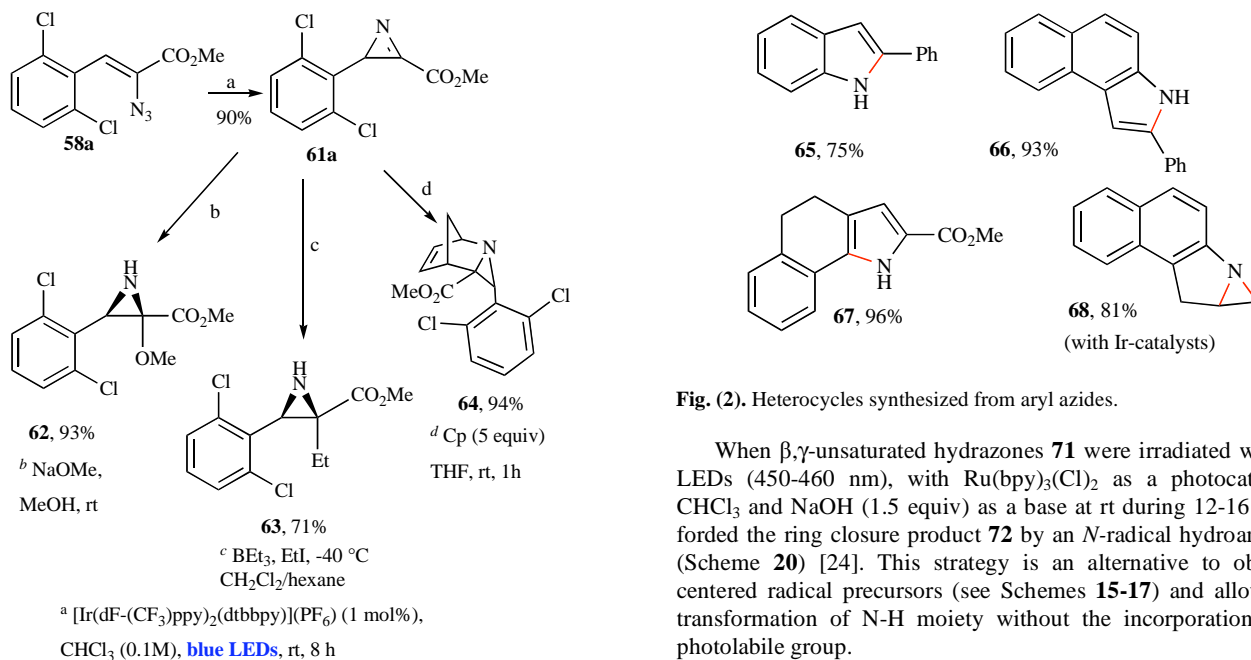
In these reactions, azirine is an intermediate because it could be isolated where subsequent ring expansion to the five-membered heterocycle is slow. In addition, azide **58a** was converted to a variety of substituted aziridines (**62-64**) by addition of nucleophiles and radicals to the C=N bond or reacted by hetero-Diels-Alder cycloaddition with cyclopentadiene (Scheme 18).

Furthermore, sensitization of aryl azides proceeded successfully to afford indoles **65** and **66** (Fig. 2). In addition, tricyclic fused heterocycles **67** were accessible from γ -substituted azido acrylates and azirine **68** from azidonaphthalene. In the last case, the triplet excited-state energy of azido naphthalene is higher, thus it could be efficiently sensitized by [Ir(dF(CF₃)ppy)₂(dtbbpy)]⁺.

Recently, Chen and Xiao *et al.* reported a highly efficient route to construct *N*-free 2-substituted indoles **70** (similar to **65**) from the readily available styryl azides **69** via a visible light-induced photo-

Scheme 16. Synthesis of substituted pyridines **57**.

Scheme 17. Mechanisms and synthesis of pyrroles from dieny azides.

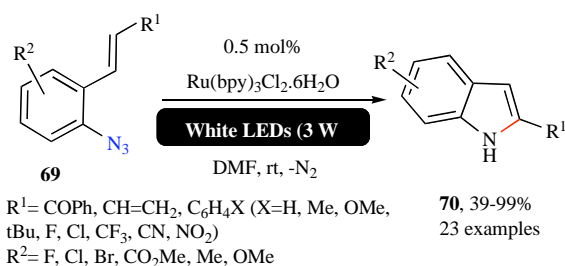
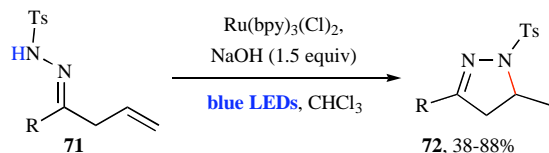
Scheme 18. Manipulation of the azirine intermediate **61a**.

catalysis (Scheme 19) [23]. Again, a plausible reaction mechanism for this photo-catalytic transformation via an energy transfer was also proposed.

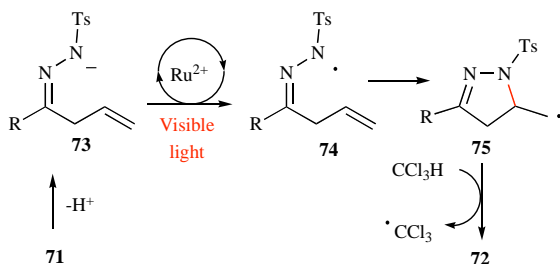
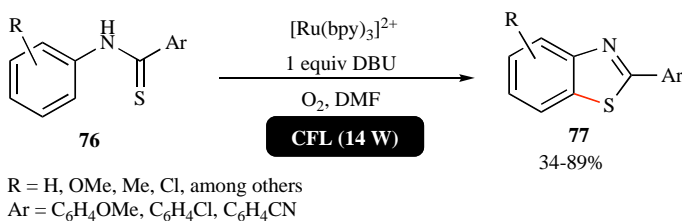
Fig. (2). Heterocycles synthesized from aryl azides.

When β,γ -unsaturated hydrazones **71** were irradiated with blue LEDs (450-460 nm), with Ru(bpy)₃(Cl)₂ as a photocatalyst in CHCl₃ and NaOH (1.5 equiv) as a base at rt during 12-16 h, it afforded the ring closure product **72** by an *N*-radical hydroamination (Scheme 20) [24]. This strategy is an alternative to obtain *N*-centered radical precursors (see Schemes 15-17) and allow direct transformation of *N*-H moiety without the incorporation of any photolabile group.

A possible reaction mechanism was proposed in Scheme 21. Deprotonation of hydrazone **71** occurs under basic conditions to give the anionic intermediate **73**, affording radical **74** by an oxidative quenching. A 5-*exo-trig* cyclization of **74** affords radical **75**. Subsequent H-transfer from CHCl₃ (a redox couple) to **75** gives

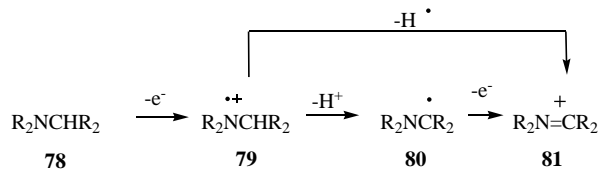
Scheme 19. Synthesis of substituted indoles **70** from azides **69**.Scheme 20. Synthesis of substituted 1-tosyl-4,5-dihydro-1H-pyrazoles **72**.

product **72**, together with generation of Cl₃C· radical, that can regenerate the photocatalyst through an ET process.

Scheme 21. Mechanism proposed for the formation of dihydropyrazoles **72**.

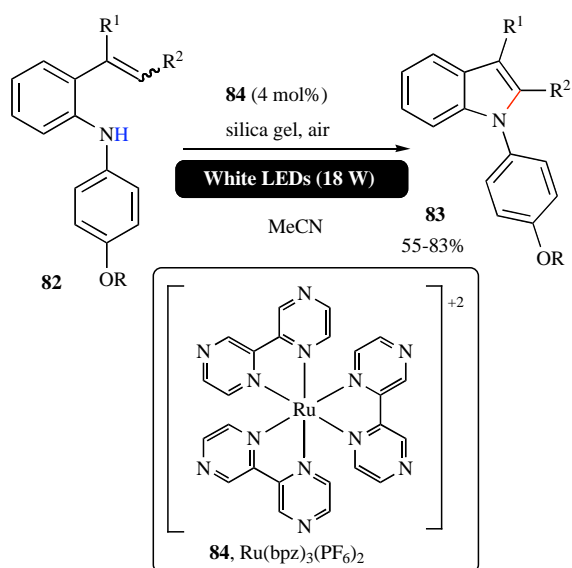
Scheme 22. Synthesis of 2-arylbenzo[d]thiazoles derivatives.

Another example that involves, as a first step, the formation of an anion followed by ET and radical cyclization reactions is the synthesis of benzothiazoles **77** (Scheme 22). In this case, photoredox catalysis has been used to obtain sulfur center radicals. The anion of thioamide **76** is oxidized in the presence of [Ru(bpy)₃]²⁺ as a photoredox catalyst to afford benzothiazoles **77** with good yields through an intramolecular HAS (Scheme 3) [25].



Scheme 23. Reaction pathways of amine radical cations.

In particular, one-electron oxidation of tertiary amines **78** is known to produce radical cations **79**, which in polar solvents undergoes facile deprotonation, subject to kinetic acidity and stereoelectronic factors, to produce α-amino radicals **80** (Scheme 23) [26]. Depending on the reaction conditions, the generated radicals

Scheme 24. Synthesis of substituted indoles **83**.

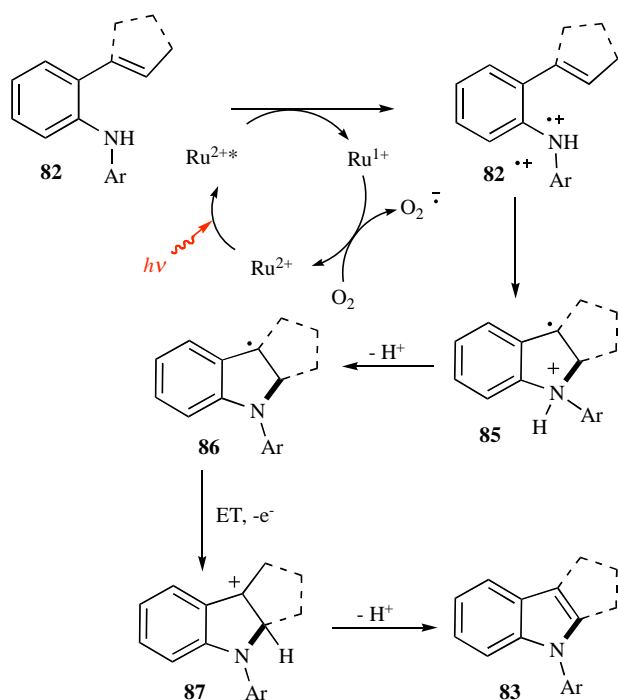
80 could react as a nucleophile with a suitable substrate or could undergo further one-electron oxidation due to their reduction potential to form iminium cation **81**, thus serving as an electrophile. Alternatively, radical cation **79** could also act as H donor to afford cation **81** in a single step. Among them, radicals **79-80** could add to unsaturated systems.

In this way, the addition of radical cations **79** to olefins is an attractive method for C–N bond formation. When styryl anilines **82** were irradiated with visible light and [Ru(bpz)₃](PF₆)₂ (**84**) as a catalyst in MeCN in air, *N*-aryl indoles **83** were obtained with good yields (Scheme 24) [27].

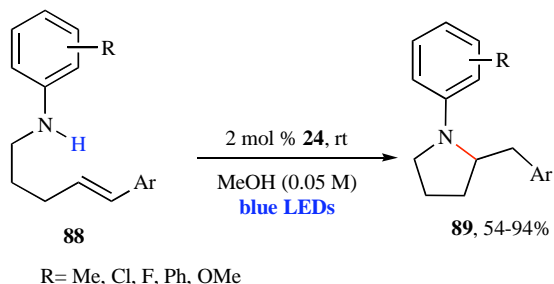
Scheme 25 outlines the catalytic cycle proposed. The key steps include: (i) conversion of amine **82** into nitrogen-centered radical cation **82^{•+}** through oxidation using the excited catalyst, (ii) electrophilic addition of **82^{•+}** to a tethered alkene to generate the benzylic radical cation **85**, (iii) deprotonation and further oxidation of benzylic radical **86** to its corresponding benzylic cation **87**, and finally (iv) aromatization through deprotonation, thus forming indole **83**.

Another example where aminium cations were used to form heterocycles is the synthesis of *N*-arylpyrrolidines **89** (Scheme 26) [28]. Fluorescence quenching assays demonstrate that ET between excited state of **24** and aryl olefins **88** to give the aminium radical intermediate is kinetically favored. Hammett analysis for a series of *para*-substituted styrenes acceptors revealed that C–N bond formation from a radical cation is the rate-limiting step.

The visible light promoted reaction of the linked indole-*N*-tosylamide **90** catalyzed by [Ru(bpy)₃Cl₂] in the presence of tetramethylguanidine (TMG) as a base give the tetrahydro-5*H*-indolo[2,3-*b*]quinolinol products **91** in good yields (49-77%) and excellent regioselectivities (dr >95.5) (Scheme 27) [29].

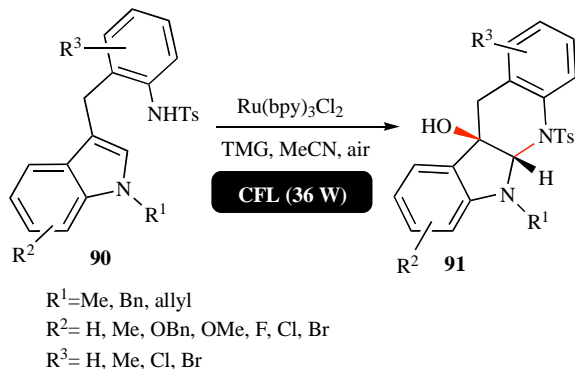


Scheme 25. Mechanisms proposed for synthesis of *N*-arylindoles.



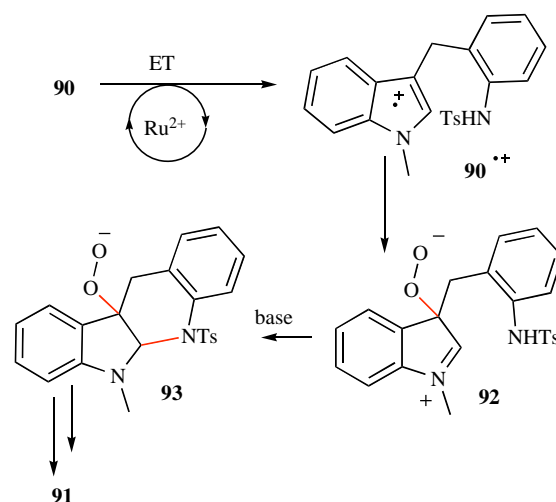
Scheme 26. Synthesis of *N*-arylpyrrolidines derivatives **89**.

Scheme **28** outlines the mechanism proposed. Excited $[\text{Ru}(\text{bpy})_3]_2^{+*}$ can undergo reductive quenching by **90** to afford radical cation $\mathbf{90}^{\bullet+}$, that is trapped with $\text{O}_2^{\bullet-}$ radical anion formed by the reaction of $[\text{Ru}(\text{bpy})_3]^+$ with O_2 , to afford zwitterion **92**. A base-promoted cyclization finally gives heterocycle **91**.



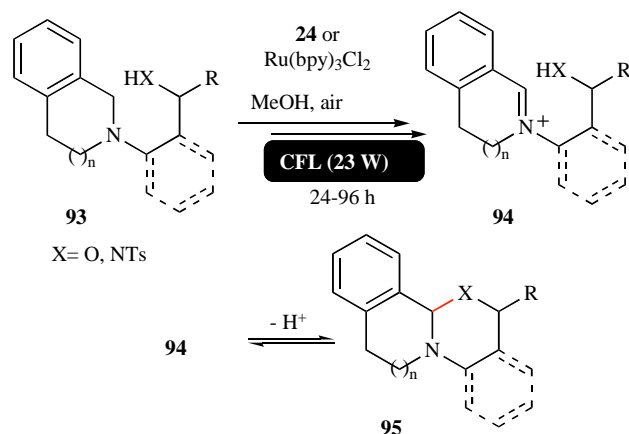
Scheme 27. Synthesis of derivatives **91**.

Oxidative amine photoredox catalysis has become more widely adopted, and many examples of nucleophilic additions to tetrahydroisoquinolines have been published using iminium ion **94** as an intermediate (similar to **81**). The versatility of these systems is impressive, and there have been many creative contributions in this



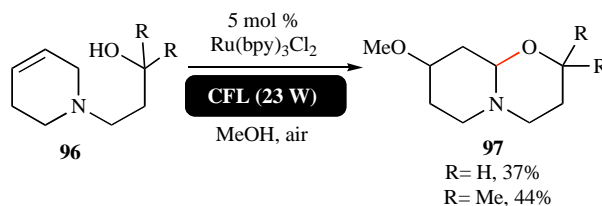
Scheme 28. Mechanisms for the oxyamidation of indoles.

context (see also Section 2.2). As a part of these studies, Xiao *et al.* developed an efficient photocatalytic method for the synthesis of isoquino[2,1-*a*][3,1]oxazine and isoquino[2,1-*a*]pyrimidine derivatives **95** (Scheme **29**) [30]. Visible light irradiation of solutions of either alcohol ($\text{X} = \text{OH}$) or tosylamide ($\text{X} = \text{NTs}$) tetrahydroisoquinolines **93** with the iridium complex $\text{Ir}(\text{ppy})_2(\text{dtbbpy})\text{PF}_6$ (**24**) was found to promote generation of fused heterocycle targets **95** in moderate to good yields (26-86 %).



Scheme 29. Reaction of tetrahydroisoquinolines **93** with nucleophiles.

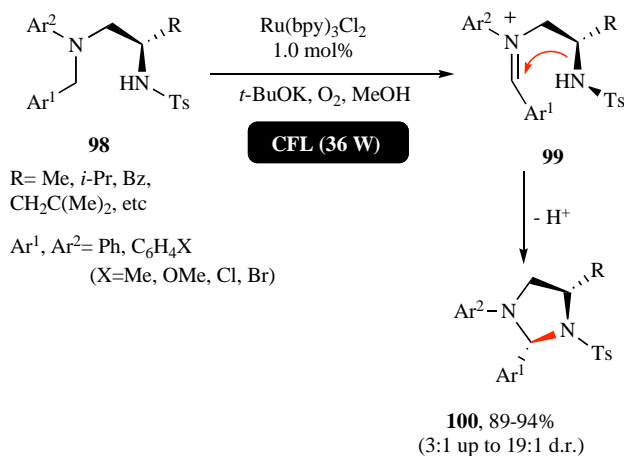
Later, as an extension of this work, Marvin *et al.* reported the synthesis of **95** from **93** using $\text{Ru}(\text{bpy})_3\text{Cl}_2$ as a catalyst in regular yields (12-52%) [31]. Moreover, unsaturated piperidines **96** were used as substrate and heterocycle formation was accompanied by the addition of methanol across the unsaturation to provide methoxy oxazine **97** as a mixture of diastereomers (Scheme **30**).



Scheme 30. Synthesis of octahydropyrido oxazines **97**.

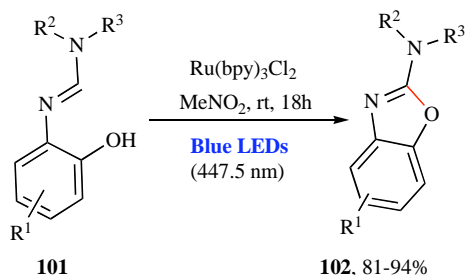
The enantiomerically pure substrate **98**, in the presence of a photoredox catalysts, *t*-BuOK and O_2 under visible light irradiation, gave tetrahydroimidazole **100** in high yields with very good di-

astereoselectivities (Scheme 31) [32]. In the mechanism proposed, the diamine **98** is oxidized to iminium intermediate **99** followed by intramolecular nucleophilic attack to afford tetrahydroimidazole **100**.



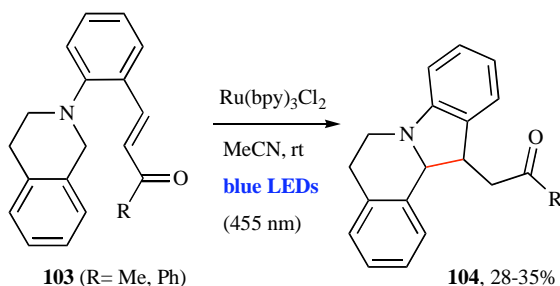
Scheme 31. Synthesis of tetrahydroimidazoles **100**.

The photocatalytic preparation of 2-aminobenzoxazoles **102** derivatives from *o*-phenolic amidines **101** was carried out by irradiation with blue LEDs in MeNO₂ with good yields (Scheme 32) [33]. This reaction formally involves oxidative functionalization of a vinyl C–H bond with C–O bond formation.



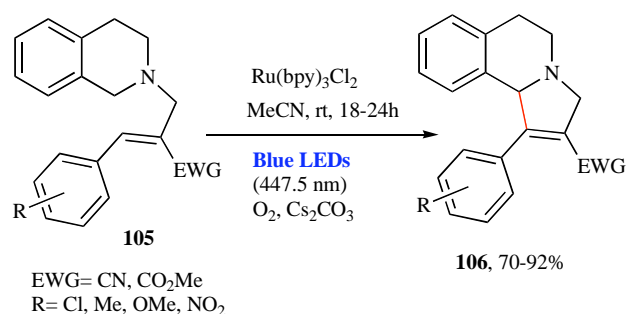
Scheme 32. Synthesis of benzoxazol-2-amine **102**.

As shown in Scheme 23, radical cations of tetrahydroisoquinolines could produce α -amino alkyl radicals. In this context, these intermediates participate in intramolecular radical addition reaction transforming aminoenones **103** into the corresponding 5,6-dihydroindolo[2,1-*a*]tetrahydroisoquinolines **104** (Scheme 33) [34].



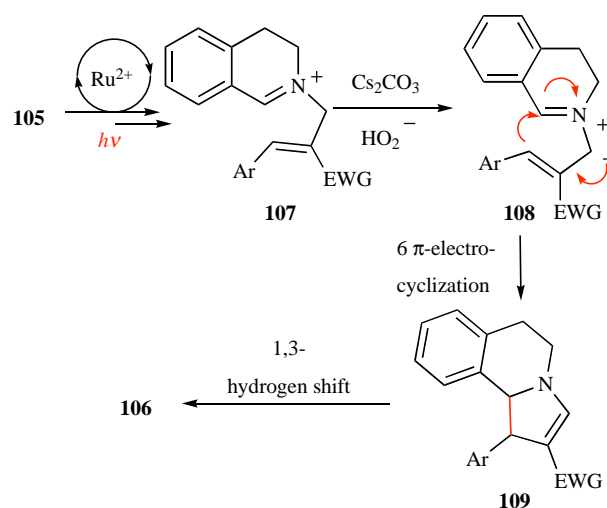
Scheme 33. Synthesis of tetrahydroisoquinolines **104**.

There is a current interest in novel syntheses of pyrrolo[2,1-*a*]isoquinoline alkaloids due to their antitumor activity [35]. The *N*-cinnamyl tetrahydroisoquinolines **105** afforded pyrrolo[2,1-*a*]isoquinoline **106** when **105** are irradiated with Ru(bpy)₃Cl₂ as catalysts in air atmosphere (Scheme 34) [36]. Electron-withdrawing groups (EWG) in the 2-position of the cinnamyl moiety are required for the cyclization reaction.



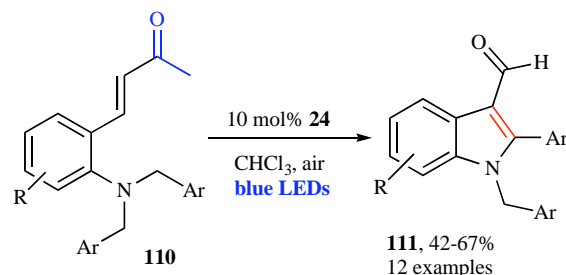
Scheme 34. Synthesis pyrrolo-isoquinoline derivatives **106**.

In this case (see Scheme 23) the iminium cation **107** is generated by reductive quenching-deprotonation and easily converted into **108** by a second deprotonation in the presence of Cs₂CO₃ and anion HO₂⁻ (Scheme 35). The *in situ* generated 6 π -electron system **108** gives electro-cyclization to afford **109**, undergoing 1,3-hydrogen shift to finally yield the product **106**.



Scheme 35. Mechanism proposed for the formation of **106**.

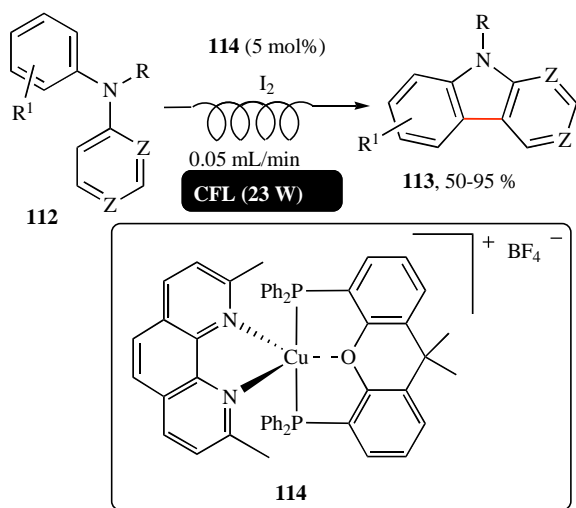
The reaction of (*E*)-4-(2-(dibenzylamino)phenyl)but-3-en-2-one **110** resulted in the unexpected formation of indole-3-carbaldehyde **111** (Scheme 36) [37]. Mechanistic investigations have been performed to elucidate the reactive intermediates and to propose a plausible reaction pathway for the photoredox catalyzed addition/aromatization/C–C bond cleavage cascade reaction via the formation of α -amino alkyl radical intermediates.



Scheme 36. Synthesis of indoles derivatives **111**.

The synthesis of carbazoles from diarylamines through C–C bond formation is an attractive synthetic route for this important class of compounds [38]. Although several strategies are reported, harsh conditions are used and substrate scope are often limited [39]. Taking this into account, triarylamines and *N*-alkyl diarylamines **112** were converted to *N*-aryl or *N*-alkyl carbazoles **113** using Cu-

based complex like **114** in a continuous-flow photochemical reactor (CFL, 23 W) (Scheme 37) [39]. In general, triaryl amines bearing electron-donating groups (EDG) tend to produce higher yields than triaryl amines possessing EWG. The incorporation of nitrogen-based heterocycles, as well as halogen-containing arenes in carbazoles skeletons, was well tolerated [40].

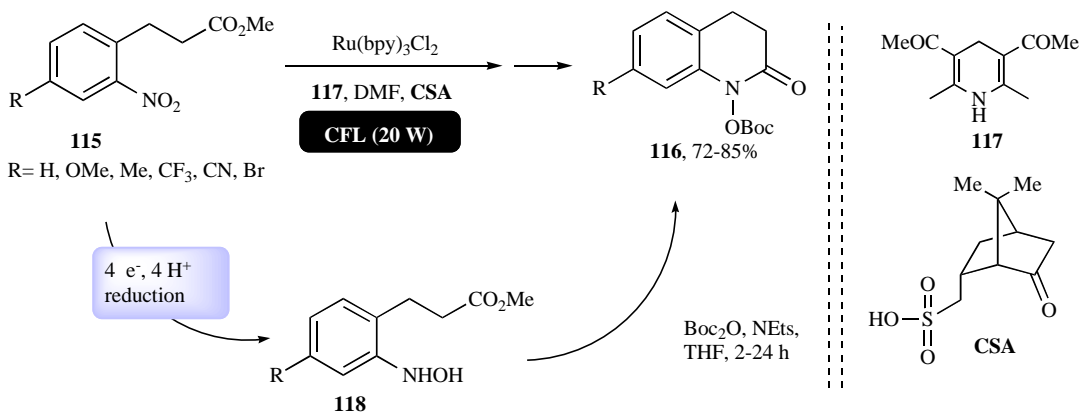


Scheme 37. Continuous-flow synthesis of carbazoles **113**.

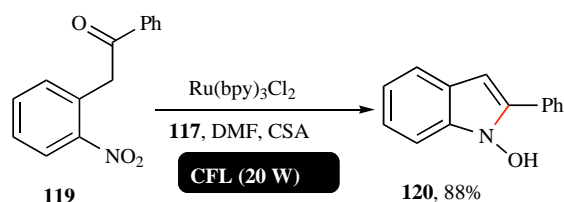
The photocatalytic reduction of nitroarenes **115** with [Ru(bpy)₃]²⁺, Hantzsch esters **117** as reductants and camphorsulfonic acid (CSA), afforded hydroxamic acids **116** in good yields (isolated as protected *N*-OBoc, Scheme 38) [41]. The mechanism proposed is a four-electron reduction to give hydroxyamino intermediate **118** that cyclized to **116**.

In the same experimental conditions, ketone **119** afforded 2-phenyl-1*H*-indol-1-ol **120** that could be isolated in 88% yield (Scheme 39) [41].

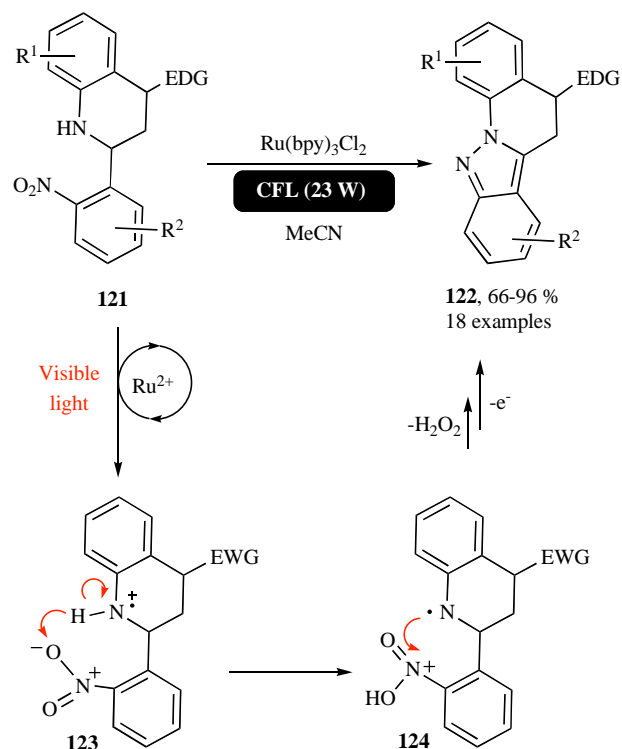
The synthesis of indazolo[2,3-*a*]quinoline **122** derivatives was reported in moderate to good yields from 2-(2-nitrophenyl)-1,2,3,4-tetrahydroquinolines **121** via visible light photoredox catalysis. The reaction involves a novel ruthenium-catalyzed intramolecular formation of the *N-N* bond of the indazole ring (Scheme 40) [42]. The mechanism proposed involves formation of radical cation **123** by oxidative quenching. This intermediate undergoes intramolecular proton transfer to the nitro oxygen to give **124**. Finally, *N-N* bond formation and ET afforded the target compound **122**.



Scheme 38. Photo-reduction of nitroarenes.



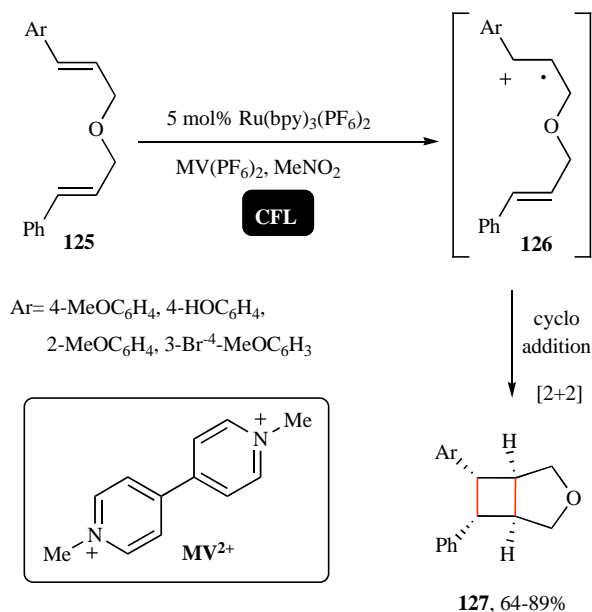
Scheme 39. Synthesis of 2-phenyl-1*H*-indol-1-ol **120**.



Scheme 40. Mechanism proposed for the formation of product **122**.

Photooxidation and photoreduction reactions of [Ru(bpy)₃]²⁺ and related ruthenium (II) chromophores have been used for design [2+2], [3+2] and [4+2] cycloaddition reactions involving radical cation and radical anion intermediates. Examples of photoredox-mediated [2+2] cycloadditions by both reductive and oxidative quenching cycle are known. For instances, the photostimulated reaction of bis(styrene) **125**, [Ru(bpy)₃](PF₆)₂ and 15 mol% of

methyl viologen [MV(PF₆)₂] gave a radical cation **126**, that underwent a subsequent [2+2] cycloaddition, affording cyclobutanes **127** in high yield with excellent diastereoselectivity (64-89%) (Scheme 41) [43]. Moreover, no cycloaddition upon irradiation of **125** with UV light under conventional photolytic conditions was observed. Furthermore, when Ar= 3-MeOC₆H₄ or Ph, no products **127** were formed [43].

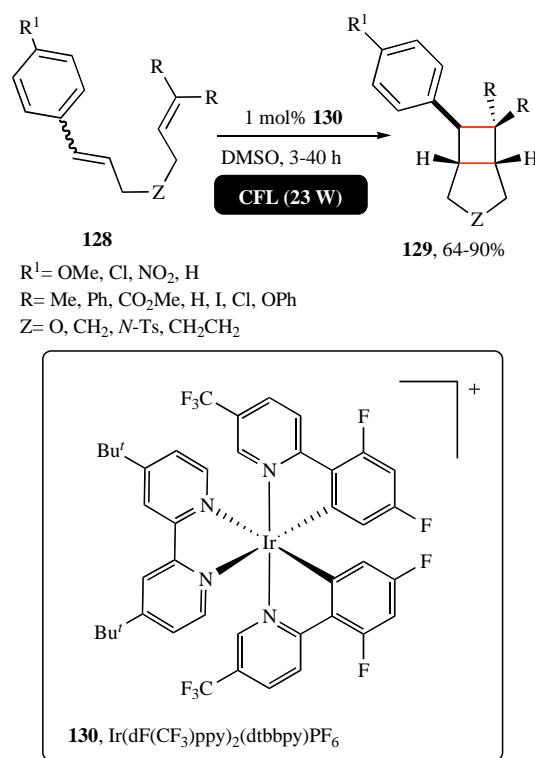


Scheme 41. Synthesis of cyclobutanes by [2+2] cycloadditions.

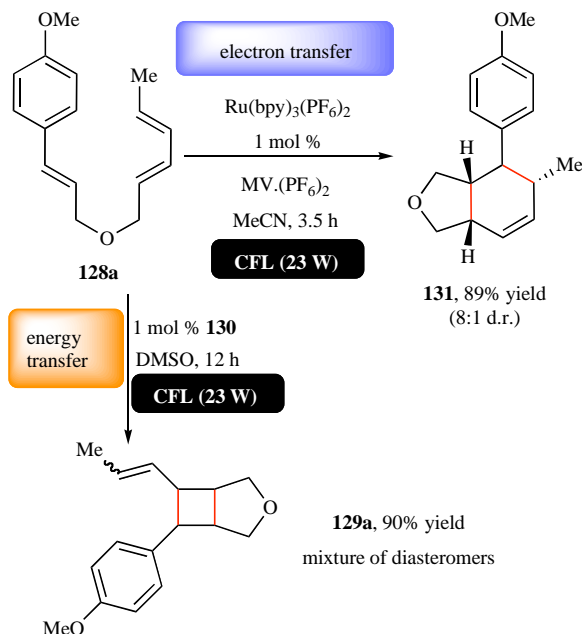
The nature of the photoinduced ET limits the scope of cycloaddition reactions of either electron-rich or electron-deficient substrate. On the other hand, an energy transfer mechanism maintains the same operational facility as that of previously reported photoredox reactions; yet the scope of this transformation is governed by the relative excited-state energies of the substrate and catalyst, rather than by their electrochemical properties. Yoon and Lu explored the [2+2] cycloaddition to several styrenes like **128** in the presence of iridium complex **130** to yield cyclobutanes **129** (Scheme 42) [44]. The reaction of *Z*-isomer of styrene **128** gave the same results than that of *E*-isomer, since *E/Z* photo-isomerization reaction is faster than cycloaddition to give **129**.

In these cases, no dramatic dependence is observed when the reactions are carried out in the presence of different solvents (CH₂Cl₂, acetone, MeOH, CHCl₃). This result is consistent with a triplet sensitization mechanism, ruling out charged intermediates. Moreover, diene **128a** was evaluated in two different sets of conditions (Scheme 43): when the radical cation of **128a** was generated in the presence of Ru(bpy)₃(PF₆)₂ catalyst, [4+2] cycloaddition product **131** was obtained in very good yield via ET mechanism. On the other hand, exposure of **128a** to iridium catalysts **130** gave a complex mixture where [2+2] cycloaddition product **129a** was identified [44].

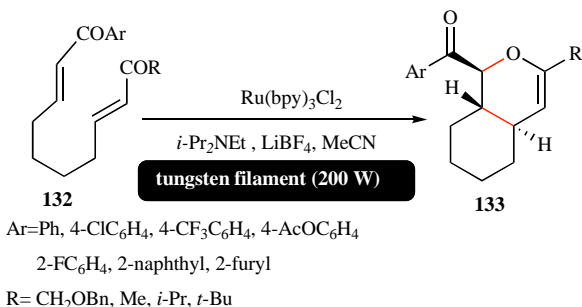
Yoon *et al.* studied the [2+2] cycloaddition reaction with visible light of the symmetrically bis(enone) **132** (R= Ar) in the presence of [Ru(bpy)₃]²⁺ with *i*-Pr₂NEt and LiBF₄ (Lewis Acid, LA) as additives. However, they found no products derived from [2+2] cycloaddition, but products **133** from a [4+2] cycloaddition in high yields (70-85% yields) with excellent diastereoselectivity (Scheme 44) [45]. Working with unsymmetrical bis(enones) **132** (Ar = Ph, R= aliphatic groups), in which two possible isomers could be formed, only one isomer (**133**) with high level of regioselectivity was obtained in regular to good yields (12-76% yield).



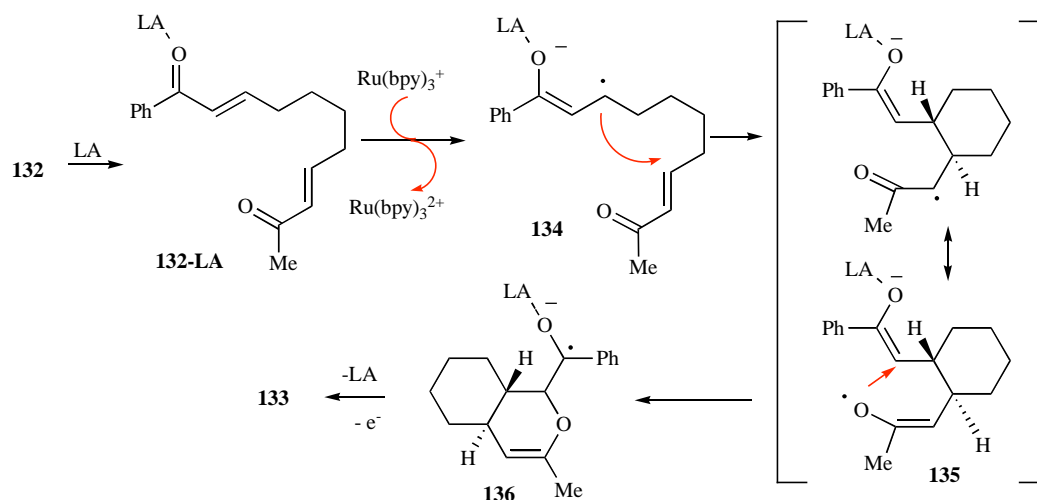
Scheme 42. Synthesis of cyclobutanes derivatives **129**.



Scheme 43. Energy transfer vs ET reactions.



Scheme 44. Synthesis of hexahydro-1*H*-isochromenes **133**.

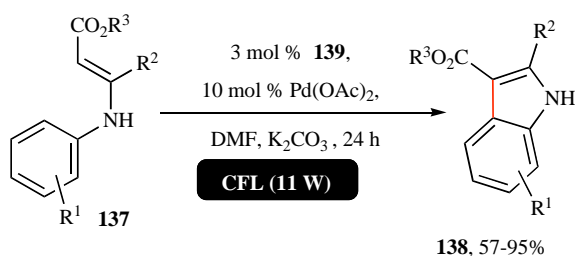


Scheme 45. Mechanism proposed for [4+2] cycloaddition.

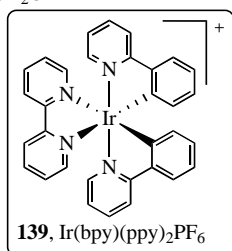
The mechanism outlined in Scheme 45, proposes that cycloaddition proceeds in a step-wise fashion. Excited $[\text{Ru}(\text{bpy})_3]^{2+*}$ undergo reductive quenching by *i*-Pr₂NEt resulting in formation of $[\text{Ru}(\text{bpy})_3]^+$. The Lewis acid-activated enone complex **132-LA** accepts an electron from $[\text{Ru}(\text{bpy})_3]^+$ reductant to afford a radical anion intermediate **134** that reacts with the pendant double bond to afford a distonic radical anion intermediate **135**. Then, formation of the conjugated radical anion **136** by C-O bond formation from **135** takes place. Finally, Diels-Alder cycloadduct **133** is produced upon loss of one electron and the Lewis acid.

2.1.1. Dual Catalysis

Synergistic dual catalysis (coupling of more than one catalytic cycle in a single transformation) is an interesting concept that combines the distinct advantages of different catalytic processes, although compatibility challenges may arise [46-48]. A combination of transition-metal catalysis with photocatalysis was applied in the synthesis of highly functionalized indoles **138** (Scheme 46). The direct C-H activation of aromatic enamines **137** was achieved using Pd(OAc)₂ and $[\text{Ir}(\text{bpy})(\text{ppy})_2]\text{PF}_6$ (**139**) in DMF [49].



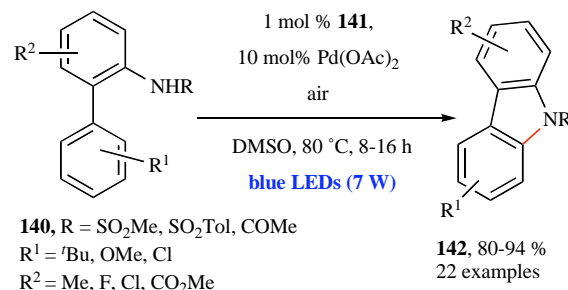
R¹ = OPh, Cl, Me, F, -OCH₂O-
 R² = Me, Ph
 R³ = Me, *t*-Bu, Ph



Scheme 46. Synthesis of substituted indoles **138**.

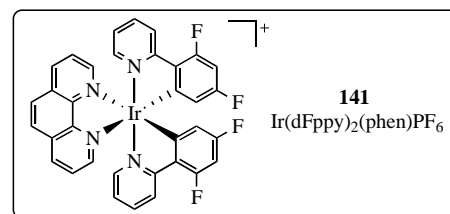
Using the same methodology, You and Cho reported a combined photoredox and Pd-catalysis for the synthesis of several *N*-substituted carbazoles **142**, through intramolecular C-H bond ami-

nation of *N*-substituted 2-amidobiaryls **140** (Scheme 47). The reactions take place under air, using Pd(OAc)₂ and **141** as catalysts in DMSO as a solvent [50].



140, R = SO₂Me, SO₂Tol, COMe
 R¹ = *t*Bu, OMe, Cl
 R² = Me, F, Cl, CO₂Me

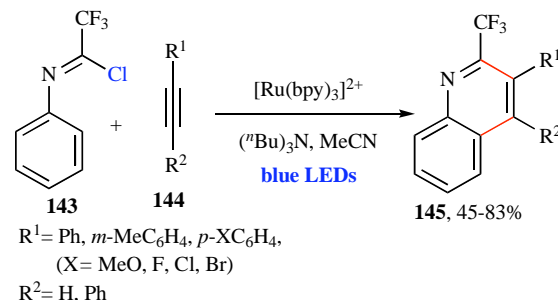
142, 80-94 %
 22 examples



Scheme 47. Synthesis of substituted carbazoles **142** by dual catalysis.

2.2. Intermolecular Process

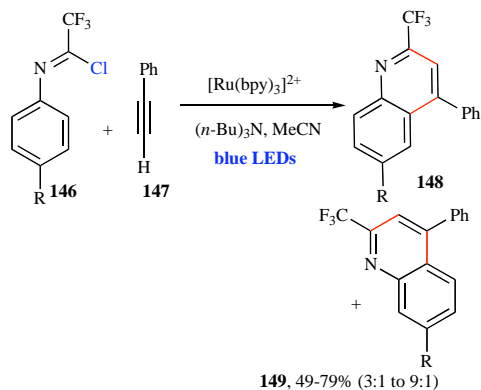
The photocatalyzed reaction of trifluoromethyl-*N*-phenylacetimidoyl chloride **143** and acetylenes **144** affords substituted quinolines **145** (Scheme 48) [51]. The reaction can tolerate various functional groups including methoxy, ester, and ketone present in alkynes **144**, giving **145** in good yields.



R¹ = Ph, *m*-MeC₆H₄, *p*-XC₆H₄,
 (X = MeO, F, Cl, Br)
 R² = H, Ph

Scheme 48. Synthesis of substituted 2-trifluoromethyl quinolines **145**.

When a *para*- substituent is introduced into the aromatic ring attached to the nitrogen, the reaction encounters regioselectivity problems. For instance, the reaction of substituted trifluoromethyl-*N*-phenylacetimidoyl chloride **146** with phenylacetylene **147** afforded quinolines **148** and **149** (Scheme 49).

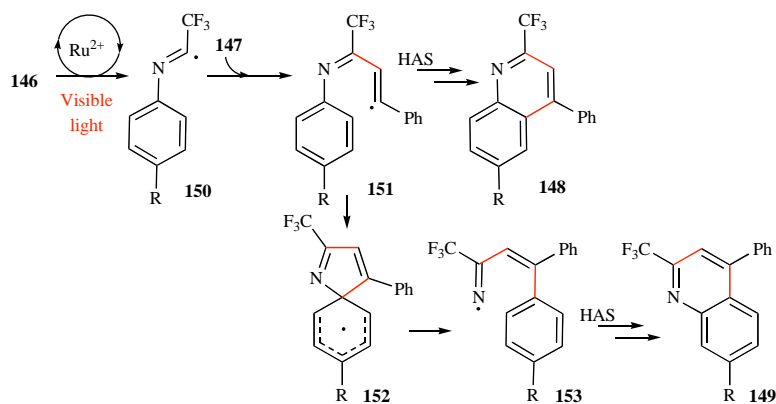


Scheme 49. Synthesis of substituted quinolines **148** and **149**.

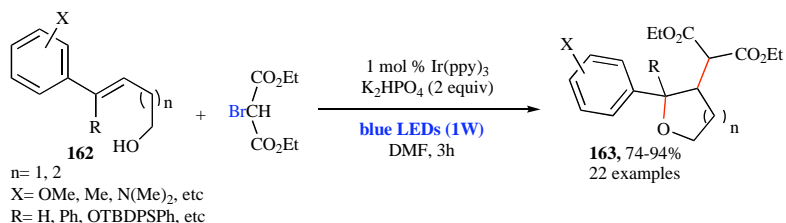
A possible mechanism includes reductive quenching to obtain radical intermediate **150** (Scheme 50). Radical **150** then undergoes intermolecular addition with phenyl acetylene **147** to give vinyl radical **151**, which reacts with the pendant benzene to give product **148** by a HAS process. It was suggested that the formation of product **149** results from an *ipso* cyclization of radical **151** followed by C-N bond cleavage to give a new radical **152**. This radical affords quinoline **149** by HAS process.

Complementary to photoredox-initiated radical additions to indoles (Schemes 4 and 5), intermolecular photoredox annulation of indoles was reported [52]. The reaction proceeds *via* diastereoselective tandem radical cyclization between *N*-(2-iodoethyl)indoles **154** and alkenes **155**, which is terminated by a reduction giving addition-reduction product **156** in the sense of Scheme 2 (Scheme 51).

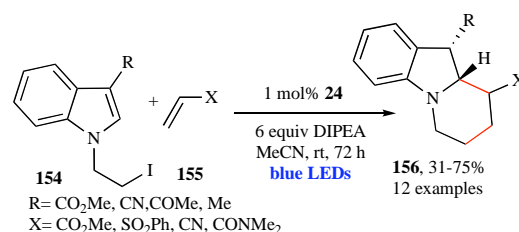
When diazonium salts **157** are irradiated with visible light (3 W white LEDs) in the presence of 4-arylhex-4-enoic acids **158** and Ru(bpy)₃(PF₆) in H₂O/MeCN, a photocatalytic arylation-



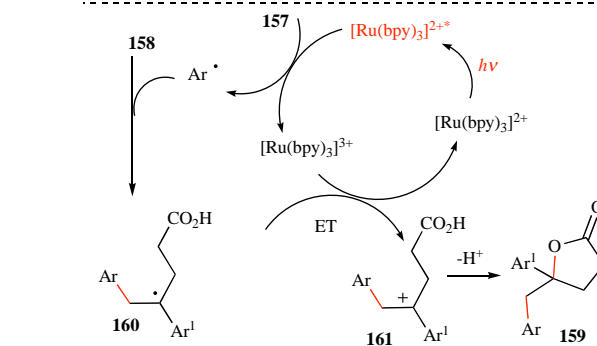
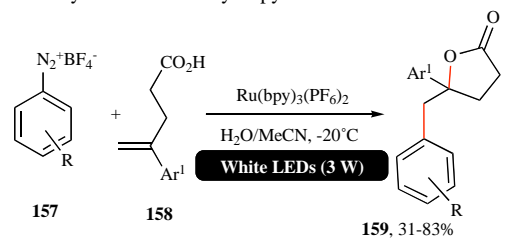
Scheme 50.



Scheme 53. Synthesis of substituted tetrahydrofurans **163**.



Scheme 51. Synthesis of hexahydropyridoindoles **156**.

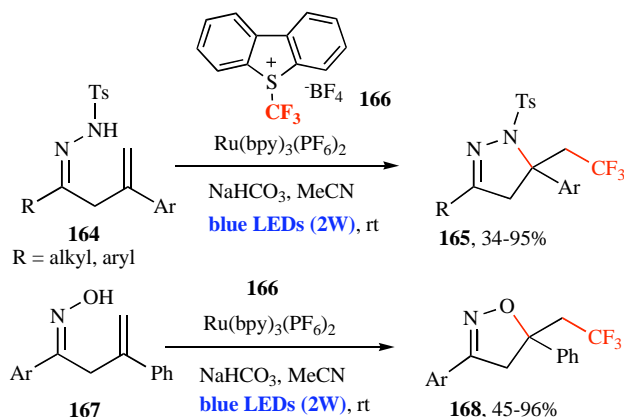


Scheme 52. Mechanism proposed for the formation of lactones **159**.

lactonization sequence affords disubstituted butyrolactones **159** in good yields (Scheme 52) [53]. When **157** receives an electron from the excited [Ru(bpy)₃]²⁺, Ar[•] radicals formed are trapped by **158** to afford radical **160**. The new radical is oxidized to cation **161** (recovering the catalyst) that is trapped with pendant acid to afford lactone **159**.

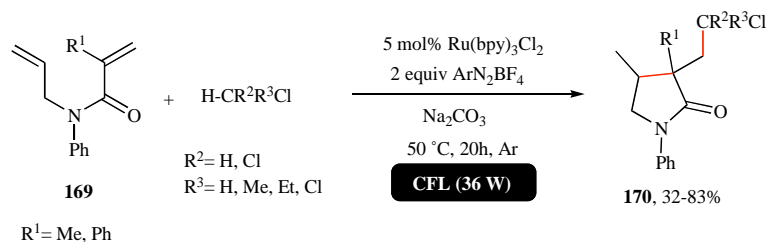
Following the same strategy, the difunctionalization of alkenes **162** through radical addition followed by intramolecular etherification might perform the synthesis of substituted tetrahydrofurans **163** (Scheme 53) [54]. In general, the reaction conditions worked well with EDG at *para* or *ortho* positions that are effective activators.

When a mixture of β,γ -unsaturated hydrazone **164** and Umemoto's reagent **166** was irradiated using the combination of NaHCO_3 and $\text{Ru}(\text{bpy})_3(\text{PF}_6)_2$ (1 mol%) as a catalyst, **165** was obtained [55]. Using the same strategy, β,γ -unsaturated oximes **167** afforded dihydroisoxazoles **168** in good yields (Scheme 54). A mechanism analogous to that depicted in Scheme 52 was proposed.

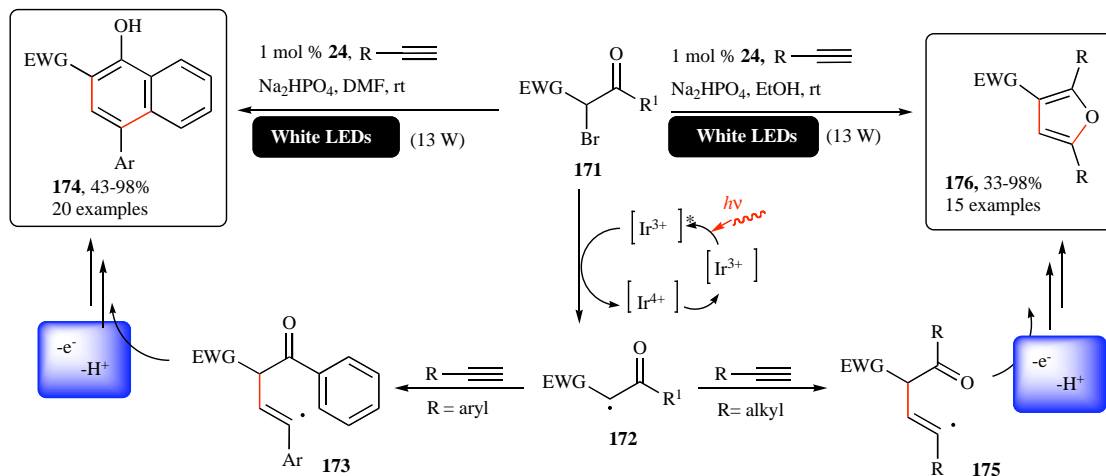


Scheme 54. Synthesis of dihydropyrazoles **165** and dihydroisoxazoles **168**.

A visible-light induced method was reported for 5-*exo-trig* cyclization of 1,6-dienes with alkyl chlorides using $\text{Ru}(\text{bpy})_3\text{Cl}_2$ and ArN_2BF_4 as the radical initiator system [56]. In this radical chain reaction, selective scission of the $\text{C}(\text{sp}^3)\text{-H}$ bond adjacent to the chloride atom allows the reaction of *N*-allyl-*N*-phenyl acrylamides **169** derivatives and alkyl chlorides $\text{H-CR}^2\text{R}^3\text{Cl}$, to produce **170** in good yield (Scheme 55) [57].



Scheme 55. Synthesis of pyrrolidin-2-ones **170** derivatives.

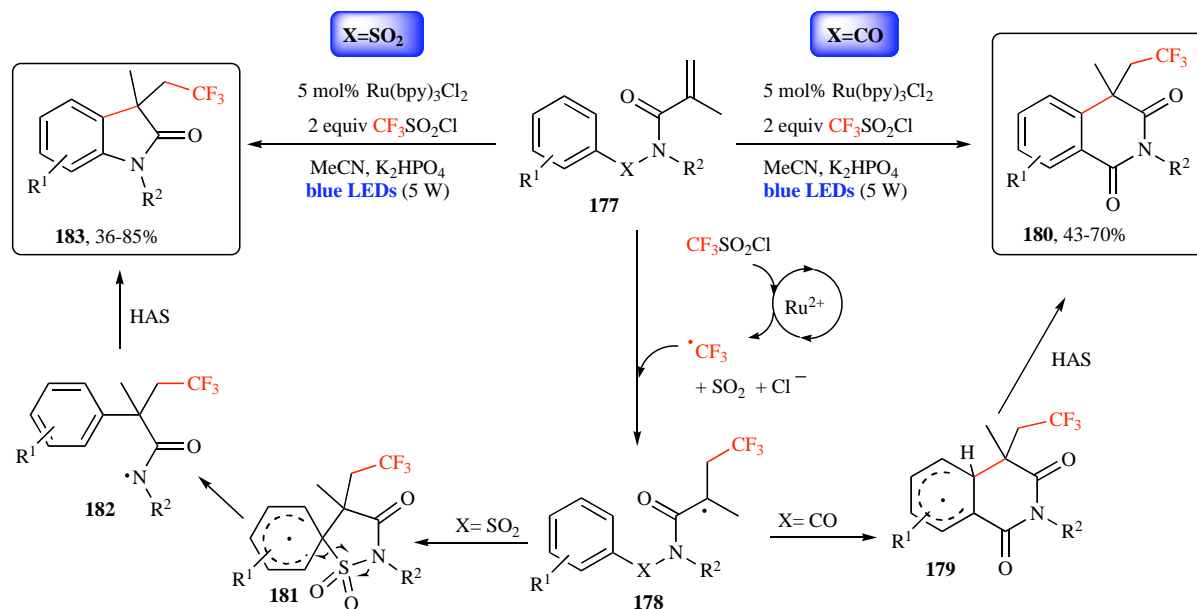


Scheme 56. *De novo* synthesis of naphthols and furans.

Moreover, using the iridium catalysts **24** $[\text{Ir}(\text{ppy})_2(\text{dtbbpy})](\text{BF}_4)$, *de novo* synthesis of polysubstituted naphthols **174** and furans **176** was carried out effectively from α -bromo-carbonyl compounds **171** and alkynes (Scheme 56) [58]. Radical **172** is generated by oxidative quenching, and depending on the nature of the substituent R^1 , two pathways are possible. If R^1 is an aromatic moiety, the coupling of radical **172** with an alkyne gives intermediate **173**, which reacts by HAS to finally yield naphthols **174**. On other hand, if R^1 is an alkyl moiety, the addition of radical **172** to alkyne affords **175**, which by oxidation and deprotonation produces furan **176**. In both cases, an oxidation step is needed to recover the catalyst.

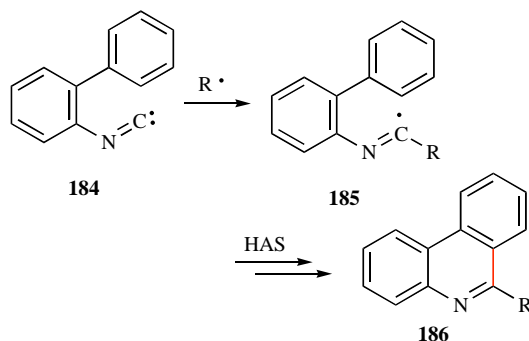
Since the pioneering works on the photocatalytic radical trifluoromethylation of aldehydes and enol silanes reported by MacMillan [59, 60], a range of elegant photocatalytic $\cdot\text{CF}_3$ radical-mediated addition/cyclization reactions has been developed for the synthesis of various biologically important CF_3 -containing carbo- and heterocycles, where alkene substrates are suitable radical acceptors. In this regard, the synthesis of trifluoromethylated isoquinolinediones **180** and oxindoles **183** were obtained from precursors **177** (Scheme 57) [61]. The excited state $[\text{Ru}(\text{bpy})_3]^{2+*}$ reduced $\text{CF}_3\text{SO}_2\text{Cl}$ and generate $\cdot\text{CF}_3$ radical, Cl^- and SO_2 . The radical $\cdot\text{CF}_3$ was trapped by **177** to give intermediate **178**. For $\text{X}=\text{CO}$, the formation of product **180** follows HAS sequence as shown in Scheme 3. Meanwhile, for $\text{X}=\text{SO}_2$ an *ipso*-cyclization of radical **178** affords amidyl radical **182** after SO_2 extrusion. Finally, HAS reaction from **182** gives oxindoles **183**.

In photoredox catalysis, alkenes, alkynes and aromatic rings as radical acceptors, have been widely used since 2008 as a synthetic approach to form new C-C bonds. However, isocyanates used as somophiles started in 2013, their use as precursors to heterocycles has been widely exploited in organic synthesis. Neutral isocyanide insertions are shown in Scheme 58. Biphenyl 2-isocyanide **184**, which incorporates an isocyanide group and a somophile (phenyl ring) into the same molecule, is selected to react with a radical R^\cdot . The radical R^\cdot adds to **184** to give the imidoyl radical **185**, which



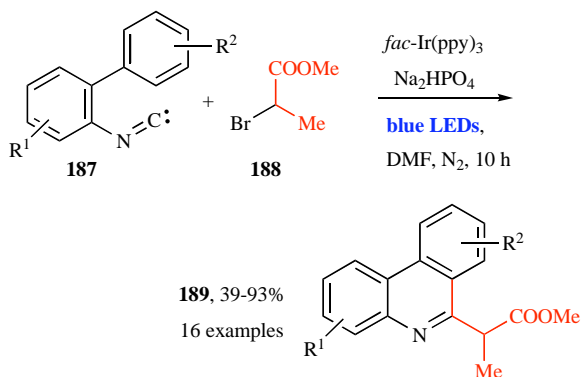
Scheme 57. Synthesis of trifluoromethylated isoquinolinones and oxindoles.

subsequently undergoes HAS to afford phenanthridine **186**. Since intramolecular HAS is faster than intermolecular radical couplings, multiple isocyanide insertions and double alkylation are avoided in this process.



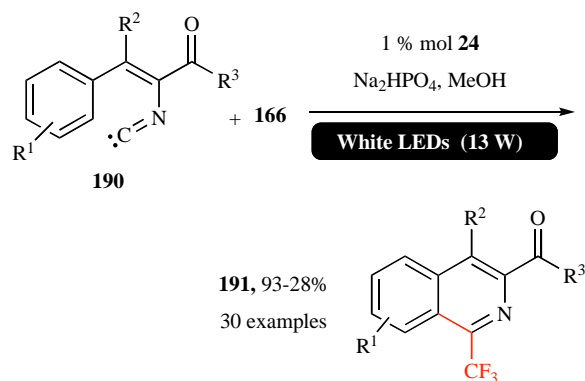
Scheme 58. General reaction for isocyanides.

Taking this into account, different alkyl bromides **188** were employed as radical precursors for the construction of 6-alkyl phenanthridine **189** (Scheme **59**) using 1 mol% of *fac*-Ir(ppy)₃ as photocatalysts [62]. Isocyanides **187**, having different functional groups on both benzene ring and isocyanide bearing naphthalene, anthracene and pyridine rings instead of the benzene ring, were also successful in this transformation with good to excellent yields.



Scheme 59. Synthesis of substituted phenanthridines **189**.

The synthesis of 1-trifluoromethylisoquinolines **191** using Umemoto's reagent **166** as the source of $\cdot\text{CF}_3$ radicals and vinyl isocyanide **190** is also described in Scheme **60** [63].

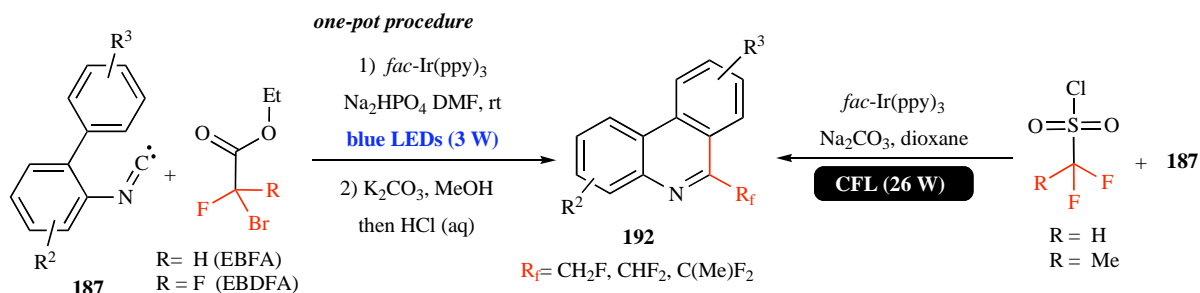


Scheme 60. Synthesis of isoquinolines derivatives **191**.

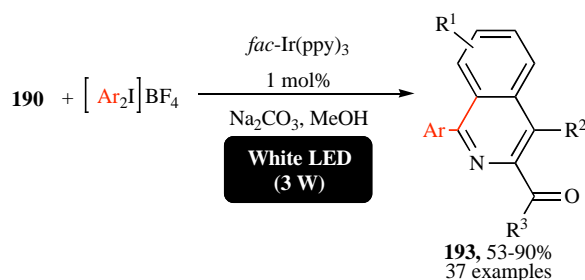
The synthetic strategy was extensively used for fluoroalkylation of biaryl isocyanides **187** to yield 6-fluoroalkylphenanthridines **192** in good to excellent yields (Scheme **61**). Several fluorine sources were used, such as ethyl bromodifluoroacetate (EBDFA) [64], ethyl bromofluoroacetate (EBFA) [64], $\text{CF}_2\text{HSO}_2\text{Cl}$ [65], and $\text{MeCF}_2\text{SO}_2\text{Cl}$ [65].

1-Arylisoquinolines **193** were synthesized from vinyl isocyanide **190** and diaryliodonium tetrafluoroborates (Scheme **62**) [66]. Diaryliodonium salts (Ar_2IX) form $\text{Ar}\cdot$ and ArI by oxidative quenching.

Using the strategy shown above, the synthesis of functionalized pyrrolo[1,2-a]quinoxaline **195** has been developed from 1-(2-isocyanophenyl)-1*H*-pyrrole **194** (Scheme **63**) [67]. In this reaction, phenyliodine(III) dicarboxylates are used as radical $\text{R}\cdot$ precursor (Scheme **64**) and are easily prepared from the corresponding functionalized carboxylic acid by ligand exchange with phenyliodine (III) diacetate ($\text{PhI}(\text{OAc})_2$). Various primary, secondary, tertiary aliphatic carboxylic acid, alkenes and alkynes (which are potentially susceptible to radical attacks), despite being partially pro-



Scheme 61. Fluoroalkylation of biarylisocyanides.

Scheme 62. Synthesis of isoquinolines derivatives **193**.

tected α -amino diacids, were effective in affording the cyclization products desired.

Changing the pyrrole moiety in **194** by imidazole, pyrazole, triazole and tetrazole, others aza-heterocycles (**196-200**) could also be obtained with good yields as depicted in Figure 3.

In addition, preparations of these compounds by integration of in-line isocyanide formation and photochemical cyclization have been achieved in a three step continuous-flow system (Fig. 4). In the last cases, residence time involved only a few minutes and was enough to reach a full conversion of the isocyanide intermediate **194** to **195**, while 5 to 24 hours of irradiation are usually required in batch setups.

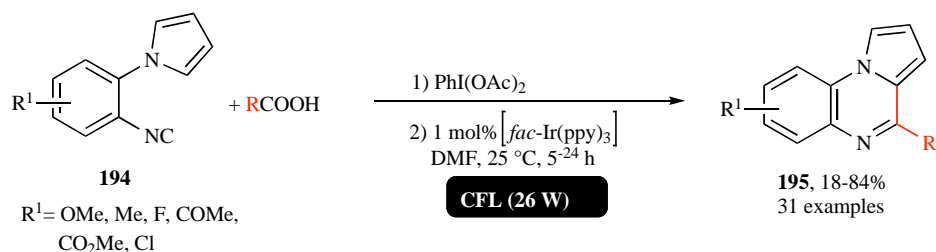
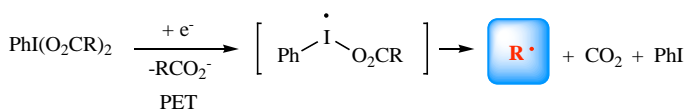
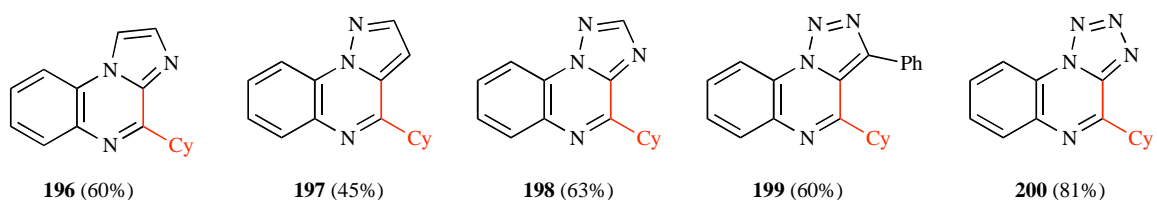
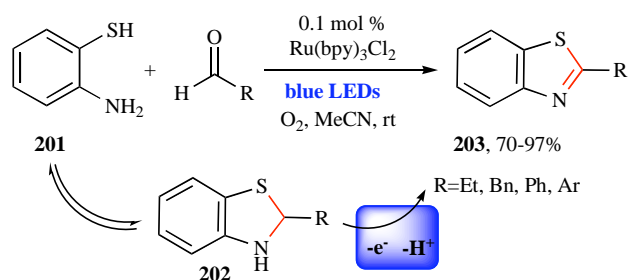
Scheme 63. Synthesis of functionalized pyrrolo[1,2-*a*]quinoxaline **195**.Scheme 64. Mechanism for the generation of radicals R[•] from phenyliodine(III) dicarboxylates.

Fig. (3). Heterocycles synthesized from isocyanides.

A method for the synthesis of 2-substituted benzothiazoles **203** has been developed. The process requires only 0.1 mol% [Ru(bpy)₃Cl₂], O₂, and visible light irradiation with substrate 2-aminothiophenol **201** and a variety of aldehydes. In the mechanism proposed the photocatalyst promoted the oxidation of a condensation product **202** (Scheme 65).

Scheme 65. Synthesis of 2-substituted benzothiazoles **203**.

Amino methyl radicals, photochemically generated from *N,N*-dimethylbenzylamine **204**, can be added to *N*-arylmaleimide **205** to yield tetrahydroquinoline products **206** in 55-98% yields (Scheme 66) [68]. The mechanism proposed involves a radical addition-HAS sequence as described above.

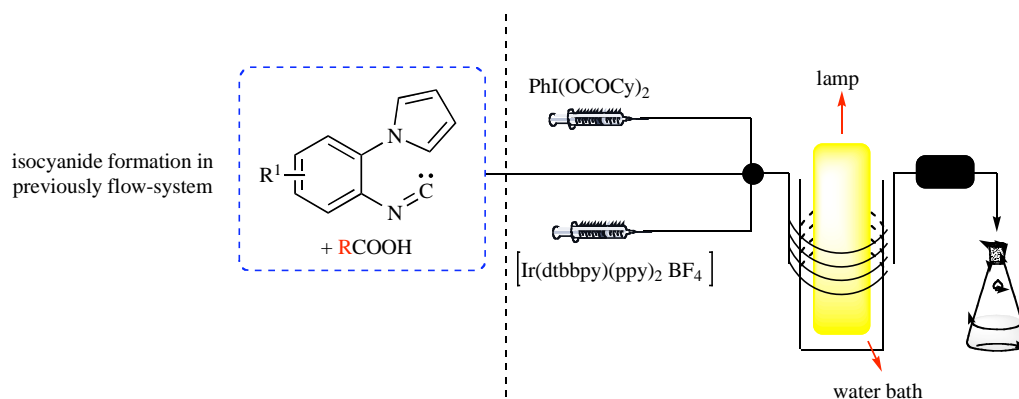
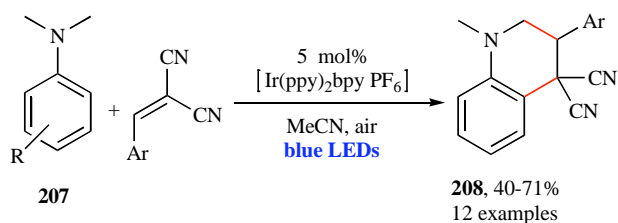
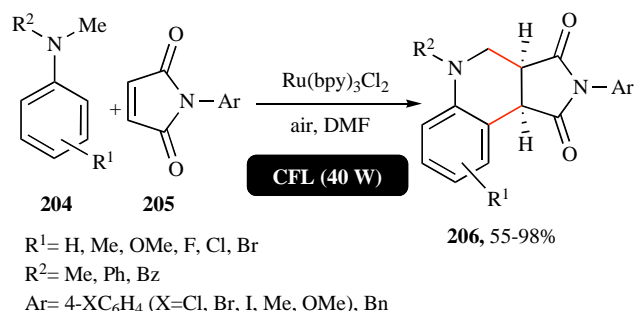


Fig. (4). Continuous-flow synthesis of pyrrolo[1,2-*a*]quinoxaline.

Moreover, α -amino alkyl radicals could add to electron-deficient alkenes where oxygen was found to act as a chemical switch to trigger two different reaction pathways by which two different types of products were obtained from the same starting material [38]. In the absence of oxygen, the intermolecular addition of *N,N*-dimethyl-anilines to electron-deficient alkenes provided γ -amino nitriles in good to high yields. By contrast, in the presence of oxygen, a radical addition/cyclization reaction occurred, resulting in the formation of tetrahydroquinoline derivatives **208** in good yields under mild reaction conditions (Scheme 67).



Scheme 67. Synthesis of tetrahydroquinoline derivatives **208**.



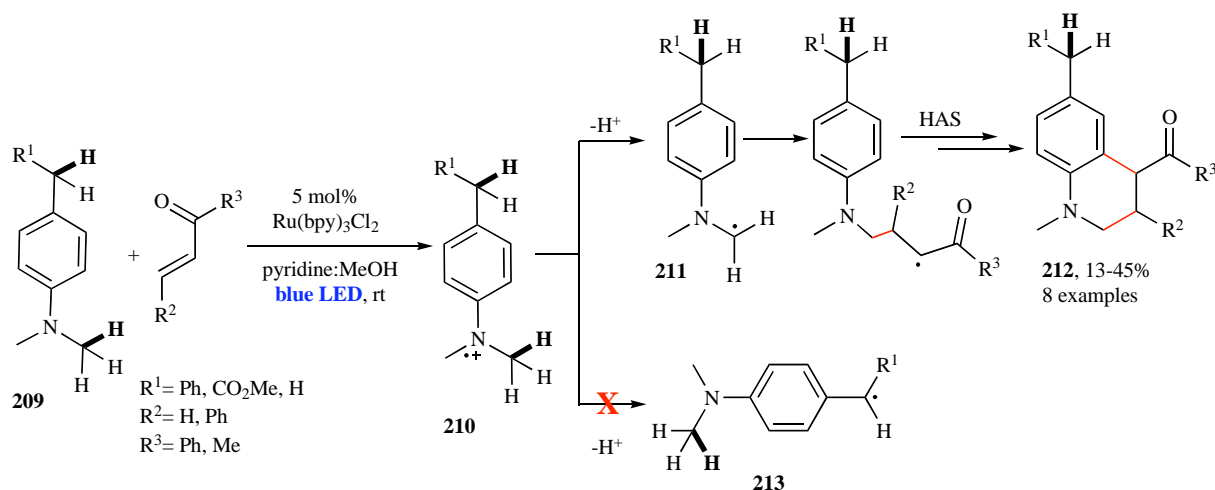
Scheme 66. Synthesis of tetrahydroquinoline products **206**.

Simultaneously the groups of Yu and Bian [68] and Rueping [38] studied tertiary amines having two possible sp^3 C-H sites available for deprotonation. Thus, the tertiary amines of type **209** having fairly acidic benzylic sp^3 C-H bonds afforded substituted tetrahydroquinolines **212** by a subsequent α -alkylation/HAS-

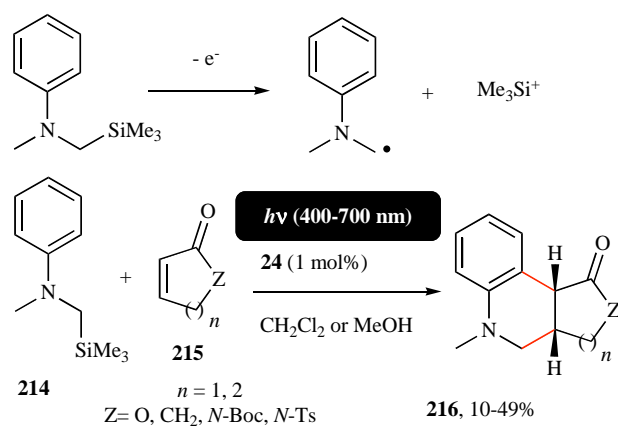
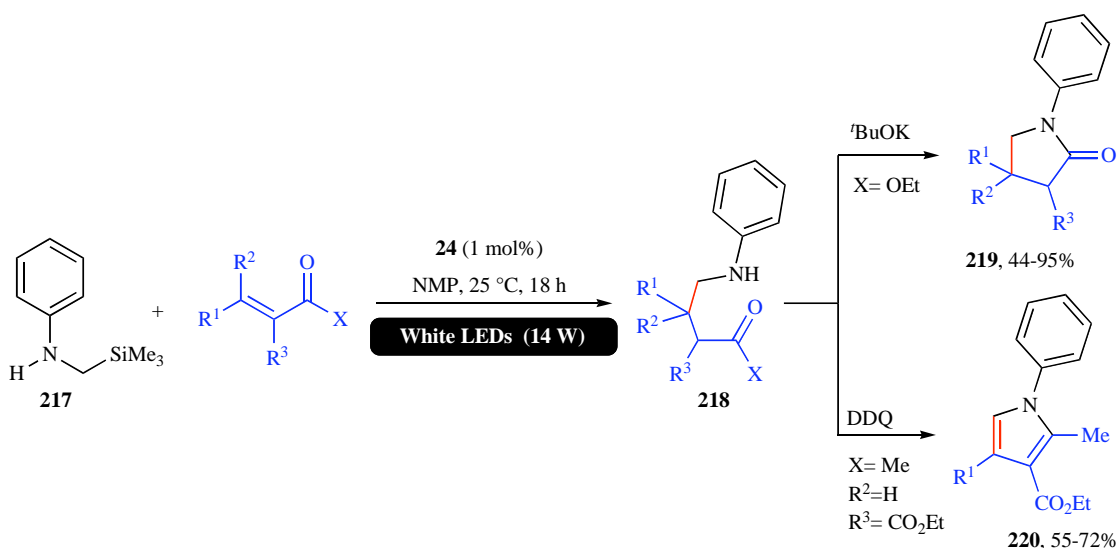
cyclization sequence (Scheme 68) [69]. This behavior could be attributed to a C-H deprotonation from **210**, allowing localization of charge on the nitrogen, and contributing to low reaction barriers for generating **211**, compared to the formation of **213** by distal C-H deprotonation.

In addition, amino methyl radicals could be generated from *N*-methyl-*N*-((trimethylsilyl)methyl) aniline. Using the same methodology as that described above, and using different cyclic α,β -unsaturated carbonyl groups **215**, interesting tricyclic products **216** were obtained by an addition-HAS cyclization sequence (Scheme 69) [70]. In all cases, the addition-reduction product was obtained in different yields (10-49%).

Starting from secondary amine *N*-((trimethylsilyl)methyl) aniline **217** and deficient alkenes, γ -amino carbonyl compounds **218** were obtained, and then converted into γ -lactams **219** ($\text{X} = \text{OEt}$) or pyrroles **220** ($\text{X} = \text{Me}$) in a one-pot process (Scheme 70) [71].

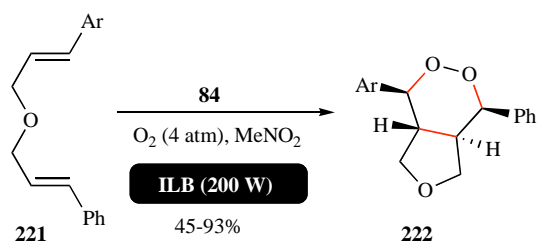


Scheme 68. Photocatalytic reaction of tertiary amines **209** with electron-deficient alkenes.

Scheme 69. Synthesis of tetrahydroquinolines **216**.Scheme 70. Synthesis of γ -lactams or pyrroles in a one-pot strategy.

When the photostimulated reaction of bis(styrenes) **221** was carried out with tris(bipyrazyl) ruthenium (II) complex ($\text{Ru}(\text{bpz})_3(\text{PF}_6)_2$ (**84**) in the presence of O_2 , the principal product yielded was the endoperoxide **222** (Scheme 71 and Fig. 5) [72]. It was pointed that a successful reaction required the presence of an EDG at the *ortho* or *para* position of one of the styrene, since with $\text{Ar} = 3\text{-MeOC}_6\text{H}_4$ or Ph, no products **222** were formed.

The mechanism proposed is described in Scheme 72 with bis-styrene **221** as a model. The photoinduced one-electron oxidation of the alkene gives radical cation **223** and $\mathbf{84}^+$ by reductive quenching.

Scheme 71. Synthesis of endoperoxides **222**.

This reactive intermediate **223** undergoes a [2+2+2] cycloaddition with triplet oxygen to afford an endoperoxide radical cation **224**. The final step involves reduction of **224** by $\mathbf{84}^+$ that continues the catalytic cycle.

[3+2]-Dipolar cycloadditions are a powerful class of reactions that allow the construction of structurally complex molecules in a

straightforward and atom-economical fashion. It has been reported that the application of photoredox catalysis of diester of 2-(3,4-dihydroisoquinolin-2(1*H*)-yl)malonates **225** reacted with *N*-substituted maleimide **226** to afford heterocycle **227** in the presence of O_2 and **84** (Scheme 73) [73].

Photostimulated formation of iminium ion **228** is obtained by reductive quenching in the presence of O_2 (see Scheme 31) which is deprotonated to yield azomethine ylide **229**. Subsequent [3+2] dipolar cycloaddition of **229** with **226** gave product **227** (Scheme 74).

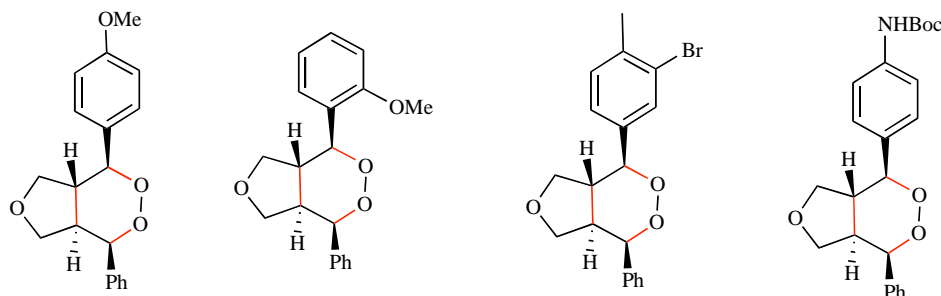
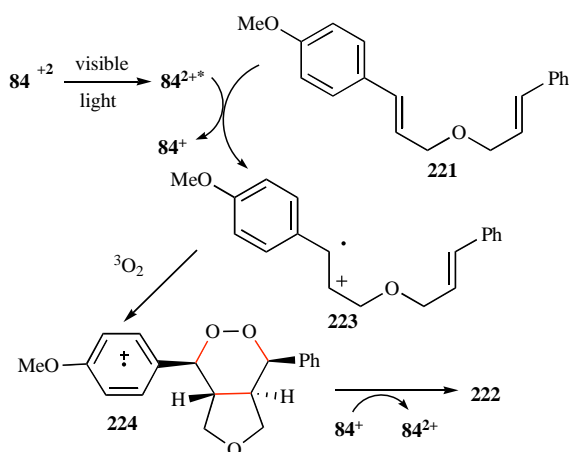
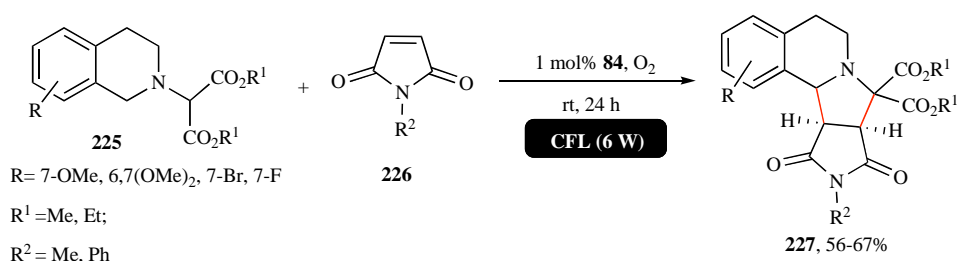
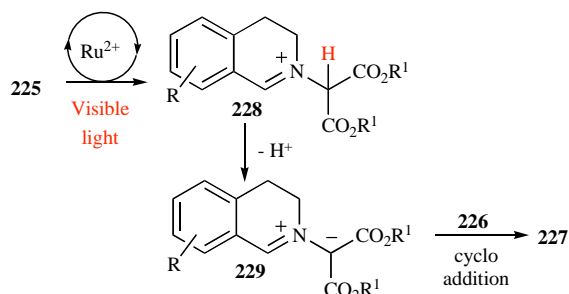


Fig. (5). Endoperoxides synthesized from bis(styrenes).



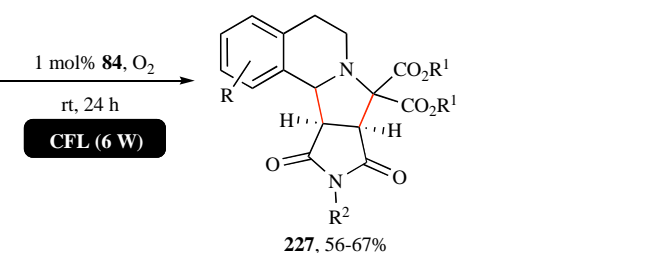
Scheme 72. Mechanistic proposal for [2+2+2] cycloaddition.

Scheme 73. Synthesis of hexahydropyrrolo isoquinolines derivatives **227**.

Scheme 74. Proposed mechanism for the azomethine ylide formation and [3+2] dipolar cycloaddition.

Following the same methodology, it was demonstrated that dihydroisoquinoline monoesters **230** react with a variety of dipolarophiles *N*-substituted maleimides **226** efficiently to give the corresponding products **232** in good to excellent yields after treatment with NBS to oxidize the dihydro-compound initially formed **231** (Scheme 75) [74]. The reaction appears quite general in relation to *N*-substitutions and other dipolarophiles, such as activated alkynes, acrylates, nitroolefins, and maleic anhydrides, which reacted smoothly to give good products yield.

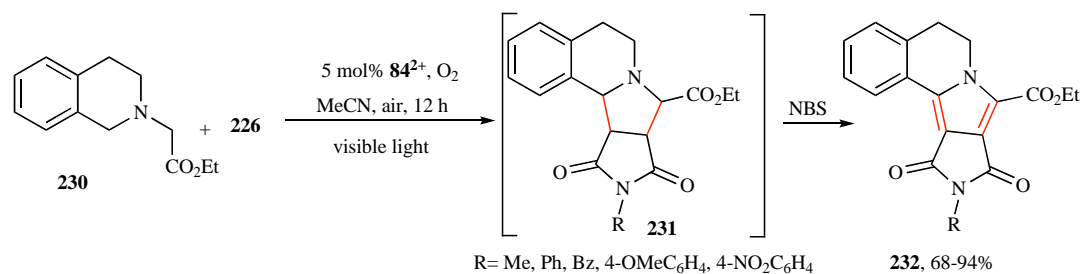
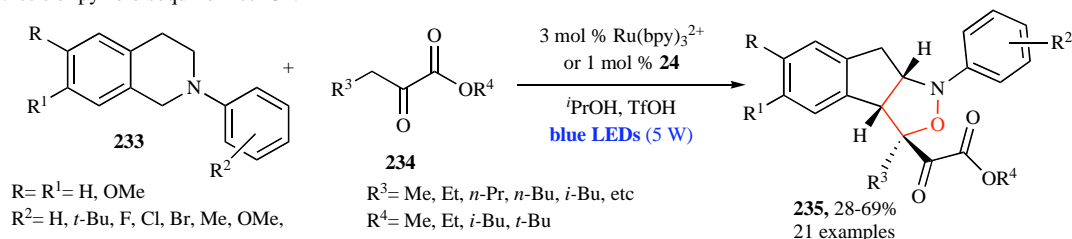
Starting from *N*-aryl dihydroisoquinoline **233** and α -keto esters **234**, isoxazolidine derivatives **235** are concisely formed in one step with excellent stereoselectivity (dr > 20:1), through a C–H activation-retro-aza-Michael-oxidation-cyclization tandem sequence using [Ru(bpy)₃]²⁺ (Scheme 76) [75]. When a EWG group was installed on the *N*-substituted aromatic ring, the reaction proceeded sluggishly under Ru-catalysts. In these cases, the use of a more



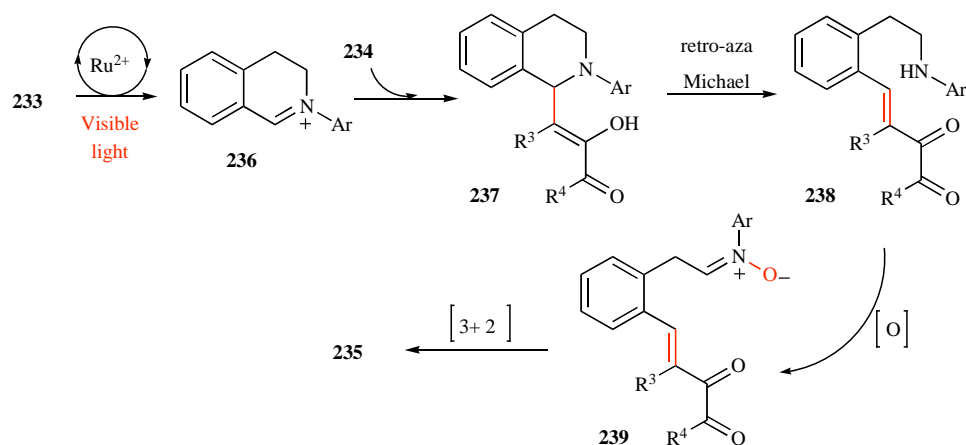
reactive iridium catalyst, Ir(ppy)₂(dtbbpy)PF₆ (**24**), can remarkably improve the reaction, furnishing the desired product **235** in moderate yields with excellent stereoselectivity.

It is proposed that iminium cation **236** is trapped by nucleophilic addition of α -keto esters **234** to give intermediate **237** (Scheme 77). The keto-enol tautomer will suffer a retro-aza-Michael to the unstable intermediate **238**. Subsequently, oxidation to nitrile oxides **239** followed by [3+2] cycloaddition produces the desired bicyclic isoxazolidines **235**.

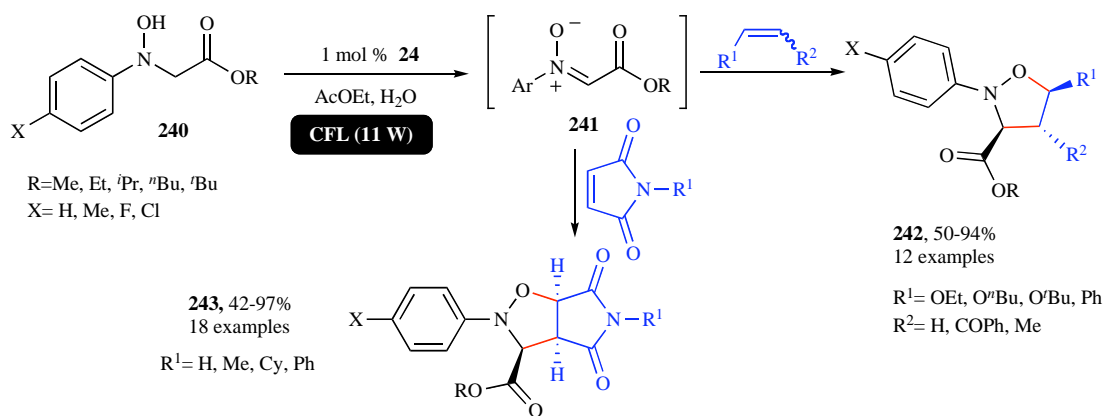
N-alkylsubstituted arylhydroxylamines **240** could be oxidized to nitrones **241** by photocatalysis via single-electron oxidation (Scheme 78) [76]. This intermediate react *in-situ* by [3+2] cycloadd-

Scheme 75. Synthesis of pyrroloisoquinolines **232**.

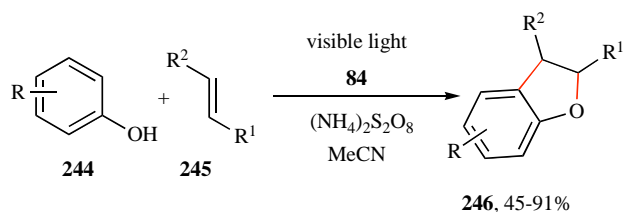
Scheme 76. Synthesis of tetrahydroindeno isoxazoles.



Scheme 77. Plausible mechanisms for aerobic C-H/C-N cleavage cascade reaction forming isoxazolines **235**.



Scheme 78. Synthesis of isoxazolidines **242** and **243**.



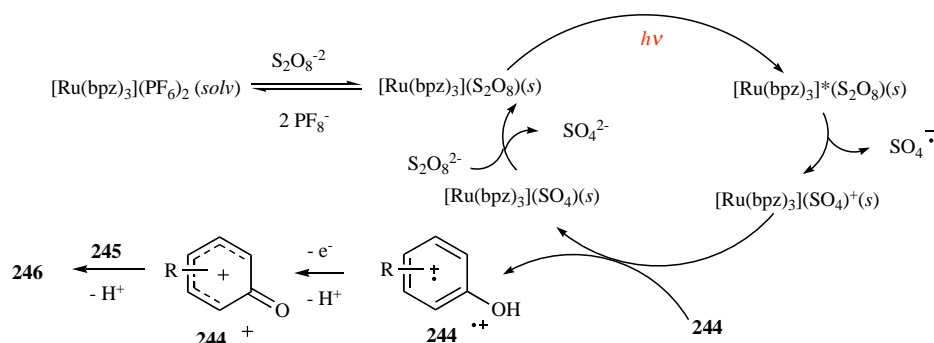
Scheme 79. Synthesis of 2,3-dihydrobenzofurans derivatives **246**.

dition with different alkenes such as vinyl ethers, and maleimides to give five-membered ring isoxazolidines **242** and **243**, respectively.

Recently a photocatalytic procedure was reported for [3+2] phenol-olefin cycloaddition, in which the use of ammonium persulfate

fate as an oxidant was crucial. Thus, when phenolic compounds **244** and an olefin **245** are treated with the complex $[\text{Ru}(\text{bpz})_3]^{2+}$ (**84**), $(\text{NH}_4)_2\text{S}_2\text{O}_8$ and irradiated with a visible light, dihydrobenzofuranes **246** are obtained with good yields (Scheme **79**) [77].

The authors proposed the mechanistic model outlined in Scheme **80**, including a solid-state photoredox catalytic cycle. Initially, a salt metathesis results in the formation of insoluble $[\text{Ru}(\text{bpz})_3](\text{S}_2\text{O}_8)$, which is the real catalyst. Photo excitation of this salt followed by oxidative quenching by $\text{S}_2\text{O}_8^{2-}$ afford $[\text{Ru}(\text{bpz})_3](\text{SO}_4)^+$ and sulfate radical anion $\text{SO}_4^{\cdot-}$. The oxidation of phenol **244** by $[\text{Ru}(\text{bpz})_3](\text{SO}_4)^+$ affords radical cation **244** $^{\cdot+}$, which can be further oxidized to give a resonance-stabilized phenoxonium cation **244** $^{++}$ that is trapped by an electron-rich olefin **245** to afford the observed dihydrobenzofuran **246**.



Scheme 80. Mechanism proposed for the oxidative [3+2] cycloaddition of phenols with alkenes using $[\text{Ru}(\text{bpz})_3]^{2+}$.

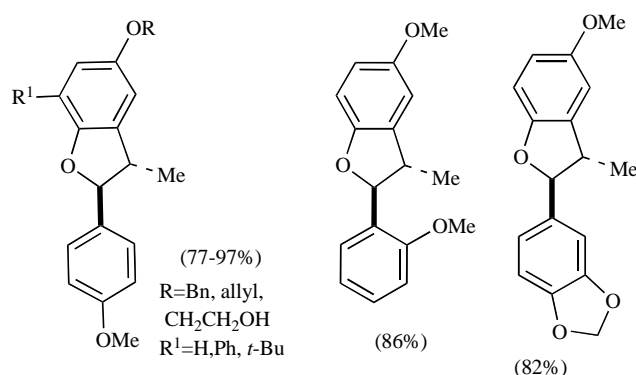


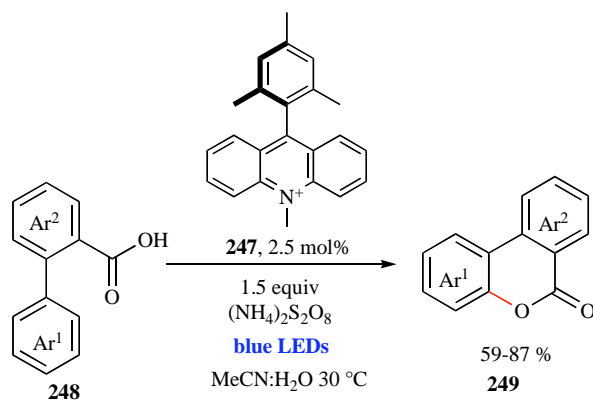
Fig. (6). Dihydrobenzofuranes **246** synthesized by [3+2] cycloaddition of phenols with alkenes.

The broad range of organic substrates that are readily oxidized by this photoredox catalysis suggests that this strategy may be applicable to a variety of useful oxidative transformations. Selected examples of this oxidative [3+2] cycloaddition of phenols with alkenes are shown in Figure 6.

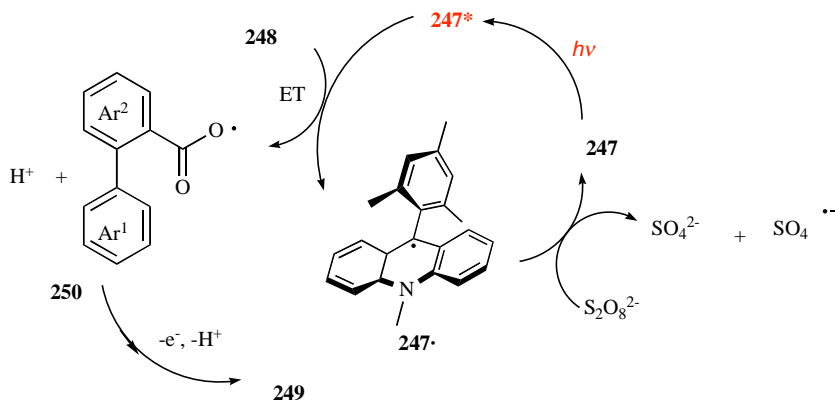
3. ORGANIC (TRANSITION METAL-FREE) PHOTOCATALYSIS

3.1. Intramolecular Reactions

Regardless of the numerous methods for the preparation of benzocumarins, new procedures are still needed, especially those in line with the principles of green chemistry. Benzocumarins were prepared by photocatalyzed dehydrogenative lactonization using an organic photocatalyst 9-mesityl-10-methylacridinium perchlorate



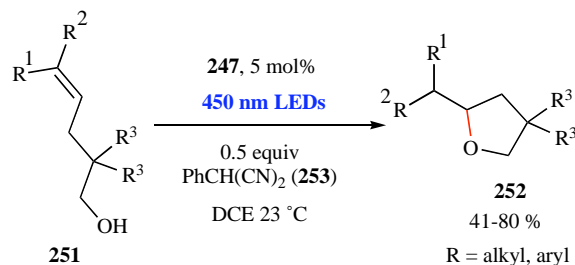
Scheme 81. Synthesis of benzocumarins **249**.



Scheme 82. Mechanism proposed for photocatalytic dehydrogenative lactonization.

247 (Scheme **81**) [78]. For this reaction an oxidant $(\text{NH}_4)_2\text{S}_2\text{O}_8$ was necessary to obtain good yields, especially when EDG are present in the aromatic rings. Mechanistic studies allowed the authors to propose a radical cyclization by a HAS reaction of the benzyloxy radical **250**, obtained by reaction of 2-arylbenzoic acid and the excited photocatalyst **247*** (Scheme **82**).

Catalyzed intramolecular cyclization of nucleophiles onto alkenes has been intensively study over the last two decades; however, most of these studies refer to a Markovnikov addition. Nicewicz's group recognized the potential of photo-catalyzed ET in achieving anti-Markovnikov addition to olefin through oxidation to a radical cation. Using commercial available **247**, they prepared a series of tetrahydrofurans **252** with good yields starting from alkenes tethered to alcohol functionality **251** (Scheme **83**) [79].



Scheme 83. Synthesis of tetrahydrofurans **252**.

This anti-Markovnikov transformation provides a reactivity profile that complements traditional Markovnikov-based Brønsted acid catalyzed reactions. Moreover, the reaction shows to be good for the preparation of lactone **254** and cyclic ethers **255** and **256** (Fig. 7).

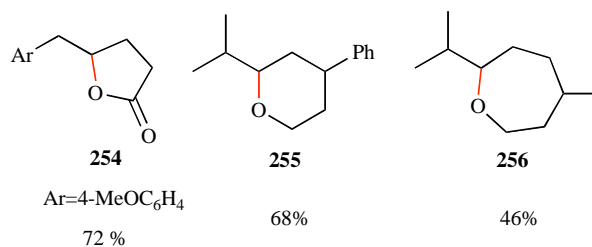
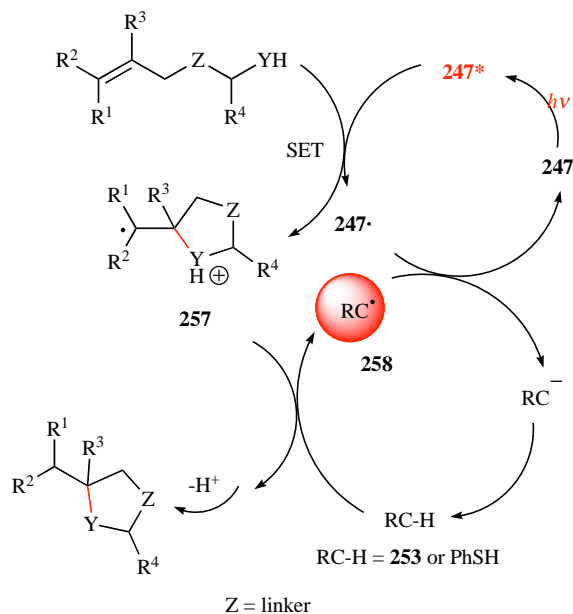


Fig. (7). Scope of photocatalyzed anti-Markovnikov transformation.

The proposed mechanism involves reductive quenching of **247*** by the substrate (Scheme **84**). Cyclization of the oxidized species gives radical **257** (distonic radical cation) which is reduced by 2-phenylmalononitrile **253** (a redox couple **RC**) via H-atom transfer

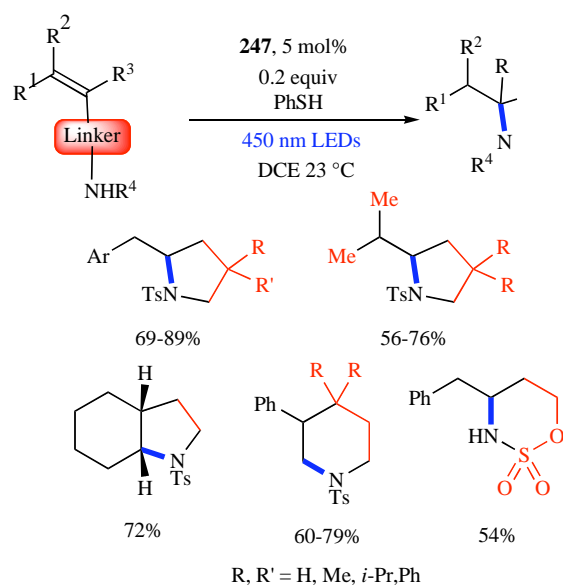
to give the product. Finally, reaction of reduced catalyst and radical **258** recovers the catalyst and the redox couple closing the catalytic cycle. The use of redox couple **253** is a key feature of this strategy, it allows efficient transformation of **257** to the product and recovery of the catalyst.



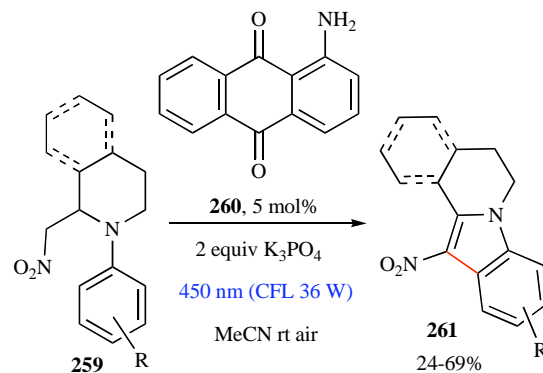
Scheme 84. Mechanisms proposed for photocatalyzed anti-Markovnikov nucleophilic addition to olefin.

The methodology was later extended to intramolecular hydroamination allowing the synthesis of pyrrolidine, piperidines and a sulfamic derivative (Scheme **85**) [80]. Potential problems with amine oxidation were anticipated and avoided using a protective group (sulfonyl, boc) over the amine. Again, selection of the redox couple was critical and **253** was replaced by PhSH to obtain the best results.

Brasholz *et al.* studied a cascade dehydrogenation/ 6π -cyclization/oxidation reaction of isoquinoline **259** in the presence of 1-aminoanthraquinone (**260**) as a photocatalyst, 12-nitroindoloisoquinolines **261** were obtained (Scheme **86**) [81]. The mechanism proposed for the dehydrogenation step involves deprotonation of a photo-generated iminium cation **262** (Scheme **34** with **260** instead

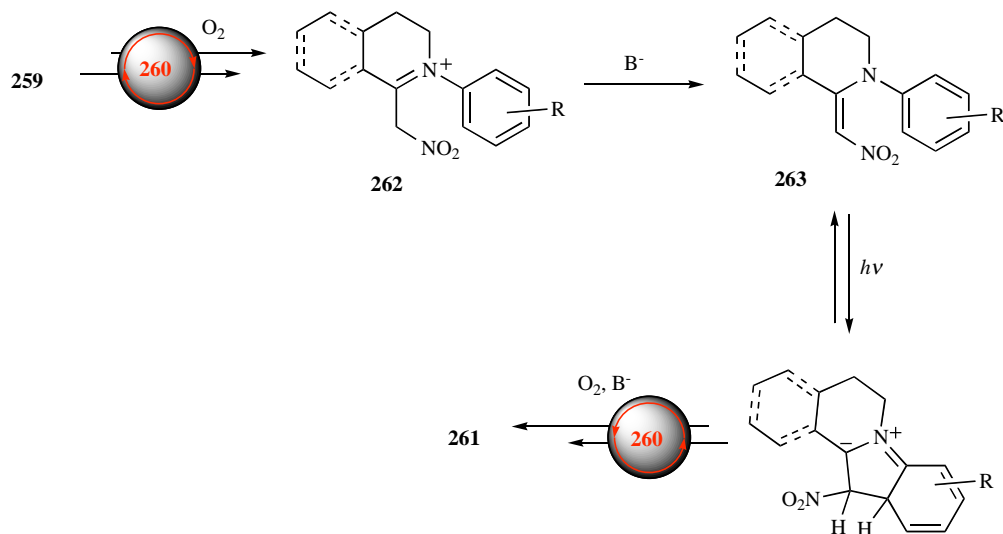


Scheme 85. Anti-Markovnikov hydroamination of alkenes catalyzed by an organic photoredox system.



Scheme 86. Synthesis of 12-nitroindoloisoquinolines **261**.

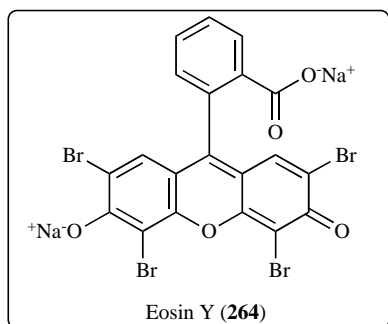
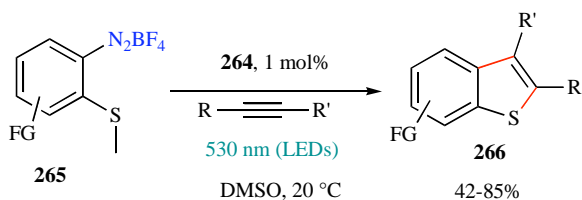
of Ru) to obtain **263**. Compound **263** would suffer photo 6π -cyclization followed by photocatalytic oxidation to the final product **261** (Scheme **87**).



Scheme 87. Mechanism proposed for cascade dehydrogenation/ 6π -cyclization/oxidation reactions.

3.2. Intermolecular Reactions

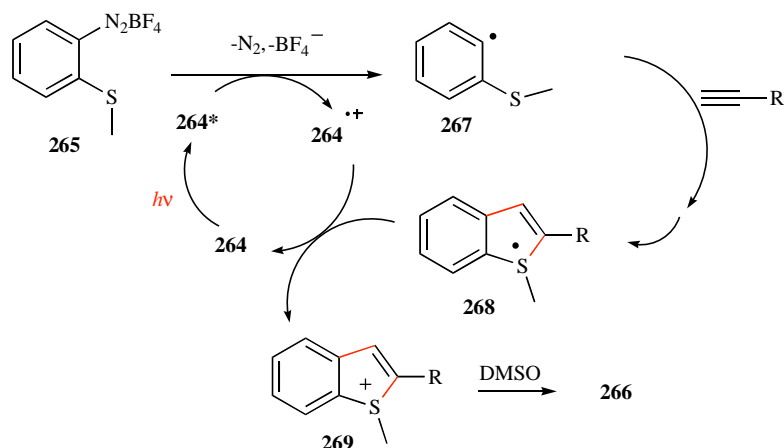
The synthesis of benzothiophenes was achieved through eosin Y (**264**) photocatalysis starting from *ortho*-methylthio diazonium salts and alkynes (Scheme **88**) [82]. Diazonium salts with EDG or halogen are well tolerated as well as alkynes with EDG and EWG. The method provides mild (green light and inexpensive organic dye) and efficient access to different types of benzothiophenes, avoiding metal catalysts and high temperatures.



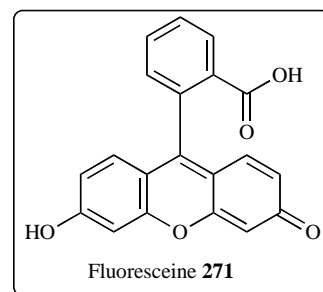
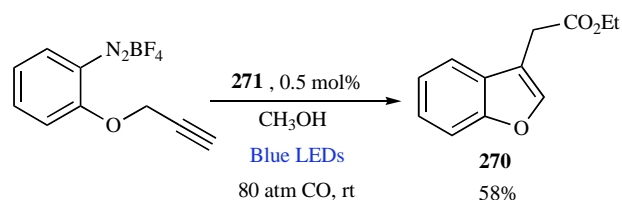
Scheme 88. Synthesis of benzothiophene **266** using Eosin Y.

The mechanism of the reaction has been proved to follow radicals as key intermediates (Scheme **89**) [82]. Reduction of diazonium salt by an oxidative quenching gives an aryl radical intermediate (**267**). Intermolecular additions to the alkyne afford an alkenyl radical which cyclizes to the sulphur atom to give sulphuranyl radical **268** [83]. Oxidation of **268** recovers the catalyst and provides cation **269** which could react with a nucleophile (solvent in this case) by the S_N2 mechanism.

In the context of an alkoxyacylation of aryldiazonium salts using CO and a photocatalyst **271**, furan **270** has been synthesized in moderate yields (Scheme **90**) [84]. As mentioned before, aryl radicals are generated, following a radical cyclization and trapping with CO. Oxidation of the final radical restores the catalyst and gives the final product after reaction with a nucleophile.



Scheme 89. Mechanism proposed for the photocatalyzed synthesis of benzothiophenes.

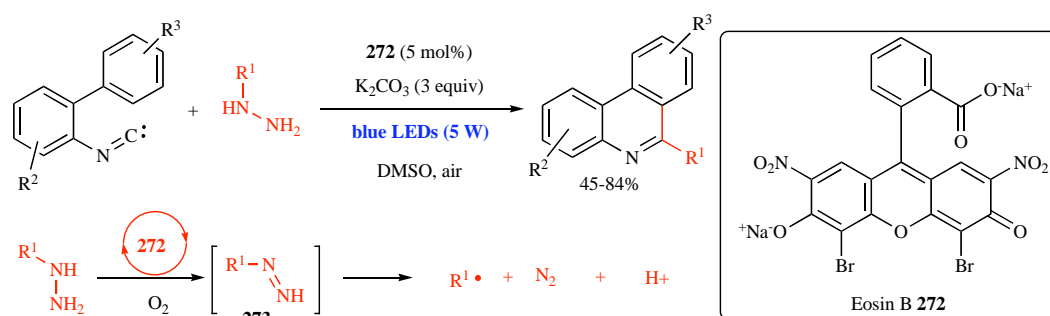


Scheme 90. Synthesis of ethyl 2-(benzofuran-3-yl)acetate **270**.

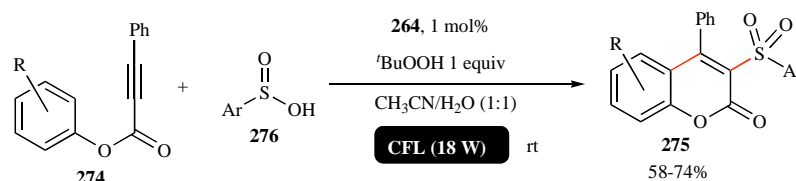
Aryl radical was also prepared by photocatalyzed oxidation of hydrazines with an organic dye [85]. The synthesis of 6-substituted phenanthridines was achieved using eosin B (**272**) as a catalyst and 2-isocyanobiphenyls with good yields (Scheme **91**). In addition, the use of hydrazines allowed the preparation of alkyl and acyl substitutions that were less explored in the diazonium salt approach due to limited availability of the corresponding precursors. The proposed mechanism involves the formation of a radical from intermediate **273**, which follows the mechanism described in Scheme **58**.

Recently, Wang *et al.* synthesized coumarins **275** through a visible-light-initiated oxidative cyclization of phenyl propiolates **274** (Scheme **92**) [86]. The reaction was proposed to go through a radical process involving a *tert*-butoxyl radical and possibly a sulfonyl radical **277** (Scheme **93**).

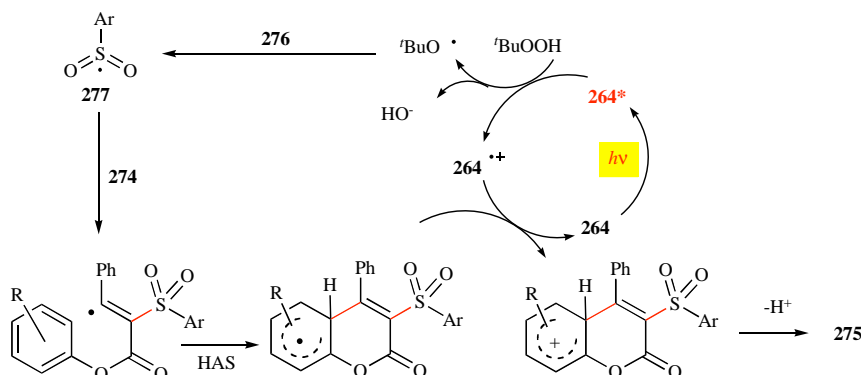
Functionalization of tetrahydroisoquinolines has been extensively studied in photoredox catalysis using O_2 as a terminal oxidant; most of them result in the reaction of the corresponding iminium anion with different nucleophiles. As was mentioned before (see Scheme **23**), photo-oxidation of an amine could give iminium cation or α -aminoradicals, and the reaction of the last one with electrophile is a valuable synthetic tool. Accordingly, the group of Ye, Jiang *et al.* prepared four different products by reaction of tetrahydroisoquinolines **278** with the same electrophile and dicyanopyrazine **279** as a photocatalyst (Scheme **94**) [87]. Chemioselectiv-



Scheme 91. Synthesis of 6-substituted phenanthridines by photooxidation.



Scheme 92. Synthesis of 3-(arylsulfonyl)-4-phenyl-2H-chromen-2-ones **275**.



Scheme 93. Mechanism proposed for the synthesis of coumarins **275**.

ity was controlled through the addition of a Lewis acid (LiPF_6), a base (Li_3PO_4), changing the solvent and modifying the temperature.

Product **280** was obtained in high yield working in a $\text{Me}/\text{H}_2\text{O}$ (1:3) mixture with LiPF_6 as additive. Although the effect of the photocatalyst is irrefutable, a slow reaction was detected without catalyst, which could not be explained. The occurrence of a radical addition to the electrophile was probed and proposed to be the first event for the formation of all products (Scheme **95**). The fate of the radical formed (**281**) determines the product obtained, affected by changing the conditions. It is proposed that, in the presence of Lewis acids radical **281** will be stabilized, favoring a HAS reaction to **280** [87].

As one of the few efforts to improve the photophysical properties of organic dyes, Huang and Zhao designed two photocatalysts with long-lived triplet state and strong absorption of visible light [88]. Combination of strong absorption of the boron-dipyrromethene (bodipy) and long-lived triplet state of C_{60} allows synthesizing C_{60} -Bodipy dyes with enhanced properties to act as photocatalysts (**282-284**, Fig. **8**).

The performance of the catalysis was probed in the synthesis of pyrrolo[2,1-*a*]isoquinoline **232** (see Scheme **75**) by tandem oxidation/[3+2] cycloaddition reactions of tetrahydroisoquinolines **230** and *N*-phenylmaleimides (Scheme **96**). Compared to the reported conditions with $\text{Ru}(\text{bpy})_3^{2+}$ (**84**) (Scheme **75**), [74] C_{60} and Bodipy **282**, the new C_{60} -Bodipys **283** and **284** photocatalyst show better catalytic activity giving higher yields in shorter times. Mechanistic

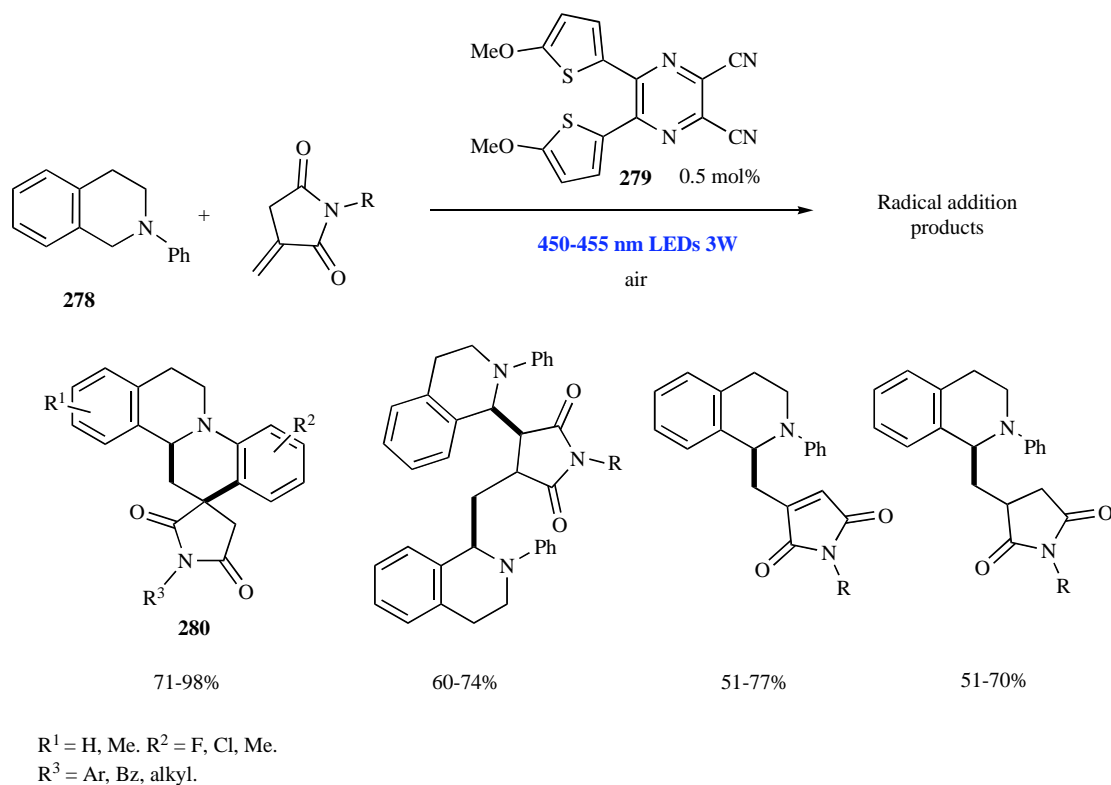
studies confirmed the same mechanism as that determined for catalyst **84**: reductive quenching of photocatalyst with oxygen as a terminal oxidant (see Scheme **74**).

In another effort to obtain photocatalyst with better properties, a supported bodipy photocatalyst (Figure **8**, **285**) was prepared, proving its use in the same reaction (Scheme **96**). Once again, a better performance was obtained with good product yield and shorter reaction times than those with $\text{Ru}(\text{bpy})_3^{2+}$.

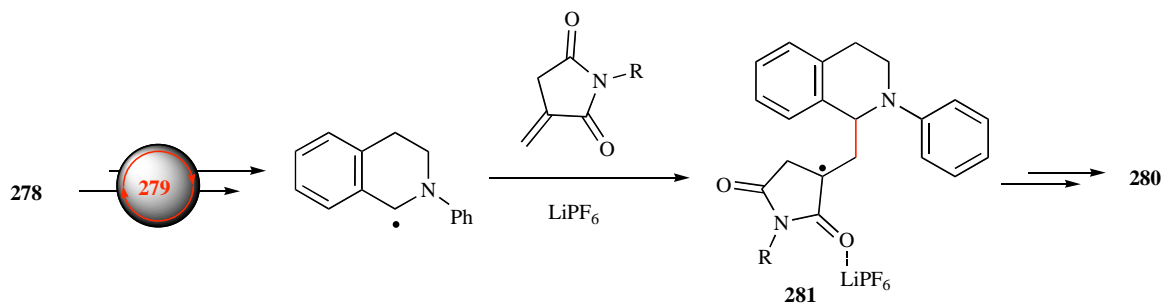
A further example of pyrrolo[2,1-*a*]isoquinoline by a tandem oxidation/[3+2] cycloaddition was reported using Rose Bengal **286** as a photocatalyst (Scheme **96**) [89]. Moderate to good yields were obtained in longer reaction times as compared to bodipys (**283** and **284**) and $\text{Ru}(\text{bpy})_3^{2+}$. However, its lower performance is acceptable considering its lower cost. In addition, different setups were used by the authors by changing light source, power, geometry, etc.; making a global comparison particularly difficult.

Catalyst **286** also catalyzed the [3+2] cycloaddition of tetrahydroisoquinolines **287** with alkynes **288** to pyrrolo[2,1-*a*]isoquinoline **289** in moderate yield (Scheme **97**) [89].

N-Aryl-tetrahydroisoquinolines **290** have also been used to prepare 12-nitro-5,6-dihydroindolo[2,1-*a*]isoquinoline (**261**) by reaction with nitromethane and 1,5-diaminoanthraquinone (**291**) as photocatalyst (Scheme **98**) [81]. This cascade reaction involves four steps including photocatalytic cross-dehydrogenative coupling / dehydrogenation / 6π -cyclization / oxidation reactions.



Scheme 94. Chemio-diverse functionalization of tetrahydroisoquinolines.



Scheme 95. Mechanism for the formation of 280.

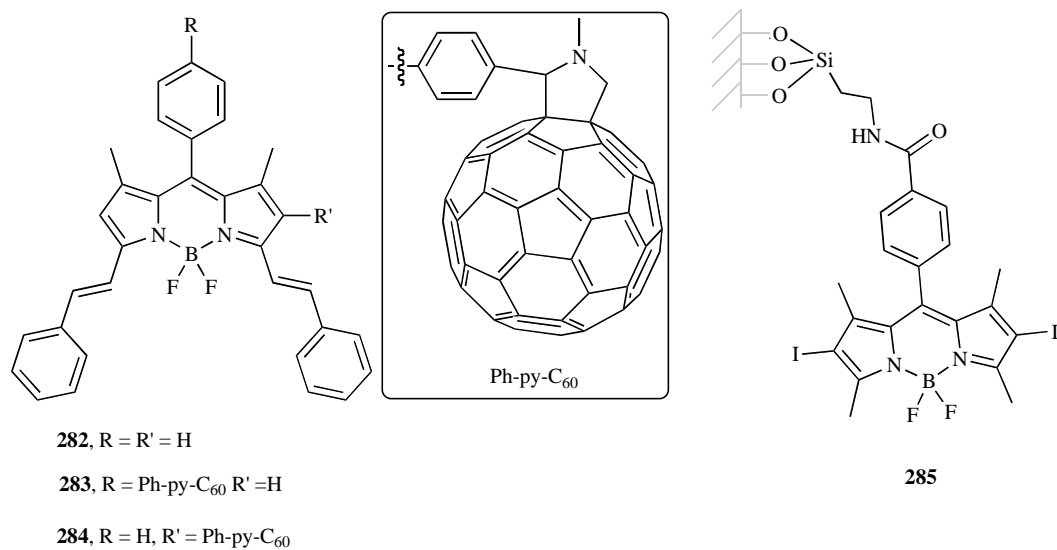
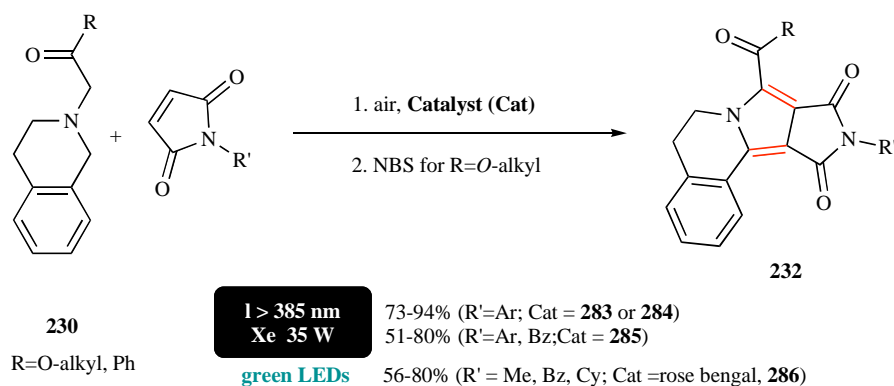
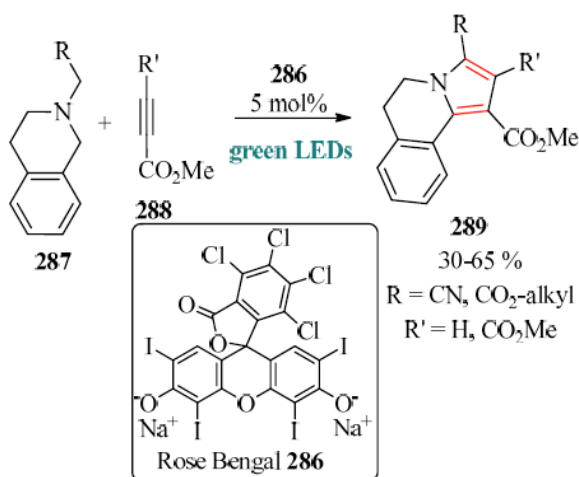
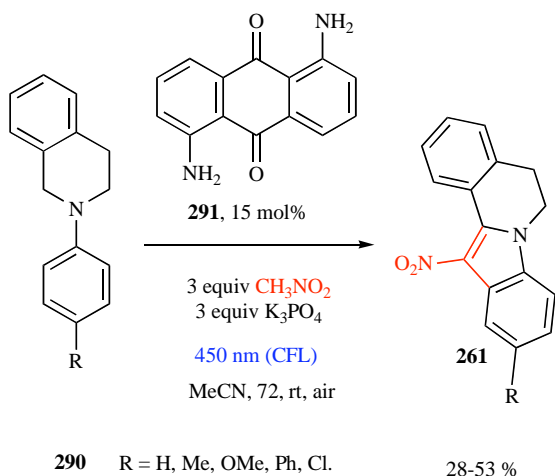
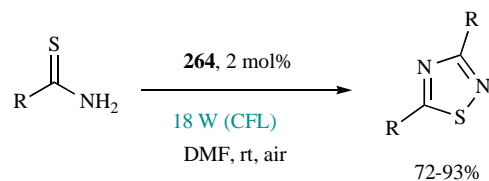


Fig. (8). Boron-dipyrromethene (bodipy) photocatalysts.

Scheme 96. Synthesis of dihydropyrrolo isoquinolines derivatives **232**.Scheme 97. Synthesis of 5,6-dihydropyrroloisoquinolines derivatives **289**.Scheme 98. Synthesis of 12-nitro-5,6-dihydroindolo[2,1-a]isoquinoline **261**.

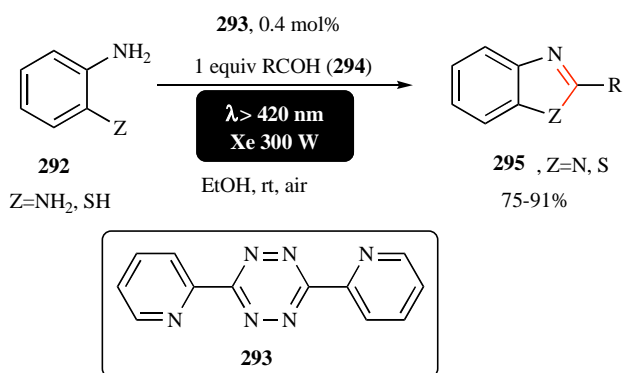
Photocatalytic cross-dehydrogenative coupling had been previously reported with transition-metal complex (see for example Scheme **34**) but not through a dehydrogenation/ 6π -cyclization/oxidation. Optimization of these steps (see above Scheme **86** and Scheme **87**) allows the author to find suitable conditions to perform the cascade reaction with good yields. Eosin Y (**264**) has also been used to synthesize 1,2,4-thiadiazoles by oxidative cyclization of primary thioamides (Scheme **99**) [90]. Photocatalysis allows re-

placement of stoichiometric chemical oxidant by oxygen, working at rt and short times. The mechanism proposed involves two photocatalytic oxidations to get the final product, yet, it was not probed with mechanistic studies.



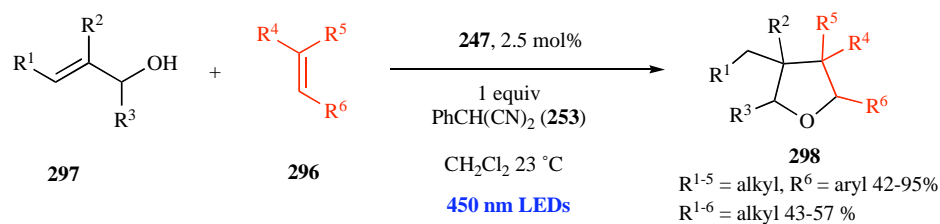
Scheme 99. Synthesis of 1,2,4-thiadiazole derivatives.

Benzimidazoles and benzothiazoles **295** have been synthesized by photoinduced oxidative cyclization in mild and environmentally benign conditions using tetrazine **293** as a photocatalyst (Scheme **100**) [91]. Photostimulation of aldehydes **294** and 2-amino or 2-thioanilines (**292**) was performed at rt and oxygen as a terminal oxidant. The reaction involves an initial condensation reaction of **294** and **292** to give an imine followed by oxidation to promote cyclization (similar to Scheme **65**).

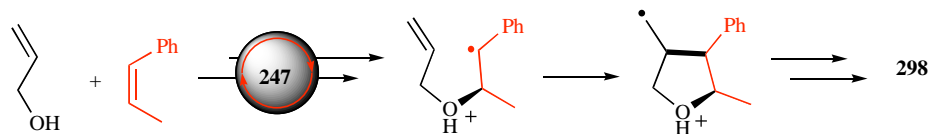
Scheme 100. Synthesis of substituted benzimidazoles and benzothiazoles **295**.

Substituted tetrahydrofurans **298** were synthesized by a radical-cross-over cycloaddition (Scheme **101**) [92]. The authors extended their work in the intramolecular addition of nucleophiles onto radical cation of alkenes (Scheme **83**) [79], and built the cycle from alkenes **296** and alkenols **297**. The reaction mechanism resembles that shown in Scheme **84** with a 5-*exo* radical cyclization (Scheme **102**) taking place before reduction by H-donor **253**.

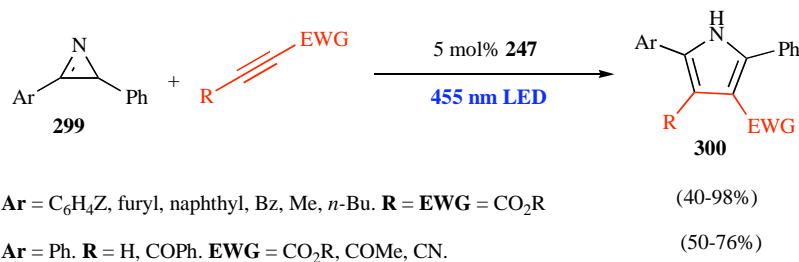
Xiao *et al.* developed a photocatalyzed coupling of 2*H*-azirines (**299**) and alkynes to obtain pyrroles **300** which avoid transition-metals and UV light irradiation (Scheme **103**) [93]. Using catalyst



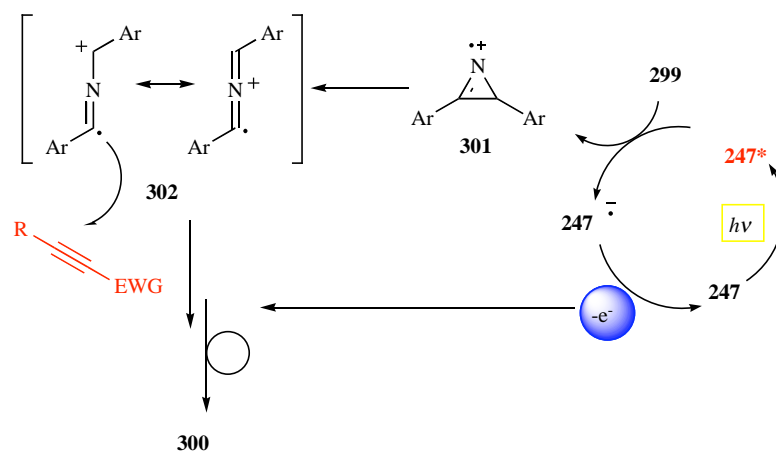
Scheme 101. Synthesis of tetrahydrofurane derivatives **298**.



Scheme 102. Mechanism proposed for the synthesis of tetrahydrofurans **298**.



Scheme 103. Synthesis of substituted pyrroles **300**.



Scheme 104. Mechanisms proposed for the photocatalyzed reaction of 2*H*-azirines and alkynes.

247, high yields of the expected products were obtained in a formal [3+2] cycloaddition. Mechanistic studies confirm a reductive quenching of the excited catalyst by **299** (Scheme **104**). Ring opening of **301** produces radical cation **302** that reacts with the alkyne to finally give **300**.

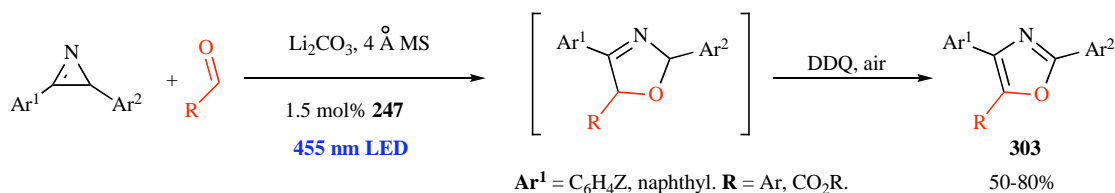
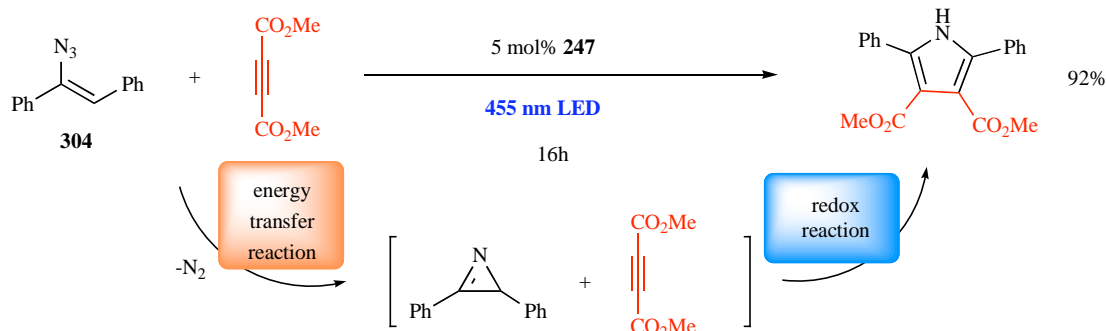
The same group extended the synthetic utility of 2*H*-azirines to obtain oxazoles **303** by reaction with aldehydes (Scheme **105**) [94]. The reaction mechanism was proposed to be the same as that reported (Scheme **104**) with cation **302** as the key intermediate. In this work, the authors also showed that reaction of 2*H*-azirines with alkenes and imines was possible to obtain pyrroles and dihydroimidazoles; however the scope was not explored.

An interesting example in Xiao's group was the preparation of pyrroles by a photocascade catalysis involving energy transfer and redox reactions (Scheme **106**) [93]. Previous studies in the photosensitization of azide derivatives to azirine (see Scheme **17**) [24] encouraged the authors to carry out a photocascade catalysis start-

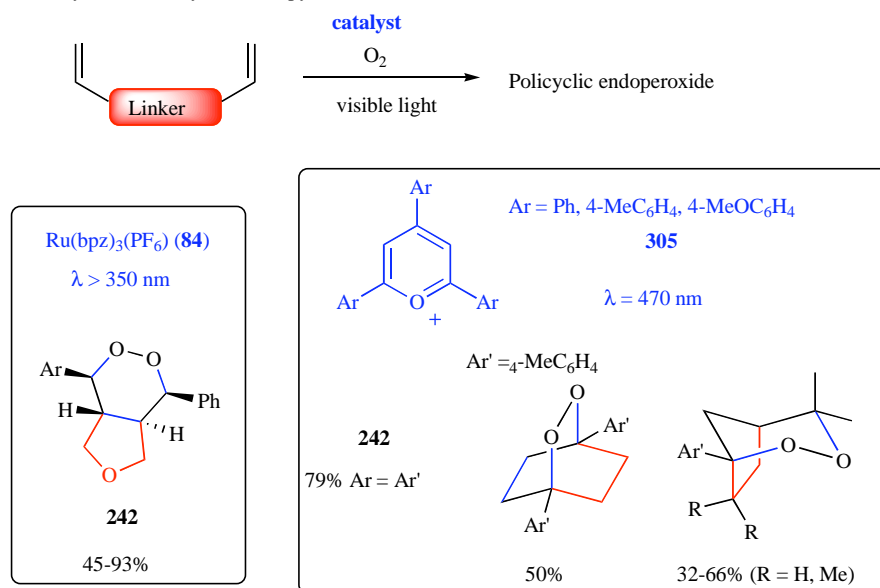
ing from azide **304** and an alkyne. It was shown that **247** was effective in both reactions affording 92% yield of the desired product (Scheme **106**).

Photocatalysis represents a good opportunity for the construction of complex labile molecules such as endoperoxides. In 1988 Miyashi *et al.* [95] synthesized some endoperoxides using 9,10-dicyanoanthracene (DCA) as part of an structural study of radical cation dienes using UV light irradiation. Inspired by this work, Yoon *et al.* (Scheme **73** and Fig. **5**), [72] and Nicewicz [96] synthesized different endoperoxides with good yields using visible light irradiation (Scheme **107**).

Organic dyes based catalyst **305** (Scheme **107**) perform better than Ru, as shown by Nicewicz *et al.* They obtained similar yields of the same compound with one of this catalyst using less catalyst loading. All studies support the mechanism shown in Scheme **72**, replacing Ru catalyst by **305**. As noted before, key intermediate radical cation **223** is obtained by SET to the excited photocatalyst.

Scheme 105. Synthesis of substituted oxazoles **303**.

Scheme 106. Metal-free photocatalytic cascade synthesis of pyrrole.



Scheme 107. Synthesis of endoperoxides by photocatalysis.

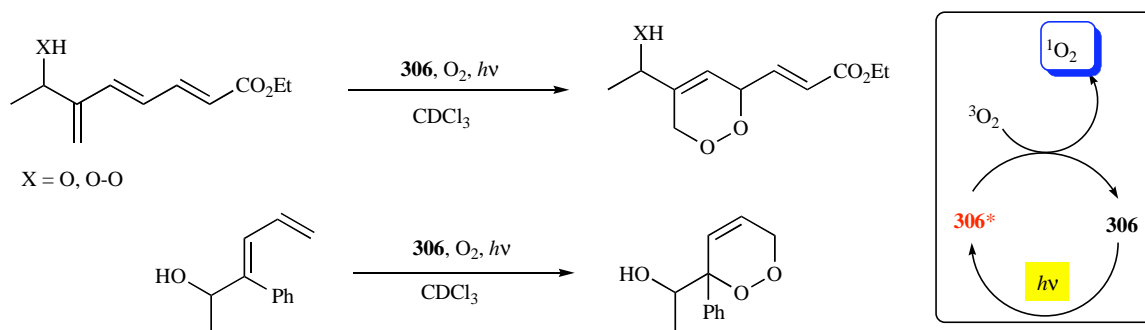
In a slightly different approach, Griesbeck *et al* reported the polyoxygenation of polyenes to obtain some endoperoxides with moderate yields (Scheme **108**) [97]. The authors used tetraphenylporphyrin **306** to promote a singlet oxygen functionalization of the substrates.

An interesting synthesis of Artemisinin, a currently used anti-malarial drug, was reported by Seeberger *et al.* (Scheme **109**) [98]. The author used a photocatalyzed oxidation with singlet oxygen followed by acid catalyzed oxidation in a continuous-flow reactor. Careful optimization resulted in a process characterized by short residence times, good power consumption and simplicity. **306** and 9,10-dicyanoanthracene (DCA) could act as photocatalyst but DCA was better since allows mixture of all component at the beginning of the flow reactor.

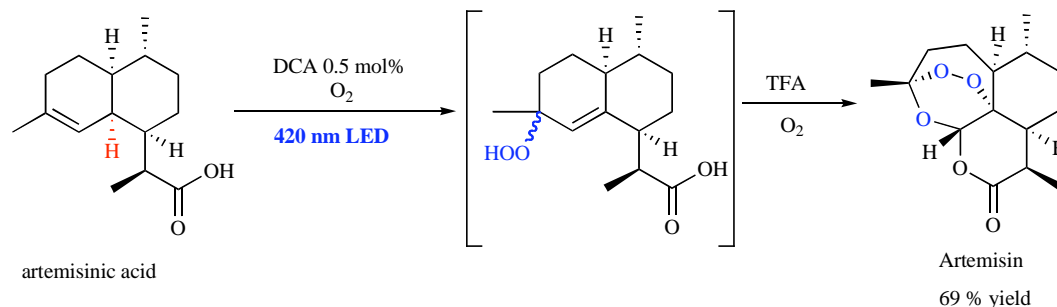
4. CONCLUSION AND REMARKS

The development in visible light photoredox catalysis research has demonstrated that this new synthetic approach is growing in

importance in synthetic organic chemistry. This approach allows the formation of reactive radical intermediates by photoredox and energy-transfer catalysis generated at rt with mild reaction conditions. Most published works use simple light sources such as fluorescent lamps or LED's the potential to use solar light is evident as opposed to UV photochemistry, light does not excite most functional groups, a fact that is not generally allowed through traditional high-energy UV photolysis or pyrolysis. In this review we have been able to illustrate the fact that photocatalysis with visible light is a powerful synthetic tool for the formation of several heterocycles such as indoles, pyrroles, tetrahydroisoquinolines, endoperoxides, benzothiazoles, phenanthridines, quinolines, etc. In these syntheses, diverse reactive intermediates were generated via ET: reduction or oxidation. As we have shown, these intermediates included C-centered alkyl radicals, heteroatom-centered radicals, electrophilic α -carbonyl radicals, iminium ions, aryl radicals, cations, among others. These reactive intermediates have been used in typically radical and radical ions reactions that include insertion to double and triple bond, HAS, dipolar cycloadditions, etc.



Scheme 108. Photooxygenation of polyenes with singlet oxygen.



Scheme 109. Continuous-Flow Process for the Synthesis of Artemisinin.

Although photocatalysis with transition-metal complexes has received widespread attention, today's organic catalyst emerges as a real alternative to produce the same transformation in line with the principles of green chemistry. Particularly remarkable for any visible light photocatalyst is that fact that the use of visible light is clean, renewable and inexpensive.

However, further development is needed in the optimization of photocatalysts to achieve ideal catalyst characteristics with high quantum yields and TON numbers. We expect that the photocatalytic approach expands the research field of radical reactions and stimulates development of novel reactive radical precursors. Furthermore, newly designed photocatalysts will be developed to achieve novel transformations and to improve the actual ones.

LIST OF ABBREVIATIONS

bodipy	=	Boron-dipyrrromethene
CFL	=	condensed/compact fluorescent light
CSA	=	camphorsulfonic acid
Cy	=	cyclohexane
DBU	=	1,8-diazabicycloundec-7-ene
DCE	=	dichloroethane
DCA	=	9,10-dicyanoanthracene
DDQ	=	2,3-dichloro-5,6-dicyanobenzoquinone
DIPEA	=	<i>N,N</i> -Diisopropylethylamine
DMF	=	dimethylformamide
EA	=	electron acceptor
ED	=	electron donor
EDG	=	electron donating groups
EP	=	energy transfer photocatalyst
ET	=	electron transfer
EWG	=	Electron-withdrawing groups
HAS	=	homolytic aromatic substitution

IET	=	intramolecular electron transfer
ILB	=	incandescent lamp bulb
LA	=	Lewis acid
LG	=	leaving group
MS	=	molecular sieve
MV	=	methyl viologen
NBS	=	<i>N</i> -bromosuccinimide
PCn	=	photocatalyst
PG	=	protecting group
Pht	=	phtalimide moiety
PRC	=	photoredoxcatalysis
rt	=	room temperature
SET	=	single electron transfer
TFA	=	trifluoroacetic acid
TMG	=	tetramethylguanidine

CONFLICT OF INTEREST

The author(s) confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

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REFERENCES

- [1] Xu, J.; Stevenson, J. Drug-like Index: A New Approach To Measure Drug-like Compounds and Their Diversity. *J. Chem. Inf. Model.* **2000**, *40*, 1177–1187.

- [2] Walter, H. Bioactive Heterocyclic Compound Classes. *Bioact. Heterocycl. Compd. Classes Agrochem.* **2012**, 175–193.
- [3] Angnes, R. A.; Li, Z.; Correia, C. R. D.; Hammond, G. B. Recent Synthetic Additions to the Visible Light Photoredox Catalysis Toolbox. *Org. Biomol. Chem.* **2015**, *13*, 9152–9167.
- [4] Lu, L.-Q.; Chen, J.-R.; Xiao, W.-J. Development of Cascade Reactions for the Concise Construction of Diverse Heterocyclic Architectures. *Acc. Chem. Res.* **2012**, *45*, 1278–1293.
- [5] Xie, J.; Jin, H.; Xu, P.; Zhu, C. When C–H Bond Functionalization Meets Visible-Light Photoredox Catalysis. *Tetrahedron Lett.* **2014**, *55*, 36–48.
- [6] Teplý, F. Photoredox Catalysis by [Ru(bpy)₃]²⁺ to Trigger Transformations of Organic Molecules. Organic Synthesis Using Visible-Light Photocatalysis and Its 20th Century Roots. *Collect. Czechoslov. Chem. Commun.* **2011**, *76*, 859–917.
- [7] Hari, D. P.; König, B. Synthetic Applications of Eosin Y in Photoredox Catalysis. *Chem. Commun.* **2014**, *50*, 6688–6699.
- [8] Nicewicz, D. A.; Nguyen, T. M. Recent Applications of Organic Dyes as Photoredox Catalysts in Organic Synthesis. *ACS Catal.* **2014**, *4*, 355–360.
- [9] Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis. *Chem. Rev.* **2013**, *113*, 5322–5363.
- [10] Tucker, J. W.; Narayanan, J. M. R.; Krabbe, S. W.; Stephenson, C. R. J. Electron Transfer Photoredox Catalysis: Intramolecular Radical Addition to Indoles and Pyrroles. *Org. Lett.* **2010**, *12*, 368–371.
- [11] Tucker, J. W.; Nguyen, J. D.; Narayanan, J. M. R.; Krabbe, S. W.; Stephenson, C. R. J. Tin-Free Radical Cyclization Reactions Initiated by Visible Light Photoredox Catalysis. *Chem. Commun.* **2010**, *46*, 4985–4987.
- [12] Tucker, J. W.; Stephenson, C. R. J. Tandem Visible Light-Mediated Radical Cyclization-Divinylcyclopropane Rearrangement to Tricyclic Pyrrolidinones. *Org. Lett.* **2011**, *13*, 5468–5471.
- [13] Ju, X.; Liang, Y.; Jia, P.; Li, W.; Yu, W. Synthesis of Oxindoles via Visible Light Photoredox Catalysis. *Org. Biomol. Chem.* **2012**, *10*, 498–501.
- [14] Kim, H.; Lee, C. Visible-Light-Induced Photocatalytic Reductive Transformations of Organohalides. *Angew. Chemie Int. Ed.* **2012**, *51*, 12303–12306.
- [15] Nguyen, J. D.; D'Amato, E. M.; Narayanan, J. M. R.; Stephenson, C. R. J. Engaging Unactivated Alkyl, Alkenyl and Aryl Iodides in Visible-Light-Mediated Free Radical Reactions. *Nat. Chem.* **2012**, *4*, 854–859.
- [16] Dong, W.; Liu, Y.; Hu, B.; Ren, K.; Li, Y.; Xie, X.; Jiang, Y.; Zhang, Z. Visible Light Induced Radical Cyclization of O-Iodophenylacrylamides: A Concise Synthesis of Indolin-2-One. *Chem. Commun.* **2015**, *51*, 4587–4590.
- [17] Fu, W.; Zhu, M.; Xu, F.; Fu, Y.; Xu, C.; Zou, D. An Approach to 6-Trifluoromethyl-Phenanthridines through Visible-Light-Mediated Intramolecular Radical Cyclization of Trifluoroacetimidoyl Chlorides. *RSC Adv.* **2014**, *4*, 17226–17229.
- [18] Dong, X.; Hu, Y.; Xiao, T.; Zhou, L. Synthesis of 2-Trifluoromethyl Indoles via Visible-Light Induced Intramolecular Radical Cyclization. *RSC Adv.* **2015**, *5*, 39625–39629.
- [19] Kachkovskiy, G.; Faderl, C.; Reiser, O. Visible Light-Mediated Synthesis of (Spiro)annelated Furans. *Adv. Synth. Catal.* **2013**, *355*, 2240–2248.
- [20] Sukhorukov, A. Y.; Ioffe, S. L. Chemistry of Six-Membered Cyclic Oxime Ethers. Application in the Synthesis of Bioactive Compounds. *Chem. Rev.* **2011**, *111*, 5004–5041.
- [21] Jiang, H.; An, X.; Tong, K.; Zheng, T.; Zhang, Y.; Yu, S. Visible-Light-Promoted Iminyl-Radical Formation from Acyl Oximes: A Unified Approach to Pyridines, Quinolines, and Phenanthridines. *Angew. Chemie Int. Ed.* **2015**, *54*, 4055–4059.
- [22] Farney, E. P.; Yoon, T. P. Visible-Light Sensitization of Vinyl Azides by Transition-Metal Photocatalysis. *Angew. Chemie Int. Ed.* **2014**, *53*, 793–797.
- [23] Xia, X.-D.; Xuan, J.; Wang, Q.; Lu, L.-Q.; Chen, J.-R.; Xiao, W.-J. Synthesis of 2-Substituted Indoles through Visible Light-Induced Photocatalytic Cyclizations of Styryl Azides. *Adv. Synth. Catal.* **2014**, *356*, 2807–2812.
- [24] Hu, X.-Q.; Chen, J.-R.; Wei, Q.; Liu, F.-L.; Deng, Q.-H.; Beauchemin, A. M.; Xiao, W.-J. Photocatalytic Generation of N-Centered Hydrazonyl Radicals: A Strategy for Hydroamination of β,γ-Unsaturated Hydrazones. *Angew. Chemie Int. Ed.* **2014**, *53*, 12163–12167.
- [25] Cheng, Y.; Yang, J.; Qu, Y.; Li, P. Aerobic Visible-Light Photoredox Radical C–H Functionalization: Catalytic Synthesis of 2-Substituted Benzothiazoles. *Org. Lett.* **2012**, *14*, 98–101.
- [26] Hu, J.; Wang, J.; Nguyen, T. H.; Zheng, N. The Chemistry of Amine Radical Cations Produced by Visible Light Photoredox Catalysis. *Beilstein J. Org. Chem.* **2013**, *9*, 1977–2001.
- [27] Maity, S.; Zheng, N. A Visible-Light-Mediated Oxidative C–N Bond Formation/Aromatization Cascade: Photocatalytic Preparation of N-Arylindoles. *Angew. Chemie Int. Ed.* **2012**, *51*, 9562–9566.
- [28] Musacchio, A. J.; Nguyen, L. Q.; Beard, G. H.; Knowles, R. R. Catalytic Olefin Hydroamination with Aminium Radical Cations: A Photoredox Method for Direct C–N Bond Formation. *J. Am. Chem. Soc.* **2014**, *136*, 12217–12220.
- [29] An, J.; Zou, Y.-Q.; Yang, Q.-Q.; Wang, Q.; Xiao, W.-J. Visible Light-Induced Aerobic Oxidation of Indoles: A Photocatalytic Strategy for the Preparation of Tetrahydro-5H-indolo[2,3-b]quinolins. *Adv. Synth. Catal.* **2013**, *355*, 1483–1489.
- [30] Xuan, J.; Feng, Z.-J.; Duan, S.-W.; Xiao, W.-J. Room Temperature Synthesis of isoquino[2,1-a][3,1]oxazine and isoquino[2,1-a]pyrimidine Derivatives via Visible Light Photoredox Catalysis. *RSC Adv.* **2012**, *2*, 4065–4068.
- [31] Mathis, C. L.; Gist, B. M.; Frederickson, C. K.; Midkiff, K. M.; Marvin, C. C. Visible Light Photooxidative Cyclization of Amino Alcohols to 1,3-Oxazines. *Tetrahedron Lett.* **2013**, *54*, 2101–2104.
- [32] Xuan, J.; Cheng, Y.; An, J.; Lu, L.-Q.; Zhang, X.-X.; Xiao, W.-J. Visible Light-Induced Intramolecular Cyclization Reactions of Diamines: A New Strategy to Construct Tetrahydroimidazoles. *Chem. Commun.* **2011**, *47*, 8337–8339.
- [33] Srivastava, V.; Yadav, L. Visible-Light-Triggered Oxidative C–H Aryloxylation of Phenolic Amidines; Photocatalytic Preparation of 2-Aminobenzoxazoles. *Synlett* **2013**, *24*, 2758–2762.
- [34] Kohls, P.; Jadhav, D.; Pandey, G.; Reiser, O. Visible Light Photoredox Catalysis: Generation and Addition of N-Aryltetrahydroisoquinoline-Derived α-Amino Radicals to Michael Acceptors. *Org. Lett.* **2012**, *14*, 672–675.
- [35] Pässler, U.; Knölker, H. J. The Pyrrolo[2,1-A]isoquinoline Alkaloids. *Alkaloids Chem. Biol.* **2011**, *70*, 79–151.
- [36] Yadav, A. K.; Yadav, L. D. S. Visible-Light-Driven Electrocyclization of Activated Allylic Amines via Azomethine Ylide Formation. *Tetrahedron Lett.* **2015**, *56*, 686–689.
- [37] Zhu, S.; Das, A.; Bui, L.; Zhou, H.; Curran, D. P.; Rueping, M. Oxygen Switch in Visible-Light Photoredox Catalysis: Radical Additions and Cyclizations and Unexpected C–C Bond Cleavage Reactions. *J. Am. Chem. Soc.* **2013**, *135*, 1823–1829.
- [38] Schmidt, A. W.; Reddy, K. R.; Knölker, H. J. Occurrence, Biogenesis, and Synthesis of Biologically Active Carbazole Alkaloids. *Chem. Rev.* **2012**, *112*, 3193–3328.
- [39] Hernandez-Perez, A. C.; Collins, S. K. A Visible-Light-Mediated Synthesis of Carbazoles. *Angew. Chemie Int. Ed.* **2013**, *52*, 12696–12700.
- [40] Hernandez-Perez, A. C.; Caron, A.; Collins, S. K. Photochemical Synthesis of Complex Carbazoles: Evaluation of Electronic Effects in Both UV- and Visible-Light Methods in Continuous Flow. *Chem. - A Eur. J.* **2015**, *21*, 16673–16678.
- [41] Cismesia, M. a.; Ischay, M. a.; Yoon, T. P. Reductive Cyclizations of Nitroarenes to Hydroxamic Acids by Visible Light Photoredox Catalysis. *Synthesis* **2013**, *45*, 2699–2705.
- [42] Lin, W.; Yang, D. Visible Light Photoredox Catalysis: Synthesis of Indazol[2,3-a]quinolines from 2-(2-Nitrophenyl)-1,2,3,4-Tetrahydroquinolines. *Org. Lett.* **2013**, *15*, 4862–4865.
- [43] Ischay, M. a.; Lu, Z.; Yoon, T. P. [2+2] Cycloadditions By Oxidative Visible Light Photocatalysis. *J. Am. Chem. Soc.* **2010**, *132*, 8572–8574.
- [44] Lu, Z.; Yoon, T. P. Visible Light Photocatalysis of [2+2] Styrene Cycloadditions by Energy Transfer. *Angew. Chemie Int. Ed.* **2012**, *51*, 10329–10332.
- [45] Hurlley, A. E.; Cismesia, M. a.; Ischay, M. a.; Yoon, T. P. Visible Light Photocatalysis of Radical Anion Hetero-Diels-Alder Cycloadditions. *Tetrahedron* **2011**, *67*, 4442–4448.
- [46] Hoffmann, N. Homogeneous Photocatalytic Reactions with Organometallic and Coordination Compounds-Perspectives for Sustainable Chemistry. *ChemSusChem* **2012**, *5*, 352–371.
- [47] Rueping, M.; Koenigs, R. M.; Poschary, K.; Fabry, D. C.; Leonori, D.; Vila, C. Dual Catalysis: Combination of Photocatalytic Aerobic Oxidation and Metal Catalyzed Alkynylation Reactions-C–C Bond Formation Using Visible Light. *Chem. - A Eur. J.* **2012**, *18*, 5170–5174.
- [48] Sahoo, B.; Hopkinson, M. N.; Glorius, F. Combining Gold and Photoredox Catalysis: Visible Light-Mediated Oxy- and Aminoarylation of Alkenes. *J. Am. Chem. Soc.* **2013**, *135*, 5505–5508.
- [49] Zoller, J.; Fabry, D. C.; Ronge, M. a.; Rueping, M. Synthesis of Indoles Using Visible Light: Photoredox Catalysis for Palladium-Catalyzed C–H Activation. *Angew. Chemie Int. Ed.* **2014**, *53*, 13264–13268.
- [50] Choi, S.; Chatterjee, T.; Choi, W. J.; You, Y.; Cho, E. J. Synthesis of Carbazoles by a Merged Visible Light Photoredox and Palladium-Catalyzed Process. *ACS Catal.* **2015**, *5*, 4796–4802.
- [51] Dong, X.; Xu, Y.; Liu, J. J.; Hu, Y.; Xiao, T.; Zhou, L. Visible-Light-Induced Radical Cyclization of Trifluoroacetimidoyl Chlorides with Alkynes: Catalytic Synthesis of 2-Trifluoromethyl Quinolines. *Chemistry* **2013**, *19*, 16928–16933.
- [52] Mühlmeil, S.; Alpers, D.; Hoffmann, F.; Brasholz, M. Iridium(III) Photocatalysis: A Visible-Light-Induced Dearomatization Tandem [4+2] Cyclization to Furnish Benzindolizidines. *Chem. - A Eur. J.* **2015**, *21*, 12308–12312.
- [53] Guo, W.; Cheng, H.-G.; Chen, L.-Y.; Xuan, J.; Feng, Z.-J.; Chen, J.-R.; Lu, L.-Q.; Xiao, W.-J. De Novo Synthesis of γ,γ-Disubstituted Butyrolactones through a Visible Light Photocatalytic Arylation-Lactonization Sequence. *Adv. Synth. Catal.* **2014**, *356*, 2787–2793.
- [54] Lin, R.; Sun, H.; Yang, C.; Shen, W.; Xia, W. Visible Light-Induced Difunctionalization of Electron-Enriched Styrenes: Synthesis of Tetrahydrofurans and Tetrahydropyrans. *Chem. Commun.* **2015**, *51*, 399–401.
- [55] Wei, Q.; Chen, J.-R.; Hu, X.-Q.; Yang, X.-C.; Lu, B.; Xiao, W.-J. Photocatalytic Radical Trifluoromethylation/Cyclization Cascade: Synthesis of CF₃-Containing Pyrazolines and Isoxazolines. *Org. Lett.* **2015**, *17*, 4464–4467.
- [56] *Encyclopedia of Radicals in Chemistry, Biology and Materials*; Chatgililoglu, C., Studer, A., Eds.; John Wiley & Sons, Ltd: Chichester,

- UK, 2012.
- [57] Liu, Y.; Zhang, J.-L.; Song, R.-J.; Li, J.-H. Visible-Light-Facilitated 5-*Exo-Trig* Cyclization of 1,6-Dienes with Alkyl Chlorides: Selective Scission of the C(sp³)-H Bond in Alkyl Chlorides. *European J. Org. Chem.* **2014**, 1177–1181.
- [58] Jiang, H.; Cheng, Y.; Zhang, Y.; Yu, S. De Novo Synthesis of Polysubstituted Naphthols and Furans Using Photoredox Neutral Coupling of Alkynes with 2-Bromo-1,3-Dicarbonyl Compounds. *Org. Lett.* **2013**, *15*, 4884–4887.
- [59] Nagib, D. A.; Scott, M. E.; MacMillan, D. W. C. Enantioselective α -Trifluoromethylation of Aldehydes via Photoredox Organocatalysis. *J. Am. Chem. Soc.* **2009**, *131*, 10875–10877.
- [60] Pham, P. V.; Nagib, D. A.; MacMillan, D. W. C. Photoredox Catalysis: A Mild, Operationally Simple Approach to the Synthesis of α -Trifluoromethyl Carbonyl Compounds. *Angew. Chemie Int. Ed.* **2011**, *50*, 6119–6122.
- [61] Zheng, L.; Yang, C.; Xu, Z.; Gao, F.; Xia, W. Difunctionalization of Alkenes via the Visible-Light-Induced Trifluoromethylarylation/1,4-Aryl Shift/Desulfonylation Cascade Reactions. *J. Org. Chem.* **2015**, *80*, 5730–5736.
- [62] Jiang, H.; Cheng, Y.; Wang, R.; Zheng, M.; Zhang, Y.; Yu, S. Synthesis of 6-Alkylated Phenanthridine Derivatives Using Photoredox Neutral Somophilic Isocyanide Insertion. *Angew. Chemie Int. Ed.* **2013**, *52*, 13289–13292.
- [63] Cheng, Y.; Yuan, X.; Jiang, H.; Wang, R.; Ma, J.; Zhang, Y.; Yu, S. Regiospecific Synthesis of 1-Trifluoromethylisoquinolines Enabled by Photoredox Somophilic Vinyl Isocyanide Insertion. *Adv. Synth. Catal.* **2014**, *356*, 2859–2866.
- [64] Sun, X.; Yu, S. Visible-Light-Mediated Fluoroalkylation of Isocyanides with Ethyl Bromoacetates: Unified Synthesis of Mono- and Difluoromethylated Phenanthridine Derivatives. *Org. Lett.* **2014**, *16*, 2938–2941.
- [65] Zhang, Z.; Tang, X.; Dolbier, W. R. Photoredox-Catalyzed Tandem Insertion/Cyclization Reactions of Difluoromethyl and 1,1-Difluoroalkyl Radicals with Biphenyl Isocyanides. *Org. Lett.* **2015**, *17*, 4401–4403.
- [66] Jiang, H.; Cheng, Y.; Wang, R.; Zhang, Y.; Yu, S. Synthesis of Isoquinolines via Visible Light-Promoted Insertion of Vinyl Isocyanides with Diaryliodonium Salts. *Chem. Commun.* **2014**, *50*, 6164.
- [67] He, Z.; Bae, M.; Wu, J.; Jamison, T. F. Synthesis of Highly Functionalized Polycyclic Quinoxaline Derivatives Using Visible-Light Photoredox Catalysis. *Angew. Chemie Int. Ed.* **2014**, *53*, 14451–14455.
- [68] Ju, X.; Li, D.; Li, W.; Yu, W.; Bian, F. The Reaction of Tertiary Anilines with Maleimides under Visible Light Redox Catalysis. *Adv. Synth. Catal.* **2012**, *354*, 3561–3567.
- [69] Pandey, G.; Jadhav, D.; Tiwari, S. K.; Singh, B. Visible Light Photoredox Catalysis: Investigation of Distal sp³ C-H Functionalization of Tertiary Amines for Alkylation Reaction. *Adv. Synth. Catal.* **2014**, *356*, 2813–2818.
- [70] Lenhart, D.; Bach, T. Visible-Light-Induced, Ir-Catalyzed Reactions of N-Methyl- N -((trimethylsilyl)methyl)aniline with Cyclic α,β -Unsaturated Carbonyl Compounds. *Beilstein J. Org. Chem.* **2014**, *10*, 890–896.
- [71] Nakajima, K.; Kitagawa, M.; Ashida, Y.; Miyake, Y.; Nishibayashi, Y. Synthesis of Nitrogen Heterocycles via α -Aminoalkyl Radicals Generated from α -Silyl Secondary Amines under Visible Light Irradiation. *Chem. Commun.* **2014**, *50*, 8900–8903.
- [72] Parrish, J. D.; Ischay, M. a.; Lu, Z.; Guo, S.; Peters, N. R.; Yoon, T. P. Endoperoxide Synthesis by Photocatalytic Aerobic [2 + 2 + 2] Cycloadditions. *Org. Lett.* **2012**, *14*, 1640–1643.
- [73] Rueping, M.; Leonori, D.; Poisson, T. Visible Light Mediated Azomethine Ylide Formation—photoredox Catalyzed [3+2] Cycloadditions. *Chem. Commun.* **2011**, *47*, 9615.
- [74] Zou, Y. Q.; Lu, L. Q.; Fu, L.; Chang, N. J.; Rong, J.; Chen, J. R.; Xiao, W. J. Visible-Light-Induced oxidation/[3+2] Cycloaddition/oxidative Aromatization Sequence: A Photocatalytic Strategy to Construct pyrrolo[2,1-*a*]isoquinolines. *Angew. Chemie Int. Ed.* **2011**, *50*, 7171–7175.
- [75] Xie, J.; Xue, Q.; Jin, H.; Li, H.; Cheng, Y.; Zhu, C. A Visible-Light-Promoted Aerobic C–H/C–N Cleavage Cascade to Isoxazolidine Skeletons. *Chem. Sci.* **2013**, *4*, 1281–1286.
- [76] Hou, H.; Zhu, S.; Pan, F.; Rueping, M. Visible-Light Photoredox-Catalyzed Synthesis of Nitrones: Unexpected Rate Acceleration by Water in the Synthesis of Isoxazolidines. *Org. Lett.* **2014**, *16*, 2872–2875.
- [77] Blum, T. R.; Zhu, Y.; Nordeen, S. a.; Yoon, T. P. Photocatalytic Synthesis of Dihydrobenzofurans by Oxidative [3+2] Cycloaddition of Phenols. *Angew. Chemie Int. Ed.* **2014**, *53*, 11056–11059.
- [78] Ramirez, N. P.; Bosque, I.; Gonzalez-Gomez, J. C. Photocatalytic Dehydrogenative Lactonization of 2-Arylbenzoic Acids. *Org. Lett.* **2015**, *17*, 4550–4553.
- [79] Hamilton, D. S.; Nicewicz, D. a. Direct Catalytic Anti-Markovnikov Hydroetherification of Alkenols. *J. Am. Chem. Soc.* **2012**, *134*, 18577–18580.
- [80] Nguyen, T. M.; Nicewicz, D. a. Anti-Markovnikov Hydroamination of Alkenes Catalyzed by an Organic Photoredox System. *J. Am. Chem. Soc.* **2013**, *135*, 9588–9591.
- [81] Rusch, F.; Unkel, L.-N.; Alpers, D.; Hoffmann, F.; Brasholz, M. A Visible Light Photocatalytic Cross-Dehydrogenative Coupling/Dehydrogenation/6 π -Cyclization/Oxidation Cascade: Synthesis of 12-Nitroindoloisoquinolines from 2-Aryltetrahydroisoquinolines. *Chem. - A Eur. J.* **2015**, *21*, 8336–8340.
- [82] Hari, D. P.; Hering, T.; König, B. Visible Light Photocatalytic Synthesis of Benzothiophenes. *Org. Lett.* **2012**, *14*, 5334–5337.
- [83] Leardini, R.; Pedulli, G. F.; Tundo, A.; Zanardi, G. Reaction Pathways for the Cyclization of Ortho-Thioalkyl and Ortho-Thioaryl Substituted Phenyl Radicals with Alkynes. Reaction of O-Methylthioarenediazonium Tetrafluoroborates with Alkynes to Give 2-Substituted Benzo[*b*]thiophenes. *J. Chem. Soc. Chem. Commun.* **1985**, No. 20, 1390.
- [84] Guo, W.; Lu, L.-Q.; Wang, Y.; Wang, Y.-N.; Chen, J.-R.; Xiao, W.-J. Metal-Free, Room-Temperature, Radical Alkoxyacylation of Aryldiazonium Salts through Visible-Light Photoredox Catalysis. *Angew. Chemie Int. Ed.* **2015**, *54*, 2265–2269.
- [85] Xiao, T.; Li, L.; Lin, G.; Wang, Q.; Zhang, P.; Mao, Z.; Zhou, L. Synthesis of 6-Substituted Phenanthridines by Metal-Free, Visible-Light Induced Aerobic Oxidative Cyclization of 2-Isocyanobiphenyls with Hydrazines. *Green Chem.* **2014**, *16*, 2418–2421.
- [86] Yang, W.; Yang, S.; Li, P.; Wang, L. Visible-Light Initiated Oxidative Cyclization of Phenyl Propiolates with Sulfinic Acids to Coumarin Derivatives under Metal-Free Conditions. *Chem. Commun.* **2015**, *51*, 7520–7523.
- [87] Liu, X.; Ye, X.; Bureš, F.; Liu, H.; Jiang, Z. Controllable Chemoselectivity in Visible-Light Photoredox Catalysis: Four Diverse Aerobic Radical Cascade Reactions. *Angew. Chemie Int. Ed.* **2015**, *54*, 11443–11447.
- [88] Huang, L.; Zhao, J. C₆₀-Bodipy Dyad Triplet Photosensitizers as Organic Photocatalysts for Photocatalytic Tandem oxidation/[3+2] Cycloaddition Reactions to Prepare pyrrolo[2,1-*a*]isoquinoline. *Chem. Commun.* **2013**, *49*, 3751–3753.
- [89] Vila, C.; Lau, J.; Rueping, M. Visible-Light Photoredox Catalyzed Synthesis of Pyrroloisoquinolines via Organocatalytic oxidation/[3 + 2] Cycloaddition/oxidative Aromatization Reaction Cascade with Rose Bengal. *Beilstein J. Org. Chem.* **2014**, *10*, 1233–1238.
- [90] Srivastava, V.; Yadav, A.; Yadav, L. Eosin Y Catalyzed Visible-Light-Driven Aerobic Oxidative Cyclization of Thioamides to 1,2,4-Thiadiazoles. *Synlett* **2013**, *24*, 465–470.
- [91] Samanta, S.; Das, S.; Biswas, P. Photocatalysis by 3,6-Disubstituted-S-Tetrazine: Visible-Light Driven Metal-Free Green Synthesis of 2-Substituted Benzimidazole and Benzothiazole. *J. Org. Chem.* **2013**, *78*, 11184–11193.
- [92] Grandjean, J. M. M.; Nicewicz, D. a. Synthesis of Highly Substituted Tetrahydrofurans by Catalytic Polar-Radical-Crossover Cycloadditions of Alkenes and Alkenols. *Angew. Chemie - Int. Ed.* **2013**, *52*, 3967–3971.
- [93] Xuan, J.; Xia, X.-D.; Zeng, T.-T.; Feng, Z.-J.; Chen, J.-R.; Lu, L.-Q.; Xiao, W.-J. Visible-Light-Induced Formal [3+2] Cycloaddition for Pyrrole Synthesis under Metal-Free Conditions. *Angew. Chemie Int. Ed.* **2014**, *53*, 5653–5656.
- [94] Zeng, T.-T.; Xuan, J.; Ding, W.; Wang, K.; Lu, L.-Q.; Xiao, W.-J. [3 + 2] Cycloaddition/Oxidative Aromatization Sequence via Photoredox Catalysis: One-Pot Synthesis of Oxazoles from 2 H -Azirines and Aldehydes. *Org. Lett.* **2015**, *17*, 4070–4073.
- [95] Miyashi, T.; Konno, A.; Takahashi, Y. Evidence for a Chair Cyclohexane-1,4-Radical Cation Intermediate in the Single Electron-Transfer-Induced Cope Rearrangement of 2,5-Diaryl-1,5-Hexadienes. *J. Am. Chem. Soc.* **1988**, *110*, 3676–3677.
- [96] Gesmundo, N. J.; Nicewicz, D. a. Cyclization–endoperoxidation Cascade Reactions of Dienes Mediated by a Perylium Photoredox Catalyst. *Beilstein J. Org. Chem.* **2014**, *10*, 1272–1281.
- [97] Griesbeck, A. G.; de Kiff, A.; Kleczka, M. Tetraphenylporphyrin-Catalyzed Tandem Photooxygenation of Polyenes and 1,4-Dienes: Multiple and Diverse Oxyfunctionalizations. *Adv. Synth. Catal.* **2014**, *356*, 2839–2845.
- [98] Kopetzki, D.; Lévesque, F.; Seeberger, P. H. A Continuous-Flow Process for the Synthesis of Artemisinin. *Chem. - A Eur. J.* **2013**, *19*, 5450–5456.