International Journal of Enhanced Research in Science, Technology & Engineering
ISSN: 2319-7463, Vol. 14 Issue 5, May-2025

Photoredox Catalysis in Organic Synthesis

Pooja

Email - poojadahiya459@gmail.com

ABSTRACT

These days, the visible light photoredox concept is quickly applied to catalytic reactions in contemporary organic synthesis, providing highly effective, selective, and ecologically friendly methods for various bond creation. For C–B, C–O, C–S, and analogous couplings, this bond formation can be accomplished via desulfonylation, decarboxylation, and radical-mediated cleavage to the activation of aryl halides. In contemporary organic synthesis, we can also employ defluorinative techniques, alkene di-functionalization, bio-orthogonal photocatalytic processes, and visible light-driven C–H functionalisation of heteroarenes. This technique allows us to modify physiologically active compounds, increasing their usefulness in material science and pharmaceuticals, in addition to altering the functional groups and link formation. The most current developments in photoredox catalysis are included in this review, along with the mechanistic pathway, substrate scope, and applications. Future insights on how photoredox catalysis will continue to shape creative approaches in synthetic chemistry are provided by the discussion of remaining issues, such as catalyst design, reaction scalability, and sustainable integration.

Key Words: Visible Light Photoredox, Water Splitting, Carbon Dioxide Reduction.

INTRODUCTION

Numerous unconventional bond structures in organic chemistry have been made possible during the past century by the discovery, advancement, and application of light-mediated catalysis. The science of photocatalysis has had a major rebirth in recent years, and once again, a number of novel activation modes have given rise to a wide range of novel bond-forming protocols and synthetic techniques.1 The field of photocatalysis includes an ever-growing number of generic activation modes in which photonic energy is selectively directed to a specially engineered photon-absorbing catalyst (a photocatalyst) that, when excited, can induce an accompanying substrate, reagent, or secondary catalyst to participate in special reaction pathways that were previously unachievable under thermal control. The most popular methods by which photocatalysts can simultaneously perform selective molecule activation and convert light into chemical energy are (i) energy transfer, (ii) organometallic excitation, (iii) light-induced atom transfer, and (iv) photoredox catalysis. These methods will all be covered in detail in this special issue. However, for the sake of this Perspective, we shall limit our discussion to the effects and applications of photoredox catalysis in organic synthesis. We will first look at the usefulness of photoredox catalysis from a historical perspective. After that, we will talk about the area's amazing recent influence on the field of organic reaction innovation and its use in both academic and industrial settings. Reports that highlight the special qualities of photoredox catalysis and the genuinely innovative nature of the concomitant reactions it can produce have received special attention because this paper's coverage cannot be (and is not intended to be) exhaustive.

Water splitting, carbon dioxide reduction, and the creation of new solar cell materials have all benefited greatly from photoredox catalysis over the past forty years. However, the potential of using this catalytic platform for organic synthesis has only recently started to materialise. The realisation that easily accessible metal polypyridyl complexes and organic dyes might enable the conversion of visible light into chemical energy under extraordinarily mild conditions has played a significant role in the recent yet explosive expansion of this activation platform. These molecules can easily access open-shell reactive species by participating in single-electron transfer (SET) interactions with organic (and organometallic) substrates upon excitation.5 Here, the photoredox catalyst is selectively excited by exposure to visible light at wavelengths that are not absorbed by typical organic molecules. A reaction environment specific to organic chemistry is made possible by the resulting excited species' ability to function as both a strong oxidant and a strong reductant at the same time (Figure 1). In fact, this electronic duality stands in stark contrast to conventional redox reaction manifolds (such as electrochemistry), where the reaction medium can be either reductive or oxidative (but not both), opening up hitherto unreachable redox-neutral reaction platforms.

Numerous innovative synthesis techniques have been made possible by recent developments in contemporary photoredox catalysis.

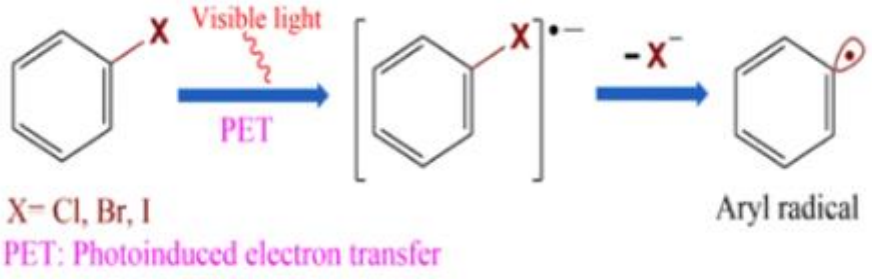

Figure 1. Generation and transformations of aryl radicals.

One of the most basic and widely used concepts in contemporary synthetic chemistry is the creation of carbon–carbon (C–C) bonds. The use of transition-metal catalysts to activate various C–X bonds, including C–H, C–O, and C–N, has advanced significantly in recent years.*Corresponding Writer: The creation of various molecular compounds is made possible by Shakirali Manusiya. It's interesting to note that sulfonyl-based molecules, which were previously thought to be extremely stable and chemically inert, have recently gained attention as useful precursors for the creation of C–C bonds through visible light-driven desulfonylation. The range of synthetic procedures is expanded by the selective reaction of sulfonyl chlorides, sulfinates, sulfonamides, and sulfones utilising visible light under mild and environmentally benign photocatalytic conditions.

These methods have a significant advantage in that they can modify a broad variety of functional groups, allowing for the late modification of complex, physiologically active compounds without the requirement for protective groups on sensitive functionalities like hydroxyl, amine, or amide. These developments demonstrate their critical importance in drug discovery and large-scale synthesis. [1]. Simultaneously, the creation of aryl radicals has become a potent method for producing various aromatic molecules. Pharmaceuticals, natural goods, and sophisticated functional materials frequently contain aryl and heteroaryl groups. Arylation reactions have historically relied mostly on transition-metal catalysis, which calls for costly catalysts, ligands that are sensitive to moisture or air, and challenging reaction conditions. By enabling the reduction of aryl halides under mild, sustainable, and economical conditions to yield highly reactive aryl radical intermediates, visible-light photoredox catalysis has completely transformed this field (Figure 1). Aryl halides continue to be the most readily available and useful aryl sources when compared to other precursors such diazonium salts, iodonium salts, or triflates.

Despite the fact that these substances often have high redox potentials, improvements in photocatalytic systems, such as semiconductor-based catalysts, organic dyes, and transition-metal complexes, have made their reduction much more possible. As a result, a variety of C–C and C–heteroatom bond-forming processes are now feasible. Crucially, these techniques have also proven to be very useful for late-stage alteration of complex bioactive compounds, creating new potential in materials science and medicinal chemistry. In addition to organic synthesis, photoredox catalysis has significantly advanced bioorthogonal chemistry by offering several potent methods for modifying biomolecules in living systems without interfering with normal cellular functions. A reaction must proceed quickly and selectively in physiological settings while staying completely compatible with aquatic surroundings in order to be referred to as bioorthogonal (Figure 2). Recent advancements have demonstrated that photocatalytic techniques are particularly well-suited to fulfil these requirements because to their precise spatiotemporal control, adjustable reactivity, and mild operating conditions.

There is a clear link between synthetic chemistry and biological applications because visible-light-driven mechanisms have already been applied in a variety of fields, such as in-situ biomolecule labelling, targeted activation, and catalytic transformations inside living cells. Even if there are still issues like catalyst deactivation and maintaining tight orthogonality in intricate biological systems, photocatalysis is gradually becoming recognised as a flexible and promising platform for broadening the toolkit of bioorthogonal processes. These developments show how visible-light photoredox catalysis transforms aryl radical production, C–C bond formation, and bioorthogonal chemistry. With a focus on mechanistic insights, important representative reactions, and their numerous applications in organic synthesis and associated techniques, we summarise current advancements in these fields in this review. [3].

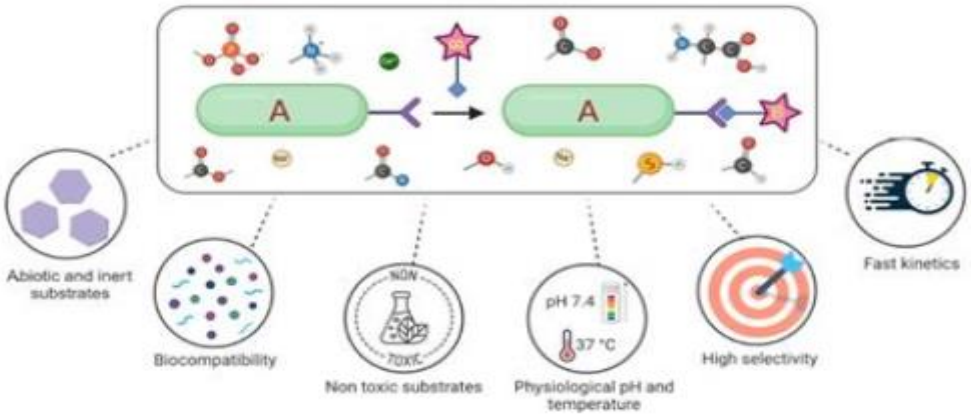

Figure 2. Overview of general reaction of bioorthogonal chemistry

2. C–C Bond Formation under Visible Light Photoredox Catalysis

In this article, we discuss the various transformations that could be based on the photoredox reaction as well as the various ways that different catalysts can facilitate the production of c-c bonds.

2.1 Desulfonylative C–C Bond Formation

Visible-light-driven arylation and alkylation for the production of C–C bonds have garnered a lot of attention recently, mainly due to the fact that these reactions can occur under moderate, ecologically benign, and frequently transition-metal-free circumstances. Significant advancements have also been made in the desulfonylative transformations of sulfonyl derivatives, such as sulfonyl chlorides, sulfinates, sulfonamides, and sulfones, when exposed to visible light. Desulfonylative reactions typically involve three main molecular routes. In the first pathway, a single electron transfer (SET) reaction between the activated photocatalyst and sulfonyl substrate 1 results in the production of sulfonyl radical anion 2. If R^2 serves as an appropriate leaving group, fragmentation results in the anionic species R^2 and sulphur dioxide, producing R^1 radical 3, which can go through several transformations to generate C–C bonds. Alternatively, the organic sulfonyl anion is expelled when R^2 is a non-leaving group, like an alkyl substituent, leaving the R^1 radical 3. In a third situation, compound 1 may be attacked by an external radical species 4 that originates from a different mechanism if the excited photocatalyst does not directly activate sulfonyl compound 1. Through the creation of a C–C bond, this radical substitution produces product 5 while releasing the sulfonyl radical, which is then reduced to the subsequent sulfonyl anion through interaction with another intermediate.

A. Sulfonyl Chloride: By producing sulfonyl radicals when exposed to visible light, sulfonyl chlorides are frequently utilised as sulfonylation reagents. However, because fluoroalkylsulfonyl chlorides are so stable, desulfonylation usually results in the production of fluoroalkyl radicals. A photocatalytic technique for desulfonylative trifluoromethylation of C–H bonds in various heteroarenes (6 and 7) and unactivated arenes (8) was described by MacMillan in 2011. Opportunities for late-stage diversification were increased by this approach, which allowed physiologically active molecules to be selectively functionalised at locations of high electron density and possible regions of metabolic vulnerability.[5]

This technique can be used to functionalise a range of physiologically active compounds at high electron density and metabolic sensitivity locations. For example, the anti-Alzheimer's agent 13, the flavonoid 14, and the DNA base analogue 12 were all regionally selectively trifluoromethylated with exceptional efficiency, yielding 85–94%.[1]

B. Sulfinates: Although sulfinates are typically thought of as sulfonylation reagents, they can also undergo desulfonylation to serve as alkyl radical precursors. Moschitto showed that when exposed to visible light, alkyl sulfinates undergo desulfonylative alkylation of heteroarenes.

C. Sulfonamides: Because the N–S(O_2) link in sulfonamides is usually relatively stable, radical species usually begin a Smiles rearrangement during desulfonylative functionalisation. Using visible light-induced photoredox catalysis, Zhang (2016) reported an effective intramolecular aryl migration coupled with desulfonylation of sulfonamides. A specific reaction mechanism was suggested based on experimental results. In this reaction, a single electron transfer with the sulfonamide substrate creates a radical intermediate after the iridium photocatalyst is first activated under visible light irradiation.[7]

2.2 Decarboxylative Couplings

Both organic molecules and natural items frequently include carboxylic acids and their many derivatives, and their decarboxylative coupling processes have drawn a lot of interest. Recent developments in visible-light photoredox decarboxylative coupling are highlighted in this section, with particular attention on the creation of C–C and C–Y (Y = heteroatom) bonds.

A. Formation of C-C bond: Here, we go over how visible-light photoredox decarboxylative techniques, such as decarboxylative addition, alkynylation, alkenylation, allylation, and arylation, can produce C-C bonds. acceptors, 1-benzyl-1,4-dihydronicotinamide (BNAH) served as the reductant and $Ru(bpy)_3Cl_2$ as the photocatalyst. Under a nitrogen environment, the reaction proceeded in a THF–water mixture (7:3), yielding the desired product 3 [9]. This decarboxylative process was used by Overman and colleagues to synthesise (-) aplyviolene in its entirety. Using N,N-diisopropylethylamine (DIPEA) and a Hantzsch ester (HE) as reductants, compound 7 was created by visible light-mediated decarboxylative Michael addition of N-(acyloxy) phthalimide 5 to alkene 6. Compound 7 was discovered as a crucial intermediary in this work. The decarboxylation of 5 [9] resulted in the production of tertiary carbon radical 8, which carried out this transition.

B. Formation of C-Y bonds (Y=Heteroatoms): This section describes the visible-light photoredox decarboxylative formation of C-Y (Y=heteroatom) bonds, which includes the formation of C-H, C-N, C-S, C-Se, and C-F bonds.

C-H bond formation: Hydrodecarboxylation of carboxylic acids has gotten very little attention, despite the notable advancements in visible-light-driven decarboxylative coupling techniques. Using an acridinium (Acr) photoredox catalyst (PC = Mes-Acr-$Me^+BF_4^-$, Mes = 2,4,6-trimethylphenyl) in conjunction with bis(4-chlorophenyl) disulphide (DDDS) under visible light irradiation, Wallentin and colleagues established a decarboxylative reduction of carboxylic acids in 2014.[15].

Formation of C-N Bonds: Since natural products and pharmacologically active compounds frequently contain nitrogen-containing structures, it is extremely beneficial to develop effective C-N bond-forming techniques in mild environments. A photocatalytic method for decarboxylative C–N amination of arene and heteroarene substrates was reported by Sanford and associates in 2014. The nitrogen-centered radical intermediates that propel the transformation in this system are derived from trifluoromethylacyloxyphthalimide.[16].

2.3 Allylic Functionalization

In this regard, there has been a lot of interest in the combined application of Fukuzumi acridinium salts as visible-light photoredox catalysts that can remove electrons from olefins and cobalt (II/III) oximine complexes (cobaloximes) as proton acceptors [20]. Both catalytic hydrogen evolution and the direct functionalisation of unactivated alkenes are made possible by this dual system.

2.4 Dehydroxymethylation Pathways

Because of their distinct Ce(III)/Ce(IV) excitation routes, cerium-based compounds, which are both plentiful and reasonably priced, have been employed as well-organised photocatalysts. Numerous radical-mediated changes are carried out by these systems. Despite their widespread availability and frequent usage in synthesis, alcohols are rarely used directly as carbon synthons through the process of dehydroxymethylation, which removes one carbon atom as formaldehyde. Conventional methods frequently produce simple alkanes and rely on noble metals and exogenous oxidants. The Dong group created a Rhodium-catalyzed oxidative process that effectively and selectively transforms alcohols into alkenes in order to get around this restriction. Alcohols can be transformed into alkyl radicals via oxalate intermediates, according to more recent developments in photoredox catalysis. A wide range of alcohols, from basic ethanol to structurally complicated biomolecules, may now be mildly and effectively dehydroxymethylated using cerium photocatalysts. Numerous cross-coupling processes, such as alkylation, amination, hydrogenation, and oxidation, are made possible by this method.

2.5 Alkynylation via Photoredox Catalysis

Alkynes are extremely valuable compounds used in complex molecule synthesis, innovative materials, and pharmaceuticals. Their integration has historically relied on transition-metal-catalyzed Sonogashira coupling, which also necessitates high temperatures, certain ligands, and side reactions including homocoupling and β-hydride elimination. Recently, visible-light photoredox catalysis-based radical alkynylation techniques have become more popular as a way to get around these restrictions. Decarboxylative alkynylation of carboxylic acids, $C(sp^3)$–H alkynylation via benzophenone catalysis, and gold-catalyzed, sunlight-mediated alkynylation of amines are significant developments. Despite these advancements, tertiary $C(sp^3)$–C(sp) coupling is still very difficult to achieve. A possible answer is provided by tertiary alcohols, which are easily converted into radical precursors by oxalate derivatives. A technique for directly deoxyalkynylating tertiary alkyl caesium oxalates using EBX reagents has been devised based on the work of MacMillan and Overman. This technique produces high yields under benign and useful circumstances by using 4CzIPN as a photocatalyst in dichloromethane with DMF as an addition under blue LED irradiation. All things considered, photoredox-enabled alkynylation enhances traditional methods by expanding the range of $C(sp^3)$–C(sp) bond formation in a sustainable and straightforward way. A variety of organic photocatalysts, such as DCA, 4CzPN, Mes-$Acr^+ClO_4^-$, and Eosin Y, were examined for their capacity to produce the deoxyalkynylation process throughout the experimental investigations. Among these, 4CzIPN consistently produces the best yields, outperforming the others. This 4CzIPN performance highlights how important photocatalyst structure and redox potential are in controlling radical alkynylation efficiency.

2.6 Radical-Mediated C–C Bond Cleavage and Reorganization

Recently, visible-light photoredox catalysis has become well-known as a sustainable substitute for traditional thermal methods for C–C bond activation, which have poor selectivity and need severe conditions. Nitrogen-centered radicals (NCRs), particularly iminyl radicals, which can be produced under mild conditions from oxime esters or hydroxylamine derivatives by oxidative or reductive single-electron transfer (SET), are a particularly potent tactic. The generated iminyl radicals easily undergo β-C–C bond cleavage, which leads to ring-opening fragmentation and cyanoalkyl radicals. Because of their great versatility, these intermediates can be caught by a variety of π-systems, allowing for transformations including Heck-type olefinations, alkynylation, difluoroallylation, and sulfonylation. Among these, iminyl radical Heck couplings induced by visible light are significant because they offer direct access to functionalised alkenes with superior tolerance and selectivity for a variety of functional groups. The creation of a dual cobaloxime–photoredox catalytic system, in which α-imino-oxy acids undergo oxidative decarboxylation to produce iminyl radicals that support selective C–C bond clevage, is a significant advancement in this field. Cobalt captures the resulting alkyl radicals, allowing radical-olefin coupling and β-hydride elimination to give nitrile-substituted alkenes exceptional E-selectivity. Only CO2, H2, and acetone are released as non-hazardous byproducts as this reaction continues under visible light irradiation without the requirement for extra oxidants. This technique demonstrates a wide range of substrate tolerance, supporting aromatic, ester, and heteroaryl functionalities. It also emphasises the collaboration between cobaloxime and photoredox catalysis in promoting radical-mediated C–C bond cleavage and reorganisation. When combined, these techniques offer a strong foundation for the gentle and long-lasting synthesis of nitriles and functionalised alkenes.

3 - C–X (HETEROATOM) BOND FORMATION UNDER VISIBLE LIGHT

3.1 From Aryl Halides Reduction of aryl halides to aryl radicals

Aryl groups play a major role in organic synthesis and are widely used in innovative materials, medicines, and natural goods. The majority of arylation techniques used in the past relied on transition-metal catalysis, which is very efficient but necessitates costly catalysts, precisely calibrated ligands, and challenging reaction conditions. On the other hand, visible-light photoredox catalysis has become a more environmentally friendly and adaptable platform that enables the mild production of aryl radicals from low-cost raw materials. Among these, aryl halides are readily available and reasonably priced, making them appealing precursors. The scope of such conversions is limited by their high reduction potentials and the strength of the C–X (heteroatoms) bonds, especially in aryl chlorides, which present significant hurdles for conventional photocatalysts. [24]. The options available for aryl radical production have been greatly expanded by recent discoveries. Inert aryl chlorides can now be activated thanks to techniques like electron-primed photocatalysis and consecutive photoinduced electron transfer (conPET), which provide access to reduction potentials. These methods now enable net-reductive couplings under moderate settings by avoiding the inherent limits of traditional single-electron transfer procedures. This leads to great efficiency in a variety of transformations, such as hydroarylation, borylation, and other C-heteroatom bond forms. Together, these developments demonstrate visible light-mediated reduction of aryl halides as a robust and adaptable platform that not only solves long-standing problems but also broadens the synthetic C–C and C–heteroatom bond formation. [24].

C–X (B, C, O, P, S, Se) bond formation without external photocatalysts

Apart from photocatalyst-mediated reactions, a new idea is photocatalyst-free methedologies, in which aryl halides interact with visible light directly to conduct homolytic C–X bond cleavage. A variety of nucleophiles or radical acceptors can effectively trap the resultant aryl radicals, allowing for the formation of various C–X bonds, such as C–B, C–C, C–O, C–P, C–S, and C–Se bonds. These techniques demonstrate the inherent photoactivity of aryl halides and highlight their adaptability as radical precursors. Crucially, these approaches reduce reliance on costly transition-metal catalysts and external photocatalysts, offering more cost-effective, environmentally friendly, and straightforward methods for arylation processes.

3.2 C–F Bond Activation and Defluorinative Reactions (Ar-F bond formation)

3.2.1 Synthesis of Fluorinated Aromatic Compounds –

Various photocatalysts can be used to synthesise various fluorinated aromatic compounds. Fluoroalkyl groups have tremendous impacts on molecular characteristics, making their incorporation into organic molecules a highly significant alteration. In addition to increasing bioavailability and biological activity, such insertions usually improve lipophilicity, metabolic stability, and resistance to oxidative processes. Furthermore, fluoroalkyl substituents are particularly effective for medicines, agrochemicals, and innovative materials because they can provide water-repellent properties and general molecular resilience.

3.2.2 Radical routes for C-F cleavage (visible-light photoredox): One efficient technique for C-F bond cleavage is photocatalytic reduction. $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_4$, $Ir(ppy)_2(dtbbpy)PF_4$, 4CzIPN, 4DPAIPN, fac-$Ir(ppy)_3$, Rose Bengal (RB), Eosin Y, and $Ru(bpy)_3Cl_2$ are some of the catalysts that have been employed for this transition Polyfluorinated Arenes: The Weaver group demonstrated how photocatalytic C-F bond cleavage can substitute fluorine atoms in perfluorinated arenes with hydrogen, alkyl, alkenyl, or electron-rich aryl groups. The stronger reductant fac-$Ir(ppy)_3^-$ is produced when iPr_2NEt (DIPEA) single-electron reduces the excited fac-$Ir(ppy)_3$* under visible light

irradiation. This species produces perfluoroaryl radical anions by reducing perfluorinated arenes, which then push out fluoride to produce perfluoroaryl radicals. The resultant radicals can produce the hydrodefluorination (HDF) product by abstracting a hydrogen atom from the amine radical cation.

3.3 Thiol-yne and Thiol-ene Reactions

The important class of organosulfur compounds found in both nature and medicine is called thioethers. The significance of the C–S bond in pharmaceuticals is demonstrated by medications like ranitidine (anti-ulcer), butoconazole (antifungal), and montelukast (asthma therapy). Thioethers are crucial building blocks in material science because they are useful intermediates in synthetic chemistry for the synthesis of sulfoxides and sulfones. The thiol–ene/yne (hydrothiolation) reaction is a particularly useful technique for their synthesis because of its ease of usage and atom economy. Traditional radical-based techniques rely on UV or heat activation, which have adverse effects and low selectivity. Visible-light photoredox catalysis has been employed as a moderate and sustainable method to get over these restrictions. This technique has grown quickly since Yoon and Stephenson's initial contributions, offering effective and selective pathways to C-S bond production. With a focus on anti-Markovnikov and Markovnikov selectivity in synthetic approaches, this section summarises advancements in various techniques in visible-light photoredox-catalyzed thiol–ene/yne reactions.

3.4 Remote C–H Functionalization (Borylation and Heteroaromatic Systems)

Because they can change their functional groups, alkyl boronic esters are crucial intermediates in organic synthesis. Conventional approaches to their preparation include prefunctionalization and multistep processes, both of which are less effective. Direct C(sp^3)–H borylation, on the other hand, is an orthogonal and atom-efficient method. Although there have been several developments in C(sp^2)–H borylation, selective C(sp^3)–H borylation is still difficult to achieve, particularly at sterically hindered tertiary sites, because to factors like severe reaction conditions, dependence on directing groups, and catalyst deactivation. Imidazo[1,2-a] pyridines, on the other hand, are a significant class of heterocycles that include nitrogen and are frequently found in functional materials, natural goods, and medications. They have a wide range of biological actions, and this heterocycle is the source of various medications that are employed in clinical settings. Although functionalisation of these hetrocycles through C-H bond activation provides a straightforward and simple means to alter structures, current techniques frequently have drawbacks such the need for costly catalysts, strong oxidants, and limited sustainability. With the ability to selectively functionalise C–H through single-electron transfer (SET) routes in mild settings, photochemical techniques have recently surfaced as a more environmentally friendly and adaptable option.

4. APPLICATIONS IN BIOORTHOGONAL AND BIOLOGICAL SYSTEMS

The advancement of various photocatalysis techniques has increased its significance as a fundamental technique of contemporary synthesis. In order to excite electrons that can initiate single-electron transfer (SET) or energy transfer (EnT) reactions, photocatalysts absorb visible light. $[Ru(bpy)_3]^{2+}$ is a simple example that can function as both an oxidant and a reductant. Mildness, chemoselectivity, and compatibility with biological and aqueous environments are the main benefits of photocatalysis. These characteristics are utilised in biological applications as well as complicated chemical production, where photocatalysis serves as a link between biology and chemistry.

4.1 Initial Applications – Photodynamic Therapy (PDT).

Ancient light-based treatments evolved into contemporary photodynamic therapy (PDT), which uses photosensitisers to produce reactive oxygen species (ROS) to cause cytotoxicity, primarily in the treatment of cancer. Although porphyrin dyes are the most common, metal-based compounds have better stability and photophysical characteristics. Despite certain drawbacks, such as oxygen dependence, promote alternate photocatalytic approaches, such as photoactivated chemotherapy (PACT) or mitochondrial-targeted Ir(III) complexes that oxidise NADH. These established the foundation for biological abiotic photocatalysis.

4.2 Net-Oxidative and Net-Reductive Processes.

Adapting photoredox chemistry to biological applications is the subject of recent developments. Using dyes like fluorescein, Chen's team created photocatalytic deboronative hydroxylations for drug uncaging in cells. Fox created far-red tetrazine oxidation for intracellular drug activation, whereas Zou and associates created a photo-release technique for anticancer medications under hypoxia. On the reductive side, Ru(II)-catalyzed azide reductions allowed for the selective uncaging of biomolecules and nucleic acid-templated imaging, which subsequently extended to subcellularly precise photocatalysis driven by proteins and RNA.

4.3. Covalent Biopolymer Modification.

Peptides, proteins, and nucleic acids can be selectively labelled and cross-linked by the use of photocatalysis in bioconjugation. While MacMillan created photoredox peptide cyclizations via decarboxylative radical chemistry, Kodadek employed $Ru(bpy)_3^{2+}$ for tyrosine oxidation. Tyrosine, tryptophan, cysteine, and histidine residues can be fluorescently tagged, cross-linked, and functionalised using these techniques. Fox's tetrazine-based cross-linking in living mice is one example of a live system that may benefit from this.

CONCLUSION

The subject of contemporary photoredox catalysis has grown significantly in just eight years, and numerous new activation platforms and synthetic transformations have been created. The capacity of photoredox catalysts to effectively transform visible light into chemical energy is essential to the advancement of these technologies. Additionally, the redox characteristics of metal polypyridyl photoredox catalysts can be readily adjusted to fit nearly any particular application by modifying the ligand backbone. Practically speaking, the chemical community has embraced photoredox catalysis quickly due to its accessibility to highly reactive radical intermediates from bench-stable precursors and its ease of reaction setup using basic home light sources. The toxicity of the tin reagents used as radical precursors has hampered earlier research on the production and reactivity of C-centered radicals. The range of techniques for native functionalisation has been expanded by recent developments in photoredox catalysis, which have shown that a wide variety of radical intermediates can be obtained from easily accessible chemicals like carboxylic acids and halides and, in certain situations, through direct homolysis of C-H bonds. Photoredox catalysis has shown exceptional efficacy in the creation of new redox-neutral reaction manifolds in addition to offering fresh access to the targeted radical intermediates. These features have led to the development of photoredox reactions, which make it possible to access new bond disconnections and streamline synthetic approaches.

By offering many techniques for a variety of bond-forming reactions under moderate and sustainable circumstances, photoredox catalysis has developed into a potent and environmentally friendly tool in contemporary organic synthesis. The various advancements in photoredox techniques covered in this review demonstrate how visible-light-mediated ideas, such as desulfonylation, decarboxylation, defluorinative techniques, allylic functionalisation, and radical-mediated pathways, have broadened the range of C–C and C–X bond constructions. In addition to providing a more environmentally friendly alternative to conventional transition-metal catalysis, these techniques also create new opportunities for the late-stage functionalisation of intricate bioactive compounds.

Photoredox catalysis has stronger ties to bioorthogonal chemistry and biological applications in addition to synthetic applications, demonstrating its potential in drug development, bioconjugation, and photodynamic treatment. Despite the impressive advancements, there are still several issues, including compatibility with highly functionalised substrates, energy efficiency, scalability, and catalyst design. The adoption of these techniques in academia and industry is anticipated to be further accelerated by future developments in this field that concentrate on naturally occurring photocatalysts, visible to near-IR light reactions, and the relationship between chemistry and dual catalysis. However, photoredox catalysis's ongoing progress will not only advance various synthetic chemistry techniques but also broaden its uses in biological systems, materials science, and medicines.

REFERENCES

1. Xu, Xiaohong, et al. “Recent Advances in C–C Bond Formation via Visible Light-Mediated Desulfonylation and Its Application in the Modification of Biologically Active Compounds.” Molecules, vol. 29, no. 23, Nov. 2024,p. 5553.
2. Lan, Jihong, et al. “Visible-Light Photocatalytic Reduction of Aryl Halides as a Source of Aryl Radicals.” Molecules, vol. 27, no. 17, Aug. 2022, p. 5364.
3. Laha, Ramkrishna, et al. “Desulfinative Alkylation of Heteroarenes via an Electrostatic Electron Donor–Acceptor Complex.” Organic Letters, vol. 24, no. 40, Oct. 2022, pp. 7394– 99.
4. Liu, Yang, et al. “Visible-Light Photoredox Catalyzed Dehydrogenative Synthesis of Allylic Carboxylates From Styrenes.” Organic Letters, vol. 23, no. 11, May 2021, pp. 4441–46.
5. Zhang, Kaining, et al. “Dehydroxymethylation of Alcohols Enabled by Cerium Photocatalysis.” Journal of the American Chemical Society, vol. 141, no. 26, June 2019, pp. 10556–64.
6. Li, Muzi, et al. “Visible-Light-Mediated Deoxyalkynylation of Activated Tertiary Alcohols.” The Journal of Organic Chemistry, vol. 86, no. 17, Aug. 2021, pp. 12386–93.
7. “Visible-Light Photocatalytic Reduction of Aryl Halides as a Source of Aryl Radicals.” Molecules, vol. 27, no. 17, Aug. 2022, p. 5364.
8. Singh, Jitender, et al. “Visible Light Induced Photocatalyst - Free C−X (X=B, C, O, P,S, Se) Bond Formation of Aryl Halides.” Advanced Synthesis & Catalysis, vol. 366, no. 8, Feb. 2024, pp. 1719–37.
9. Kliś, Tomasz. “Visible-Light Photoredox Catalysis for the Synthesis of Fluorinated Aromatic Compounds.” Catalysts, vol. 13, no. 1, Jan. 2023, p. 94.
10. Ye, Y.; Sanford, M.S. Merging visible-light photocatalysis and transition-metal catalysis in the copper-catalyzed trifluoromethylation of boronic acids with CF3I. J. Am. Chem. Soc. 2012
11. Yin, D.; Su, D.; Jin, J. Photoredox catalytic trifluoromethylation and perfluoroalkylation of arenes using trifluoroacetic and related carboxylic acids. Cell Rep. Phys. Sci. 2020
12. Sap, Jeroen B. I., et al. “Organophotoredox Hydrodefluorination of Trifluoromethylarenes With Translational Applicability to Drug Discovery.” Journal of the American Chemical Society, vol. 142, no. 20, May 2020, pp. 9181– 87.
13. Xiao, Qian, et al. “Recent Advances in Visible-Light Photoredox Catalysis for the Thiol-Ene/Yne Reactions.”

Molecules, vol. 27, no. 3, Jan. 2022, p. 619.
14. Chalotra, Neha, et al. "Photoredox-Mediated Generation of gem-Difunctionalized Ketones: Synthesis of A,α-Aminothioketones." Organic Letters, vol. 21, no. 12, June 2019, pp. 4793– 97.
15. Cui, Huanhuan, et al. "Visible-light-induced Selective Synthesis of Sulfoxides From Alkenes and Thiols Using Air as the Oxidant." Green Chemistry, vol. 19, no. 15, Jan. 2017, pp. 3520–24. https://doi.org/10.1039/c7gc01416c.
16. Guerrero-Corella, Andrea, et al. "Thiol–ene/Oxidation Tandem Reaction Under Visible Light Photocatalysis: Synthesis of Alkyl Sulfoxides." Chemical Communications, vol. 53, no. 75, Jan. 2017, pp. 10463–66.
17. Singh, Manjula, et al. "Visible-light-activated Selective Synthesis of Sulfoxides via Thiol-ene/Oxidation Reaction Cascade." Tetrahedron Letters, vol. 59, no. 5, Dec. 2017, pp. 450–53.
18. Barman, Eliezer, et al. "Visible Light Photoredox-catalyzed Hydrothiolation of Enamides and Enecarbamates." Tetrahedron Letters, vol. 61, no. 32, July 2020, p. 152201.
19. He, Jiachen, and Silas P. Cook. "Metal-free, Photoinduced Remote C(Sp3)–H Borylation." Chemical Science, vol. 14, no. 35, Jan. 2023, pp. 9476–81.
20. Gao, Juanjuan, et al. "Recent Advances in Visible Light-Induced C-H Functionalization of Imidazo[1,2-a]Pyridines." Molecules, vol. 30, no. 3, Jan. 2025, p. 607.
21. Chang, Qing, et al. "Visible-Light-Induced Regioselective Cyanomethylation of Imidazopyridines and Its Application in Drug Synthesis." The Journal of Organic Chemistry, vol. 82, no. 10, May 2017, pp. 5391–97.
22. Huang, Huaiyi, et al. "Targeted Photoredox Catalysis in Cancer Cells." Nature Chemistry, vol. 11, no. 11, Sept. 2019, pp. 1041–48.