Journal Homepage: www.ijarpr.com ISSN: 3049-0103 (Online)

International Journal of Advance Research Publication and Reviews

Vol 03, Issue 10, pp 416-421, October, 2026

Photoredox Catalysis in Medicinal Chemistry: A Modern Approach to the Synthesis of Bioactive Molecules

Mr. Vinod Matole*, Miss. Shraddha Birajdar, Mr. Abhishek Kirkol, Miss. Asmita Kasture, Mr. Avinash Rajput, Miss. Aarti Deshmukh, Mr. Samarth Shinde

Shivai Charitable Trust's College of Pharmacy, Koregaonwadi Tal. Omerga Dist. Dharashiv-413606, Maharashtra India.

Email ID: matole7414@gmail.com

Abstract

Photoredox catalysis has developed from a specialized photochemical technique into a broadly useful platform for modern medicinal chemistry. By using light-activated catalysts to control single-electron or energy-transfer events, photoredox reactions can generate reactive intermediates under comparatively mild conditions. This capability enables carbon–carbon and carbon–heteroatom bond formation, C–H functionalization, reductive and oxidative coupling, heterocycle construction, late-stage diversification, and selective modification of complex drug-like molecules. These transformations are particularly valuable in medicinal chemistry because rapid preparation of structurally diverse analogues is central to structure–activity relationship studies and lead optimization. Visible-light photoredox chemistry can also complement conventional transition-metal catalysis and, in some cases, replace multistep functional-group manipulations with direct transformations. Organic photocatalysts, iridium and ruthenium complexes, semiconductor systems, and emerging earth-abundant-metal catalysts have all contributed to the field. Recent developments extend photoredox chemistry toward peptide functionalization, protein bioconjugation, isotopic labelling, DNA-encoded libraries, and chemical-biology applications. Despite its advantages, issues including photon penetration, reactor design, scale-up, catalyst cost, oxygen sensitivity, reproducibility, and photochemical safety remain important. This review discusses the principles, catalyst classes, reaction mechanisms, medicinal-chemistry applications, sustainability aspects, challenges, and future opportunities of photoredox catalysis, with emphasis on its role in the synthesis and diversification of bioactive molecules.

Keywords: Photoredox catalysis; visible light; medicinal chemistry; photocatalyst; radical chemistry; C–H functionalization; late-stage functionalization; drug discovery; bioactive molecules; green synthesis.

1. Introduction

Medicinal chemistry depends on the ability to construct and modify molecules rapidly while maintaining sufficient structural complexity and functional-group compatibility. Classical synthetic routes can become inefficient when a lead compound contains several sensitive groups or when an analogue must be prepared at a late stage of a project. Photoredox catalysis offers a complementary strategy because light can be used as an external source of energy to initiate electron-transfer or energy-transfer processes. Modern visible-light methods commonly employ a photocatalyst that absorbs light and reaches an electronically excited state capable of oxidizing or reducing a reaction partner.

The importance of this approach is linked to its ability to access radical intermediates under conditions that can be milder than many traditional radical-generating methods. Such intermediates can participate in bond-forming reactions that are difficult to accomplish using two-electron chemistry alone. Reviews in medicinal chemistry have highlighted applications including peptide functionalization, protein bioconjugation, C(sp3)–C(sp2) coupling, late-stage functionalization, isotopic labelling, and DNA-encoded library chemistry. Photoredox catalysis is therefore not simply a new method for making known structures; it can expand the accessible chemical space around biologically relevant scaffolds.

For pharmaceutical research, the most attractive feature is strategic flexibility. A complex molecule can sometimes be diversified without reconstructing its entire synthetic sequence. This can accelerate analogue generation and help medicinal chemists explore structure–activity relationships. At the same time, photoredox chemistry should be viewed as a toolbox rather than a universally superior replacement for conventional synthesis. Catalyst selection, irradiation wavelength, oxygen concentration, concentration, photon flux, solvent, and reactor geometry can strongly affect the outcome[1-2].

2. Fundamental Principles of Photoredox Catalysis

Photoredox catalysis combines photochemistry with redox chemistry. In a simplified cycle, a photocatalyst absorbs a photon and is promoted from its ground state to an excited state. The excited catalyst can then participate in single-electron transfer (SET) with a substrate, donor, or acceptor. The resulting radical or radical-ion intermediate undergoes bond formation, fragmentation, hydrogen-atom transfer, or another productive reaction step. Finally, a second electron-transfer event regenerates the ground-state catalyst.

Two broad catalytic modes are commonly considered. In oxidative quenching, the excited photocatalyst transfers an electron to an acceptor and the catalyst becomes oxidized. In reductive quenching, the excited catalyst accepts an electron from a donor and becomes reduced. The appropriate pathway depends on the redox potentials of the catalyst and reaction partners. Energy-transfer mechanisms provide another route in which the excited photocatalyst transfers energy rather than an electron.

Visible light is particularly attractive because it can provide sufficient excitation energy while being less energetic than ultraviolet radiation. Blue LEDs are frequently used, although green, red, or other wavelengths may be selected according to the absorption profile of the photocatalyst. The reaction vessel and light source are not passive components: distance from the lamp, photon flux, vessel geometry, stirring, and reaction concentration influence the amount of light reaching the reaction mixture[3-4].

3. Major Classes of Photocatalysts[5-7]

Photocatalysts used in synthetic photoredox chemistry can broadly be divided into transition-metal complexes, organic photocatalysts, and heterogeneous or emerging catalyst systems.

3.1 Transition-metal Photocatalyst

Polypyridyl complexes of ruthenium and iridium became important because their excited states can possess useful lifetimes and tunable redox properties. They have enabled numerous oxidative and reductive transformations. However, precious-metal content, cost, residual-metal concerns, and sustainability considerations motivate the development of alternatives.

3.2 Organic Photocatalyst

Organic dyes and donor–acceptor chromophores such as acridinium, cyanoarene, xanthene, and related systems can provide strong photoredox activity without precious metals. Their structural diversity allows tuning of absorption and redox properties. Organic photoredox chemistry has particular relevance to medicinal chemistry because metal-free methods can be attractive when metal contamination is undesirable.

3.3 Earth-abundant and heterogeneous systems

Copper, iron, nickel, cobalt, manganese, and other abundant elements are being investigated to reduce dependence on precious metals. Semiconductor and heterogeneous photocatalysts may facilitate catalyst recovery and alternative reactor configurations. Photoinduced ligand-to-metal charge transfer is also attracting attention because it can provide pathways for activation of otherwise challenging bonds.

4. General Mechanistic Pathways[8]

The central mechanistic event in many photoredox reactions is single-electron transfer. Following irradiation, the photocatalyst reaches an excited state with altered oxidation and reduction properties. Electron transfer can generate carbon-centred, nitrogen-centred, oxygen-centred, sulfur-centred, or halogen-derived radical intermediates. These species can then undergo addition, substitution, fragmentation, cyclization, coupling, or hydrogen-atom transfer.

Hydrogen-atom transfer is particularly useful for C–H functionalization. Instead of pre-installing a reactive functional group, a suitable C–H bond can be converted into a radical that subsequently reacts with another partner. The ability to functionalize aliphatic C–H bonds can be valuable for medicinal chemistry because many drug-like molecules contain numerous sp3-rich positions.

Photoredox reactions can also operate in combination with another catalytic cycle. In dual photoredox/transition-metal catalysis, light controls radical generation while a metal catalyst controls cross-coupling. This cooperative strategy has enabled bond constructions that are difficult through either catalytic mode alone.

5. Important Synthetic Transformations in Medicinal Chemistry[9-10]

5.1 C-C bond formation

Photoredox chemistry provides multiple routes to C–C bonds through radical addition, reductive coupling, decarboxylative coupling, and cross-coupling. These reactions are valuable for introducing alkyl, aryl, fluoroalkyl, and other fragments into drug-like scaffolds.

5.2 C-N, C-O and C-S bond formation

Nitrogen- and oxygen-containing groups are common in medicines. Photoredox methods can generate radicals or radical ions that react with amines, alcohol-derived species, heteroatoms, or activated partners. Such transformations can simplify access to medicinally important amination, etherification, and thioether products.

5.3 C-H Functionalization

Direct C–H functionalization is one of the most strategically important applications. It can reduce the need for prefunctionalized substrates and permit late-stage modification of complex molecules. Photoredox-enabled C–H activation may proceed through hydrogen-atom transfer, radical cation formation, or complementary catalytic mechanisms.

5.4 Heterocycle synthesis

Heterocycles dominate many bioactive molecules. Photoredox-induced cyclization and radical addition can generate rings under mild conditions and can tolerate functional groups that might be problematic under strongly acidic, basic, or high-temperature conditions.

5.5 Reductive and oxidative transformation

Light-driven electron transfer can replace some stoichiometric redox reagents. Depending on the catalyst and reaction partner, photoredox systems can promote reduction of activated substrates, oxidative coupling, deprotection-related processes, or radical precursor activation.

6. Role in Drug Discovery and Lead Optimization[11-12]

Medicinal chemistry requires repeated synthesis and testing of analogues. A method that permits selective modification of an existing scaffold can therefore have high practical value. Photoredox catalysis is particularly suited to late-stage functionalization, in which a biologically active or advanced intermediate is diversified near the end of a synthetic sequence.

Late-stage diversification can affect potency, selectivity, solubility, metabolic stability, lipophilicity, and other properties. For example, installation of a small alkyl group, halogen-containing fragment, heteroatom substituent, or isotopic label may produce an analogue with altered pharmacological behaviour without rebuilding the core structure.

Photoredox chemistry also supports the exploration of sp3-rich chemical space. Radical processes can introduce three-dimensionality and stereochemical complexity into aromatic or heteroaromatic scaffolds. This is relevant because increasing molecular three-dimensionality can help diversify the physical and biological properties of compound libraries.

Another emerging application is chemical biology. Mild photoredox conditions can be compatible with peptides and biomolecules, creating opportunities for site-selective labelling, bioconjugation, proximity labelling, and controlled modification of biological targets.

7. Natural Products and Complex Bioactive Molecules[13-14]

Natural products and natural-product-inspired scaffolds often contain dense functionality and stereochemical complexity. Photoredox catalysis has been incorporated into synthetic strategies for such structures through reductive couplings, radical cyclizations, C–H functionalization, fragmentation, and other bond-forming processes. The value of these methods lies not only in reaction yield but also in the ability to change retrosynthetic planning.

In complex-molecule synthesis, a photoredox step can sometimes merge fragments that would traditionally require several operations. Radical intermediates may also react selectively with unsaturated systems embedded in complex frameworks. This can reduce protecting-group manipulations and shorten routes.

For medicinal chemists, lessons from natural-product synthesis are transferable to the preparation of bioactive analogues. Reaction compatibility with functional groups and the ability to operate at a late synthetic stage are particularly important.

8. Sustainability and Green Chemistry Perspective[15-16]

Photoredox catalysis is often described as a sustainable technology because photons can act as traceless energy inputs and many reactions can be conducted at relatively mild temperature and pressure. Visible-light LEDs can provide efficient irradiation with lower heat generation than some conventional photochemical sources. Catalytic quantities of photocatalyst may replace stoichiometric oxidants or reductants in appropriate reactions.

Nevertheless, sustainability should be evaluated across the entire process. Precious-metal photocatalysts may create resource and purification concerns. Some organic dyes may have complex synthesis or limited recyclability. Solvent choice, reaction concentration, energy consumption of irradiation, catalyst loading, work-up, and purification all contribute to the environmental profile.

Flow photochemistry may improve photon utilization and heat management and can provide better control during scale-up. Immobilized or recyclable catalysts and earth-abundant-metal or metal-free systems are promising directions. Thus, the green value of photoredox chemistry depends on process design rather than simply on the use of visible light.

9. Applications beyond Small-Molecule Synthesis[17-18]

The influence of photoredox chemistry extends beyond traditional small-molecule synthesis. Photoredox methods have been applied to peptide functionalization and protein bioconjugation, where reaction conditions must be compatible with sensitive biomolecular structures. Selective radical generation can provide chemical handles for attaching probes or modifying specific residues.

Isotopic labelling is another important area. Photochemical strategies can facilitate incorporation of isotopes into complex molecules, supporting pharmacokinetic studies, metabolite identification, and mechanistic investigations. Photoredox concepts have also been integrated with DNA-encoded library technologies, where chemical diversity must be generated under DNA-compatible conditions.

The broader field of photochemistry in medicinal chemistry additionally includes photopharmacology, photocaging, and light-controlled biological activity. These areas are conceptually related but should be distinguished from photoredox synthesis: photoredox catalysis primarily uses light to drive chemical transformations, whereas photopharmacology uses light to control biological function or molecular conformation.

10. Challenges and Limitations[19]

Despite rapid progress, several limitations remain. First, light penetration decreases as solutions become more concentrated or optically dense, making direct translation from small laboratory scale to manufacturing scale nontrivial. Second, reaction performance may depend strongly on lamp wavelength, intensity, distance, vessel geometry, and stirring. Inadequate reporting of these parameters can reduce reproducibility.

Catalyst selection is another challenge. Precious-metal complexes can be expensive and may require stringent control of residual metals. Organic photocatalysts can overcome some of these concerns but may have limitations in absorption, stability, or redox range. Oxygen can either inhibit or intentionally participate in a reaction, so its role must be controlled.

Scale-up also raises photochemical safety and engineering issues. Heat generated by LEDs, oxygen-rich environments, solvent flammability, and reactor design must be considered. Pharmaceutical development further requires robust impurity control and demonstration that the process is reproducible at the intended scale.

Mechanistic complexity can make reaction optimization difficult. Excited-state pathways, radical chain processes, energy transfer, electron transfer, and catalyst deactivation can operate simultaneously. Advanced spectroscopic and kinetic studies are increasingly important for understanding these systems.

11. Future Perspectives[20]

The future of photoredox catalysis in medicinal chemistry is likely to involve increased integration with automation, high-throughput experimentation, flow reactors, computational catalyst design, and machine-learning-assisted reaction optimization. These technologies can systematically explore wavelength, catalyst, solvent, concentration, and stoichiometric variables.

A major direction is the development of catalysts based on abundant elements and metal-free chromophores. Improved understanding of excited-state properties and reaction kinetics should enable more predictable catalyst selection. Photoinduced ligand-to-metal charge transfer and other unconventional activation modes may expand access to strong radicals and inert bonds.

Another opportunity is selective modification of complex pharmaceuticals and biomolecules. Combining photoredox chemistry with enzyme catalysis, electrochemistry, transition-metal catalysis, or bioconjugation may generate new reaction platforms. In parallel, continuous-flow photochemistry could help overcome photon-penetration limitations and improve process control.

Ultimately, the strongest impact will come when photoredox reactions are selected because they solve a specific medicinal-chemistry problem better than available alternatives. The field is moving from proof-of-concept photochemistry toward predictable, scalable, and application-driven synthesis.

12. Conclusion

Photoredox catalysis has become an important component of modern synthetic and medicinal chemistry. Its ability to use light to regulate electron-transfer and energy-transfer events provides access to reactive intermediates under comparatively mild conditions. The resulting chemistry supports C–C and C–heteroatom bond formation, C–H functionalization, heterocycle construction, late-stage diversification, complex-molecule synthesis, and chemical-biology applications.

For drug discovery, the central advantage is strategic: photoredox methods can expand the range of transformations available for rapidly modifying drug-like molecules. This can accelerate analogue synthesis and broaden chemical-space exploration. However, the technology must be evaluated critically with respect to catalyst sustainability, reaction reproducibility, photon management, scale-up, safety, and purification.

Continued development of metal-free and earth-abundant photocatalysts, flow systems, mechanistic tools, and automated optimization is expected to strengthen the practical value of photoredox chemistry. With appropriate process design, photoredox catalysis has the potential to become not merely an alternative synthetic technique but a routine platform for generating and optimizing bioactive molecules.

13. References

1. Shaw MH, Twilton J, MacMillan DWC. Photoredox Catalysis in Organic Chemistry. J Org Chem. 2016;81(16):6898-6926. doi:10.1021/acs.joc.6b01449.

2. Narayanam JMR, Stephenson CRJ. Visible light photoredox catalysis: applications in organic synthesis. Chem Soc Rev. 2011;40:102-113. doi:10.1039/B913880N.

3. Bogdos MK, Pinard E, Murphy JA. Applications of organocatalysed visible-light photoredox reactions for medicinal chemistry. Beilstein J Org Chem. 2018;14:2035-2064. doi:10.3762/bjoc.14.179.

4. Skubi KL, Blum TR, Yoon TP. Dual catalytic photochemical processes. Chem Rev. 2016;116:10035-10074.

5. Prier CK, Rankic DA, MacMillan DWC. Visible light photoredox catalysis with transition metal complexes: applications in organic synthesis. Chem Rev. 2013;113:5322-5363.

6. Romero NA, Nicewicz DA. Organic photoredox catalysis. Chem Rev. 2016;116:10075-10166.

7. Nicholls TP, Leonori D, Bissember AC. Applications of visible light photoredox catalysis to the synthesis of natural products and related compounds.

J Chem Soc Perkin Trans 1 / Nat Prod Rep. 2016;33:1248-1254. doi:10.1039/C6NP00070C.

8. Cresswell AJ, Eey STC, Denmark SE. Catalytic, stereospecific synthesis of organoboron compounds using photoredox chemistry. Angew Chem Int Ed. 2015.

9. MacMillan DWC. Photoredox catalysis in the pharmaceutical industry. Chem Eng News / related industrial perspectives.

10. Skubi KL, Swords WB, Hofstetter H, Yoon TP. Combining photoredox and transition metal catalysis in organic synthesis. Chem Rev. 2021.

11. Pitre SP, Overman LE. Strategic Use of Visible-Light Photoredox Catalysis in Natural Product Synthesis. Chem Rev. 2022;122(2):1717-1751. doi:10.1021/acs.chemrev.1c00247.

12. Nocera DG. The merging of photochemistry and electrochemistry. J Am Chem Soc. 2012.

13. Twilton J, Le C, Zhang P, Shaw MH, Evans RW, MacMillan DWC. The merger of transition metal and photoredox catalysis. Nat Rev Chem. 2017;1:0052.

14. Huang X, Webster RD, Harrold ND, et al. Photoredox-catalyzed C-H functionalization reactions. Chem Rev. 2022;122 / related review literature.doi:10.1021/acs.chemrev.1c00311.

15. Visible-Light Photocatalysis as an Enabling Technology for Drug Discovery: A Paradigm Shift for Chemical Reactivity. ACS Med Chem Lett. 2020.

doi:10.1021/acsmedchemlett.0c00436.

16. Photochemistry in Medicinal Chemistry and Chemical Biology. 2024 review literature.

17. Yang Y, Huang X, Jin Y. Photoinduced ligand-to-metal charge transfer (LMCT) in organic synthesis: reaction modes and research advances. Chem Commun. 2025;61:1944-1961. doi:10.1039/D4CC06099G.

18. Huxter VM. Advancing Organic Photoredox Catalysis: Mechanistic Insight through Time-Resolved Spectroscopy. J Phys Chem Lett. 2024;15:7945-7953. doi:10.1021/acs.jpclett.4c00895.

19. Visible and Near-Infrared Photopharmacology: Wavelength-Redshift Strategies for Spatiotemporally Precise Therapeutics. J Med Chem. 2026;69(3):1878-1915. doi:10.1021/acs.jmedchem.5c02041.

20. Emerging Roles of Photoredox Catalysis in Biomedical Research. 2026.