Overview of green oxidation of benzyl and allyl H

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Abstract. This review focuses on green oxidation methods for benzylic and allylic C-H bonds. Traditional synthesis methods often require pre-introducing functional groups like halogens or hydroxyl groups to activate substrates. Such approaches are not only cumbersome but also pose environmental risks. In contrast, modern methods take advantage of the σ-π hyperconjugation effect, which facilitates the activation of benzylic and allylic C-H bonds. This allows for direct functionalization without pre-functionalization, aligning with the principles of green chemistry. Photocatalysis activates C-H bonds via hydrogen atom transfer (HAT) by exciting metal complexes through ligand-metal charge transfer (LMCT) and generates products in combination with green oxidants such as oxygen. Photoelectric cooperative catalysis integrates electrochemical and photochemical steps to break through the redox window limitations of single catalytic systems and achieve highly selective C-H functionalization. In terms of green oxidants, methanol as an oxygen source in electrochemical oxidation is compatible with various benzylic substrates containing functional groups, while water enables metal-free and oxidant-free carbonylation through radical-polar crossover mechanisms in photocatalysis. Challenges include nanosecond-scale radical lifetimes and low catalytic efficiency, mitigated by substrate-catalyst pre-coordination. Future directions involve dual-ligand design and "metal-photocatalyst-electrochemistry" ternary systems to enhance selectivity and atom economy for sustainable synthesis.

Keywords: Green oxidation, Photocatalysis, Photoelectric cooperative catalysis, Benzylic C-H bond; Allylic C-H bond.

1. Introduction

As early as 2011, Nerlis Paola Pájaro Castro et al. [1] proposed 12 fundamental principles, such as waste prevention, atomic economy, and the use of renewable materials, which have been widely applied in fields like medicine, agriculture, and chemical engineering. The chemical industry, as a foundational sector, is crucial for its sustainable development. Green chemical catalysis technology can help the chemical industry achieve sustainable development. At the same time, the technology meets society's demand for environmentally friendly and resource-saving solutions.

Benzene and propylene derivatives, as important basic chemical raw materials, have always occupied a wide and key application position in the industrial field. In traditional synthesis, functional groups such as halogen and hydroxyl need to be introduced in advance to activate the substrate and form C-H bonds for subsequent products. For example, toluene is first introduced with a chlorine atom through benzyl halogenation to form benzyl chloride, then the chlorine atom is converted into a hydroxyl group via hydrolysis, or it can be transformed into a cyano group through cyanidation. These approaches are used to introduce various functional groups. Ultimately, they help convert toluene into high-value-added products. However, in modern processes, people utilize the feature that the σ-π hyperconjugation effect reduces the bond energy of benzylic and allylic C-H bonds and enhances their reactivity. This allows for the direct formation of new bonds through oxidation or functionalization reactions. Such an approach avoids pre-functionalization and aligns with the principles of green chemistry.

In this paper, several green chemical methods based on photocatalysis and photoelectric synergy to break C-H and will be introduced. The generated free radicals can be directly oxidized by green and safe oxidants to further generate the target products. Compared to traditional catalysts that rely on scarce precious metals (such as platinum and palladium), these methods have more abundant

sources, effectively reducing costs and avoiding the risk of heavy metal pollution. They are safe to use and represent the cutting-edge direction in current catalysis, bringing new solutions to industries such as chemical and energy.

2. Different Types of Catalysis

2.1. Photocatalysis

Photocatalysis is a hot field in the field of chemistry in recent years. The advantages of photocatalytic reactions under mild conditions avoid the disadvantages of high temperature, high pressure and many chemical oxidants or reductants used in traditional chemical synthesis. It has a wide range of substrates and important application value in medicine, pesticides, fine chemicals and other fields.

The mechanism of photocatalysis typically involves the LMCT process when a photocatalyst absorbs photons: in metal complexes, electrons transfer from the ligand's orbitals to the empty orbitals of the central metal, causing the complex to enter an excited state. The excited state of the catalyst can activate the C-H bond of the substrate through HAT, generating free radicals that then trigger subsequent reactions.

The photocatalytic improvement of traditional processes by Chang-Cheng Wang et al. [2] is used as an example. In the industrial preparation of benzoic acid and polycarboxylic acids (BPCAs), deep oxidation of polyalkylbenzenes is primarily used. The traditional Amoco process employs liquid-phase aerobic oxidation in an acetic acid medium using a homogeneous Co-Mn-Br catalyst system, as shown in Fig1.(b). Under this system, bromine may exist in some unstable form in reaction intermediates or products. As the reaction progresses under certain conditions, these brominated substances can undergo decomposition or transformation reactions, releasing MeBr which depletes the ozone layer and corrodes production equipment. The team used $CeCl_3$ as the HAT catalyst and oxygen as the sole terminal oxidant, avoiding the use of brominated transition metal catalysts. As shown in Fig 1. (c) and (d), under light conditions, alcohols react with $CeCl_3$ to form Ce (IV)-alcohol salt intermediates. These intermediates then participate in a photoinduced ligand - metal charge transfer (LMCT) process, generating electrophilic alkoxyl radicals. The resulting radicals have high reactivity and can abstract hydrogen atoms from the C - H bond of benzyl groups, forming benzyl radicals. This step is the starting point of the entire photocatalytic reaction, where light excitation provides energy for the reaction, promoting the cleavage of chemical bonds and the formation of radicals. The free radicals could be oxidized to the final products by oxidants. In this experiment, oxygen was used as the only oxidant to gradually oxidize toluene and its derivatives into benzoic acid or benzoic acid.

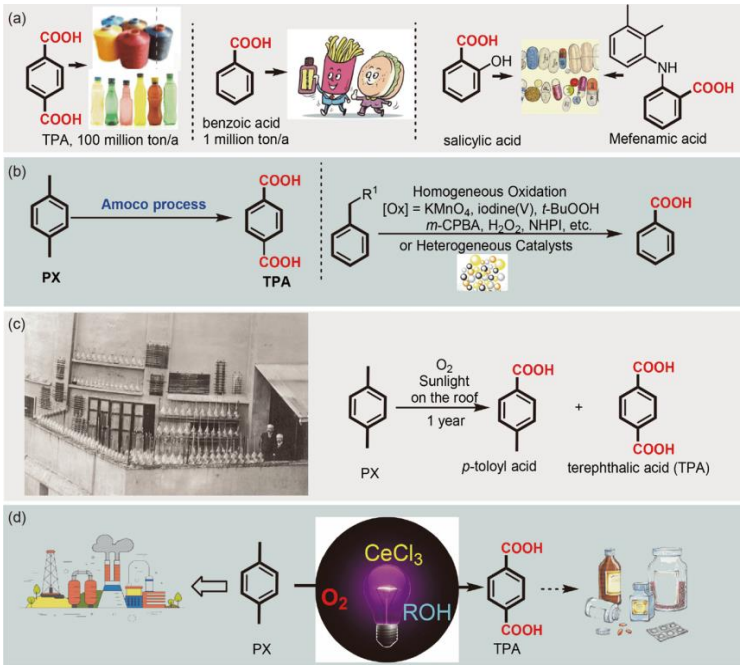

Figure 1. Photocatalysis plays a unique role in the preparation of terephthalic acid (TPA) and related chemical reactions, emerging as a key area for exploring new synthesis pathways of TPA. (a)TPA has a considerable annual output and is used in plastic products. (b) The traditional Amoco process. (c) A photocatalysis-related experiment conducted on the roof, as well as the reaction where PX generates p-methylbenzoyl acid and TPA under the action of light and oxygen. (d) Photocatalytic aromatic radical travel process

2.2. Photoelectric cooperative catalysis

In the pursuit of efficient and sustainable chemical synthesis, photoelectric cooperative catalysis has emerged as a frontier strategy, integrating light-driven electron transfer and catalytic activation to unlock novel reaction pathways. Shangze Wu et al. [3] introduced photoelectric cooperative catalysis in detail.

2.2.1. Reasons for combining light and electricity

1) Limitations of the REDOX capacity of photocatalysts

Photo-redox catalysis (PRC) reactions are limited by the redox window of the photocatalyst, which is the range of potentials where redox reactions can occur. Most visible light photons have energy that determines their redox capability, typically ranging from about 1.8 to 3.1 eV, making it difficult to achieve high-energy redox reactions. Besides, while UV photons can overcome the energy limitation, they come with many drawbacks, such as low reactor energy efficiency, high costs, safety risks, and direct excitation of substrate molecules, leading to harmful reaction pathways. Other methods, like multi-photon processes, often require large amounts of sacrificial oxidants or reductants to generate active catalyst forms or regenerate "exhausted" photocatalysts.

2) Electrodes lack selectivity

In electrolytic cell reactions, since electrodes can usually only distinguish different reaction components based on their inherent thermodynamic redox potentials and cannot make more precise differentiations, issues such as over - oxidation, over - reduction, and solvent - involved redox processes are likely to occur during the reaction, thus interfering with the progress of the main reaction.

2.2.2. Advantages of photoelectric synergy

1) Overcoming Traditional Photocatalytic Redox Limitations

E-PRC (Electrochemical-Photochemical Reaction Cycle) combines electrochemical and photochemical processes within a single catalytic cycle. By using electro-generated radical ions as

photocatalysts, it enables super oxidation and reduction reactions, breaking through the redox limitations of traditional photocatalysis. This allows reactions to occur beyond the individual redox windows of photocatalysis or synthetic electrochemistry.

2) Mild and Selective Photocatalytic HAT Reactions

Traditional photocatalytic single-electron transfer (SET) redox reactions often require high redox potentials to cleave certain chemical bonds or generate specific radicals. However, high redox potentials lead to strict reaction conditions, potential over-oxidation or -reduction of substrates, unwanted side reactions, and higher demands on equipment and catalysts. In contrast, photocatalytic hydrogen atom transfer (HAT) reactions use a milder approach. They activate HAT reagents through light excitation to abstract hydrogen atoms from substrate C-H bonds, generating specific radicals. As illustrated in Fig.2, light ("hv") removes electrons from chlorinated species, producing chlorine radicals. With bond energy (BDE) data for different substrates provided, the photocatalyst selectively targets bonds within specific energy ranges, precisely activating desired bonds while minimizing damage to others, thus enhancing reaction selectivity.

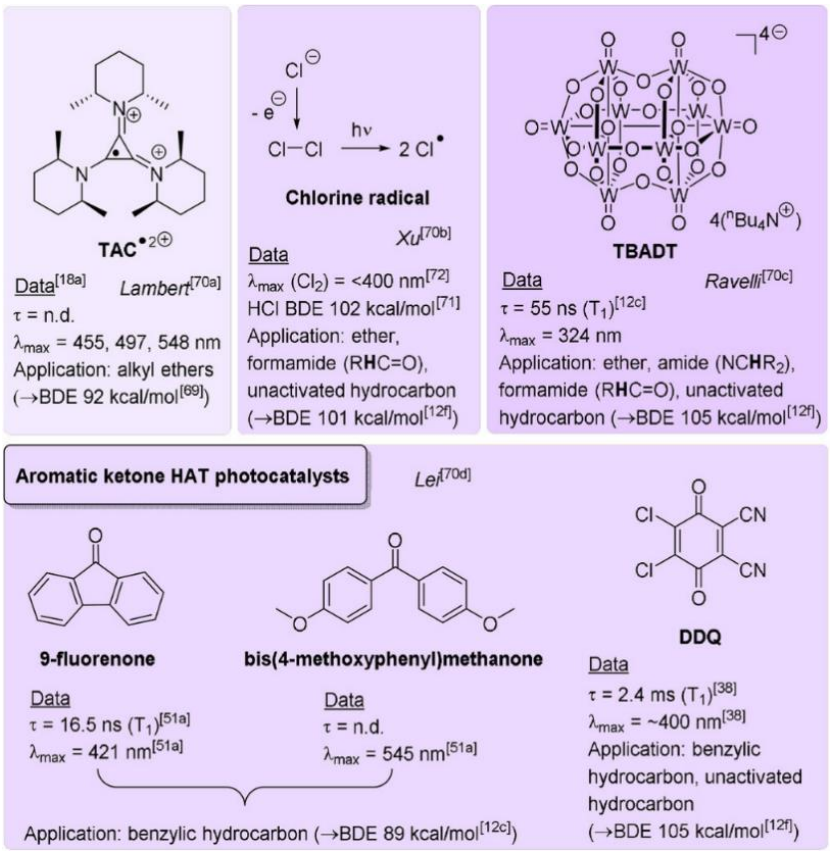

Figure 2. Different photocatalysts work for specific types of substrates, such as photocatalytic HAT reagent 9-benzyl ketone (9-fluorenone), has a λ max of 421 nm for benzyl hydrocarbon, indicating that the reagent is excited at 421nm light, with a τ of 16.5 ns and BDE of about 89 kcal/mol.

2.3. `Optical synergy and metal catalysis

Numerous studies have shown that non-noble metal and photoelectric synergistic catalysis systems exhibit potential to outperform traditional noble metal catalysis systems in terms of reaction efficiency and economy.

Referring to iron catalytic reactions, Hao Wu et al [4] mentioned that traditional photocatalytic systems using transition metals such as iridium (Ir) or ruthenium (Ru) may not be the optimal choice, and the catalytic efficiency is not as good as that of non-noble metals. Jagrit Grover et al. [5] noted that both iron and copper can be used as catalysts to produce benzyl and allyl radicals. Zhengjia Shen et al. [6] Also mentioned the synergistic catalysis of iron-nickel and copper-rhenium was also mentioned to further enhance the reaction rate.

2.4. Green oxidant

Meng Xue et al. [7] discovered that the application of oxygen in electrochemical oxidation is fraught with limitations. For instance, it often necessitates the use of hazardous electrolytes. Considering these drawbacks, the development of more practical oxidants becomes imperative.

2.4.1. Using methanol as an oxygen source

During Meng Xue et al. [7]'s research, they identified methanol as an oxygen source that demonstrates excellent compatibility with a diverse array of substrates. The study further reveals that this reaction exhibits a broad scope of application, being applicable to numerous compounds featuring benzyl C-H bonds. This includes substrates adorned with various substituents and functional groups.

As depicted in Fig. 4, regardless of whether the substrates possess long-chain alkyl groups, cyclic structures, or contain functional groups such as halogen atoms, carbonyl groups, ester groups, or boronic acid groups, they can all smoothly participate in the reaction, yielding the corresponding ketone products. This characteristic endows the reaction with greater promise in the realm of organic synthesis, enabling it to fulfill the synthesis requirements of compounds with disparate structures.

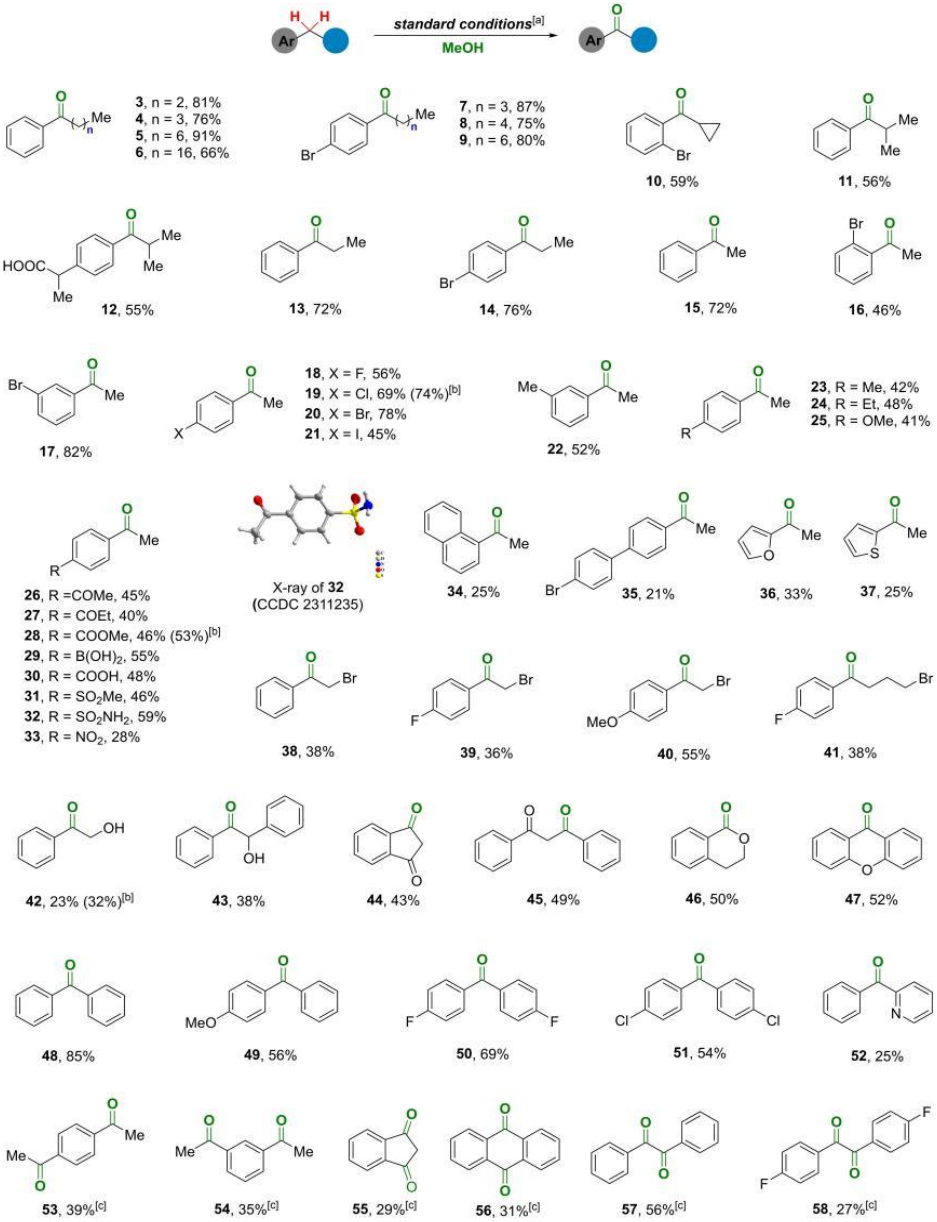

Figure 3. In the figure, it is shown that a variety of different structured substrates can react with methanol under standard conditions and produce corresponding ketones with certain yields, indicating that long-chain alkyl and cyclic structures can participate in the reaction smoothly.

At the same time, using anhydrous systems and argon atmosphere protection ensures high methanol concentration and activity. The reaction also involves a series of radical steps. In anhydrous methanol, the generation and stable presence of bromine radicals are more favorable.

2.4.2. Using Water as an oxygen source

Xiaona Yang et al. [8] introduced a visible light-mediated and metal-free method for the transformation of benzyl and allyl C-H bonds is described. The reaction conditions are mild and can be carried out at room temperature without additional heating, pressurization or complex electrode devices. As shown in Fig.4 (c), 4CzIPN acts as an organic photocatalyst that absorbs blue light and becomes excited, generating thiol radicals to participate in the formation of benzyl and allyl radicals. Water acts as a nucleophile, attacking the benzyl/allyl cations to form an intermediate alcohol. 4CzIPN then absorbs visible light and enters an excited state, acting as an oxidant to abstract electrons from the alcohol intermediate, forming alkoxy radicals and reduced photocatalysts. Through intramolecular HAT processes, the alkoxy radicals directly abstract hydrogen atoms from adjacent carbons to form aldehydes or ketones. Since water is a mild oxidizing agent, aldehydes can remain stable without being oxidized into acids.

This experiment found that all kinds of ethylbenzene derivatives, whether the aromatic ring is electron-rich or electron-deficient substituents, could be successfully reacting to produce corresponding ketone products, showing high selectivity and good functional group compatibility of this method.

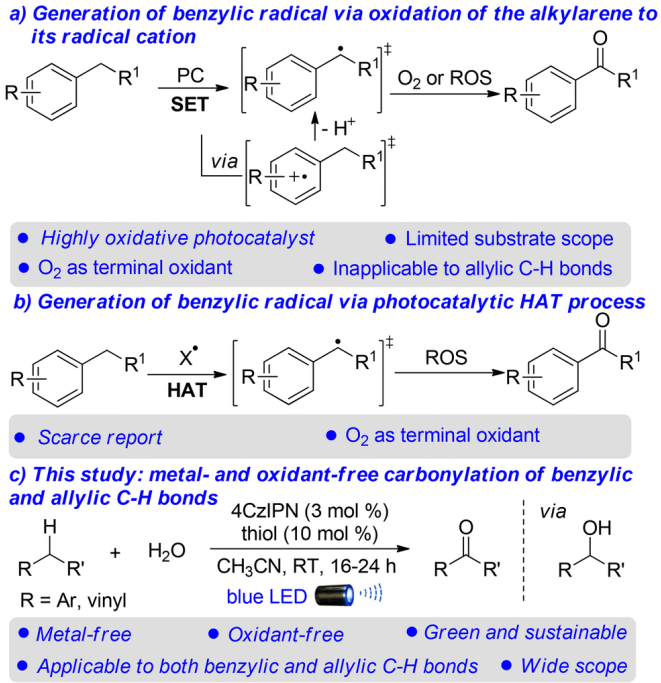

Figure 4. (a) shows a way only applicable to alkyl aromatics and completely incompatible with allylic C-H bonds, prone to conjugate isomerization. (b) shows a way theoretically can act on allylic C-H bonds, but there are very few actual research reports. Its universality and selectivity lack verification, and the presence of double bonds easily causes side reactions such as addition or isomerization. (c) This study clearly indicates that it is applicable to benzyl and allyl C-H bonds, expanding the range of substrate types that can be reached.

3. Discussion

At present, there are still many issues in the field of photocatalysis. For example, the life span of excited free radical ions is very short, and it is difficult to achieve effective reaction through diffusion control. It needs to rely on the pre-coordination of substrate and catalyst to overcome, but the mechanism and structural characterization of pre-coordination still need further study.

Alexander Reichle and Oliver Reiser [9] have discovered the pre-donation of ligands to copper (II) complexes and the photoinduced disproportionation (LIH) mechanism: through ligand exchange, Cu (II)-substrate complexes, such as Cu(II)-benzyl complexes, are formed. Ligand-metal charge transfer (LMCT) is utilized to trigger photoinduced disproportionation, generating Cu(I) and substrate radicals. The pre-donation effect enhances the binding of radicals to the metal center via intramolecular interactions, inhibiting the rapid recombination of radicals with Cu (I). At the same time, external oxidants, such as O_2, regenerate Cu (II), maintaining the catalytic cycle, capturing the formation of peroxide intermediates, and preventing the meaningless consumption of radicals, indirectly extending their effective lifespan. Yinwei Wang et al. [10] synthesizedthe pyrene-rich conjugated organic framework (COFs) QM-Py4P which can interact with free radicals through π-π interactions. This interaction stabilizes the radicals and extends their lifetime. In the photocatalytic oxidation of toluene, such stabilization promotes the activation of C−H bonds and enhances the catalytic effect.

In the future, research can focus on developing dual ligands. Combine the redox activity of metal centers with the π-π stacking/electronic interactions of framework materials (e.g., Cu-COF composites). This will realize the integration of radical generation, stabilization, and reaction. Additionally, we can explore "metal-photocatalyst-electrochemistry" ternary systems to break through the limitations of traditional single catalysis and further enhance selectivity and efficiency.

4. Conclusion

This review systematically summarizes the cutting-edge advancements in green oxidation of benzylic and allylic C-H bonds, with a focus on the core mechanisms of photocatalysis, photoelectric cooperative catalysis, and other technologies that avoid pre-functionalization steps like halogenation in traditional synthesis. Photocatalytic systems activate C-H bonds via hydrogen atom transfer (HAT) through ligand-metal charge transfer (LMCT) excitation of metal complexes, combined with green oxidants such as oxygen to generate carboxylic acids, ketones, and other products. Photoelectric cooperative catalysis breaks through the redox window limitations of single catalytic systems by coupling electrochemical and photochemical steps, such as using electrodes to regulate radical ion generation pathways and combining light excitation for highly selective C-H functionalization, thus addressing over-oxidation issues in traditional electrolysis reactions. In the field of photo-synergy and metal catalysis, traditional photocatalytic systems centered on noble metals such as iridium and ruthenium have limitations, with their catalytic efficiency being inferior to that of non-noble metals like iron and copper. Studies have shown that Fe and Cu can directly generate benzylic and allylic radicals, while metal synergistic catalysis modes such as Fe-Ni and Cu-Re further enhance the reaction rate. This provides a new pathway for reducing costs and minimizing heavy metal pollution, demonstrating the potential of non-noble metals in green catalysis.

In the application of green oxidants, methanol as an oxygen source demonstrates compatibility with various benzylic substrates in electrochemical oxidation, while water enables metal-free and oxidant-free carbonylation through radical-polar crossover mechanisms in photocatalysis, expanding the substrate scope.

Current challenges focus on the short lifetime of radical intermediates and low catalytic cycle efficiency, which rely on pre-coordination of substrates with catalysts to inhibit recombination. Future research may integrate the redox activity of metal centers with the π-π stacking effects of conjugated organic frameworks through dual-ligand design to achieve integrated regulation of radical "generation-stabilization-reaction". Additionally, the development of "metal-photocatalyst-electrochemistry" ternary systems holds promise to overcome the limitations of traditional single-catalysis modes through multi-field synergy like light excitation, potential regulation and ligand field effects, further enhancing reaction selectivity and atom economy to provide more efficient solutions for sustainable chemical synthesis.

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