

REVIEW

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Recent developments in alkene oxo-functionalization reactions governed by photoredox methods

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Alkene oxo-functionalization reactions have emerged as a powerful tool in modern synthetic organic chemistry, enabling the sequential formation of carbonyl (C=O) and various C–R bonds (R = alkyl, aryl, oxygen-, sulfur-, nitrogen- or phosphorus-compounds). Recent advances in photoredox catalysis have propelled the development of these transformations by enabling the use of mild, selective, and sustainable reaction conditions. This review provides an analysis of recent methods for alkene oxo-functionalization under photoredox conditions, with a focus on the synthesis of multifunctionalized products through single and tandem processes. Mechanistic insights into radical generation, photoexcitation pathways and oxygen sources are discussed to highlight the unique role of photoredox catalysis in these transformations. Additionally, we examine the substrate scope, functional group tolerance, and potential applications of these reactions in complex molecule synthesis and drug development. Finally, current challenges and future perspectives in the field are discussed, emphasizing how innovative photoredox approaches continue to expand new opportunities for the selective construction of C=O and C–R bonds in organic synthesis.

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1. Introduction

The carbonyl group is one of the most fundamental and versatile units in organic chemistry because it is present in many functional groups, such as amides, carboxylic acids, carba-

mates and ketones. Its significance extends from basic concepts taught in undergraduate courses to advanced applications in fields such as materials science, biochemistry, and drug development. Among carbonyl-containing functional groups, ketones play a central role in both industrial and medicinal chemistry. For example, acetone is the simplest ketone and it is obtained along with phenol *via* the Hock process,¹ which is one of the most significant methods in the chemical industry. On the other hand, the ability of ketones to participate in hydrogen bonding and dipole–dipole interactions,

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Yingmin Ji

Yingmin Ji received her BSc in Chemistry at UAB in 2023. One year later, she defended her Master's thesis at UAB in the CatSyNanoMat group. Afterwards, she enrolled in the PhD program at UAB under the supervision of Prof. A. Vallribera and Dr A. Granados, where she is studying novel photoinduced transformations.

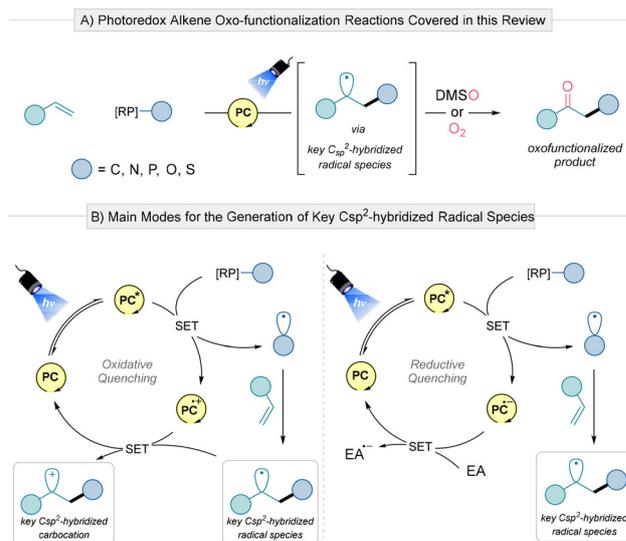


along with their polarity,² makes them essential for modulating the molecular properties of drug candidates.³

Typical synthetic routes for preparing ketones include the oxidation of secondary alcohols,⁴ Friedel–Crafts acylation reactions,⁵ hydration of alkynes,⁶ ozonolysis,⁷ and Wacker-type oxidation of alkenes,⁸ among others. The continuous development of new methods is crucial for advancing both industrial applications and pharmaceutical research.

The implementation of photoredox catalysis in organic synthesis has undoubtedly contributed to the construction of new chemical bonds, ushering in a new golden era of radical chemistry.⁹ A key factor driving the rapid growth of this technology is the ability of organic dyes and polypyridyl complexes to facilitate the conversion of visible light into chemical energy under mild reaction conditions, typically using light-emitting diodes (LEDs). Particularly, photocatalytic methods have significantly advanced the field of alkene 1,2-difunctionalization reactions by offering a sustainable and versatile platform for introducing two functional groups across a double bond in a single step.¹⁰ These methods, driven by visible light and facilitated by organophotoredox catalysts or transition-metal complexes, have enabled a broad range of transformations, including oxy-amination,¹¹ diamination,¹² carbo-amination,¹³ and dicarbofunctionalization,¹⁴ among others. These reactions typically proceed by energy transfer¹⁵ or photoredox mechanisms,¹⁶ involving radical or radical–polar crossover pathways, all initiated by the excited state of the photocatalyst. This generates reactive intermediates that enable the precise and regioselective incorporation of functional groups under mild reaction conditions. It is worthwhile to recognize innovative and photoactive electron-donor–acceptor (EDA) complexes applied to alkene 1,2-difunctionalization.¹⁷

Despite significant advancements in photoredox-mediated alkene 1,2-difunctionalization reactions, recent reviews¹⁸ do not cover alkene oxo-functionalization reactions. Remarkably, the preparation of such functionalized ketones governed by



Scheme 1 (A) Reaction design to access oxo-functionalized organic compounds *via* photoredox catalysis covered in this review. (B) Main reactivity modes for the generation of the key C_{sp}²-hybridized radical intermediate. RP = radical precursor. EA = electron-acceptor.

photoredox methods has the potential for building high molecular complexity from simple and readily available starting materials, which commonly are the corresponding redox-active species and the olefinic organic skeleton. Importantly, these photoredox approaches are governed by single-electron transfer (SET) processes. Therefore, this review offers a comprehensive guide to designing alkene oxo-functionalization strategies, emphasizing the sequential formation of C=O and C–R (R = C, N, P, O or S) bonds through photoredox chemistry (Scheme 1A). Under a suitable set of reaction conditions, a key C_{sp}²-hybridized radical species (Scheme 1A) can be generated and employed to access oxo-functionalized organic molecules. Most studies in this arena are designed around reductive or



Albert Gallego-Gamo

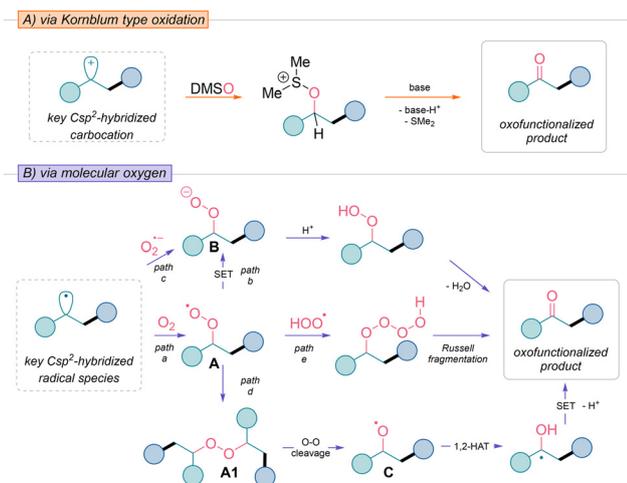
Albert Gallego-Gamo received his BSc in Chemistry in 2020 at UAB. In 2021, he defended his Master's thesis in the CatSyNanoMat group at UAB. Currently, he is a PhD student under the supervision of Dr C. Gimbert-Suriñach and Prof. A. Vallribera, working on the development of novel organic photoactive materials and photo-induced transformations. In 2024, he spent three months working in the Procter lab as a visiting student.



Carolina Gimbert-Suriñach

Dr Carolina Gimbert-Suriñach obtained her PhD at UAB under the supervision of Prof. A. Vallribera. After one year as an assistant professor at the same university, she moved to UNSW to undertake postdoctoral research with Prof. S. B. Colbran. She then worked at ICIQ in Prof. A. Llobet's group as a postdoctoral fellow and research group coordinator. After a short stay at UB as a Serra Hünter professor, she started as a Ramón y Cajal fellow and co-leader of the CatSyNanoMat group at UAB in 2021. She was promoted to Associate Professor of Organic Chemistry in 2023.





Scheme 2 Access to oxo-functionalized compounds *via* (A) a Kornblum-type oxidation process or (B) a molecular oxygen mechanism from the key Csp²-hybridized radical.

oxidative quenching photoredox cycles⁹ to access the Csp²-hybridized radical (Scheme 1B), which is ultimately oxidized to the corresponding carbonyl compound. Typically, carbonyl formation under these photoredox conditions is achieved using non-toxic oxidants such as dimethyl sulfoxide (DMSO) or molecular oxygen (O₂) (Scheme 2). Oxidation with DMSO proceeds *via* a photoredox radical/polar crossover mechanism. Here, the key Csp²-hybridized radical species is first oxidized by the photoredox cycle to the corresponding carbocation, which then reacts with DMSO, followed by a deprotonation process, analogous to the Kornblum oxidation (Scheme 2A). In contrast, oxidations utilizing molecular oxygen are proposed to proceed through distinct mechanistic pathways, as illustrated in Scheme 2B. The C-centered radical can react with O₂ (path

a) to form the alkyl peroxy radical intermediate **A**, which may then be reduced to the anion (**B**). Following protonation and dehydration, the desired carbonyl compound is obtained. Alternatively, the anionic species **B** may also be produced directly from the initial radical through reaction with superoxide (path c). Additionally, the alkyl peroxy radical **A** can undergo additional transformations, including trapping with the hydroperoxy radical (path e) to produce an intermediate that undergoes Russell fragmentation. It can also participate in radical-radical coupling with the initial Csp² radical to yield the alkoxy radical **C** (path d) *via* O–O bond cleavage from peroxide **A1**, which then undergoes intramolecular 1,2-hydrogen atom transfer (1,2-HAT), ultimately leading to the oxo-functionalized product after SET and deprotonation.

This review highlights notable studies that achieved sequential formation of C=O and Csp³-R bonds using simple photocatalysts alone. Accordingly, we exclude reactions that proceed *via* photocatalyst-free systems, photoredox/transition metal dual catalysis, or pathways lacking SET events.

2. Oxo-alkylation reactions

Alkene oxo-alkylation reactions *via* photoredox catalysis represent a powerful synthetic strategy for C–C bond formation. The section is organized according to the type of carbon-based bond formation: C–CF₃, C–CF₂R, and C–C(alkyl).

2.1 C–CF₃ bond formation

In the field of trifluoromethyl chemistry, various radical precursors have emerged over the past decade. In 2014, Akita¹⁹ introduced the Togni reagent as an effective precursor for the [•]CF₃ species, facilitating the synthesis of α-trifluoromethylated ketones from alkenes and DMSO *via* an Ir-promoted, oxidative quenching process (Scheme 3, conditions A). This approach



Adelina Vallribera

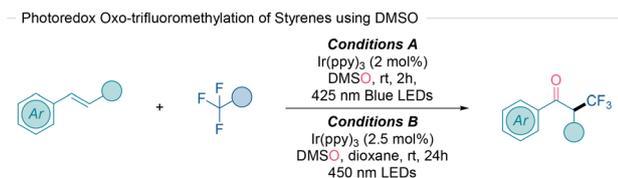
Prof. Adelina Vallribera received her PhD in Chemistry in 1993 from UAB under the supervision of Prof. J. Marquet. After a post-doctoral stay at the Laboratoire de Chimie Organique de Synthèse in Belgium in the group of Prof. L. Ghosez, she joined the group of Prof. M. Moreno-Mañas at UAB. She became an assistant professor in 1997 in the Organic Chemistry Unit at the Department of Chemistry at UAB and was promoted to Full Professor in 2017.



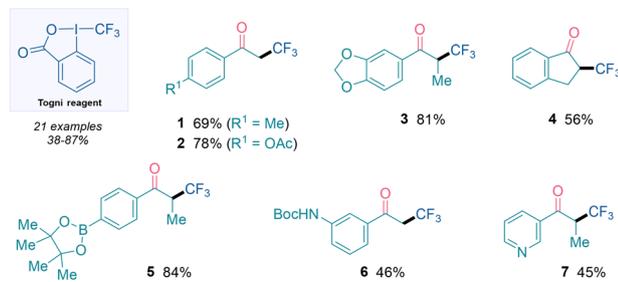
Albert Granados

Dr. Albert Granados received his MSc in Electrochemistry, Science, and Technology in 2014. He then joined the Vallribera group at UAB, where he obtained his PhD with a special award in 2018. Subsequently, he pursued post-doctoral studies with Prof. R. Pleixats and Prof. A. Vallribera at UAB. In 2021, he began another post-doctoral stint in the Molander group at the University of Pennsylvania (UPenn). In early 2023, he started as a Lecturer in Organic Chemistry in the CatSyNanoMat group at UAB and was promoted to Associate Professor in mid-2024. He was appointed as a Member of the Science of Synthesis Early Career Advisory Board for the 2025–2027 period.

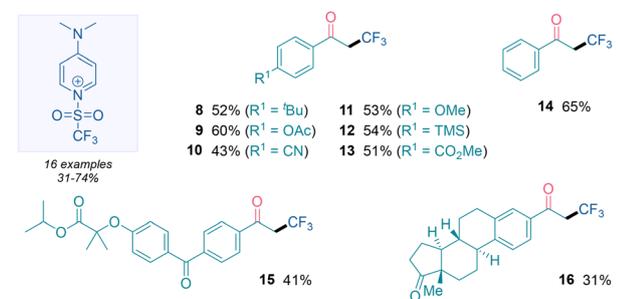




Akita 2014 — Conditions A



Xiao 2024 — Conditions B

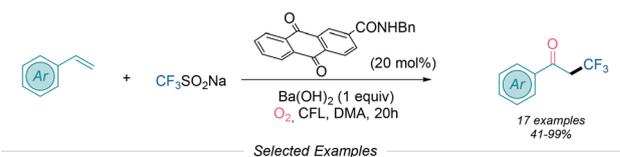


Scheme 3 Photoredox oxo-trifluoromethylation reactions of alkenes described by Akita¹⁹ and Xiao.²⁰

generally achieved high yields with styrenes containing electron-donating groups (1–3), while substrates with electron-withdrawing groups showed reduced yields due to the formation of β -trifluoromethylstyrene as a side product. Notably, sensitive boronic esters are well tolerated (5). Endocyclic styrenes provided the desired ketones in good yield (4).

Recently, Xiao²⁰ presented a new trifluoromethylation reagent capable of single-electron reduction to produce $\cdot\text{CF}_3$. This method tolerates a wide range of functional groups (Scheme 3, conditions B), including nitriles (10), esters (9 and 13), halogens, and silyl groups (12), and has shown promise for late-stage functionalization (15 and 16). Both methods employ Ir(ppy)₃ as a photocatalyst to initiate the $\cdot\text{CF}_3$ radical *via* SET. Subsequently, this open-shell species undergoes Giese addition with alkenes, forming a key benzylic radical intermediate that is further oxidized to a benzylic carbocation. Finally, in both cases, DMSO served as the oxidant, converting the intermediate to the desired α -trifluoromethylated ketones *via* Kornblum type oxidation (see Scheme 2A) assisted by the base *o*-iodobenzoate in Akita's method and a pyridine derivative in Xiao's work.

In 2018, Itoh²¹ reported a reductive quenching approach to synthesize α -trifluoromethylated ketones using the Langlois reagent in the presence of molecular oxygen (Scheme 4) using a compact fluorescent lamp (CFL). Here, the organic dye 2-ben-

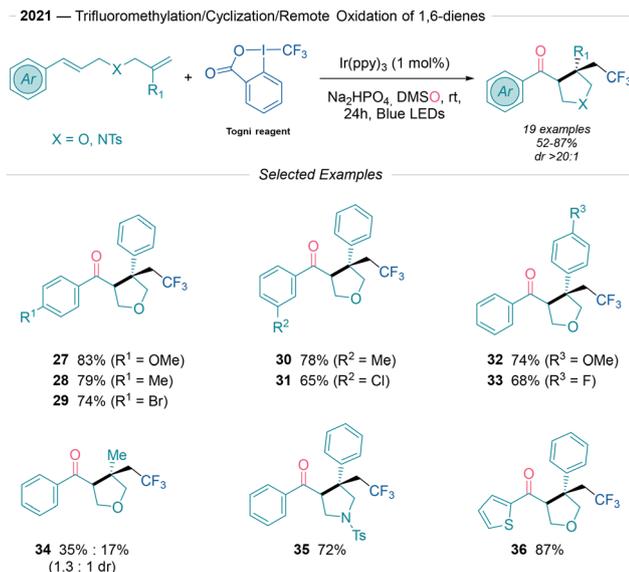
2018 — Oxo-trifluoromethylation of Alkenes using O₂ as Oxidant

Scheme 4 Photoredox synthesis of α -trifluoromethylketones reported by Itoh.²¹

zylamideanthraquinone served as the most convenient photocatalyst, with Ba(OH)₂ as base. This reaction proceeds well with both electron-withdrawing and electron-donating group-substituted styrenes (17–20), although strongly electron-withdrawing groups, such as methyl ester or nitrile (20), yield lower amounts. Steric effects were observed among *ortho*-, *meta*-, and *para*-methyl-substituted styrenes (17, 21 and 22). Notably, the reaction tolerates sensitive protecting groups (24–25) including acetals and *tert*-butyldimethylsilyl ethers (OTBS). The mechanistic investigation of this transformation was supported by radical-trapping experiments and ¹⁸O labelling. The authors proposed that after generating the $\cdot\text{CF}_3$ radical *via* SET from the excited photocatalyst, the radical undergoes Giese addition with styrenes to yield a benzylic radical intermediate. Finally, this intermediate reacts with molecular oxygen, which is reduced to a peroxy anion, and the desired product is formed by protonation, followed by decomposition (path a and b, Scheme 2B).

In 2021, Zhu and collaborators²² developed a mild protocol to access CF₃-substituted tetrahydrofurans and tetrahydropyrroles from 1,6-dienes and the Togni reagent (Scheme 5). This reaction proceeds under photoredox oxidative quenching conditions using Ir(ppy)₃ and DMSO. The scope includes both electron-rich and electron-poor arenes, with yields ranging from 65% to 83% (27–33) and excellent diastereoselectivity. Additionally, the method is compatible with *N*-protected 1,6-dienes (35) and thiophene-substituted (36) aromatic rings, although it is unsuitable for alkyl 1,6-dienes. The protocol can be scaled up to the gram-scale. Mechanistic studies, including TEMPO radical-trapping and ¹⁸O labelling experiments with DMS-¹⁸O, suggest that the CF₃ radical generated *via* SET undergoes radical addition to the terminal alkene of the 1,6-diene to yield a C-centered radical intermediate, which undergoes an intramolecular cyclization process yielding a benzylic radical species. Subsequently this intermediate is oxidized to the carbonyl as depicted in Schemes 1B and 2A.

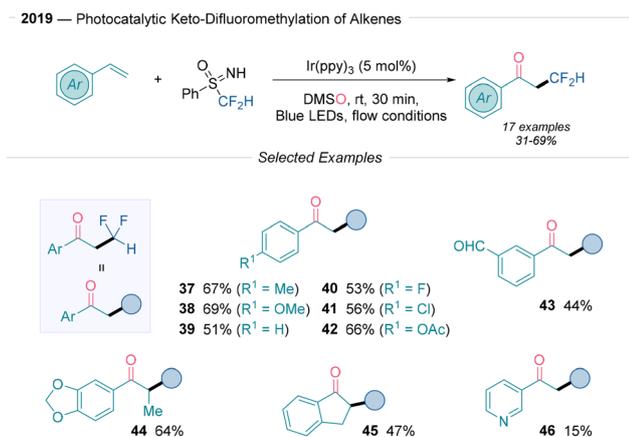




Scheme 5 Photoredox trifluoromethylation/cyclization/oxidation of 1,6-dienes.²²

2.2 C–CF₂R bond formation

In 2019, Akita and Koike²³ reported the synthesis of α -CF₂H-substituted ketones through an Ir(ppy)₃ photoredox approach using aromatic alkenes and the novel *N*-tosyl-*S*-difluoromethyl-*S*-phenylsulfonimine as the CF₂H radical source, with DMSO serving as both a solvent and mild oxidant (Scheme 6). The difluoromethyl group is a fruitful structural motif that acts as a bioisostere for alcohol and thiol functional groups.²⁴ This reaction was carried out on a preparative scale in a photocatalytic flow reaction (MiChS flow reactor) at room temperature and with only 30 minutes of illumination. The substrate scope includes styrenes with *para* electron-rich substituents with yields ranging between 49 and 69% (for example 67% for 37) and halogens yielding 43–56% yields. Internal alkenes such as *trans*-stilbene, isosafrole, indene (45) and 2-methyl-

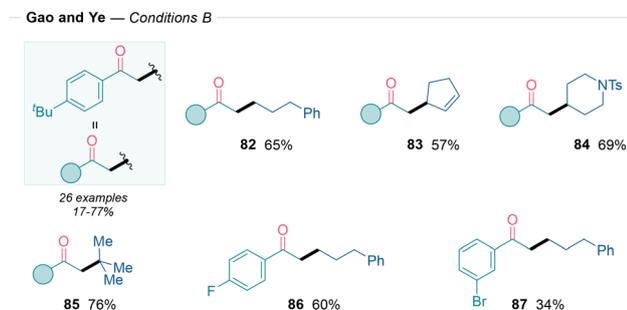
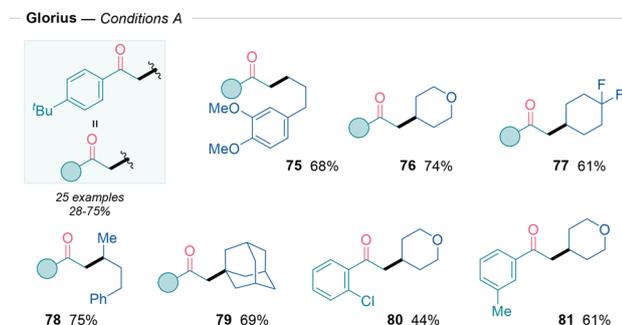
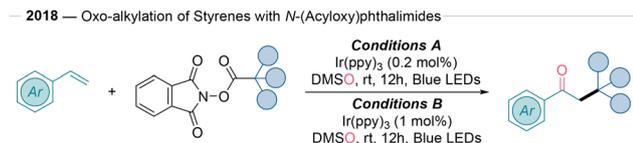


Scheme 6 Direct keto-difluoromethylation of alkenes under photoredox conditions reported by Akita and Koike.²³

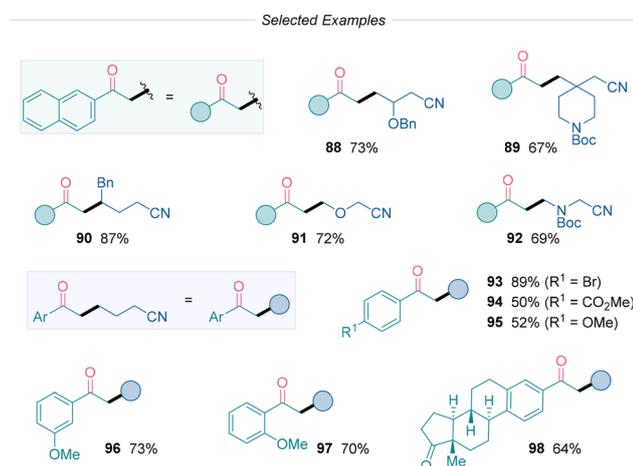
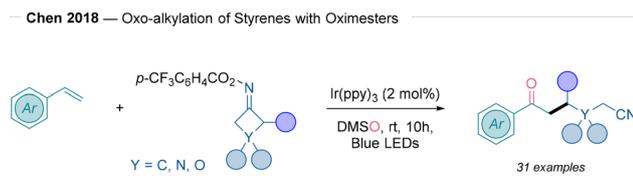
indene required a longer residence time despite giving the CF₂H-ketone products in moderate yields (31–64% yields). Electron deficient styrenes and aliphatic alkenes did not react under these conditions. A plausible reaction mechanism is proposed based on radical trapping experiments with TEMPO, intermittent light irradiation experiments and determination of the photochemical quantum yield. The reaction is governed by an oxidative quenching photoredox cycle followed by the oxidation shown in Scheme 2A. Interestingly, when the base is omitted a single-electron reduction of the sulfonium intermediate (Scheme 2A) followed by O–S bond homolysis is also proposed. The resulting alkoxy radical (C in Scheme 2B) undergoes 1,2-HAT and single-electron oxidation to give the CF₂H-ketone.

Subsequently, four more contributions were published in 2019 on visible-light-promoted oxo-difluoroalkylation of alkenes using DMSO. The notable α -difluoroalkylated (α -CF₂R) ketones represent valuable building blocks with bioactive properties. The first example details a visible-light-induced oxo-difluoroacetylation to access α,α -difluoroketones from styrenes and bromodifluoroacetates using Ir(ppy)₃ under blue LEDs and in the presence of stoichiometric AgTFA (Scheme 7, conditions A).²⁵ This difunctionalization showed moderate to good yields and excellent regioselectivity. Styrenes with *para* electron-donating groups (47–48) and weakly electron-withdrawing groups (49–50) produced the desired compounds in yields that ranged from 63 to 74%. Internal alkenes also demonstrated good reactivity (53–54), with both *meta* and *ortho* substituents being well tolerated. Additionally, a bromodifluoroacetamide example afforded the corresponding ketone in decent yield (55). A scale-up reaction demonstrated the synthetic utility of this approach. The proposed mechanism is supported by radical trapping and labelled DMS-¹⁸O experiments. It involves the photoexcitation of Ir(ppy)₃, which generates a strongly reducing excited state that triggers the generation of the [•]CF₂COOEt radical assisted by Ag^I, likely through AgBr formation. Continuing radical addition to the alkene, the key Csp²-hybridized radical is produced and furnishes the final product *via* Kornblum oxidation (Scheme 2A). Ye²⁶ described an alternative set of reaction conditions for oxo-difluoroacetylation using 2 equivalents of KH₂PO₄ as weak base to optimize yields by preventing HF elimination (Scheme 7, conditions B). Styrenes with *para* electron-donating groups (56 and 57) performed well (66–76% yields), while weakly electron-withdrawing groups (58 and 59) yielded around 46% yield. Moreover, *meta* (60) and *ortho* (61) substituents also yielded products within 43–58% yields and moderate yields were obtained for internal alkenes (62 and 63). Bromodifluoroacetamides produced aniline- (64) and indole-derived ketones in moderate yields, although aliphatic alkenes failed under standard conditions. Scale-up of the reaction using 5 mmol of styrene further demonstrated this method's synthetic utility. Mechanistic studies suggest that the reaction proceeds *via* excitation of Ir(ppy)₃, which reduces the BrCF₂CO₂Et radical precursor and generates a carbon-centered radical. Then, the mechanism follows the pathway depicted in



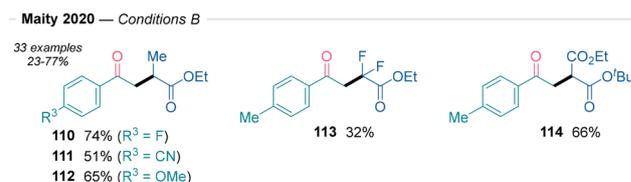
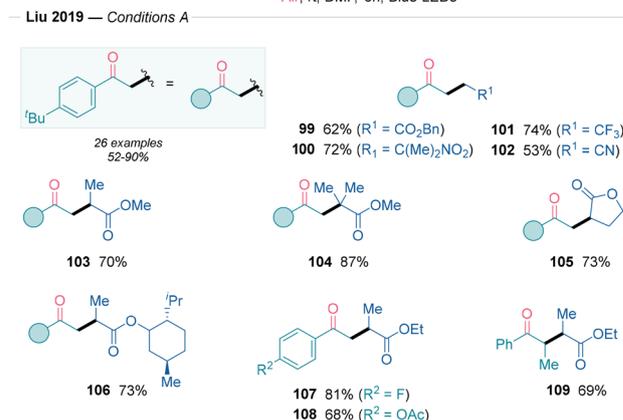
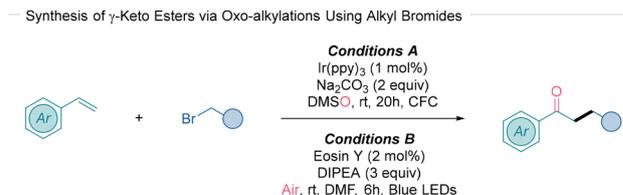


Scheme 9 Oxo-alkylation protocols described by Glorius²⁹ and Ye³⁰ in 2018.



Scheme 10 Use of oximesters as radical precursors for alkene oxo-alkylation reactions reported by Chen.³¹

reaction mechanism involves an iminyl radical-triggered C–C bond cleavage from an oximester reagent, followed by a radical Giese addition to the alkene and subsequent Kornblum oxi-



Scheme 11 Photoredox approaches^{32,33} for accessing γ -keto esters using alkyl bromides and alkenes.

dation (Scheme 2A). These conditions showed functional group tolerance for ethers (**88**) and *N*-Boc amines (**89** and **92**).

Additionally, it was applied to a broad range of cyclobutane-derived *O*-acyl oximes (**93–98**). Moreover, the reaction enabled efficient product formation with various styrenyl-based radical acceptors, including biologically relevant derivatives (**98**).

The synthesis of γ -keto esters from styrenes under photoredox conditions has been independently reported by Liu³² and Maity³³ (Scheme 11). Liu first introduced an Ir-based oxidative quenching photoredox method using α -bromoesters as convenient radical precursors and DMSO as the oxidant (Scheme 11, conditions A). Notably, other electron-withdrawing groups, such as NO₂ (**100**), CF₃ (**101**), and CN (**102**) derivatives, could also be incorporated using the same reaction conditions. Primary, secondary, and tertiary radicals (**99**, **103** and **104**) were successfully introduced into the styrenyl radical acceptor. This protocol was also applicable to various styrenes (**107** and **108**), including β -methylstyrene (**109**). Radical trapping experiments and the use of tetramethylene sulfoxide confirmed that the reaction proceeds *via* a photoredox cycle, where the cationic intermediate is oxidized by DMSO (Scheme 2A). Later, in 2020, Maity described an organophotoredox approach under aerobic conditions using α -bromocarbonyls (Scheme 11, conditions B). The combination of eosin Y as a photocatalyst and DIPEA as a base in



DMF was crucial for the reaction's success. The substrate scope included α -bromoesters (**110–113**), α -bromoketoesters, α -bromomalonates (**114**), α -bromoketones, and α -bromoamides. Various styrene derivatives, including endocyclic alkenes and β -substituted styrenes, were well tolerated. The reaction mechanism was investigated through radical trapping studies, Stern–Volmer fluorescence quenching, and radical-clock experiments. Photoexcited eosin Y reduces the corresponding α -bromocarbonyl to a carbon-centered radical *via* SET. Oxidized eosin Y is then regenerated by DIPEA that acts as a sacrificial electron-donor. The generated radical undergoes Giese addition to the double bond, forming a benzylic radical intermediate. This intermediate reacts with O₂ to form the peroxy radical, which follows path d in Scheme 2B. The authors proposed that the generated α -hydroxy-C-centered radical is oxidized to the final product by either DIPEA⁺ (chain termination) or by another substrate molecule (chain propagation). The authors also noted the possibility of a reductive quenching photoredox cycle, since Stern–Volmer experiments indicate that DIPEA can quench the excited state of eosin Y.

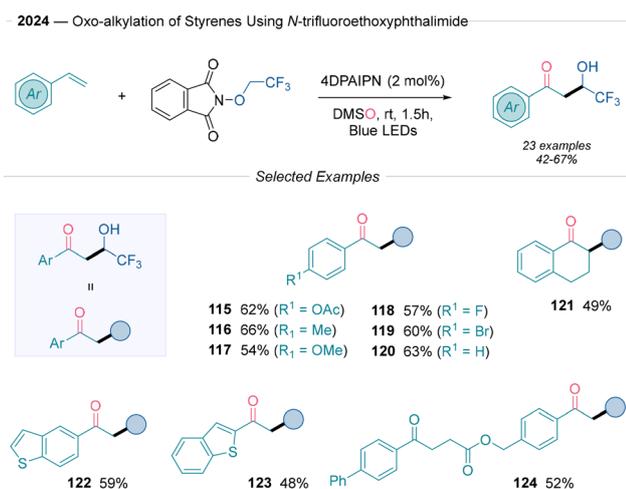
The trifluoroethanol moiety is significant in medicinal chemistry.³⁴ Recently, access to 2-hydroxy-1,1,1-trifluoroethylacetophenones has been reported *via* the oxo-alkylation of alkenes under oxidative quenching photoredox conditions (Scheme 12).³⁵ Interestingly, this chemical space is explored using *N*-trifluoroethoxyphthalimide as a radical precursor. This redox-active ether can be reduced to the trifluoroethoxy radical using the cost-effective and readily available 1,3-dicyano-2,4,5,6-tetrakis(diphenylamino)benzene (4DPAIPN) photocatalyst in the presence of DMSO. Notably, the reaction is completed in 90 minutes, with a broad substrate scope, including heteroaromatics (**122** and **123**) and complex molecules (**124**), making it ideal for late-stage functionalization.

Importantly, the reaction can be scaled up to 2.5 mmol without loss of efficiency, and access to CF₂H analogs is also

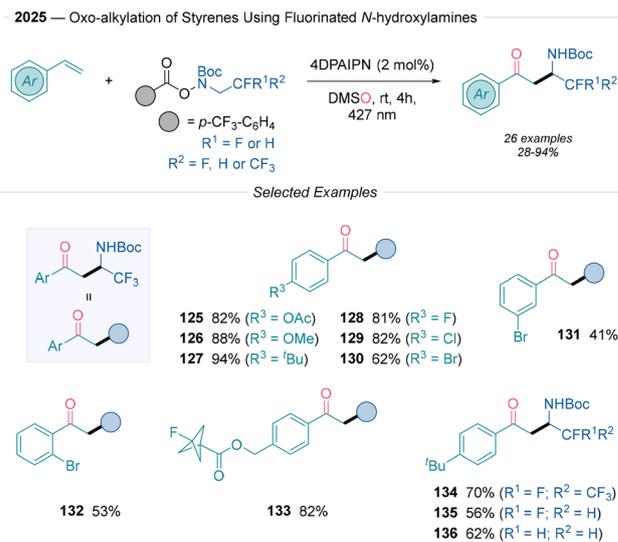
feasible under the same conditions. The authors noted that the solvent not only facilitates the formation of carbonyl through Kornblum oxidation but also is crucial for generating the key C-centered radical *via* intramolecular 1,2-HAT from the trifluoroethoxy radical. This radical then undergoes Giese addition to the olefin, followed by a SET event, leading to Kornblum oxidation (Scheme 2A). This plausible mechanism has been proposed after extensive mechanistic investigation, including Stern–Volmer luminescence quenching studies, radical trapping experiments and cyclic voltammetry investigations.

The preparation of β -trifluoromethyl β -amino ketones is feasible under organophotoredox conditions, starting from styrenes and a fluorinated redox-active hydroxylamine (Scheme 13).³⁶ This reaction is catalyzed by 4DPAIPN as the photocatalyst, which upon photoexcitation, can reduce the radical precursor to the corresponding *p*-CF₃-benzoate anion and the nitrogen-centered radical species. Subsequently, a carbon-centered radical species is formed *via* intramolecular 1,2-HAT, which then undergoes a Giese addition to the alkene. The resulting Csp²-hybridized species is oxidized to the corresponding carbonyl, as depicted in Scheme 2A. The mechanism is supported by Stern–Volmer luminescence quenching studies, cyclic voltammetry and isotope labelling experiments. This three-component reaction proceeds efficiently (**125–133**), with yields ranging from 41% to 94%, demonstrating its utility in synthesizing these valuable compounds. Notably, the reaction's scalability retains its efficiency, and the method is not restricted to the preparation of CF₃ derivatives, but other fluorinated groups such as pentafluoroethyl (CF₂CF₃, **134**), difluoromethyl (CF₂H, **135**), and monofluoromethyl (CH₂F, **136**) derivatives are also accessible.

The Katayev lab³⁷ recently developed a carbo-heterofunctionalization method *via* Ir-photoredox radical/polar crossover,



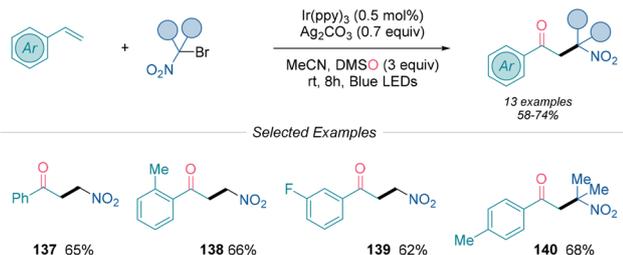
Scheme 12 Visible light-mediated synthesis of 2-hydroxy-1,1,1-trifluoroethylacetophenones.³⁵



Scheme 13 Photoredox synthesis of β -trifluoromethyl β -amino ketones.³⁶



2025 — Oxidative Alkylation of Styrenes under Photochemical Conditions

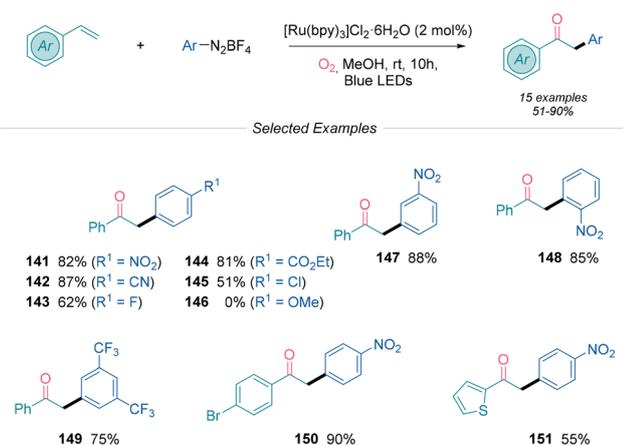
Scheme 14 Photoredox keto-alkylation developed by Katayev.³⁷

enabling the synthesis of 2-nitroketones and other nitro derivatives (Scheme 14). In this protocol, geminal bromo-nitroalkanes serve as precursors to generate key carbon-centered radical intermediates, which undergo Giese addition with olefins. The presence of DMSO facilitates the formation of the final ketone *via* Kornblum-type oxidation (Scheme 2A). The reaction demonstrates broad substrate compatibility, performing well with various styrene derivatives, including *ortho*- (138), *meta*- (139), and *para*-substituted (140) examples; however, it does not extend to heterocycles. Furthermore, both secondary and tertiary β -nitro ketones (140) can be accessed by modifying the geminal reagent under identical reaction conditions. The proposed radical/polar crossover mechanism is supported by extensive mechanistic investigations, including radical-clock and control experiments and radical trapping studies.

3. C=O and C–Csp² bond formation

Cai³⁸ presented a mild protocol for the preparation of 1,2-dia-rylethan-1-ones through oxidative arylation of styrenes using aryldiazonium salts under photoreductive conditions (Scheme 15). This transformation mandates the use of [Ru

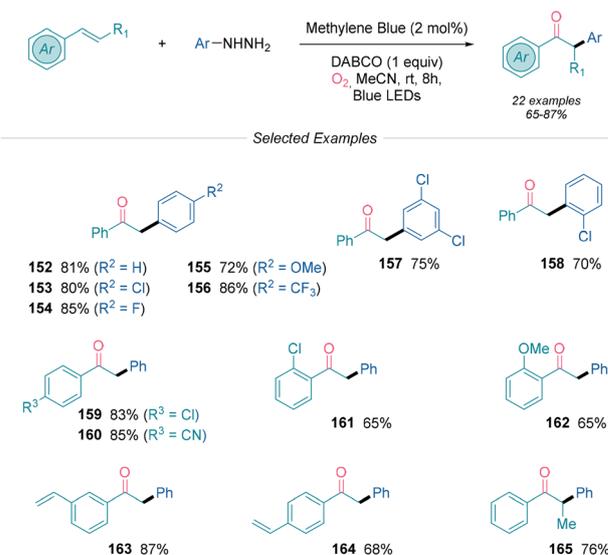
2015 — Oxidative Arylation of Styrenes under Photochemical Aerobic Conditions

Scheme 15 Keto-arylation of alkenes using aryldiazonium salts under photoredox conditions described by Cai.³⁸

(bpy)₃]Cl₂·6H₂O as a photocatalyst under an oxygen atmosphere, resulting in good yields. The difunctionalization reaction is effective, although limited by the electronic nature of the aryldiazonium salt used. Electron-poor aryldiazonium salts efficiently produced the desired 1,2-dia-rylethan-1-ones in yields ranging from 51% to 88%, tolerating nitro (141), nitrile (142), and ester (144) groups, as well as halides (145). In contrast, electron-donating substituents did not work under the established reaction conditions (146). Notably, a heteroaryl system also produced the corresponding ketone successfully (151). Steric effects had little impact on yields (141, 148), and a range of additional organic backbones, including variously substituted styrenes, were evaluated, with tolerance for both electron-donating and electron-withdrawing groups on the phenyl ring. The mechanistic operation of this transformation was studied through radical trapping experiments using TEMPO, 2,3-dimethyl-2-butene, and 1,4-diazabicyclo[2.2.2]octane (DABCO). The authors propose that after the generation of the aryl radical *via* SET, the radical undergoes Giese addition to the styrene to yield a benzylic radical intermediate. This intermediate reacts with molecular oxygen that follows path d in Scheme 2B. The produced α -hydroxy-carbon-centered radical yields the final carbonyl compound after single electron oxidation from the Ru^{III} species and the subsequent deprotonation event.

In 2017, Zhu³⁹ introduced a metal-free method for synthesizing ketones *via* oxidative radical addition of arylhydrazines as radical precursors to styrenes (Scheme 16). This aerobic process employs blue LEDs to activate methylene blue as a photocatalyst, achieving complete transformation in 8 hours. Using DABCO as a non-nucleophilic base was crucial to optimize yields. This protocol remained highly efficient when scaled up to 10 mmol, and a broad substrate scope was

2017 — Photoredox Oxidative Arylation of Styrenes Using Aryl Hydrazines

Scheme 16 Aryl hydrazines as aryl radical precursors for the keto-arylation of alkenes by Zhu.³⁹

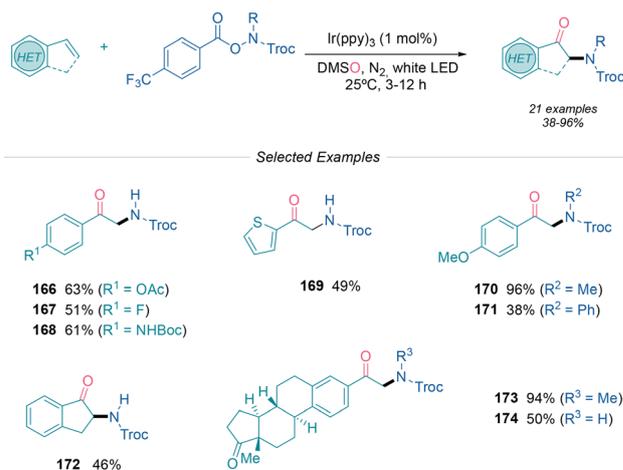
explored, yielding excellent results across aryl hydrazines with diverse substituents, including halides (**153** and **154**), ethers (**155**), and strongly electron-withdrawing groups (**156**). *ortho*-Chlorine substituents (**158**) led to slightly lower yields due to steric hindrance. The reaction tolerated various substituents on the radical acceptor, including halides or nitriles (**159** and **160**) and selectively produced mono-ketones from divinylbenzene substrates in high yields (**163** and **164**). Additionally, the reaction was not restricted to terminal alkenes, but also β -methyl styrene proved to be efficient toward the synthesis of **165** in 76% yield. Mechanistic studies, including Stern–Volmer quenching, suggest that methylene blue's excited state is quenched by the redox-active aryl hydrazine, forming an aryl radical *via* oxidation and deprotonation. This sp^2 -hybridized radical undergoes Giese addition with the olefin to produce a benzyl radical intermediate. The final ketone formation may proceed *via* two possible pathways; in the first, the benzyl radical is intercepted by a hydroperoxyl radical, forming a hydroperoxyl intermediate that decomposes to yield the ketone; in the second, the benzyl radical follows path a and e shown in Scheme 2B.

4. C=O and C–N bond formation reactions

In 2017, Yu⁴⁰ presented the first example of oxo-functionalization involving the construction of a C(sp^3)–N bond (Scheme 17). In their study, a hydroxylamine derivative was used as a N radical source, initiated *via* a SET process by an Ir photocatalyst, followed by homolytic cleavage of the O–N bond. After a Giese addition and a Kornblum-type oxidation, this method enabled the synthesis of various α -amino ketones in moderate to excellent yields. Notably, both *para*- and *ortho*-substituted arenes demonstrated high efficiency, although yields were slightly lower for *meta*-substituted arenes. Additionally, the scope was extended to complex scaffolds, including thiophenes (**169**), naphthalenes, indenes (**172**), and estrone (**173–174**) derivatives. Importantly, this work also explored alternative hydroxylamine precursors bearing Ph or Me groups (**170–171**), showing how these modifications impacted final yields. Experimental findings confirmed the involvement of radical species, with DMSO acting as the oxidant. The authors proposed the general mechanism described in Scheme 2A.

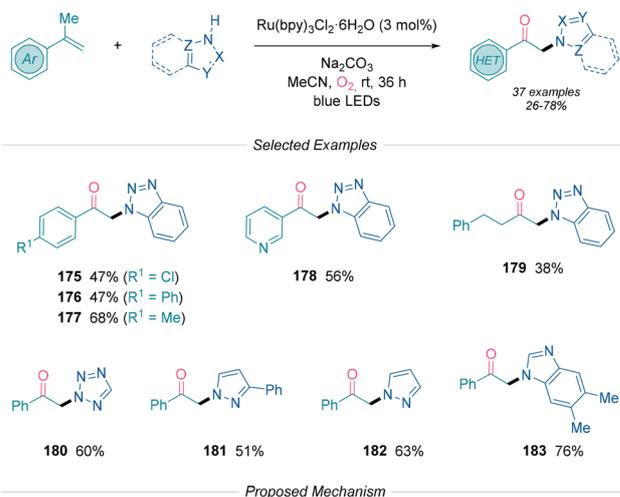
Shao⁴¹ recently developed an aerobic method for synthesizing aminoketones using photoredox catalysis, leveraging molecular oxygen as a green oxidant in conjunction with a Ru catalyst to achieve moderate to good yields (Scheme 18). The method allows the incorporation of medicinally relevant nitrogen containing heteroaromatics under mild conditions. Different heteroaromatics (**175**, **180–183**) were well tolerated, although indoles, imidazoles or pyrroles are shown to be unproductive under these conditions. Mechanistic investigations demonstrated a β -scission step *via* a labelling experiment with α -deuterated methylstyrene, which yielded the non-

2017 — Photoinduced Oxo-amination of Styrenes via Kornblum Oxidation



Scheme 17 Oxo-amination photoredox method described by Yu and collaborators.⁴⁰

2023 — Photoinduced Aerobic Synthesis of α -Amino Ketones



Scheme 18 Photochemical synthesis of α -aminoketones described by Shao.⁴¹

deuterated product. Additionally, EPR experiments detected radical adducts of singlet O_2 or $O_2^{\cdot -}$ confirming the presence of key radical intermediates. Based on these findings, the authors propose two potential pathways for the generation of

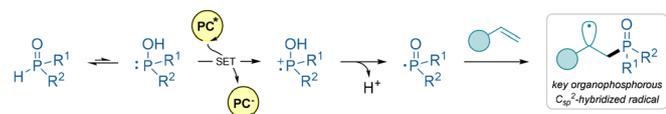


the nitrogen radical, converging into a unified mechanism. On the one hand, energy transfer (EnT) from the excited photocatalyst to O_2 generates a singlet oxygen state, which then engages in a SET with the heteroaromatic reagent and proton loss. Alternatively, a direct SET between the reagent and the excited photocatalyst followed by proton release is also proposed. Subsequently, this N-centered radical species undergoes Giese addition to the α -methylstyrene derivative. The generated key-benzylic radical reacts with *in situ* formed $O_2^{\cdot-}$ and H^+ to form an alkyl hydroperoxide, which subsequently undergoes homolytic cleavage of the O–O bond to release $\cdot OH$. Finally, β -scission induced by the resulting alkoxy radical produces the final ketones after losing a $\cdot Me$ radical.

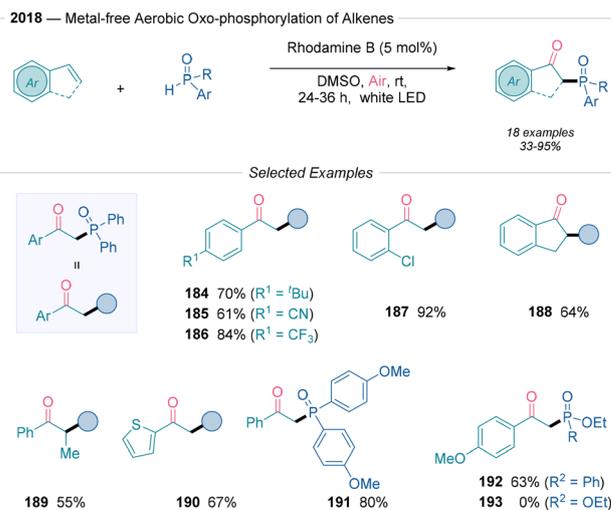
5. C=O and C–P bond formation reactions

β -Ketophosphine oxides are valuable intermediates in organic synthesis due to their versatility in constructing complex molecular structures. All the presented methods below utilize disubstituted phosphine oxides as radical progenitors. Importantly, these organophosphorous compounds exist in equilibrium with the minor tautomer disubstituted phosphinous acid, which is able to undergo SET under a suitable set of reaction conditions. Then this P-centered radical undergoes addition to the olefin (Scheme 19).

Zhu⁴² introduced the first metal-free oxo-phosphorylation of alkenes, enabling aerobic oxidative incorporation of a phosphoxide unit into a variety of activated alkenes (Scheme 20). The reaction utilizes rhodamine B as the photocatalyst, diaryl phosphine oxides, DMSO as the solvent, and white light as the energy source. Notably, the authors do not confirm that O_2 is solely responsible for the oxidation step since no control experiments were conducted under an inert atmosphere, thus leaving open a possible Kornblum-type oxidation process (Scheme 2A). Nonetheless, the method demonstrates impressive scope and high yields, successfully transforming various 2-, 3-, and 4-substituted styrenes (**184**–**187**), as well as internal alkenes (**188**–**189**) and thiophenes (**190**), which highlights its compatibility with heteroaromatic systems. Diarylphosphine oxides showed the best reactivity, although a single example using ethyl phenylphosphinate (**192**) was investigated and dialkyl phosphites were ineffective (**193**). Mechanistic investigations included only a radical scavenger experiment. The authors suggest that the minor organophosphorous tautomer undergoes SET with the excited state of the photocatalyst, gen-



Scheme 19 Main mechanistic pathway for the generation of the organophosphorous C_{sp^2} -hybridized radical in this section.



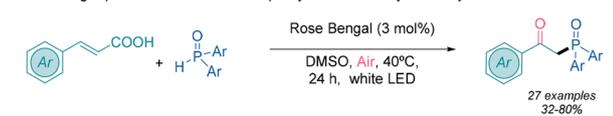
Scheme 20 Photoredox alkene oxo-phosphorylation conditions presented by Zhu.⁴²

erating a phosphorus-centered radical cation. After deprotonation, the P-centered radical adds to the styrene skeleton and subsequently reacts with preformed $O_2^{\cdot-}$ following the general mechanism described in Scheme 2A path c.

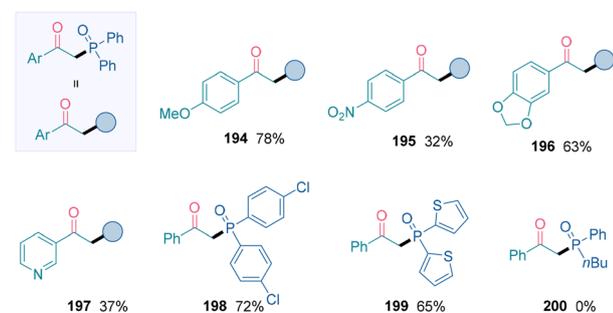
In 2018, Zou and collaborators⁴³ described a pioneering method for the oxidative phosphorylation of alkenyl carboxylic acids *via* an organophotoredox relay approach. This reaction uses cinnamic acid derivatives with diarylphosphine oxides, rose bengal as an organophotocatalyst, DMSO as the solvent, under an oxygen atmosphere and at 40 °C (Scheme 21). This transformation is effective using different styrene derivatives, including both electron-rich (**194**) and electron-deficient (**195**) systems. Some heteroaromatics also showed compatibility (**197**), although furans suffered from decreased yields or were entirely unreactive. The method allows the use of some diverse phosphorus oxides, including a dithiophene derivative (**199**), although alkyl and alkoxy substituents on phosphorus were incompatible (**200**). Radical scavengers suppressed the desired transformation and the use of an acrylamide derivative instead of the aromatic olefin led to the formation of a phosphorus oxide oxindole product. These experiments confirmed the involvement of the phosphoryl radical species. Furthermore, EPR spectroscopy allowed the detection of both $O_2^{\cdot-}$ and $\cdot POH_2$ species. However, given the presence of DMSO it is important to consider a Kornblum-type oxidation mechanism since there are not enough control experiments. Based on the authors' observations, an oxidative quenching photoredox cycle operates this transformation. The PC^* species is quenched by O_2 to form $O_2^{\cdot-}$ and the oxidized state of the photocatalyst. Subsequently, the diarylphosphinous acid tautomer undergoes SET yielding the radical phosphoxide after deprotonation and adds to the cinnamic acid derivative. The generated intermediate follows the general mechanism described in Scheme 2B, path c, where an additional decarboxylation event is promoted by SET.



2018 — Light-promoted Oxidative Phosphorylation of Alkenyl Carboxylic Acids



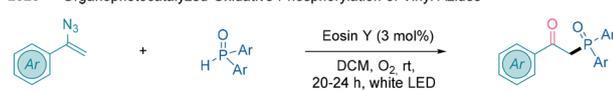
Selected Examples



Scheme 21 Rose bengal promoted synthesis of β -oxophosphine oxides described by Zou.⁴³

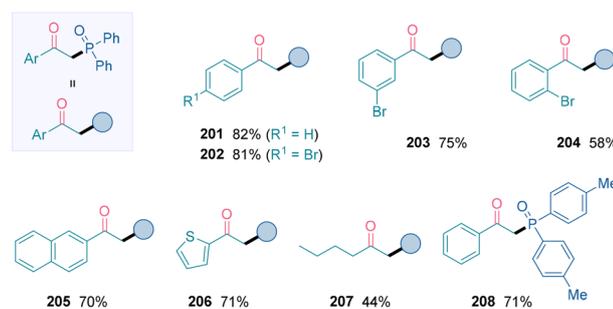
Kim presented two oxo-phosphorylation methods utilizing different substituted vinyls. First in 2020,⁴⁴ the installation of diphenylphosphine oxides onto vinyl azides under eosin Y catalysis was enabled using open-air conditions (Scheme 22). Although requiring pre-functionalization of the olefin, its implementation into non-styrene derivatives (**207**) is remarkable, broadening the substrate scope. These conditions tolerated various styrene derivatives, including halogen- and alkyl-

2020 — Organophotocatalyzed Oxidative Phosphorylation of Vinyl Azides

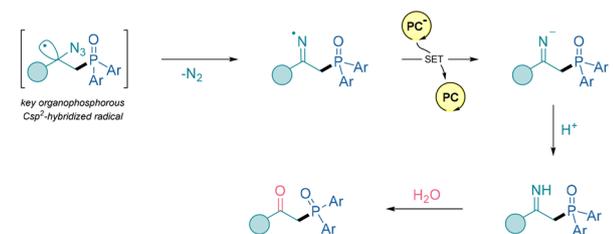


11 examples
44-89%

Selected Examples



Proposed Mechanism

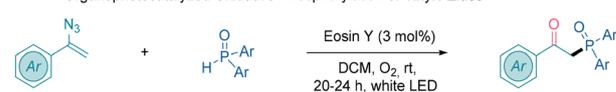


Scheme 22 Visible-light mediated synthesis of β -oxophosphine oxides reported by Kim.⁴⁴

substituted 2-, 3-, and 4-styrenes (**201–204**), and demonstrated scalability, retaining efficiency at the gram-scale. Mechanistically, the authors proposed a general oxidative quenching photoredox pathway based on a TEMPO experiment and related literature. The excited eosin Y yields the P-centered radical after deprotonation, which adds to the alkene generating nitrogen gas and an iminyl radical. Lastly, this intermediate is reduced to the corresponding imine anion, and upon protonation, it is hydrolyzed to the targeted carbonyl.

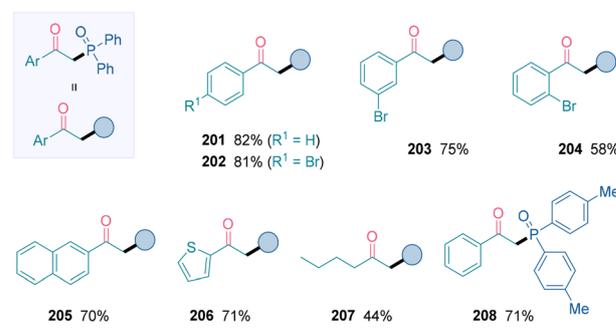
Recently, the same group⁴⁵ expanded this reactivity by introducing phosphine oxides into bromovinyls under similar organophotocatalyzed reaction conditions (Scheme 23). This method successfully incorporated phosphine oxides into electron-rich styrenes, although it struggled with electron-poor systems (**209** and **211**). Notably, the transformation retained efficiency at the gram-scale and it could be performed on allylbenzene (**213**), albeit in lower yields. The proposed mechanism parallels the initial method, starting with the phosphine oxide's equilibrium and undergoing SET with eosin Y, generating the phosphorus-centered radical. Following Giese addition and oxygen incorporation, a SET regenerates the catalyst, and the formed anionic intermediate is protonated. A hydroxyl transfer to a phosphine oxide radical cation yields a bromoalcohol intermediate, which, after the loss of HBr, forms the desired acetophenone derivative.

2020 — Organophotocatalyzed Oxidative Phosphorylation of Vinyl Azides

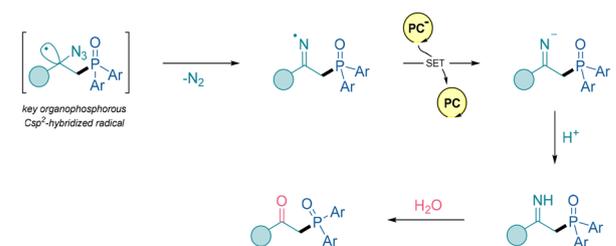


11 examples
44-89%

Selected Examples

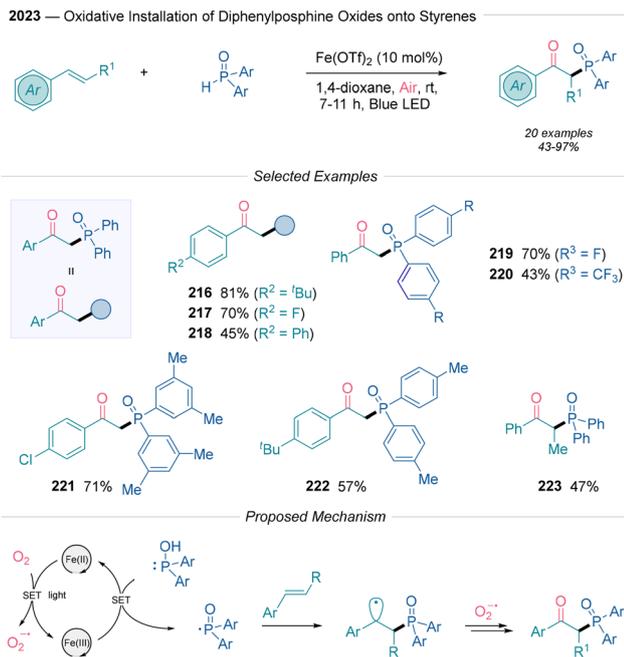


Proposed Mechanism



Scheme 23 Synthesis of β -oxophosphine oxides from α -bromostyrenes described by Kim.⁴⁵





Scheme 24 Light-induced and iron-catalyzed oxo-phosphorylation of alkenes described by Huang and Darcel.⁴⁶

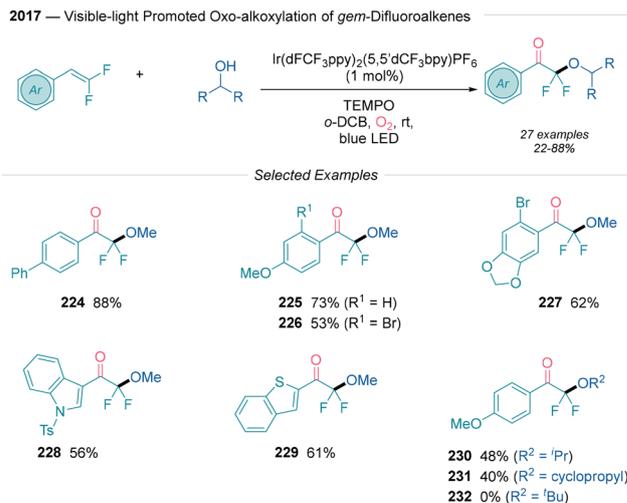
In a nice contribution by Huang and Darcel,⁴⁶ the installation of phosphine oxides onto vinyl arenes through a photo-induced iron-catalyzed method is detailed (Scheme 24). This work highlighted the potential of Earth-abundant iron complexes as cost-effective alternatives to traditional Ir- or Ru-based photocatalysts. The reaction involved combining diaryl phosphine oxides with styrenes as radical acceptors in the presence of $\text{Fe}(\text{OTf})_2$ in 1,4-dioxane without additives, leveraging ambient aerobic conditions. The scope was broad among alkyl- and halide-substituted arenes (**216–222**), although reactivity was limited when strongly electron-donating or withdrawing groups were present. Additionally, the reaction was effective for β -methylstyrenes (**223**). Mechanistic studies using radical scavengers confirmed the presence of phosphine oxide and benzylic radicals, and control experiments highlighted the necessity of aerobic conditions for product formation. The authors proposed a mechanism involving an initial photoinduced SET between the diaryl phosphine oxide and Fe^{II} , producing an Fe^{III} species and a radical cation. This cation releases a proton, generating a phosphine oxide radical that undergoes Giese addition with styrene to form a benzylic radical. This radical then couples with an $\text{O}_2^{\cdot-}$ species generated from Fe^{III} , oxygen, and light, leading to the formation of the final ketones *via* path c shown in Scheme 2B.

6. C=O and C–O/S bond formation

In this section the sequential formation of C=O and C–O/S bonds is discussed. All the upcoming methods have in common the use of O_2 as an oxidant that yields the carbonyl

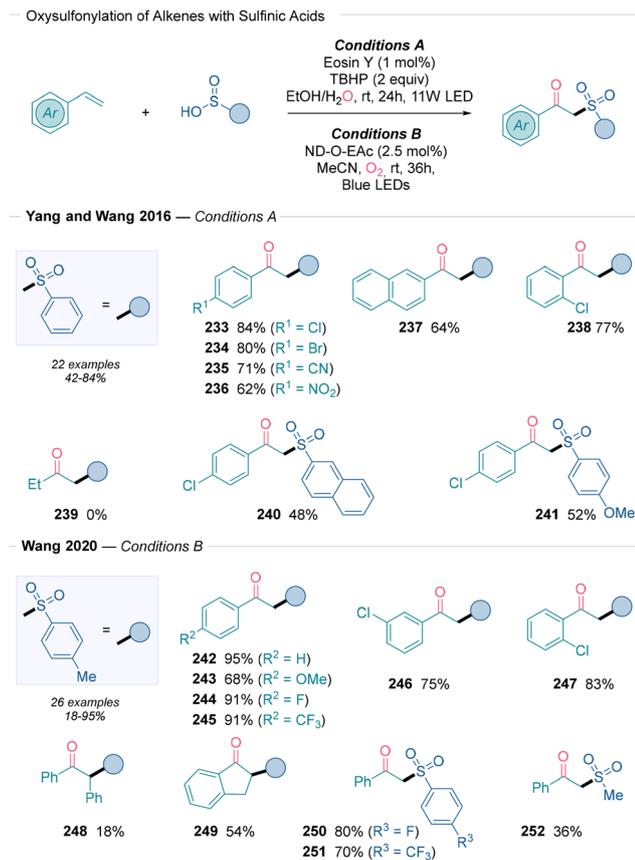
moiety. Wu and Feng⁴⁷ addressed the unique oxo-alkoxylation method of (*gem*-difluoro)alkenes (Scheme 25), overcoming significant challenges related to β -fluoride elimination and high redox potentials. These difluorovinyl species, especially in the electron-deficient context, often fail to form stable benzylic radicals, instead leading to anionic species that can trigger side reactions. The optimized method requires an Ir-based photocatalyst, TEMPO as an additive and *o*-dichlorobenzene (*o*-DCB) as solvent. The reaction demonstrated high yields for a variety of mono-, di-, and tri-substituted styrenes (**224–227**), as well as compatibility with heteroaromatic (**228** and **229**) compounds like benzothiophenes and indoles. However, electron-poor alkenes remain challenging organic backbones. Secondary alcohols showed good reactivity (**230–231**), while tertiary alcohols (**232**) did not react due to steric hindrance. Stern–Volmer luminescence quenching experiments indicated that the difluoroalkene quenched the Ir photocatalyst more effectively than the alcohol, while isotope labelling confirmed the role of O_2 as the oxygen source. The proposed mechanism involves an initial reductive quenching photoredox cycle where the $\text{Ir}^{\text{III}*}$ species oxidizes the organofluorinated styrenes to the radical cation. Subsequently, this species reacts with the desired alcohols followed by proton release yielding a benzylic radical. This intermediate reacts with the generated $\text{O}_2^{\cdot-}$ species generated by Ir^{II} to yield the final ketone through the general mechanism depicted in Scheme 2B path c.

In 2016, Yang and Wang⁴⁸ pioneered the synthesis of β -ketosulfones from alkenes and sulfinic acids under photoredox conditions, utilizing eosin Y as an organophotocatalyst and di-*tert*-butyl peroxide (TBHP) as a sacrificial oxidant (Scheme 26, conditions A). This protocol showed broad substrate compatibility, yielding β -ketosulfones from a variety of substituted alkenes. Both electron-donating and electron-withdrawing groups (**233–236**) on the aryl ring delivered moderate to good yields, including nitro- and cyano-substituents.



Scheme 25 Method disclosed by Wu and Feng for photoredox oxo-alkoxylation of alkenes.⁴⁷





Scheme 26 Synthetic methods enabling β -ketosulfones *via* photoredox reported by Yang, Wang⁴⁸ and Wang.⁴⁹

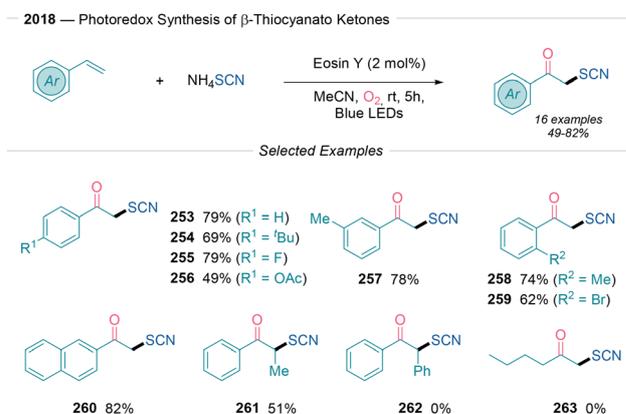
Naphthyl-substituted alkenes were also well tolerated (237). A minimal effect from steric hindrance was observed (233, 238), although aliphatic alkenes such as but-1-ene (239) proved unreactive. Mechanistic insights from Stern–Volmer luminescence quenching experiments and photochemical quantum yield measurements suggested a photoredox cycle. Isotope-labelling with H₂¹⁸O revealed that carbonyl formation derives from both H₂O and TBHP, with products containing 52% O¹⁸-labeled carbonyls and 48% unlabeled. The proposed mechanism involves SET between TBHP and excited eosin Y* to generate hydroxyl anions and *tert*-butoxy radicals, with the latter facilitating HAT with sulfinic acid to produce the S-centered radical. This radical adds to the alkene, forming a key C-centered radical intermediate that is then oxidized by eosin Y* to form a carbocation (Scheme 1B, left cycle), followed by carbonyl formation *via* water or hydroxyl addition and subsequent oxidation.

In 2020, Wang⁴⁹ extended this methodology using a naphthalimide-based photocatalyst (ND-O-EAc in Scheme 26, conditions B) with sulfinic acids as sulfone sources, expanding the β -keto sulfone synthesis to a broader range of alkenes, including styrenes (242–247), stilbenes (248), and heteroaromatics, achieving yields up to 95% and scalability to gram-scale reactions. However, challenges arose with aliphatic

alkenes and vinyl-pyridine, which yielded hydroxylated or non-oxidized products. Mechanistic studies indicated a reductive quenching photoredox cycle, with the excited photocatalyst accepting an electron from the sulfinic acid derivative to generate the sulfonyl radical, similar to Yang and Wang's mechanism discussed above. Notably, a Russell fragmentation pathway (Scheme 2B) was also proposed for this system, adding depth to the mechanistic understanding.

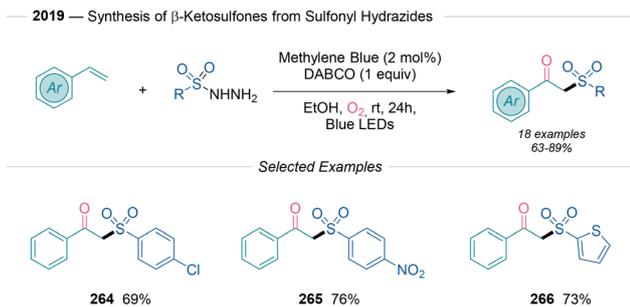
In 2018, Yue and Nan⁵⁰ described a photocatalytic formation of C=O and C–S bonds, introducing a method for β -thiocyanato ketone synthesis through styrene difunctionalization (Scheme 27). This reaction utilizes eosin Y as the photocatalyst with oxygen serving as the oxidant and NH₄SCN as the thiocyanide source. The substrate scope of this transformation is amenable to different styrenes containing alkyls (254), ethers, halides (255) or acetates (256). No steric effects were observed when assessing the methyl group at different positions of the aromatic ring (257 and 258). Extension to β -methylstyrene (261) is also feasible although stilbenes and aliphatic alkenes were incompatible (262 and 263). The mechanistic investigation included radical trapping experiments and Stern–Volmer quenching studies. The excited eosin Y* species undergoes SET with the thiocyanate anion to yield the corresponding open-shell species, which adds to the alkene *via* Giese addition. Then, the authors suggested that the generated C-centered radical species reacts with either O₂ or O₂^{•−} *via* paths a and b or c shown in Scheme 2B, with NH₄⁺ serving as the proton source.

One year later, Zhu's team⁵¹ synthesized β -keto sulfones *via* alkene difunctionalization using sulfonyl hydrazides as precursors and methylene blue as an organic photocatalyst (Scheme 28). The olefin scope is applicable to different alkyls, halides and ethers attached to the phenyl ring. Of note, divinylbenzene substrates could efficiently react at only one side. On the other hand, the arylsulfonylhydrazide substrate scope is limited to only five examples, yet a heteroaromatic thiophene derivative can be accessed in excellent yield (266). Mechanistically, the reaction involves three initial single elec-



Scheme 27 Synthetic method presented by Yue for accessing β -thiocyanato ketones.⁵⁰

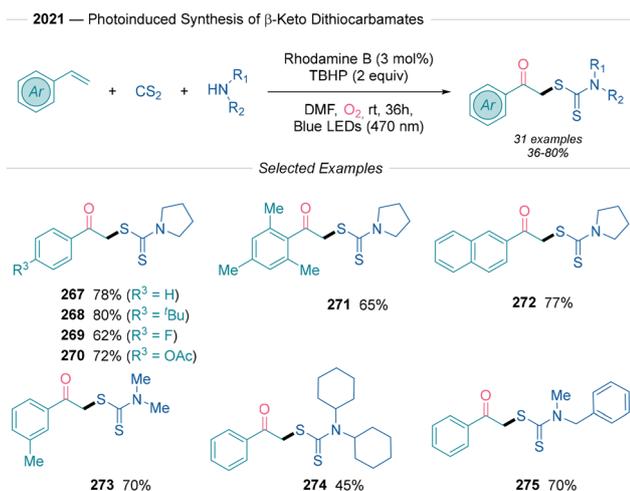




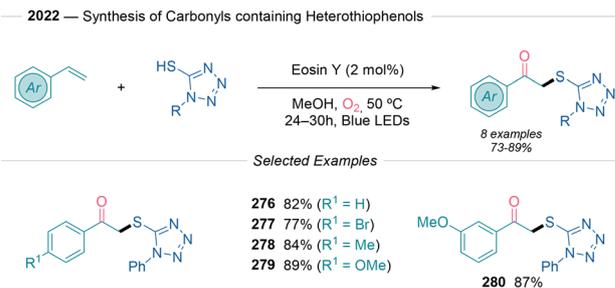
Scheme 28 Photoredox β -ketosulfone synthesis described by Zhu.⁵¹

tron oxidation processes of the sulfonyl hydrazine derivative through the photoredox cycle, which ultimately releases N_2 and forms a sulfonyl radical that adds to the olefin. Finally, the authors suggest that the produced benzyl radical intermediate proceeds through the general mechanism shown in Scheme 2B path a and e, or directly reacts with HOO^\bullet species to form the final ketone after dehydration.

In 2021, Singh⁵² developed a method for synthesizing β -keto dithiocarbamates using styrenes, carbon disulfide and secondary amines (Scheme 29). Rhodamine B catalyzes this transformation *via* reductive quenching, with the reaction showing remarkable broad substrate compatibility and achieving moderate to good yields. Different electron-donating (268, 270) and electron-withdrawing (269) groups tethered to the aromatic olefin showed good reactivity, including bulky mesitylene (271). The amenability of this transformation to (hetero) cyclic, symmetric non-cyclic and asymmetric non-cyclic secondary amines is remarkable (272–275). The use of TBHP as a sacrificial electron-acceptor significantly improved the yield. The mechanism initiates with amine nucleophilic attack on carbon disulfide to form dithiocarbamic acid, which, after SET with excited rhodamine B, yields a sulfur-centered radical that adds to styrene, producing a benzyl radical. The authors



Scheme 29 Visible-light mediated synthesis of β -keto dithiocarbamates described by Singh.⁵²



Scheme 30 Eosin Y facilitated photoredox difunctionalization process reported by Maiti.⁵³

suggest that this radical either reacts with $tBuOO^\bullet$ followed by Kornblum–DeLaMare rearrangement or follows the general radical mechanism shown in paths a and e in Scheme 2B.

Finally, in 2022, Maiti⁵³ advanced this field using aromatic thiols as sulfur sources in alkene difunctionalization (Scheme 30). Among the different methods presented, access to β -keto sulfides (276–280) is possible using eosin Y under an oxygen atmosphere after 24–30 hours of illumination at 50 °C. Despite showing a limited scope of 8 examples, the protocol demonstrated promising yields (75–89%). The authors propose that the synthesis of these organosulfur compounds proceeds *via* the Russell fragmentation pathway (see path a and e in Scheme 2B).

7. Conclusions

In conclusion, recent developments in alkene oxo-functionalization through photoredox catalysis have significantly expanded the toolkit of synthetic organic chemists, providing versatile and sustainable pathways for creating complex molecular architectures. Photoredox methods have demonstrated exceptional ability to promote selective formation of C=O and C–R bonds under mild conditions, with broad substrate scope and tolerance to diverse functional groups using mainly DMSO or O_2 as mild and non-toxic oxidants. Understanding the mechanisms behind radical generation and photo-excitation pathways highlights the ability to precisely control reaction dynamics, enabling the synthesis of complex multifunctional molecules and opening new avenues in medicinal chemistry. Despite considerable progress, some challenges remain. Reaction optimization for more challenging substrates beyond styrenes, stereoselective methods, and scalability for industrial applications are areas where additional advancements could enhance the impact of photoredox-driven alkene oxo-functionalization. As researchers continue to innovate within this field, it is anticipated that new catalytic systems, novel oxygen sources, and refined reaction conditions will drive further development, expanding the scope and applicability of these reactions in organic synthesis. Overall, photoredox catalysis stands poised to play an increasingly central



role in the future of sustainable and efficient synthetic strategies for alkene difunctionalization.

Author contributions

YJ and AGG contributed equally. All authors have given approval to the final version of the manuscript.

Data availability

No primary research results, software or code have been included and no new data were generated or analyzed as part of this review.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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