Acyl Radical Chemistry via Visible-Light Photoredox Catalysis

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Abstract
Visible-light photoredox catalysis enables easy access to acyl radicals under mild reaction conditions. Reactive acyl radicals, generated from various acyl precursors such as aldehydes, α-keto acids, carboxylic acids, anhydrides, acyl thioesters, acyl chlorides, or acyl silanes, can undergo a diverse range of synthetically useful transformations, which were previously difficult or inaccessible. This review summarizes the recent progress on visible-light-driven acyl radical generation using transition-metal photoredox catalysts, metallaphotocatalysts, hypervalent iodine catalysts or organic photocatalysts.

1 Introduction

Acyl radicals are nucleophilic in nature and serve as versatile synthetic intermediates in Giese-type additions to activated alkenes, Minisci-type acylations of heteroarenes, and for the preparation of a wide range of natural and biologically active molecules. Conventional approaches to the generation of acyl radicals, however, generally require harsh reaction conditions such as UV irradiation or high temperatures. One way to access these intermediates is by generation of alkyl radicals from alkyl iodides through photophysical and thermal initiation and subsequent carbonylation by CO (Scheme 1, method A). The use of acyl selenides in the presence of an organotin reagent such as Bu3SnH together with a radical initiator is an alternative means of generating acyl radicals (method B). Through the photochemical cleavage of the RC(O)–X bond of acyl tellurides (X = Te–R), benzylphosphine oxides [X = P(O)Ph2] can also afford acyl radicals. α-Hydroxy or α-amino ketones RC(O)–X [X = CH(OH)R or CH(NH2)R] can also deliver acyl radicals (method C). In addition, peroxide-mediated homolytic abstraction of a hydrogen atom from aldehydes and α-keto acids is a viable option for the generation of an acyl radical (method D). Many directed or non-directed C–H acylation processes catalyzed by transition metals have been developed in the last decades using this strategy. However, from a synthetic viewpoint, their utility was somewhat limited due to the requirement of high energy conditions such as high temperatures, UV irradiation, or stoichiometric amounts of toxic reagents or oxidants.

Recently, visible-light photoredox catalysis has emerged as a powerful tool for the synthesis of organic scaffolds that are difficult to prepare by traditional methods. Upon excitation with visible light, photoredox catalysts (PC) generate...
an excited photocatalyst (*PC) which can act by single-electron transfer (SET) processes, not only as a one-electron oxidant or a one-electron reductant but also as an energy donor, activating acceptor molecules by an energy-transfer (EnT) process. This photoredox strategy, therefore, provides a new platform for radical reactions by obviating the need for radical initiators and a stoichiometric amount of strong reducing agents. All these features make photoredox catalysis a sustainable alternative from the viewpoint of radical reactions and one that can be utilized as an elegant method to access acyl radicals.

2 The Scope of This Review

Over the past decade, various research groups have reported the visible-light-mediated generation of acyl radicals using photoredox catalysts, metallaphotocatalysts, hypervalent iodine photocatalysts, or organic photocatalysts. This review aims to provide an overview of recent progress in such visible-light-driven acyl radical generation using aldehydes, α-ketocarboxylic acids, carboxylic acids, carboxylic acid anhydrides, acyl thiocarbamates, acid chlorides, or acyl silanes as acyl radical precursors (Scheme 2). The scope, limitations, and the proposed reaction mechanism of each transformation are discussed. It is noteworthy that most of the reactions described in this review proceed through photoredox catalytic cycles, but the radical chain mechanism cannot be excluded.

Scheme 2 Various modes of acyl radical generation by visible-light photocatalysis

Biographical Sketches

Arghya Banerjee was born in West Bengal, India. He obtained his B.Sc. degree in chemistry from Ramakrishna Mission Vidyamandira, Belur in 2008. After completing his M.Sc. at IIT Guwahati, India in 2010, he undertook his Ph.D. at the same institute under the guidance of Prof. Bhism K. Patel. In 2017, he joined Stony Brook University as a postdoctoral associate under the supervision of Prof. Ming-Yu Ngai. His current research is focused on the development of novel acylation strategies using photoredox catalysis.

Zhen Lei was born in Xi’an, China. In 2011, he graduated with a B.Sc. degree in chemistry from Sichuan University, China. He continued his studies at the State University of New York at Binghamton, where he worked with Prof. Susan L. Bane on borazine-containing bioorthogonal reactions and was awarded his M.Sc. degree in 2015. In the same year, he began his Ph.D. studies at Stony Brook University under the guidance of Prof. Ming-Yu Ngai. His current research focuses on the development of photoredox-catalyzed C–H functionalization and asymmetric reactions.

Ming-Yu Ngai was born in Fuching, China and graduated with a B.Sc. degree from the University of Hong Kong in 2003. After receiving his Ph.D. degree with honors in chemistry from the University of Texas at Austin under the guidance of Prof. Michael J. Krische in 2008, he worked with Prof. Barry M. Trost at Stanford University as a Croucher postdoctoral fellow (2009–2011) and then with Prof. Tobias Ritter at Harvard University as a postdoctoral associate (2011–2013). In 2013, he was appointed as an assistant professor at the Department of Chemistry at Stony Brook University. His research focuses on the development of photoredox catalysis and fluorine chemistry.
3 Aldehydes as a Source of Acyl Radicals

Aldehydes are abundant, readily available, and versatile intermediates that are commonly converted into acyl radicals through hydrogen atom transfer (HAT). In this process, a radical species generated from a HAT reagent abstracts the hydrogen atom of aldehydes forming an acyl radical. Common HAT reagents such as persulfates and tert-butyl hydroperoxide, which are used in traditional thermal radical chemistry, are also applicable to photoredox catalysis. Compounds such as quinuclidine and Eosin Y have also emerged as new HAT reagents for activation of aldehydes. The bond dissociation energies (BDEs) of the C–H of different aldehydes are strikingly similar within 88.0 kcal/mol to 89.4 kcal/mol, while the BDEs of common HAT reagents can range from 88.2 kcal/mol to 106.3 kcal/mol (Scheme 3).

![Scheme 3](image)

In 2013, Cho et al. reported a synthesis of carboxylic acids through photocatalytic oxidation of aldehydes using molecular O₂ as an oxidant and a HAT reagent (Scheme 4). Both electron-deficient and electron-rich aromatic aldehydes, as well as aliphatic aldehydes, were oxidized to carboxylic acids in excellent yields (90–99%).

![Scheme 4](image)

It was proposed that the excited **Ir(dFppy)** (E传媒 = 60.1 kcal/mol) (E传媒 = triplet state energy of the excited photocatalyst) converts triplet O₂ into singlet O₂ via photoinduced energy transfer. Singlet O₂ then serves as a HAT reagent that abstracts an aldehyde hydrogen atom to form an acyl radical 5.2 and a hydroperoxyl radical (5.3). These two radicals recombine to give a peroxy acid 5.4, which reacts with another molecule of the aldehyde to afford an adduct 5.5. This compound then undergoes a Baeyer–Villiger rearrangement to form the desired carboxylic acid product 5.6 (Scheme 5).

![Scheme 5](image)

In 2014, Zeng et al. published a photoredox catalysis method to generate benzoyl radicals from benzaldehydes for the acylation of phenanthridine (Scheme 6). Although various benzaldehydes with halogen, alkyl, methoxy, and acetoxy substituents could serve as benzoyl radical donors, phenanthridine was the only radical acceptor reported in this work. The reaction afforded the desired products in yields ranging from 27–73%, but aldehydes with strong electron-donating groups such as p-NO₂ or strong electron-withdrawing groups such as p-NO₂ failed to afford the desired products.

![Scheme 6](image)

The proposed mechanism of this reaction is shown in Scheme 7. The persulfate salt 7.1 (E₂/² = 0.35 V vs SCE) oxidizes the excited **Ir(dppy)** (E₂/² = –1.73 V vs SCE) via single-electron transfer (SET) to form a sulfate ion 7.3 and a sulfate radical anion 7.2. The resulting sulfate radical anion abstracts a benzaldehyde hydrogen atom via a HAT process to give the benzoyl radical 7.5. Subsequent addition of the benzoyl radical to phenanthridine generates an amideyl radical 7.8, which is deprotonated by SO₂⁻ to afford a radical anion 7.9. This radical anion is then oxidized by the **Ir(dppy)** to form the final product 7.10.
t-Butyl hydroperoxide (TBHP) is a versatile HAT reagent. While single-electron reduction of TBHP generates the t-butoxy radical, single-electron oxidation of deprotonated TBHP affords the t-butoxy peroxo radical (Scheme 8). Both of these radical species efficiently abstract an aldehyde hydrogen atom, giving an acyl radical.\(^27\) Consequently, combining TBHP with photoredox catalysis provides a useful and mild tool for the formation of acyl radicals from aldehydes.

In 2015, Wang and Li reported a synthesis of \(\alpha,\beta\)-epoxy ketones from styrenes and benzaldehydes under photocatalytic conditions using TBHP as a HAT reagent.\(^28\) Aromatic aldehydes with halogen, alkyl, and methoxy substituents and thiophencarboxaldehyde reacted well, giving 61–83\% yields (Scheme 9). In terms of the styrene scope, arenes with halogen, alkyl, and methoxy substituents, pyridine, naphthalene, and 1,1-disubstituted arenes including 1,1-diphenylethylene and \(\alpha\)-methylstyrene underwent coupling to afford the desired products in 51–85\% yields.

Wang and Li proposed that the \(t\)-butyl hydroperoxide serves two roles in the reaction. First, TBHP oxidizes the excited *Ru\(^{III}\)* (*E\(\text{I}_{1/2}\)\(^{III/II}\) = –0.81 V vs SCE) to form a hydroxide and a \(t\)-butoxy radical ‘BuO\(^-\)’, which subsequently abstracts a hydrogen atom from the aldehyde to give a benzyl radical. Second, deprotonation of the TBHP by the hydroxide ion \(\text{OH}^-\) gives a \(t\)-butoxy peroxide anion ‘BuOO\(^-\)’, which reduces the oxidized Ru\(^{III}\)(bpy)\(^{2+}\) regenerating the photocatalyst and forming a \(t\)-butoxy peroxo radical ‘BuOO\(^-\)’. Recombination of the \(t\)-butoxy peroxo radical with the radical intermediate 10.7 affords a \(\beta\)-peroxy ketone 10.8, which undergoes base-promoted elimination of ‘BuO\(^-\)’ to produce the final product 10.9 (Scheme 10).

In 2017, Hong et al. reported an intramolecular cyclization and epoxidation (Scheme 11), developed in analogy to the intermolecular method reported by Wang and Li,\(^28\) using TBHP as the HAT reagent.\(^29\) The reaction conditions were applicable to both allyloxy and allylamino substrates.
to produce the desired spiroepoxy chroman-4-ones and enamiones. Interestingly, a three-step tandem process starting from benzyl alcohol and using 8 equivalents of TBHP also occurred, albeit with lower yields being obtained.

It was reported that addition of TEMPO completely inhibits the reaction and forms the TEMPO adduct, which indicates the involvement of a radical intermediate. Exposure of the β-peroxy ketone 12.10 to a solution of K₂CO₃ in ᵃ₋P-rOAc afforded the desired α-carbonyl epoxide 12.11, suggesting that the product is derived from the β-peroxy ketone intermediate. Based on these experimental results and the observation that benzylclic alcohols also afforded the desired spiroepoxy chroman-4-ones, tandem oxidation of the benzylclic alcohols to aldehydes followed by radical cyclization was proposed (Scheme 12). TBHP (12.1) oxidatively quenches the excited *Ru(bpy)₃²⁺ to generate Ru(bpy)₃²⁺ and a t-butoxy radical (tBuO⁻) (12.2). This radical abstracts an α-hydrogen atom from the benzylclic alcohol 12.3 to generate an α-hydroxy radical 12.5, which is oxidized and deprotonated to form benzaldehyde 12.7. Once the benzaldehyde is formed, the rest of the reaction mechanism is parallel to the catalytic cycle proposed by Wang and Li.²⁰

Following Wang’s discovery using TBHP for the generation of acyl radicals, Cho and Iqbal, in 2016, disclosed a photocatalytic amide formation protocol from aldehydes and amines (Scheme 13).³⁰ It was proposed that reduction of TBHP affords hydroxide and the t-butoxy radical, which undergoes HAT with benzaldehyde to form the benzoyl radical 13.5 (path a). This radical abstracts the chlorine atom from N-chlorosuccinimide, forming benzoyl chloride 13.8, which reacts with an amine to afford the amide product. The reaction proceeds with a sub-stoichiometric quantity of TBHP, leading to speculation that other radical species such as the t-butyl peroxy radical (path b) and the succinimide radical (path c) generated in the reaction mixture might also be responsible for the HAT of benzaldehyde leading to the benzoyl radical.

This reaction has a broad substrate scope. Both electron-rich and electron-poor benzaldehydes with substituents such as alkyl, halogens, cyano, and CF₃ underwent coupling to afford the desired amides in 65–87% yields. Primary and secondary amines, anilines, and aminopyridines were all viable substrates giving the desired products in 58–82% yields. This strategy was used in the synthesis of the antidepressant moclobemide 6 and the D₃ receptor GR103691 intermediate (Scheme 13).

**Scheme 12** Photocatalytic cycle involving benzaldehyde and benzylclic alcohol²⁰

**Scheme 13** Photocatalytic amide synthesis from benzaldehydes using TBHP³⁰
In 2017, Glorius et al. reported a photocatalytic alkylation of aldehydes, formates, and formamides using alkynylbenziodoxolones as the alkyne source and the resulting benziodoxolonyl radical as a HAT reagent. This reaction has a broad substrate scope and a wide range of alkyl, vinyl, aryl, and heteroaryl aldehydes, formates, and formamides reacted with various aryl or silyl alkynylbenziodoxolones to afford the desired alkylnlated products in 46–90% yields (Scheme 14). The carbonyl radicals generated under the optimized conditions failed to react with double bonds, and thus the method is compatible with α,β-unsaturated aldehydes. This transformation is also compatible with late-stage alkylnlation of complex substrates such as cholesterol, lithocholic acid, probenecid, and adapalene derivatives, giving the desired products in 48–78% yields.

Stern–Volmer quenching experiments showed that the 2-iodobenzoxo group was the only component that quenched the photocatalyst. In the presence of TEMPO, the formation of the alkynylated product was completely inhibited, and a TEMPO-trapped adduct was obtained. On the basis of these results, the authors proposed that 2-iodobenzoate (Scheme 15). Hydrogen atom abstraction of the aldehyde hydrogen by the benziodoxolonyl radical as a HAT reagent.

In 2017, MacMillan et al. reported a triple catalytic protocol for arylation, vinylation, and alkylation of aldehydes via an acyl radical intermediate using aryl, vinyl, and alkyl bromides as coupling partners and quinuclidine, NII, and a photocatalyst as catalysts (Scheme 16). This approach has a very broad scope and is insensitive to the electronic nature of the aryl bromides. Heteroaryl, cyclic and acyclic vinyl, and alkyl bromides are viable substrates and afforded the desired ketones in 50–90% yields. Regarding the aldehyde scope, both alkyl and aryl aldehydes coupled well to afford the desired products in 70–90% yields, although 6–10 equivalents of aryl aldehydes were needed.

The mechanistic hypothesis for this triple catalysis is shown in Scheme 17. SET from quinuclidine (E_{1/2}^{ox} = +1.21 V vs SCE) to form IrIII and the 2-iodobenzyloxy radical (Scheme 15). Hydrogen atom abstraction of the aldehyde hydrogen by 15.2 provides a carbonyl radical 15.5 that reacts with alkynylbenziodoxolone 15.6 to form the desired product 15.8, simultaneously releasing the benziodoxolonyl radical 15.7. Reduction of 15.7 with IrII forms 15.1 and regenerates the ground state Ir photocatalyst. Alternatively, since 15.7 is in equilibrium with 15.2, it can undergo a HAT reaction directly.
atom to form the acyl radical 17.5. The α-amino C–H bond also exhibits hydridic bond polarization and is subjected to hydrogen atom abstraction.34 The authors discovered that the reaction performed in 1,4-dioxane circumvented the unwanted competing α-amino C–H activation affording exclusively the desired acylated product, whereas MeCN or DMSO solvents delivered the α-amino arylation product in addition to the desired product. Oxidative addition of the aryl bromide to NiII on the other hand delivers an aryl-NiII species 17.7, which is intercepted by the acyl radical 17.5 to form acyl-NiII complex 17.8. Subsequently, reductive elimination forms the desired ketone product and a Ni species 17.9. A single-electron transfer between IrIII and NiII regenerates the IrIII and NiII catalysts and completes the catalytic cycle.

Also in 2017, Liu et al. used the quinuclidine catalyst to generate the acyl radical from aldehydes under photoredox conditions (Scheme 18).35 Both aromatic and aliphatic aldehydes were viable substrates under the dual-catalytic conditions. The synthetic utility was also well demonstrated by a variety of electron-deficient olefin acceptors.

With a mechanism similar to that described in Scheme 17, reductive quenching of the excited *IrIII catalyst by quinuclidine (19.1) forms a HAT reagent 19.2, which abstracts the aldehyde hydridic hydrogen to form an acyl radical. The acyl radical is then intercepted by an olefin to give the carbon radical intermediate 19.7. A single-electron transfer from IrIII to this intermediate, followed by protonation, delivers the desired product and regenerates the IrIII catalyst (Scheme 19).

In the same paper,35 Liu et al. presented their preliminary results of a catalytic cross-coupling process using the Ir photocatalyst and NiCl2. In contrast to MacMillan’s work,33 Liu et al. used a stoichiometric amount of quinuclidine, and the scope of the reaction was significantly limited as a result of the unwanted reduction of aryl bromides (Scheme 20).

In 2018, Itoh et al. used 2-t-butylanthraquinone (2-t-Bu-AQN) as a photocatalyst and benzoyl peroxide (BPO) as an oxidant in the presence of potassium carbonate to synthesize 3-acyl-4-arylcoumarin derivatives (Scheme 21).36 Alkyl, alkoxy, and acetoxyl groups on both the benzaldehyde and propynate substrates were well tolerated. The authors showed that many of their coumarin products had potential biological applications as demonstrated by their effectiveness in the inhibition of PSA secretion and the proliferation of androgen-dependent prostate cancer.

The proposed mechanism for this reaction is depicted in Scheme 22. Photoexcited 2-t-butylanthraquinone 22.2 acts as a HAT reagent and abstracts the formyl hydrogen atom of the desired product.
benzaldehyde, forming the semiquinone radical\(^{27}\) AQH\(^{+}\) (22.3) and the benzyloxy radical 22.5. Addition of the benzyloxy radical to the propynyl 22.6 generates a vinyl radical intermediate 22.7, which undergoes 5-\textit{exo-trig} cyclization to afford a spirocyclic species 22.8. This spirocyclic intermediate is then oxidized by either BPO or the benzoyloxyl radical 22.13 to form a carboxylation 22.9. 1,2-Ester migration and deprotonation afforded the desired product 22.11. Oxidation of AQH\(^{+}\) by BPO, followed by deprotonation produced benzoic acid, the benzoyloxyl radical and the ground state AQN catalyst. This reaction also proceeds under thermal conditions, where a 54% yield was obtained in the absence of the photocatalyst, indicating that the benzyloxy radical formed from the thermal decomposition of benzyloxy peroxide can also function as an alternative HAT reagent.

In 2018, Wu et al. reported that excited Eosin Y, functioning as a HAT reagent, can abstract the aldehyde hydrogen atom under irradiation with an 18 W white LED light (Scheme 23).\(^{21}\) Alkyl, aryl and heteroaryl aldehydes reacted with electron-deficient 1,1-dicyano-2-phenylethylene to afford the desired products in 83–94% yields. Benzaldehyde can react with a SOMOphile such as methyl 2-[(phenylsulfonyl)methyl]acrylate to form an alllylation product in 48% yield. It should be noted that the major focus of Wu’s work was on the alllylation of a wide range of C–H bonds with electron-deficient alkenes under photocatalytic conditions. The C–H partners include THF, thioethers, amides, alcohols, and cyclohexane. However, these coupling reactions are outside the scope of this review.

Anionic Eosin Y is commonly engaged in SETs under photoredox-catalyzed conditions. However, neutral Eosin Y, which was used by Wu et al.,\(^{21}\) is inactive in SET processes.\(^{18}\) It was shown that neither THF nor phenyl vinyl sulfone quenches the excited Eosin Y indicating that the reaction did not proceed through single-electron transfer or energy transfer. Transient absorbance experiments showed that the excited *Eosin Y absorbs at both 329 nm and 543 nm, whereas Eosin Y–H absorbs at 366 nm. In the presence of phenyl vinyl sulfone, a radical acceptor, the decay of Eosin Y–H was much faster than took place in the absence of the alkene (Scheme 24), demonstrating the feasibility of HAT...
between Eosin Y-H and radical intermediates formed during the coupling process. The quantum yield of the reaction was estimated to be 0.40.

On the basis of these mechanistic studies, Wu et al. proposed the direct photocatalytic hydrogen atom transfer mechanism shown in Scheme 25. Photoexcitation of Eosin Y (25.1) affords excited \*Eosin Y (25.2), which abstracts an aldehyde hydrogen atom to form an acyl radical species 25.5 and Eosin Y-H (25.3). The acyl radical is subsequently trapped by an electron-deficient alkene to form the alkyl radical intermediate 25.7. At this stage, there are two reaction pathways accounting for the formation of the desired product and regeneration of the Eosin Y catalyst. In path a, a reverse hydrogen atom transfer (RHAT) between the Eosin Y-H and radical species 25.7 affords the final product and the Eosin Y catalyst. In path b, aldehyde 25.4 undergoes HAT with the radical species 25.7 to form the desired product 25.8 and an acyl radical 25.5. The acyl radical reacts with Eosin Y-H via RHAT to afford an aldehyde and regenerate the Eosin Y catalyst. Although the authors performed computational and deuterium labeling studies, they could not distinguish between these two pathways.

Salles et al., in 2018, achieved acyl-epoxylation and hydroacylation of alkenes using methylene blue (MB) as a photoredox catalyst and \( K_2 S_2 O_8 \) as an oxidant in air-equilibrated water solution (Scheme 26). With high loading of the photocatalyst and oxidant (2.50 mol% and 2.00 equiv, respectively), simple benzaldehydes with the arene moiety substituted with Me, Cl, F, MeO or CF\(_2\) reacted with styrenes or 2-vinylpyridine to afford the desired epoxide products in 75–92% yields. 1-Naphthaldehyde and cyclohexanecarboxaldehyde were also viable substrates forming the final products in 84% and 79% yields. With lower loading of the photocatalyst and oxidant (0.50 mol% and 1.00 equiv, respectively), benzaldehydes coupled with long-chain aliphatic alkenes to deliver the hydroacylated products in 67–89% yields.

The reaction of benzaldehyde and styrene using \( K_2 S_2 O_8 \) in the absence of \( K_2 C O_3 \) only afforded trace acyl-epoxylated product, whereas the reaction proceeded well using \( H_2 O_2 \) in the presence of \( K_2 C O_3 \). Based on these observations and literature precedents, a reaction mechanism involving a hydroperoxide anion as a HAT reagent was proposed and is shown in Scheme 27. Persulfate anion 27.1 reacts with water under basic conditions to generate the hydroperoxide anion 27.2 (\( E_{1/2}^{\text{red}} = -0.88 \text{ V vs SHE} \)), which undergoes single-electron oxidation with excited MB* (\( E_{1/2}^{\text{red}} = -1.21 \text{ V vs SHE} \)) to form a hydroperoxyl radical (27.3) and methylene blue neutral radical \( \text{MB}^* \). Oxidation of \( \text{MB}^* \) by the \( S_2 O_8^{2-} \) or \( O_2 \) regenerates the methylene blue catalyst. The hydroperoxyl radical abstracts an aldehyde hydrogen atom to form an acyl radical 27.6, which adds onto an alkene to give the alkyl radical intermediate 27.8. With the lower loading of the photocatalyst and oxidant, the alkyl radical 27.8 undergoes HAT with an aldehyde substrate to afford the desired hydroacylation product 27.9 via a radical-chain propaga-
tion process. With a higher loading of the photocatalyst and persulfate anion, the alkyl radical \( 27.8 \) is trapped by the hydroperoxyl radical to deliver the \( \beta \)-peroxyl adduct \( 27.10 \). Finally, base-promoted elimination affords the desired epoxide product \( 27.11 \).

### 4 \( \alpha \)-Keto Acids as a Source of Acyl Radicals

Conversion of \( \alpha \)-keto acids into the acyl radical equivalents can be achieved via single-electron transfer of the corresponding carboxylate by photocatalytic oxidation and subsequent decarboxylation. Alternatively, installation of a good leaving group (X), e.g., as in \( N \)-hydroxyphthalimide, generates a keto ester that can be reduced by a photoredox catalyst (PC) and forms an acyl radical after further decarboxylation (Scheme 28).

![Scheme 28](image)

In 2014, Lei and Lan reported the first visible-light-mediated photocatalytic oxidative decarboxylation of \( \alpha \)-keto acids in the synthesis of amides. This efficient radical decarboxylative coupling was catalyzed by the photocatalyst \([\text{Ru(phen)}_2\text{Cl}_2](E^{1/2} = +0.82 \text{ V vs SCE})^{44}\) and molecular oxygen as an oxidant. A wide range of electron-donating and electron-withdrawing aromatic \( \alpha \)-keto acids reacted smoothly under these reaction conditions to afford the desired amides in good yields (64–85\%) (Scheme 29). Heteroaromatic and aliphatic \( \alpha \)-keto acids provided the desired products in 48–40\% yields. Various electron-rich aromatic and aliphatic amides gave the corresponding products in 40–79\% and 25–77\% yields, respectively.

![Scheme 29](image)

A series of studies was conducted to examine the reaction mechanism. For example, cyclic voltammetry (CV) experiments on a \( \alpha \)-keto acid salt (PhCO\( \text{CONHR}_2\)) suggest an oxidative decarboxylation path, TEMPO-trapping experiments confirm the formation of an acyl radical, and DFT calculations support the reaction between aroyl radicals and amines followed by deprotonation leading to an amide radical anion. Interestingly, in the absence of the \( \alpha \)-ketocarboxylic acid, EPR studies of this photocatalytic reaction detected two peaks: \([\text{Ru(phen)}_2\text{Cl}_2]^{2+}\) and an amine radical. Addition of an \( \alpha \)-ketocarboxylic acid diminishes the organic radical peak and only the \([\text{Ru(phen)}_2\text{Cl}_2]^{2+}\) peak remains. Thus, the authors proposed that the oxidation of \([\text{Ru(phen)}_2\text{Cl}_2]^{2+}\) by molecular oxygen is crucial and probably the rate-determining step of this process. Based on these results, a possible reaction mechanism was proposed and is shown in Scheme 30. Reductive quenching of the excited photocatalyst \([\text{Ru(phen)}_2\text{Cl}_2]^{2+}\) by an amine forms an amine radical cation \( 30.2 \) and \([\text{Ru(phen)}_2\text{Cl}_2]^{2+}\). Single-electron oxidation of \([\text{Ru(phen)}_2\text{Cl}_2]^{2+}\) by molecular oxygen affords the ground state photoredox catalyst, \([\text{Ru(phen)}_2\text{Cl}_2]\), and a superoxide radical anion, which deprotonates and oxidizes the ammonium \( \alpha \)-ketocarboxylate salt \( 30.3 \) to produce the dicarbonyl radical intermediate \( 30.5 \). Decarboxylation of \( 30.5 \) gives acyl radical \( 30.6 \), which is then trapped by amine \( 30.1 \) followed by deprotonation in the presence of a hydrogen peroxide anion \( \text{HO}_2^-\) (30.4) to produce the amide radical anion \( 30.7 \). Oxidation of \( 30.7 \) via a SET process affords the desired amide product \( 30.8 \).

![Scheme 30](image)

This method was also applied to anilines, \( \alpha \)-substituted with \( \text{NH}_2 \), \( \text{OH} \), and \( \text{SH} \) groups, to construct important heterocyclic compounds such as benzimidazoles (68–93\%), benzoazoles (39–46\%), and a benzothiazole (32\%) in good yields (Scheme 31).

Following initial studies by Lei and Lan on photoredox-catalyzed decarboxylative amidation, this acyl radical generation from \( \alpha \)-keto acids has been employed in several radical coupling reactions. For example, in 2015, Macmillan et al. reported the first decarboxylative arylation of \( \alpha \)-keto acids using aryl halides via a merger of visible-light phot-
toredox catalysis and nickel catalysis.\textsuperscript{45} Substituted aromatic and aliphatic α-keto acids are compatible under the reaction conditions and provide moderate to excellent yields (57–92\%) of the desired ketones (Scheme 32). A sterically hindered α-substituted α-keto acid was also efficiently coupled under the same reaction conditions and provided the desired product in high yield (92\%). Halo-arenes (halo = Br, I) and halo-heteroarenes containing electron-donating and electron-withdrawing substituents also provided the desired ketones in 70–90\% and 64–85\% yields, respectively.

Further generalization of this method was demonstrated by successfully coupling hindered vinyl halides and cyclopentyl bromide with α-keto acids under the optimized reaction conditions to generate a vinyl ketone and a dialkyl ketone in good yields (73–88\%). This strategy was also elaborated for the synthesis of fenofibrate, a cholesterol-controlling drug (Scheme 33).

The authors proposed that the strongly oxidizing excited \[ ^1 \text{Ir}([\text{dF(CF}_3\text{)}\text{ppy}]_2\text{dtbbpy})^+ \] (34.2) \( (E^\text{III/II} = +1.21 \text{ V vs SCE in MeCN}) \) generated upon visible-light irradiation, reacts with the α-ketocarboxylate via single-electron oxidation to generate the corresponding carboxyl radical species and the reduced photocatalyst 34.4. This carboxyl radical species subsequently delivers the acyl radical species 34.5 via decarboxylation. SET from the strong reducing Ir\textsuperscript{iii} species 34.4 \( (E^\text{III/II} = −1.37 \text{ V vs SCE in MeCN}) \) to the in situ generated Ni\textsuperscript{iii}–dtbbpy complex would afford the Ni\textsuperscript{0} catalyst 34.6, which initiates the second catalytic cycle through oxidative addition to the aryl halide to generate the Ni\textsuperscript{ii} aryl complex 34.8. The addition of the nucleophilic acyl radical 34.5 to 34.8 produces the nickel acyl complex 34.9. Final reductive elimination from this Ni\textsuperscript{iii} complex provides the desired ketone 34.10 with the regeneration of the Ni\textsuperscript{ii}–dtbbpy complex 34.11 (Scheme 34).

In the last decades, palladium has been widely used in various transition-metal-catalyzed decarboxylative cross-coupling reactions.\textsuperscript{46} A typical example is the decarboxylative acylation of aryl halides using α-keto acids.\textsuperscript{47} In 2015, Shang and Fu combined photoredox and palladium catalysis and achieved such decarboxylative cross-coupling reactions for the first time.\textsuperscript{48} The reported decarboxylative coupling strategy of aryl halides with α-ketocarboxylic acids provides access to various unsymmetrical ketones. The electronic and steric effects of the substituents present in aryl halides have no substantial effects on the yields of the products (74–96\%). Interestingly, aryl iodosides containing a t-butoxy carbonyl (Boc)-protected phenylalanine ester and an aryl boronic pinacol ester both provided the corresponding products in 88\% and 70\% yields. This reaction is compatible with electron-donating aryl groups (82–95\%) as well as heteroaryl (46–89\%) and alkyl α-ketocarboxylic acids (60–89\%), but the presence of electron-withdrawing substituents on the aryl ring of the α-ketocarboxylic acids sharply decreased the product yield to ~10\%. The use of an external phosphine ligand (NiXantphos) in the case of bromoarenes is due to their relatively slow oxidative addition to the Pd\textsuperscript{0} catalyst when compared to iodoarenes (Scheme 35).
Radical trap experiments showed that addition of 4 equivalents of TEMPO completely shut down the reaction and a stoichiometric amount of the corresponding TEMPO adduct was isolated (Scheme 36). These experiments strongly suggest a radical mechanism in which the excited iridium catalyst (IrIII) oxidizes the α-ketocarboxylate to generate the acyl radical and IrI species. Although in this context the oxidation of IrII is possible by either the PdI, PdII or PdIII species, DFT calculations support the involvement of the PdII species 36.9.

Merging transition-metal-catalyzed o-directed C–H bond activation with photochemically generated radical intermediates in a dual-catalytic fashion is an attractive strategy with which to form the desired bonds in a shortened and mild reaction pathway. In 2015, Wang and Li disclosed a protocol for room-temperature decarboxylative o-acylation of acetanilides with α-ketocarboxylic acids via a novel Eosin Y/Pd dual catalysis.50 Various aromatic and aliphatic α-ketocarboxylic acids all coupled with acetanilide and provided the desired products in 70–84% and 51–62% yields, respectively (Scheme 37). o-Substituted aryl α-ketocarboxylic acids were also compatible with these reaction conditions providing good yields of the o-acylated products (78–85%). A range of electron-donating and electron-withdrawing acetanilide derivatives all afforded the desired products in good yields (68–82%) when coupled with α-ketophenylacetic acid. However, more hindered o-substituted acetanilides such as o-ethyl, o-(isopropyl), and (o-t-butyl) acetanilides failed to afford the o-acylated products under the reported conditions.

On the basis of TEMPO trapping experiments and confirmation of a superoxide radical anion (O2−) by electron paramagnetic resonance (EPR), the authors proposed a plausible reaction pathway shown in Scheme 38.50 The excited *Eosin Y (38.2) oxidizes aryglyoxylic acid 38.3 to form (Eosin Y)+ (38.5) and aryglyoxylic radical cation 38.4, which undergoes deprotonation and decarboxylation to give aryl radical 38.8. (Eosin Y)+ is oxidized by molecular oxygen regenerating Eosin Y and producing the superoxide radical anion O2− (38.6). The Pd-catalytic cycle is initiated by C–H activation of acetanilide forming a palladacyclic intermediate 38.7, which subsequently reacts with the nucleophilic aryl radical 38.8 to afford a PdIII intermediate 38.9. This PdIII intermediate is further oxidized by the superoxide radical anion to generate a PdIV intermediate 38.10 along with the formation of HO2− and H2O2. Finally, reductive elimination of the PdIV intermediate affords the desired product 38.11 and an active PdII catalyst for the next catalytic cycle.

By merging Pd catalysis with organic photocatalysis, the same group further developed a protocol for efficient ortho C–H acylation of azo and azobenzene through α-keto acids in 2016 (Scheme 39).51 A range of aromatic as well as heteroaromatic α-ketocarboxylic acids reacted with azobenzene under the optimized reaction conditions and provided coupled products in 66–79% and 62% yields, respectively. Naphthyl α-ketocarboxylic acids gave the desired products...
in 77–84% yields. However, no reaction was observed when aliphatic \(\alpha\)-oxocarboxylic acid was used as the acyl surrogate. Disubstituted azo- and azoxybenzenes also afforded the desired \(o\)-acylated products in decent yields (57–78%) regardless of their electronics, however, \(o\)-disubstituted azo- and azoxybenzene derivatives gave lower yields (37–56%) due to steric problems.

A series of mechanistic studies were conducted to establish the reaction mechanism.\(^1\) A TEMPO trapping experiment suggests the generation of acyl radicals. The intermolecular kinetic isotopic effect observed (\(k_\text{H}/k_\text{D} = 3.7\)) in the reaction identifies the \(C\–H\) activation as the rate-determining step, and an EPR spectroscopic data confirms the generation of a superoxide radical anion (\(O_2^-\)) in the reaction medium. On the basis of these results, the authors proposed a mechanism that begins with the photoexcitation of mesityl acridinium catalyst (PC)\(^{40.1}\) generating the excited photocatalyst (*PC)\(^{40.2}\). Oxidation of \(\text{PC}^*\) by molecular oxygen affords \(\text{PC}^+\)\(^{40.3}\) and a superoxide radical anion. Subsequently, \(\text{PC}^+\) oxidizes the \(\alpha\)-ketocarboxylic acid to regenerate the ground state photocatalyst PC along with the corresponding carboxyl radical species that leads to the formation of an aryl radical species \(\text{PC}^\cdot\). On the other side, a Pd catalytic \(C\–H\) activation of the azobenzene forms the palladacyclic intermediate \(\text{PC}^\cdot\). Addition of the in situ generated radical \(\text{PC}^\cdot\) to this palladacyclic intermediate \(\text{PC}^\cdot\) affords the Pd\(^{40.5}\) or Pd\(^{40.6}\) species \(\text{PC}^\cdot\) in analogy to the observation of Wang and Li in Scheme 38. At this stage, reductive elimination from \(\text{PC}^\cdot\) affords the desired acylated product \(\text{PC}^\cdot\) with the formation of the Pd\(^{40.7}\) intermediate \(\text{PC}^\cdot\), which is further re-oxidized by the superoxide radical anion to regenerate the Pd\(^{40.8}\) catalyst, completing the catalytic cycle (Scheme 40).

Acyl radicals, generated by photocatalytic decarboxylation, were also reported by Shang and Fu in 2015 for acyl reductive Michael addition with various Michael acceptors.\(^5\) Various aromatic and heteroaromatic \(\alpha\)-ketocarboxylic acids were decarboxylated in the presence of photoredox catalysts to form (hetero)aryl radicals. These radicals underwent Michael addition to various \(\alpha,\beta\)-unsaturated esters, ketones, amides, aldehydes, nitriles, and sulfones to afford the corresponding products in 45–94% yields (Scheme 41).

The authors reported that the product yield was significantly decreased by reducing the loading of the base to a catalytic amount, which demonstrates the role of the carboxylate anion in quenching the excited photoredox catalyst.\(^5\) The reaction has been proposed to proceed via a reductive quenching cycle of photoexcited \(\text{PC}^*\) by the \(\alpha\)-ketocarboxylate...
as depicted in Scheme 42. The acyl radical 42.4, generated via the decarboxylation of an \( \alpha \)-ketocarboxylate radical, was subsequently trapped by a Michael acceptor affording the radical 42.6. This radical oxidizes the \( \text{Ir}^\text{III} \) catalyst regenerating the photocatalyst \( \text{Ir}[[\text{dF(CF}_3\text{)}_2\text{ppy}]_2\text{phen}]\text{PF}_6 \) and forming the anion 42.7, which readily protonates to provide the 1,4-addition product 42.8 (Scheme 42). Acrylic acid is an ineffective Michael acceptor under these reaction conditions due to its possible reductive quenching in competition with the 2-ketocarboxylate. \( \beta \)-Dimethylated and \( \beta \)-phenyl-substituted alkene substrates are also incompatible Michael acceptors due to their ability to form stable tertiary or benzylic radicals with a lower oxidation potential to oxidize \( \text{Ir}^\text{III} \).

The use of TEMPO under the standard reaction conditions completely inhibited the product formation, indicating a radical process. The use of the oxidant \( \text{t-butyldihydroperoxide} \) under the standard reaction conditions was unproductive which rules out the possibility of benzylic oxidation. The absence of the base in the optimized reaction conditions provided the desired enone product in 10% yield along with the detection, by NMR analysis, of the fluoro-acetylated product. From their observations in control experiments, Zhu et al.33 proposed a mechanism which starts with the visible-light irradiation of the photocatalyst \([\text{Ir}([\text{dF(CF}_3\text{)}_2\text{ppy}]_2\text{dtbbpy})]\text{PF}_6 \), generating a long-lived excited state \( *\text{Ir}^\text{III} \) 44.2 (Scheme 44). With the aid of Selectfluor, \( *\text{Ir}^\text{III} \) can oxidizes the \( \alpha \)-ketone to give the aroyl radical species 44.5, which reacts with styrene derivatives to deliver the benzylic radical 44.6. Fluorination of 44.6 by Selectfluor produces aroyl-fluorinated species 44.8 and the corresponding radical dication 44.7 which oxidizes the reduced \( \text{Ir}^\text{III} \) to the ground state \( \text{Ir}^\text{III} \) species, thereby completing the photoredox cycle. Finally, the aroyl-fluorinated product delivers the final \( \alpha,\beta \)-unsaturated ketone product 44.9 via a base-mediated elimination process.
In 2016, Overman’s group reported the use of N-hydroxyphthalimido esters for the efficient generation of alkyl as well as methoxycarbonyl radicals via a photoredox-catalyzed reductive SET.54 Based on this idea, in 2017, Taylor and Donald reported the generation of carbamoyl radicals from N-hydroxyphthalimido oxamides and used them for the synthesis of 3,4-dihydroquinolin-2-ones under mild photocatalytic conditions (Scheme 45).55 This method provides access to a diverse collection of o-, m- or p-substituted oxamides for the successful generation of 3,4-dihydroquinolin-2-ones in good yields (41–80%). However, a clear trend of increasing yields was observed for oxamides containing electron-withdrawing substituents compared to their electron-donating counterparts. Several mono- and disubstituted alkenes, as well as exocyclic alkenes, all afforded the desired 3,4-dihydroquinolin-2-ones containing fused cyclic (38–81%) and spirocyclic systems (43–71%).

The proposed mechanistic cycle begins with the irradiation of the photocatalyst fac-*Ir(ppy)$_3$ with visible light, which could lead to the photoexcited state fac-*Ir(ppy)$_3$ (46.2). Excited fac-*Ir(ppy)$_3$ (E$_{1/2}^{III}$ = −1.73 V vs SCE)56 reduces the N-hydroxyphthalimido oxamide 46.3 to form the radical anion 46.5, which rapidly fragments releasing CO$_2$, NPhth$^-$, and the carbamoyl radical 46.6. The carbamoyl radical undergoes Michael addition to an electron-deficient olefin followed by cyclization to produce cyclohexadienyl radical 46.8. Oxidation of 46.8 by the photocatalyst (E$_{1/2}^{IV/III}$ = +0.77 V vs SCE)56 forms cyclohexadienyl cation 46.9, which is deprotonated and rearomatized to give 3,4-dihydroquinolin-2-one 46.10 along with simultaneous regeneration of the ground state Ir$^{III}$ catalyst (Scheme 46).

In contrast to the earlier reductive approach to the generation of a carbamoyl radical from an oxamide (Scheme 45), Feng et al. reported, in 2018, a photocatalytic oxidative decarboxylation approach by taking oxamic acids as the carbamoyl precursor for the synthesis of analogous 3,4-di-hydroquinolin-2(1H)-ones (Scheme 47).57 A variety of electron-donating and electron-withdrawing oxamic acids are compatible with the reaction under the optimized conditions, affording a wide variety of 3,4-dihydroquinolin-2(1H)-ones in moderate (41–74%) yields. A range of mono, disubstituted and exocyclic alkenes are compatible with these reaction conditions leading to the desired products containing fused cyclic (31–60%) and spirocyclic systems (41%).

From the reaction of N-methyl-N-phenyloxamic acid with ethyl acrylate under the standard conditions, a trace amount of N-methyl-N-phenylformamide was isolated, and the addition of the radical scavenger TEMPO to the standard reaction mixtures gave only a trace amount of the desired product. Both of these results indicate the formation of a carbamoyl radical in the reaction medium. On the basis of these results, the authors proposed a mechanistic cycle in which the photoexcited catalyst *Ir$^{III}$ 48.2 undergoes a reductive quenching to generate Ir$^0$ and carbamoyl radical intermediate 48.5 (Scheme 48). Analogous to Scheme 46, addition of the carbamoyl radical to the electron-deficient olefin followed by intramolecular cyclization forms a cyclohexadienyl radical intermediate 48.7. Final oxidation of reduced Ir$^0$ by molecular oxygen affords the ground state Ir$^{III}$.
and a superoxide radical anion, which abstracts a hydrogen atom from cyclohexadienyl radical 48.7 to deliver the desired 3,4-dihydroquinolin-2(1H)-one 48.8.

NMR studies and the formation of alkynylation products using a BI-keto acid complex in place of α-keto acids and BI-OAc, under otherwise identical reaction conditions, confirms the formation of a BI-keto acid complex in the reaction medium. The luminescence quenching of [Ru(bpy)]3+ was much weaker in the presence of the α-keto acid compared to BI-OAc, indicating that BI-OAc is primarily the oxidative quencher in this reaction. In accordance with observations from control experiments, the authors proposed that the benziodoxole-oxoacid complex 50.6 (BI–OAc)′, generated in situ from an α-keto acid and BI-OAc, is oxidized by RuIII to liberate carbon dioxide, a benziodoxole cation (BI+ or BI-OAc), [Ru(bpy)]3+ and the aryl radical 50.7 (Scheme 50).58 The aryl radical undergoes α-addition to the BI-alkyne followed by elimination of a benziodoxolyl radical (BI•) to yield the alkynone 50.9. BI+ oxidizes the photoexcited [Ru(bpy)]3+ to complete the photoredox cycle.

In 2015, Li and Wang used a BI-OH reagent instead of BI-OAc to activate α-ketocarboxylic acids for the successful development of sunlight-driven decarboxylative alkynylation.59 A range of aromatic α-keto acids reacted with (bromoethyl)benzene under the optimized conditions to afford the corresponding alkynes in 44–76% yields. 4-Methyl-2-oxopentanoic acid, an aliphatic α-keto acid, reacted with a series of α-, m- and p-substituted 2-aryl-1-bromoethylenes to provide the desired products in good yields (60–74%). Irrespective of steric and electronic effects, substituted alkyl, aryl, and heteroaryl α-keto acids were well tolerated and afforded the desired products in 57–87% yields. Aryl α-keto acid substrates bearing sensitive functional groups such as allyl esters, propargyl esters, alcohols, and azides were also well tolerated under these reaction conditions giving the desired alkynylation products in 62–74% yields.

The combination of visible-light photocatalysis with hypervalent iodine reagents (HIR) was successfully employed by Chen et al. in 2015 for the generation of an acyl radical.58 This chemoselective decarboxylative alkynylation strategy shows a broad substrate scope in terms of HIR-bound alkynes as well as the α-keto acids. Aryl-substituted benziodoxolonyl-alkynes (BI-alkynes) containing electron-donating and electron-withdrawing substituents as well as alkyI-bound BI-alkynes all reacted well to deliver the desired alkynylation products in 65–93% and 65–85% yields, respectively (Scheme 49). The trisopropylsilyl (TIPS)-substituted BI-alkynes, which can be easily deprotected to generate terminal alkynes, also provided good (61–70%) yields of the desired products. Irrespective of steric and electronic effects, substituted alkyl, aryl, and heteroaryl α-keto acids were well tolerated and afforded the desired products in 57–87% yields. Aryl α-keto acid substrates bearing sensitive functional groups such as allyl esters, propargyl esters, alcohols, and azides were also well tolerated under these reaction conditions giving the desired alkynylation products in 62–74% yields.
The trapping of a TEMPO adduct in the presence of TEMPO and trapping of the benzoyl as well as the benziodoxolonyl radicals by BHT under the standard conditions confirms the formation of benziodoxolonyl and benzoyl radicals in the reaction medium. Using an equivalent amount of BI-alkyne and α-keto acid, the desired product was obtained in 66% yield only in the presence of 30% of the BI-OH (HIR) catalyst. Separately synthesized BI-keto acid (BI-OCOCPh), when reacted with bromoacetylne, gave a good yield of the desired product. These results indicate the involvement of BI-alkynes and a BI-keto acid complex in this reaction. From these mechanistic studies, it was proposed that BI-OH (52.1) reacts with the ketocarboxylic acid 52.2 to form the BI-oxoac complex 52.3 (Scheme 52). This complex generates the benziodoxolonyl radical 52.4 and a ketocarbonyl radical 52.5 under irradiation by sunlight. Subsequently, 52.4 reacts with bromoacetylne to give the BI-alkyne 52.7 and releases a Br radical. At the same time, decarboxylation of 52.5 produces an aryl radical that adds to the BI-alkyne to form 52.8, which releases the alkynone product 52.9 and the benziodoxolonyl radical. This radical recombines with the Br radical, and this is followed by hydrolysis to regenerate BI-OH and complete the catalytic cycle.

In 2016, Wang et al. reported BI-OAc as an efficient HIR catalyst for the decarboxylative 1,2-acylarylation/tandem cyclization of acrylamides with α-ketocarboxylic acids in the presence of only visible light (Scheme 53). Regardless of steric and electronic effects, various N-methyl-N-aryl-methacrylamides as well as aromatic ketocarboxylic acids afforded the desired products in moderate to good (58–78%) yields. Methyl substitution at the α-position of the N-methyl-N-aryl-methacrylamide provided a regiosomeric product (70%) in a 3:2 ratio, but acrylamides containing a free amine or alcohol failed to couple under the reaction conditions. Rather than N-methyl-N-aryl-methacrylamides, other acrylamides such as N-ethyl-N-aryl-methacrylamide and N-benzyl-N-aryl-methacrylamide formed the desired products in 70–84% yields. However, N-phenyl-N-aryl-acrylic acid was unproductive under the optimized reaction conditions.

The catalytic cycle is initiated by the reaction of BI-OAc and the ketocarboxylic acid 54.1 to generate the BI-keto acid intermediate 54.2. Visible-light-mediated homolytic cleavage of the BI–O bond of 54.2 liberates CO₂, a benzoyl radical 54.3, and a benziodoxolonyl radical (54.4). Addition of 54.3 across the double bond of arylmethacrylamides 54.5 followed by cyclization gives intermediate 54.7, which undergoes hydrogen atom abstraction by 54.4 to deliver the desired 3,3-disubstituted 2-oxindole 54.8 and BI-H (54.9). The reaction of 54.9 with the ketocarboxylic acid 54.1 liberates hydrogen gas and generates the BI-oxo acid intermediate 54.2 for the next cycle (Scheme 54).
5 Carboxylic Acids as a Source of Acyl Radicals

Simple and inexpensive carboxylic acids can be an alternative source from which to generate the acyl radical by visible-light photoredox catalysis (PC). Base-mediated photocatalytic oxidation, decarboxylation and further carboxylation of the in situ generated alkyl radical by carbon monoxide (CO) can afford acyl radicals. Alternatively, the carboxylic acid is converted into its redox-active ester by the use of a hypervalent iodine bound alkynyl as the activating agent (X = active electrophile) which can be reduced by the photoredox catalyst (PC) to form the acyl radical (Scheme 55). The redox properties of some carboxylates and anhydrides are listed in Scheme 55.\(^{61,62}\)

The use of 2-cyclopropylacetic acid as the carboxylic acid substrate afforded a ring-opened alkene-alkyne product in 52\% yield under the standard reaction conditions, which confirms the intermediacy of an alkyl radical. On the basis of this radical clock experiment, the author proposed a tentative mechanism, in which the excited state \*Ir\(^{III}\) phototocatalyst (\(E_{1/2}^{III/II} = +1.21\) V vs SCE)\(^{61}\) reacts with carboxylic acid \(57.3\) [\(E_{1/2}^{II/III}\) (cyclohexyl carboxylate) \(= +1.18\) V vs SCE]\(^{61}\) to form the alkyl radical \(57.5\) with the release of CO\(_2\). This alkyl radical further produces acyl radical \(57.6\) in the presence of carbon monoxide. Addition of this acyl radical to the BI-alkyne \(57.7\) followed by the release of the BI radical \(57.9\) \(^{61}\) provides the alkynone product \(57.10\). The BI radical oxidizes Ir\(^{III}\) to regenerate the ground state Ir\(^{III}\) photocatalyst and form the carboxylate \(57.11\) (Scheme 57).

In 2015, Wallentin et al. employed for the first time the activating agent dimethyl dicarbonate (DMDC) to generate an acyl radical from carboxylic acids using visible-light photocatalysis (Scheme 58).\(^{62}\) A range of substituted methacrylamides, when reacted with benzoic acid under the standard reaction conditions, afforded the 3,3-disubstituted 2-oxindole derivatives in good to excellent yields (74–95\%). Benzoeic acids bearing substituents at the \(o\)-, \(m\)- or \(p\)-position as well as carboxylic acids with extended aromatic systems all reacted very well (76–97\%) under the optimized reaction conditions. Surprisingly, \(o\)- and \(p\)-methyl- as well as \(p\)-hydroxy- and \(p\)-trifluoromethylbenzoic acids reacted...
very poorly under the standard conditions, however, after replacing DMDC with Boc₂O and 1 equivalent of MgCl₂ and increasing the loading of fac-Ir(ppy)₃ to 2.5 mol%, the desired products were produced in good (72–99%) yields. These new reaction conditions [Boc₂O, 1 equiv of MgCl₂ and 2.5 mol% of fac-Ir(ppy)₃] were very effective for heteroaromatic carboxylic acids and afforded the 1,2-acylarylation products in good (33–78%) yields.

When a mixed anhydride synthesized separately from the reaction of benzoic acid and DMDC reacted with methacryl-oximides using carboxylic acids, very poorly under the standard conditions, however, after replacing DMDC with Boc₂O and 1 equivalent of MgCl₂ and increasing the loading of fac-Ir(ppy)₃ to 2.5 mol%, the desired products were produced in good (72–99%) yields. These new reaction conditions [Boc₂O, 1 equiv of MgCl₂ and 2.5 mol% of fac-Ir(ppy)₃] were very effective for heteroaromatic carboxylic acids and afforded the 1,2-acylarylation products in good (33–78%) yields.

In 2017, the Wallentin group merged the concept of photocatalytic acyl radical formation from carboxylic acids with multicomponent reactions (Scheme 60). Strategically combining electron-poor and electron-rich alkenes with acyl radicals generated from mixed anhydrides of DMDC and carboxylic acids, the method was able to provide access to the synthetically challenging 1,2-dicarbofunctionalization of alkenes. This strategy yielded 1,2-difunctionalized products in good (33–97%) yields when reacted with substituted aromatic as well as heteroaromatic carboxylic acids with different silanol ethers and methyl acrylate. The scope of the reaction was further extended to other electron-poor...
olefins beyond methyl acrylates, with these reactions affording the desired difunctionalized products in 41–66% yields.

The reaction pathway for the formation of the acyl radical 61.5 is the same as that proposed in Scheme 59. The nucleophilic acyl radical first adds to the electron-poor olefin 61.6 forming the radical intermediate 61.7 (Scheme 61). This electron-deficient radical species reacts selectively with silyl enol ether 61.8 to deliver 61.9, which is oxidized by fac-Ir(ppy)3 and this is followed by desilylation to produce the desired product 61.10.

Using the idea of in situ generation of anhydrides as the acyl radical precursors, Zhu’s group reported three photocatalytic reactions in 2017. After first, they reported the photocatalytically catalyzed hydroacylation reaction of olefins using carboxylic acids as acyl radical precursors and tris(trimethylsilyl)silane (TMS-Si-H) as a hydrogen atom source (Scheme 62). A range of electron-donating and electron-withdrawing substituted styrenes, such as α,β-substituted or unsubstituted vinyl esters, a vinyl sulfone, and an aliphatic olefin all reacted well with benzoic acid to afford the corresponding hydroacylated products in 36–84% yields. Both aromatic and heteroaromatic carboxylic acids were viable substrates and coupled with styrene to give the desired products in 53–70% yields.

TEMPO additives completely shut down this hydroacylation reaction, which indicates the radical nature of this process (Scheme 63). The mechanism starts with the excitation of fac-Ir(ppy)3 63.1 to excited fac-Ir(ppy)3 63.2 by visible-light irradiation. Single-electron reduction of the mixed anhydride 63.3, generated by reacting the carboxylic acid with DMDC, by the excited fac-Ir(ppy)3 forms acyl radical 63.5 with the extrusion of CO2 and OMe. Subsequent addition of the acyl radical to the activated olefins forms radical intermediate 63.7. This radical intermediate then quickly abstracts the proton from TMS-Si-H 63.8 to give the desired hydroacylation product 63.9. The final SET process between fac-Ir(ppy)3 and 63.10 regenerates the ground state fac-Ir(ppy)3 for the next cycle.

Shortly after their photocatalytic hydroacylation of activated alkenes, Zhu et al. reported the selective photocatalytic reduction of aromatic carboxylic acids to the corresponding aldehydes using the fac-Ir(ppy)3 and tris(trimethylsilyl)silane (TMS-Si-H) system (Scheme 64). Aromatic carboxylic acids, regardless of the position and electronic properties of the substituents including free alkynyl, amide, and ester groups, reacted smoothly under the optimized reaction conditions to afford the corresponding aldehydes in 82–92% yields. Heteroaromatic carboxylic acids and a few complex aryl carboxylic acids were successfully reduced to...
the desired aldehydes as well. However, aliphatic carboxylic acids such as 3-phenylpropanoic acid, cyclohexane carboxylic acid, and N-Boc-glycine were all unproductive under the standard reaction conditions.

The proposed mechanism up to the formation of the acyl radical 65.5 by excited fac-Ir(ppy)$_3$ (65.2) (Scheme 65) is the same as the hydroacylation reaction mechanism using carboxylic acids (Scheme 63). Once the reactive acyl radical 65.5 is generated, it rapidly reacts with TMS$_2$Si-H (65.6) to form the corresponding aldehyde 65.7. Regeneration of fac-Ir(ppy)$_3$ occurs in the final stage by the reaction of fac-Ir(ppy)$_3$ and 65.8.

The third reaction developed by Zhu’s group in 2017 was an efficient deoxygenative intramolecular acylation/radical cyclization via photoredox catalysis for the synthesis of valuable fluorenone products.$^{59}$ A variety of functionalized biarylcarboxylic acids containing o- and p-substituents on the 2-aryl ring afforded fluorenones in 54–85% yields, while the m-substituted aromatics gave regioisomeric products. Electron-donating or electron-withdrawing substituents on the aromatic moiety of the carboxylic acid were well tolerated under the standard reaction conditions (61–86%) (Scheme 66).

A plausible mechanism for this intramolecular radical cyclization process is shown in Scheme 67. The aroyl radical 67.6 generated from the mixed anhydride 67.4 adds to the ortho position of the 2-aryl ring to give intermediate 67.7. Oxidation of intermediate 67.7 by fac-Ir(ppy)$_3$ followed by deprotonation regenerates the ground state Ir(ppy)$_3$ and affords the desired product 67.8.

In 2018, Zhu et al. merged phosphoranyl radical chemistry with photoredox catalysis to form acyl radicals from carboxylic acids via C–O cleavage using Ph$_3$P or Ph$_2$POET. These acyl radicals added to alkenes and imines to give the desired hydroacylation products (Scheme 68).$^{70}$ The scope of the reaction is very broad. Various aryl and heteroaryl carboxylic acids reacted with a wide array of electronically diverse alkynylpyridines, styrenes, and Michael acceptors such as acrylate, phenyl vinyl sulfone, diethyl vinylphosphonate, cyclohexanone and lactones to give the desired ketones in 38–89% yields. However, alkyl, alkenyl, and alkylnyl carboxylic acids failed to give the desired products. Notably, the reaction is amenable to late-stage functionalization of complex carboxylic acids and alkenes in yields of 40–76%. The reaction is also applicable to the hydroacylation of imines generated in situ under the reaction conditions to afford α-amino-ketone products.

Based on a series of mechanistic studies including radical trapping, deuterium- and $^{18}$O-labeling, and Stern–Volmer quenching experiments, a proposed reaction mechanism is depicted (Scheme 69). Photoexcited Ir$^+[(df(CF$_3$_3)ppy)$_2$](dtbbpy)]PF$_6$ ($E_{1/2}^{III/II}$ = +1.21 V vs SCE)$^{36}$ undergoes reductive quenching by PPh$_3$ ($E_{1/2}^{red}$ = +0.98 V vs SCE)$^{71}$ to form Ir$^{II}$ and the triphenylphosphine radical cation 69.1. Deprotonation of an aryl or heteroaryl carboxylic acid by K$_2$PO$_4$ forms a carbamate, which reacts with 69.1 to form a phosphoranyl radical 69.3. β-Scission of the phosphoranyl radical 69.3 liberates triphenylphosphine oxide and aroyl radical 69.4, which then adds to olefin 69.5 to deliver the alky radical intermediate 69.6. Reduction of 69.6 by Ir$^{II}$
When radical acceptors such as carbonyl and iminyl derivatives or alkenes were ortho to the carboxylic acid group on a benzene ring, intramolecular acyl radical addition took place to form cyclized products in 50–93% yields (Scheme 71). Aliphatic carboxylic acids could cyclize to form five-membered lactone and ketone products in 43% and 44% yields, respectively.

Generation of the acyl radical is similar to the mechanism proposed by Zhu (Scheme 69).20 Once the acyl radical 72.3 is formed, it abstracts a hydrogen atom from an arylthiol 72.4 to give the desired aldehyde 72.5 and an arylthiyl radical 72.6 (Scheme 72). Reduction of 72.6 by IrIII regenerates the IrIII photoredox catalyst and thiolate 72.7, which upon protonation forms the arylthiol 72.4.
6 Anhydrides as a Source of Acyl Radicals

Rather than the in situ formation of anhydrides from carboxylic acids in the presence of DMDC or Boc₂O, the direct use of anhydrides is an alternate means of generating acyl radicals using visible-light photoredox catalysis. In 2016, Wallentin et al. employed aromatic carboxylic anhydrides as the direct acyl radical source for olefinic radical acylation under photoredox conditions. The method efficiently yielded 3,3-disubstituted 2-oxindoles (45–98%) using a variety of symmetrical electron-withdrawing aromatic anhydrides. This protocol was also applied to variously substituted N-phenylacrylamides to give the corresponding products in 80–98% yields (Scheme 73). Interestingly, the Lewis acid activation of more challenging electron-rich aromatic and heteroaromatic carboxylic anhydrides was found to be necessary for the generation of the corresponding carbonyl radicals and the efficient synthesis of the desired products in 31–95% yields.

![Scheme 72 Proposed mechanism for the photocatalytic acyl radical formation using Ph₃P as a deoxygenating reagent.]

Radical trapping experiments with TEMPO confirmed the formation of an aryl radical. Stern–Volmer experiments, on the other hand, indicated that a Hantzsch ester is the main quencher of the photoexcited fac-*Ir(ppy)₃ at low concentrations. However, the same excited photocatalyst can be quenched by higher concentrations of carboxylic anhydride and iPr₃NET. Based on the above experiments, a plausible mechanism is proposed in Scheme 75 which begins with the photoexcitation of fac-*Ir(ppy)₃ with visible light. The photoexcited fac-*Ir(ppy)₃ 75.2 undergoes single-electron transfer with the Hantzsch ester (E₁/₂, red = +0.887 V vs SCE) to form Ir⁺ and iPr₃NET forming Ir⁺ species 75.3 and the Hantzsch ester (HEH) or iPr₃NET radical cation (75.5 or 75.4). Anhydride 75.6 is reduced by 75.3 (E₁/₂, red = −2.19 V vs SCE in MeCN), then fragments to provide the aryl radical 75.7 which reacts with alkene 75.8 to form α-carbonyl...
7 Acyl Thioesters as a Source of Acyl Radicals

In 2017, Gryko et al. reported the visible-light-driven vitamin-B₁₂-catalyzed generation of an acyl radical from 2-S-pyridyl thioesters (acyl-X reagent) via a single-electron reduction and the subsequent reaction of an acyl radical with electron-deficient olefins. Scheme 76 demonstrates the superiority of pyridyl thioesters compared to other acylating reagents employed in this reaction. The higher activity of thioesters compared with active esters results from the stronger electrophilic character of the carbonyl group in the thioester derivatives.

Olefins bearing electron-withdrawing groups such as esters, nitriles, sulfones, amides, and ketones all produced the desired ketones in 58–99% yields (Scheme 77). While α-substituted olefins afforded the desired products in good (62–82%) yields, β-substituted olefins gave lower yields (27–47%), probably for steric reasons. Aryl, heteroaryl, and alkyl thioesters reacted equally well under the reaction conditions and formed the desired products in 62–97% yields. In the case of aryl thioesters containing strongly electron-withdrawing groups such as CN or CF₃, the desired products were obtained in lower yields (26–60%), presumably due to their higher susceptibility to reduction (for the compound with a Me substituent: Eᵥc = −1.77 V; CF₃: Eᵥc = −1.49 V, CN: Eᵥc = −1.36 V vs Ag/AgCl).  

LCMS detection of the reaction aliquot showed the presence of the acyl-cobalt complex 78.4 in the medium and TEMPO trapping experiments indicated the acyl radical formation. In the absence of the reducing agent zinc, no reaction was observed using Co²⁺ or Co⁺-vitamin B₁₂, which confirms the formation of an acyl-cobalt complex by the reaction of Co⁻-vitamin B₁₂ generated in situ with thioesters. Addition of ND₄Cl in place of NH₄Cl showed deuteration incorporation at the α-position relative to the electron-withdrawing group, indicating the role of NH₄Cl as a proton source during the final step of the reaction. Light ON/OFF experiments support the formation of an acyl radical under constant irradiation of light. The proposed mechanism starts with the reduction of the thioester by Co⁰ and the generation of acyl-cobalt complex 78.4 under irradiation with visible light (Scheme 78). Subsequent addition of the nucleophilic acyl radical to activated olefin 78.7 generates 78.8, which is reduced by Zn and protonated by NH₄Cl to deliver the desired product 78.9. The Co⁰-catalyst is reduced to Co⁺-vitamin B₁₂ by Zn to complete the catalytic cycle.

Scheme 75 Mechanism for the hydroacylation of electron-deficient olefins

Scheme 76 Investigation of various acyl derivatives

Scheme 77 Vitamin-B₁₂-catalyzed radical acylation of electron-deficient olefins

Scheme 78 Mechanism for the vitamin-B₁₂-catalyzed reductive acylation of olefins
In 2018, McErlean et al. used a thioester as the acyl radical precursor for the hydroacylation of olefins under photocatalytic conditions (Scheme 79). With 10 equivalents of tributylamine and formic acid, intramolecular acyl radical–olefin addition occurs to form the desired chromanone and indane derivatives in 18–71% yields (Scheme 79, a). When 2 equivalents of tributylamine and alkenes such as cyclohexene and allyltrimethylsilane were employed in the absence of formic acid (based on McErlean’s Supporting Information), intermolecular coupling reactions took place to afford the desired products in 10–37% yields (Scheme 79, b).

When 2.06 equivalents of tributylamine and formic acid (based on McErlean’s Supporting Information) were used, the ketone products were further reduced to form ketyl radicals, which dimerized, forming pinacol-type products (Scheme 80, a). The authors also conducted a one-pot intramolecular cyclization–intermolecular radical–olefin addition reaction, which afforded the two- and three-component coupling products in 29% and 24% yields, respectively (Scheme 80, b).

The unique feature of this reaction is the formation of an acyl radical from the thioester, triggered by the generation of an aryl radical. The idea was inspired by the work of Crich and Yao. It is proposed that reductive quenching of the excited \( ^1{\text{Ir}[(ppy)_3]_2} \) \( (E_{1/2}^{\text{ox}} = +0.31 \text{ V vs SCE}) \) by tributylamine (triethylamine: \( E_{1/2}^{\text{ox}} = +0.83 \text{ V vs SCE} \)) produces the tributylamine radical cation \( \text{81.1} \) and \( \text{Ir}[(ppy)_3]^– \) \( (E_{1/2}^{\text{ox}} = +0.31 \text{ V vs SCE}) \) (Scheme 81). This strongly reducing species reduces the iodo benzene moiety of thioester \( \text{81.2} \) (iodobenzene: \( E_{1/2}^{\text{red}} = -1.59 \text{ V vs SCE} \)) via SET to form the aryl radical \( \text{81.3} \), which attacks the sulfur to release dihydrobenzothiophene \( \text{81.4} \) and an acyl radical \( \text{81.5} \). Trapping of \( \text{81.5} \) with an olefin forms an alkyl radical intermediate \( \text{81.6} \), which abstracts a hydrogen atom from tributylamine radical cation \( \text{81.1} \), liberating the desired product \( \text{81.7} \).

8 Acyl Chlorides as a Source of Acyl Radicals

Acyl chlorides are versatile intermediates and have been widely used as electrophilic acylating reagents in organic synthesis. Their electrophilic property can be reversed by a single-electron reduction to generate acyl radicals. An early example of the formation of an acyl radical intermediate from an acyl chloride was reported by van der Kerk et al. in 1957 using triphenyltin hydride. Under their conditions, triphenyltin chloride and benzaldehyde were formed. A systematic study of the reaction between triphenyltin hydride and benzoyl chloride was conducted by Kuivila in 1960. A mechanism that involved the generation of an acyl radical was further demonstrated by Kuivila in 1966. The formation of an acyl radical from an acyl chloride via SET with \( \text{SmI}_2 \) was reported by Kagan et al. in 1981, and the
acyl radical was further reduced to an acyl anion under their reaction conditions.\textsuperscript{84} Only recently, photoredox catalysis was used for acyl radical formation from acyl chlorides.\textsuperscript{84} In 2017, Xu et al. reported the first protocol to convert a benzoyl chloride into a benzoyl radical, which then reacted with 1,7-enynes to form fused pyran derivatives (Scheme 82).\textsuperscript{84} The reaction starts with excitation of \textit{fac}-Ir(ppy)\textsubscript{3} by a blue LED and then the excited \textit{fac}-Ir(ppy)\textsubscript{3} ($E_{1/2}^\text{IV/III} = -1.73$ V vs SCE)\textsuperscript{84b} is involved in single-electron reduction of a benzoyl chloride ($E_p = -1.02$ V vs SCE)\textsuperscript{84b} forming \textit{fac}-Ir\textsuperscript{IV}(ppy)\textsubscript{3} and benzoyl radical 82.2. The benzoyl radical then attacks the carbon–carbon double bond of 82.3 to afford an alkyl radical intermediate 82.4, which undergoes radical cyclization with the alkyne triple bond to form a vinyl radical intermediate 82.5. Oxidation of the vinyl radical intermediate by \textit{fac}-Ir\textsuperscript{IV}(ppy)\textsubscript{3} gives a vinyl cation species 82.6. The acyl carbonyl oxygen then attacks the vinyl cation center to form an oxonium ion 82.7, which is then deprotonated to give the desired product 82.8.

In Scheme 82, proposed catalytic cycle for the photocatalytic synthesis of fused pyran derivatives from benzoyl chlorides and 1,7-enynes. Adapted with permission from ref 84a. Copyright (2017) American Chemical Society.

Anilides with different N-protecting groups such as benzy1, acyl, and tosyl were competent, delivering the products in 67–70\% yields. Aryl-ester–linked 1,7-enynes were also viable substrates.

In the same year, Xu et al. extended the scope of the reaction to substrates without an alkyne motif (Scheme 84).\textsuperscript{84b} In this reaction, the \(\alpha\)-carbonyl radical intermediate 84.4, generated from the reaction of \(N\)-phenylmethylcarbamide (84.3) and the acyl radical 84.2, undergoes intramolecular cyclization to form intermediate 84.5, which is oxidized by Ir\textsuperscript{IV} then deprotonated to give a 3,3-dialkyl 2-oxindole derivative. The reaction scope is similar to that described in Xu’s previous report (Scheme 83).\textsuperscript{84a}

Acyl radicals formed from acyl chlorides can add directly to alkenes. In 2017, Tang et al. synthesized a diverse group of 3-acylspirotrienones via ipso-carboacylation of \(N\)-(p-methoxy aryl)propiolamides with acyl chlorides.\textsuperscript{84c} The p-methoxy group on the arene ring is critical to formation of the desired products. The reaction conditions worked well with benzoyl chlorides bearing alkyl, methoxy, and halogen substituents and thiophenecarbonyl chloride, affording the desired products in 60–86\% yields (Scheme 85). \(N\)-(p-Methoxyaryl)propiolamides containing a benzyl, 2-iodobenzyl acyl or allylic groups on the nitrogen atom were tolerated, providing the 3-acylspirotrienones in 69–73\% yields. In terms of the alkynyl substituents (R\textsuperscript{3}), penty1, thiophene, pyridine, naphthalene, and arenes bearing alkyl, methoxy, acyl, CF\textsubscript{3}, or halogen groups were compatible and afforded the desired products in 57–88\% yields. Mechanistically, the authors proposed that after the initial photocatalytic acyl radical formation followed by a two-step tandem acyl radical–alkyne coupling and radical cyclization, a cyclic radical species 85.1 is generated. An \textsuperscript{18}O-labeling experiment suggests that 85.1 is attacked by an exogenous \(\text{H}_2\text{O}\) molecule with assistance from 2,6-lutidine to give a radical.
anion intermediate 85.2. Removal of the methoxy group gives 85.3, which is then oxidized by Ir\(^{IV}\) to afford the desired product 85.4 (Scheme 85).

In 2018, Tang et al. further expanded this type of acyl radical chemistry to the synthesis of 3-acylcoumarins (Scheme 86).\(^\text{85}\) Although thiophencarboxyl chloride and benzoyl chlorides bearing methyl, methoxy, and halogen substituents were well tolerated, alkyl, vinyl, and electron-deficient (e.g., \(p\)-O\(_2\)NCC\(_2\)H\(_4\)) acyl chlorides failed to produce the desired products. Aryl 3-phenylpropiolates possessing methyl, halogen, methoxy, Ac and CF\(_3\) groups at the \(p\)-position of the phenoxy ring underwent the reaction smoothly, affording the products in 68\% to 80\% yields. With respect to the scope of alkynyl substituents, arenes bearing electron-donating and electron-withdrawing groups were compatible under the reaction conditions.

The proposed reaction mechanism is depicted in Scheme 87. Once the radical intermediate 87.4 is formed, it undergoes an intramolecular 5-exo-trig cyclization followed by oxidation, giving the cationic species 87.6. 1,2-Ester migration leads to 87.7, which upon deprotonation affords the desired product 87.8. Notably, both Tang’s\(^\text{85}\) and Itoh’s\(^\text{76}\) (Scheme 22) methods involve the formation of a 5-exo-trig cyclic intermediate, which is distinct from the transition-metal-catalyzed acyl radical addition reported by Wu\(^\text{86}\) and Wang\(^\text{87}\) in which a 6-endo-trig cyclization process was proposed.

9 Acyl Silanes as a Source of Acyl Radicals

The first isolation of acyl silanes was reported by Brook in 1957.\(^\text{88}\) Acyl silanes are often regarded as unusual carbonyl compounds as a result of the unique feature of an sp\(^2\)
carbon that is bonded to both a silicon and oxygen atom. In 1969, Brook and Duff reported that photolysis of acyl silanes led to the formation of acyl radical intermediates via Norrish type I cleavage of the acyl–silicon bond. Electrochemical oxidation of acyl silanes leading to the formation of acyl radicals was described extensively by Keiji and Yoshida between 1986 and 1992. Application of acyl silanes in the formation of acyl radicals under photocatalytic conditions was described by Fagnoni et al. in 2017 (Scheme 88). Acyl- and benzyoltrimethylsilanes (acylTMS and benzoylTMS) have higher oxidation potentials ($E_{1/2}$) than most of the common transition-metal photocatalysts such as fac-Ir(ppy)$_3$ ($E_{1/2}^{	ext{III/II}} = +0.31$ V vs SCE) and Ru(bpy)$_2^+$ ($E_{1/2}^{II/III} = +0.77$ V vs SCE). Thus, photocatalysts with stronger oxidizing power are needed to oxidize acylTMSs to acyl radicals. Fagnoni et al. discovered that photoexcited tetraethylammonium decatungstate (TBADT) and 9-mesityl-10-methylacridinium tetrafluoroborate (Acr$^-$-Mes) (Scheme 88) could be used to enable the acylation of electron-deficient alkenes. The authors proposed that the excited photocatalyst oxidizes an acylTMS ($E_{1/2}$) to an acylTMS radical cation ($E_{1/2}$), which then loses the TMS group to form a nucleophilic acyl radical 88.3. The formation of the acyl radical was supported by their TEMPO trap experiments. The alkyl radical intermediate 88.5 formed by the addition of the acyl radical to alkene 88.4 accepts an electron from the reduced photocatalyst to give a carbon anion 88.6, which is then protonated to form the final product 88.7.

Regeneration of the TBADT catalyst through oxidation by the carbon radical intermediate was reported by Fagnoni. Although the absorption spectrum of TBADT is not in the visible light region, it overlaps with the spectrum of sunlight, supporting this catalyst’s capacity as a ‘windowledge’ catalyst. For the Acr$^-$-Mes-catalyzed reaction, “Acr$^-$-Mes oxidizes the acylTMS to form an acyl radical and Acr$^-$...
drides, acyl thioesters, acyl chlorides, and acyl silanes. The mild conditions also enable the reactions of acyl radicals with a diverse set of coupling partners to construct molecular architectures that are otherwise difficult to prepare. Since the use of photoredox catalysis in acyl radical chemistry only began in 2013 and is still in its infancy, we anticipate that more innovative transformations involving acyl radical intermediates will continue to emerge in the near feature.

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**References**


We used benzaldehyde as the hydrogen donor to illustrate the mechanism.


We used benzaldehyde as the hydrogen donor to illustrate the mechanism.


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