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Recent advances in visible-light-induced defluorinative functionalization of α-trifluoromethyl arylalkenes

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Fluorine-containing organic molecules have been widely utilized in the fields of medicinal chemistry, synthetic chemistry, agrochemistry and materials science, due to their higher lipophilicity, metabolic stability, cell membrane permeability, bioactivity, and other advantageous properties. Among these, *gem*-difluoroalkenes have emerged as privileged carbonyl bioisosteres in drug design, exemplified by antimalarial difluoroartemisinin derivatives. Recent breakthroughs in visible-light photocatalysis have enabled mild, radical-mediated allylic defluorination of these substrates through single-electron transfer (SET) processes followed by β-fluorine elimination. This review highlights cutting-edge photochemical strategies (2022–2025) for constructing *gem*-difluoroalkenes, emphasizing mechanistic insights and functional group compatibility. The development of these sustainable methods addresses critical challenges in fluoroorganic synthesis while expanding accessible molecular diversity for medicinal applications.

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1 Introduction

Visible-light photoredox catalysis has emerged as a transformative synthetic platform, combining unique reactivity patterns, exceptional selectivity, and mild operating conditions to enable previously challenging transformations.[1] Photoredox catalysis has reshaped contemporary organic synthesis through the rational development of various visible-light-absorbing photocatalysts, including Ru/Ir complexes and organic dyes. Mechanistically, photoexcitation of the catalyst enables electron acceptance from a donor species, forming a

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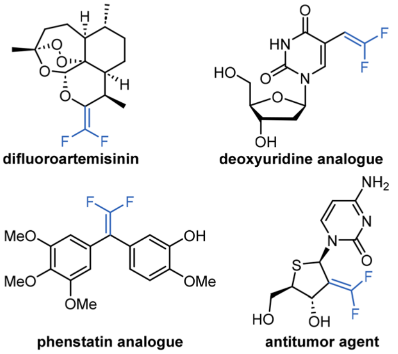
strongly reducing one-electron-reduced intermediate capable of single-electron transfer (SET) processes.

Fluorine-containing organic molecules have been widely utilized in the fields of medicinal chemistry, synthetic chemistry, agrochemistry and materials science, due to their higher lipophilicity, metabolic stability, cell membrane permeability, bioactivity, and other advantageous properties compared to their parent molecules.[2] Over 20% of pharmaceuticals include at least one fluorine atom in their molecular structures.[3] Specifically, *gem*-difluoroalkene units, which act as bioisosteres for the carbonyl group while offering improved biostability, have attracted significant interest in drug design and medicinal chemistry.[4] For instance, isosterically modifying the carbonyl group in artemisinin with a *gem*-difluoroalkene moiety to create a difluoroartemisinin significantly enhances antimalarial activity, and a deoxyuridine analogue modified in this manner exhibits antiherpetic activity (Scheme 1).[5] These developments not only expand the field of medicinal chemistry but also pave the way for novel therapeutic strategies. *gem*-Difluoroalkenes can serve as key precursors for a range of valuable fluoroorganic compounds, including monofluoroal-kenes, difluoromethylenes, difluorocyclopropanes, and trifluoromethylated products.[6] Moreover, fluorine atom environmental management differs notably between pharmaceuticals and agrochemicals: pharmaceuticals release only trace C–F byproducts due to low dosages, while fluorinated agrochemicals pose substantial contamination risks *via* large-scale, annual use. Pesticide adjuvants, used in far greater quantities than active ingredients, further worsen risks by facilitating fluorinated compounds' migration and bioaccumulation. This highlights the urgent need for highly selective defluorinative strategies to minimize byproducts and optimize environmental degradation pathways.



Scheme 1 Bioactive molecules containing *gem*-difluoroalkene scaffolds.

Many synthetic methodologies have been established to synthesize *gem*-difluoroalkenes. Traditional methods for synthesizing *gem*-difluoroalkenes include difluoroolefination of carbonyl, diazo, or hydrazone compounds, and organometallic- or strong base-mediated nucleophilic S_N2'-type addition to α-trifluoromethyl alkenes, followed by β-F elimination.[7] The difluoroolefination of carbonyl compounds (*via* Wittig, Julia–Kocienski, or Horner–Wadsworth–Emmons reaction) is an effective synthetic strategy for constructing *gem*-difluorovinyl architectures (Scheme 2a, left).[7b,e,f,8] Nevertheless, these transformations typically necessitate strongly basic reaction conditions. The reaction between diazo compounds and difluorocarbene precursors also represents a viable method for synthesizing *gem*-difluoroethylenes (Scheme 2a, right).[7d,g,h,9] The trifluoromethyl group in α-trifluoromethyl alkenes serves as a widely utilized fluorine-containing synthon. The electron-deficient trifluoromethyl

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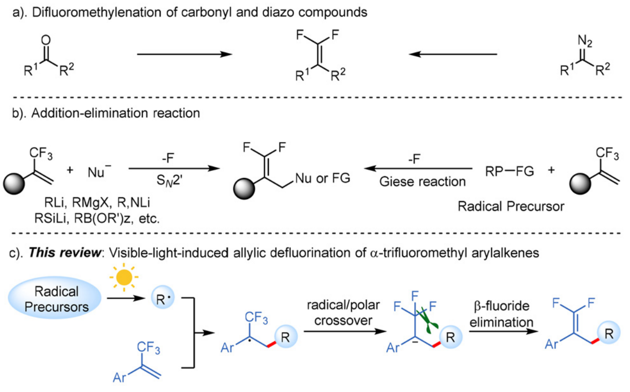


Scheme 2 Synthetic routes to access *gem*-difluoroalkenes.

group in α-trifluoromethyl alkenes readily undergoes nucleophilic S_N2' attack (Scheme 2b, left)[7g,10] or Giese addition (Scheme 2b, right),[11] often followed by β-fluorine elimination to form *gem*-difluoroalkenes. However, the nucleophilic S_N2'-type reaction involving organometallic reagents (*e.g.*, organolithium or Grignard reagents) is air- and moisture-sensitive, leading to lesser substrate scope and lower functional group tolerance.[12] In contrast to harsh basic conditions required for S_N2'-type methods, visible light-induced radical addition of α-trifluoromethyl arylalkenes with various radical precursors offers a milder and more versatile approach to *gem*-difluoroethylene synthesis (Scheme 2c).[6c,11a,c,13] In this scenario, developing efficient and mild approaches through allylic defluorination of α-trifluoromethyl arylalkenes for preparing structurally diverse *gem*-difluoroalkenes with good group tolerability is undoubtedly in high demand and has garnered special interest in organic and medicinal chemistry.

Consequently, substantial advances have been made in visible-light-driven allylic defluorination of α-trifluoromethyl arylalkenes *via* SET-triggered radical pathways, providing a general strategy for *gem*-difluoroalkene synthesis, in which the β-F elimination of CF_3 is achieved by a photo-induced radical/polar cross-cover (Scheme 2c). It is noted that alternative strategies for defluorinative functionalization of α-trifluoromethyl arylalkenes, such as transition-metal catalysis[14] and electrochemical[14b,15] approaches have also been well summarized, providing critical complementary insights into this field. Although Sun *et al.* have discussed the recent advance in the transformations of trifluoromethyl alkenes,[14c] we would provide a more comprehensive focus on the recent advance in visible-light-induced defluorinative functionalization of α-trifluoromethyl arylalkenes in this perspective review.

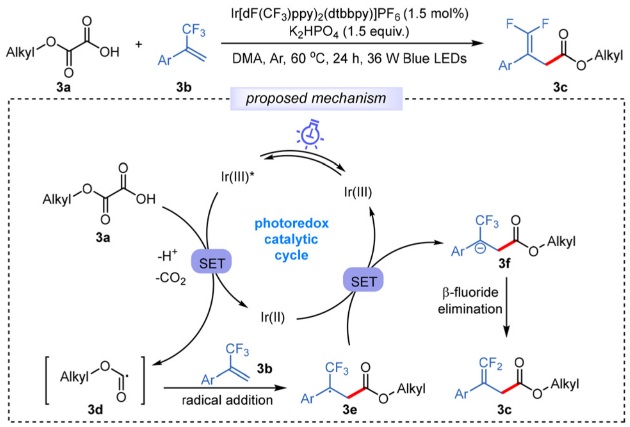
2 Metal-based photocatalysts

2.1 Ir-based photocatalysts

Alcohol-derived oxalate esters have emerged as versatile alkyl radical precursors in recent years, enabling efficient construction of diverse carbon–carbon bonds through photoredox or thermal activation.[16] In 2022, Fu's group reported an effective method for synthesizing the structural diversity of β-*gem*-difluoroalkene esters through visible light-induced defluorinative alkoxycarbonylation of α-trifluoromethyl arylalkenes **3b** with oxalates **3a** (Scheme 3).[17] Preliminary mechanistic studies indicated the involvement of alkoxycarbonyl radicals in the catalytic process. The long-lived excited state Ir(III)* could oxidized the oxalates **3a** *via* a SET process, producing reduced Ir(II) species and the alkoxycarbonyl radicals **3d** by releasing one equivalent of CO_2. **3e** were then obtained by radical addition of **3d** to the electron-deficient α-trifluoromethyl arylalkenes **3b**. **3e** were reduced by Ir(II) species to produce carbanions **3f**, which rapidly eliminated anionic β-F to form β-*gem*-difluoroalkene esters **3c**. Notably, the success of this strategy relied on intermolecular alkoxy-carbonyl radical addition to the electron-deficient α-trifluoromethyl arylalkene scaffold.

In 2022, Shen and co-workers introduced a general strategy for the defluorinative alkylation of readily available α-trifluoromethyl alkenes **4b** using α-silyl alcohols **4a** as the radical precursors under irradiation of 6 W blue LEDs at room temperature, in which $[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$ was employed as the photocatalyst, collidine was used as additive in DCM (Scheme 4).[18] A diverse array of α-trifluoromethyl alkenes **4b** were tolerated with electron-poor, electron-rich, or neutral properties, successfully providing the desired difluoro allylic cyclobutanols **4c**. Notably, several alkyl-substituted α-trifluoromethyl alkenes also proved suitable for this reaction, offering a versatile and modular platform for the synthesis of diverse *gem*-difluoroalkenes.

The *gem*-difluoroalkene structure serves as a critical pharmacophoric element in numerous agricultural insecticides. Syngenta's research demonstrated that the insecticidal efficacy of 1,1-difluorododec-1-ene derivatives is determined by this structural parameters: the pharmacophore configuration, the tail groups modifications, and the chain length of the bridging carbon chain.[19] In 2022, Zhou *et al.* synthesized *gem*-difluoroalkenes **5c** containing a distal carbonyl group through a defluorinative ring-opening *gem*-difluoroallylation of cycloalka-



Scheme 3 Defluorinative alkoxycarbonylation of α-trifluoromethyl arylalkenes with oxalates.

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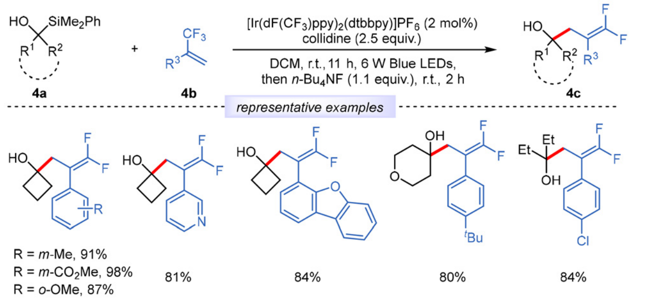
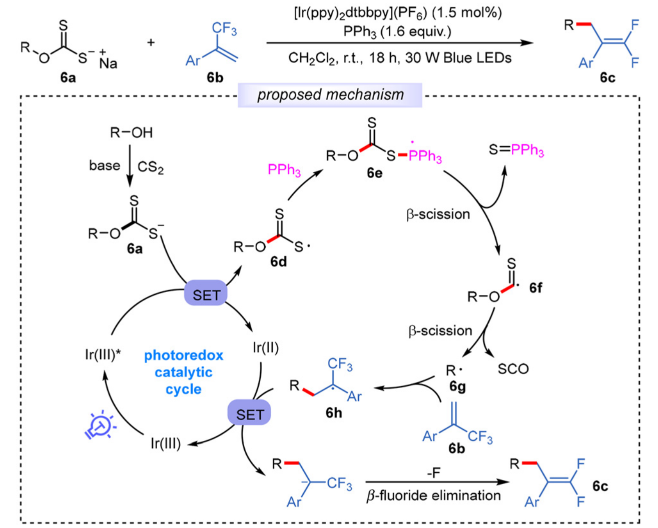


Scheme 4 Defluorinative alkylation of α-trifluoromethyl alkenes with α-silyl alcohols.



Scheme 6 Deoxygenative *gem*-difluorovinylation of aliphatic alcohols with α-trifluoromethyl arylalkenes.

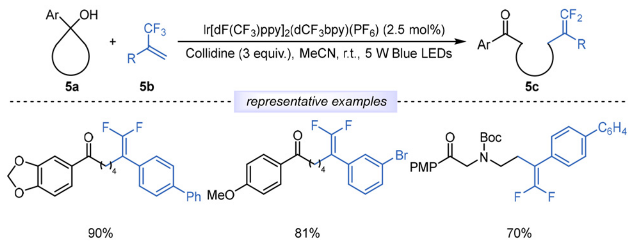
nols **5a** with α-trifluoromethyl alkenes **5b** in the presence of Ir(dFCF$_3$ppy)$_2$(dCF$_3$bpy)(PF$_6$) and collidine in MeCN under blue LEDs irradiation at room temperature (Scheme 5).[20] The ring size and substituent on the alkyl chain of cycloalkanols can easily change the bridge between C=CF$_2$ and the carbonyl group. Therefore, the strategy allows modification of three structural elements in a single reaction for synthesizing more effective insecticides.

In 2022, Hu and colleagues successfully developed a mild photocatalytic protocol for the coupling of xanthate salts **6a** with α-trifluoromethyl arylalkenes **6b** to produce the *gem*-difluoroallylation products **6c** (Scheme 6).[21] A proposed mechanism was suggested as follows. Initially, the xanthate anions **6a** were oxidized by the photoexcited Ir(III)* to generate sulfur-centered radicals **6d**. Subsequently, radicals **6d** underwent rapid coupling with Ph$_3$P to produce the crucial phosphoranyl radicals **6e**, which then underwent β-scission to form radical intermediates **6f**. The fragmentation of **6f** led to the formation of alkyl radicals **6g** through the release of carbonyl sulfide. Addition of radicals **6g** to the α-trifluoromethyl arylalkenes **6b** generated new radical intermediates **6h**. Subsequent reduction and β-fluoride elimination afforded the corresponding *gem*-difluoroalkene products **6c**. This protocol disclosed a visible-light photocatalytic strategy for the highly efficient deoxygenative *gem*-difluorovinylation of aliphatic alcohols mediated by phosphoranyl radicals.

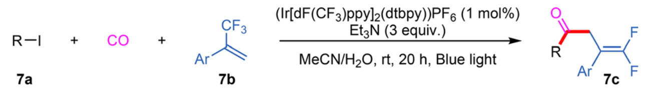
Since Otto Roelen's pioneering work on the Fischer–Tropsch reaction documented transition-metal-catalyzed carbonylation in 1938, carbonylation has become an indispensable tool for synthesizing carbonyl-containing compounds in both academic and industrial.[22] In 2022, Wu's group described a novel visible-light-mediated defluorinative carbonylation procedure that involves the cross-coupling of alkyl iodides **7a** and α-trifluoromethyl arylalkenes **7b** to access *gem*-difluoroalkenes **7c** under mild reaction conditions (Scheme 7).[23] This work employs (Ir[dF(CF$_3$)ppy]$_2$(dtbpy))PF$_6$ as the photocatalyst under visible light to generate acyl radicals in the presence of carbon monoxide.

Alkyl radicals derived from organoboron species have been extensively utilized due to their readily available from both commercial and synthetic sources. In 2022, Wang *et al.* reported an Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ catalyzed defluorinative alkylation of a series of α-trifluoromethyl arylalkenes **8b** using various alkylboronic acids **8a** as radical precursors, assisted by K$_3$PO$_4$ in ethyl acetate (EA), under the irradiation of a 36 W blue LED at room temperature (Scheme 8).[24] The pivotal progress in the proposed mechanism was the complex **A**, composed of alkylboronic acids and K$_3$PO$_4$, that were oxidized by the excited state of photocatalyst to generate alkyl radicals, which subsequently underwent similar processes to give the desired *gem*-difluoroethylenes **8c**. In this study, the authors disclosed that the pre-activation of alkylboronic acids by an organophosphorus reagent was crucial to reduce their oxidation potentials.

The [1,2]-Brook rearrangement reaction, which has been widely used in anion relay chemistry, is a reversible mechanism that converts α-silyl oxyanions into α-silyloxy carbanions



Scheme 5 Defluorinative ring-opening *gem*-difluoroallylation of cycloalkanols with α-trifluoromethyl alkenes.



Scheme 7 Defluorinative carbonylation of alkyl iodides with α-trifluoromethyl arylalkenes.

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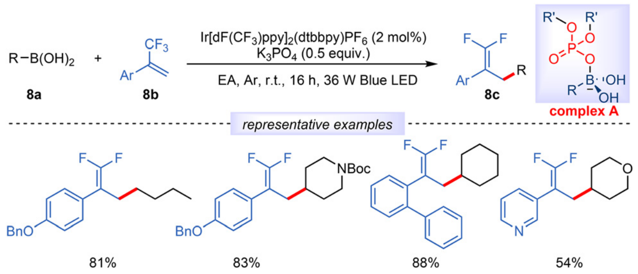
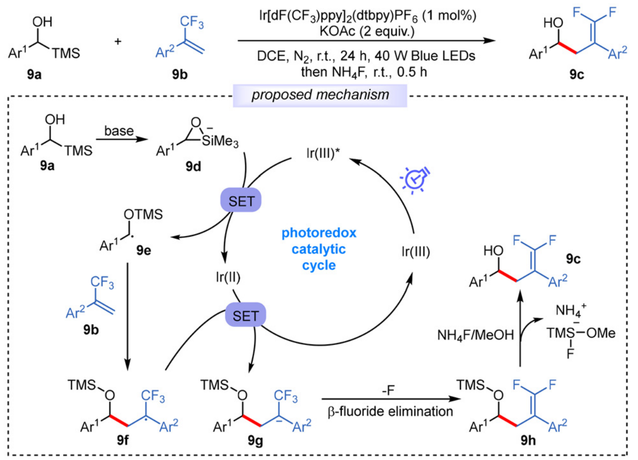
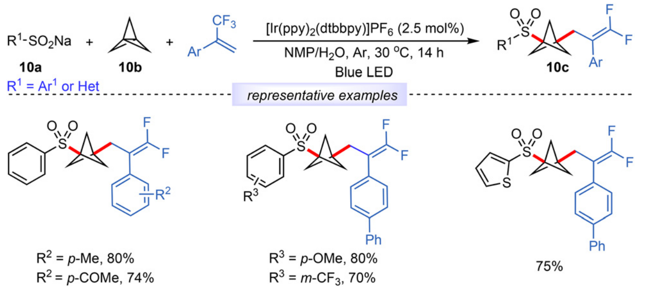


Scheme 8 Defluorinative alkylation of α-trifluoromethyl arylalkenes with alkylboronic acids.

via a pentacoordinate silicon intermediate.[25] Nevertheless, radical Brook rearrangements mediated by SET process remain underexplored, primarily owing to the challenging generation of alkoxy radical intermediates.[26] In 2023, Zhang and co-workers reported the facile construction of *gem*-difluoro homoallylic alcohol derivatives **9c** through radical [1,2]-Brook rearrangement by reacting α-trifluoromethyl arylalkenes **9b** with aryl substituted silyl alcohols **9a** (Scheme 9).[27] Based on the control experiments and previous reports, a possible mechanism was suggested. The excited Ir(III)* was reductively quenched by intermediates **9d** to form the carbon centered radicals **9e**. Subsequently, intermediates **9e** added to the α-trifluoromethyl arylalkenes **9b**, then the radical intermediates **9f** were reduced to form the anions **9g** through a single electron-transfer step. Finally, a consecutive β-fluoride elimination of carbanions **9g**, followed by a fluoride-promoted desilylation of intermediates **9h**, afforded the expected products **9c**. Notably, this work introduced a complementary defluorinative strategy for probing the reactivity and synthetic utility of *gem*-difluoroalkenes and trifluoromethyl alkenes.



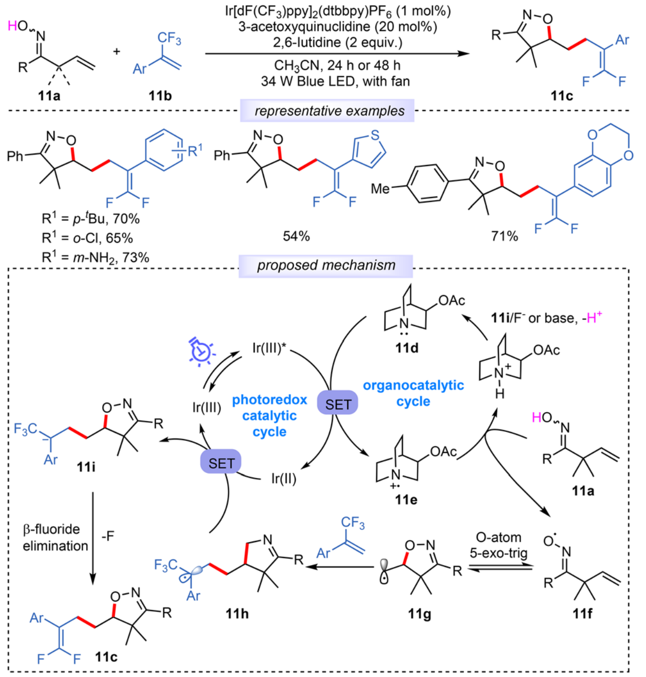
Scheme 9 Defluorinated alkylation of α-trifluoromethyl arylalkenes with aryl substituted silyl alcohols.



Scheme 10 Defluorinative *gem*-difluoroallylation of [1.1.1]propellane to access *gem*-difluoroallylic bicyclo[1.1.1]pentanes.

In contemporary drug design, bicyclo[1.1.1]pentanes (BCPs) represent a significant class of compounds frequently employed as linear spacer units to improve pharmacokinetic properties. Fluorine-containing BCPs are critical building blocks in pharmaceutical research.[2b,3b,28] In 2023, Jiang and co-workers reported a multicomponent reaction to construct *gem*-difluoroallylic bicyclo[1.1.1]pentanes **10c** by defluorinative *gem*-difluoroallylation of [1.1.1] propellane **10b** under blue LED irradiation at 30 °C in the presence of [Ir(ppy)$_2$(dtbbpy)]PF$_6$ in NMP : H$_2$O = 10 : 1 (Scheme 10).[29] This methodology utilizes commercially accessible arylsulfinates **10a** to generate radical precursors and showed good functional group compatibility under mild reaction conditions.

Oxygen radicals play important roles in organic synthesis and biological processes.[30] In 2023, Rueping *et al.* reported a study on the O–H bond activation of β,γ-unsaturated oximes using 3-acetoxyquinuclidine as the hydrogen atom transfer (HAT) reagent and Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ as the photoredox catalyst (Scheme 11).[31] Leveraging this strategy, a range of β,γ-unsaturated oximes **11a** with diverse functional groups



Scheme 11 Defluorinative *gem*-difluoroallylation of β,γ-unsaturated oximes with α-trifluoromethyl arylalkenes.

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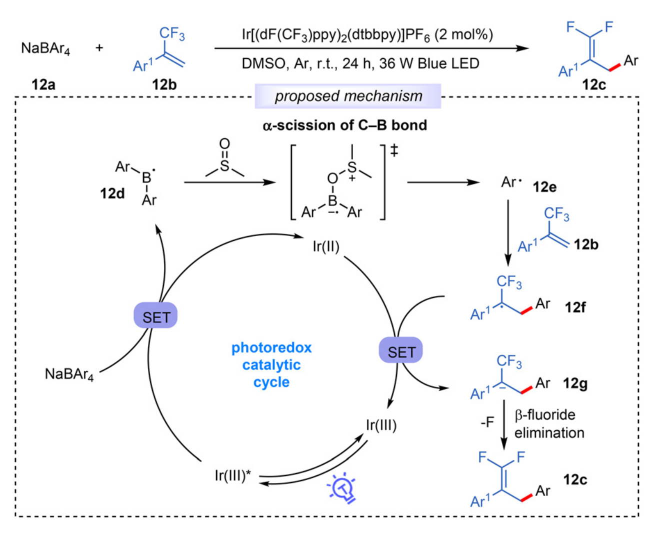
and different radical acceptors—particularly α-trifluoromethyl arylalkenes **11b**, were investigated. Moreover, this transformation was substrate-dependent, proceeding efficiently only with α-trifluoromethyl arylalkenes bearing electron-donating or weakly electron-withdrawing substituents on the aryl ring.

The proposed mechanism was shown in Scheme 11. First, the 3-acetoxyquinuclidine **11d** was oxidized by the excited state Ir(III)* to give amine radical cation **11e**. Then, the β,γ-unsaturated oximes **11a** donated a hydrogen atom to **11e** to form the iminoxyl radicals **11f**, which subsequently underwent a 5-*exo-trig* radical cyclization to produce the carbon-centered isoxazoline alkyl radicals **11g**. The radical intermediates **11g** afterwards added to the α-trifluoromethyl arylalkenes **11b** to form the radical intermediates **11h**, which were reduced to form the anions **11i** through a single electron-transfer step. Finally, defluorination of **11i** delivered the desired products **11c**. The strategy efficiently tackles the high redox potential of oximes, complements the activation of the O–H bond by quinuclidine, and provides a general pathway for the formation of iminoxyl radicals.

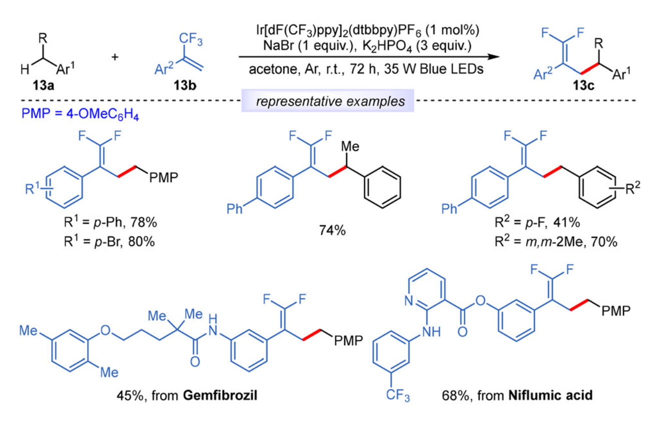
In 2023, Wang' group developed a defluorinative alkylation method for α-trifluoromethyl arylalkenes **12b** using sodium tetraphenylborate **12a** as the aryl radical precursor under the Ir$[dF(CF_3)ppy]_2(dtbbpy)PF_6$ catalysis, with irradiation from a 36 W blue LEDs at room temperature (Scheme 12).[32] Crucially, bond α-scission and efficiently generate aryl radicals **12e**. The DMSO served not only as a solvent but also as an activation reagent, enabling diarylboron radicals **12d** to underwent C–B addition of these aryl radicals to α-trifluoromethyl arylalkenes **12b** gave the carbon-centered radicals **12f**, which were further reduced by Ir(II) to generate the carbanion intermediates **12g** while regenerating the photocatalyst Ir(III). Finally, β-fluoride elimination afforded the *gem*-difluoroalkene products **12c**. This method employed tetraarylborate salts as unconventional aryl radical precursors, which underwent visible-light-induced homolysis to generate aryl radicals in the presence of DMSO as an activating agent.



Scheme 12 Defluorinative *gem*-difluoroallylation of sodium tetraphenylborate with α-trifluoromethyl arylalkenes.

Benzylic C–H bonds are prevalent in natural products, pharmaceuticals, agrochemicals, and functional materials.[33] Significant attention has been devoted to developing various approaches for the direct functionalization of benzylic C–H bonds.[34] In 2023, Ji and colleagues realized a photoredox-catalyzed approach for the defluorinative benzylation of α-trifluoromethyl arylalkenes **13b** with alkylarenes **13a** (Scheme 13).[35] The reaction, conducted in acetone solvent using 1 mol% $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ as catalyst, 1.0 equivalent of NaBr and 3.0 equivalent of K_2HPO_4 under argon atmosphere, smoothly produced various structurally valuable benzylated *gem*-difluoroalkenes **13c** in moderate to good yields (34–80%). Especially, several substrates bearing drug moieties were effectively converted into the desired products with good efficiencies. In the substrate scope, diverse functional groups were tolerated, enabling late-stage functionalization of structurally complex and functionalized molecules.

The radical-mediated 1,*n*-hydrogen atom transfer (1,*n*-HAT) strategy has proven effective for site-selective modification of $C(sp^3)$–H bonds over the past decade.[36] For instance, *N*-directed γ-$C(sp^3)$–H functionalization of sulfamate esters through unique 1,6-HAT processes has opened new avenues in chemical synthesis. However, methods involving coupling partners remain in their infancy.[37] In 2024, Qin *et al.* discovered a protocol for photoredox-catalyzed *N*-directed defluorinative γ-$C(sp^3)$–H allylation of sulfamate esters **14a** with α-trifluoromethyl arylalkenes **14b** to give the target products **14c** in the presence of $Ir[(dFCH_3ppy)_2(dtbbpy)]PF_6$ as catalyst.[38] A proposed mechanism for this transformation was described in Scheme 14. First, a PCET-based *N*-radicals **14d** formed through the combined action of Brønsted base and photoredox catalysis. Second, the *N*-radicals **14d** underwent favorable *N*-directed 1,6-HAT to generate alkyl radical precursors **14e**, which subsequently followed analogous steps to yield the target *gem*-difluoroalkene products **14c**. Moreover, water served as an environmentally benign co-solvent in this transformation. Notably, this work offered a straightforward and practi-



Scheme 13 Defluorinative benzylation of α-trifluoromethyl arylalkenes with alkylarenes.

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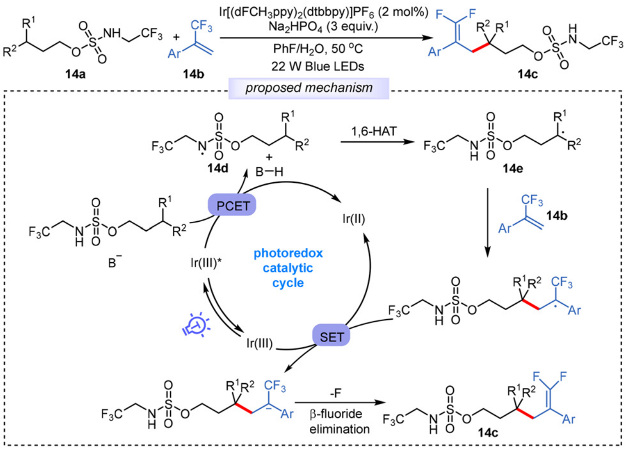
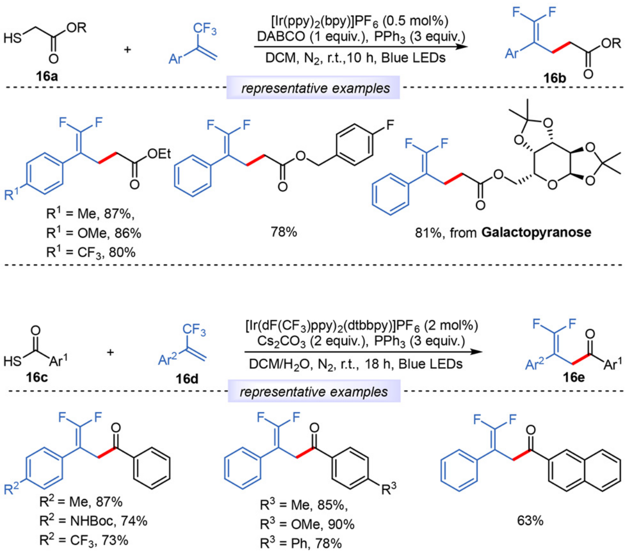


Scheme 14 N-directed defluorinative γ-C(sp^3)–H allylation of sulfamate esters with α-trifluoromethyl arylalkenes.

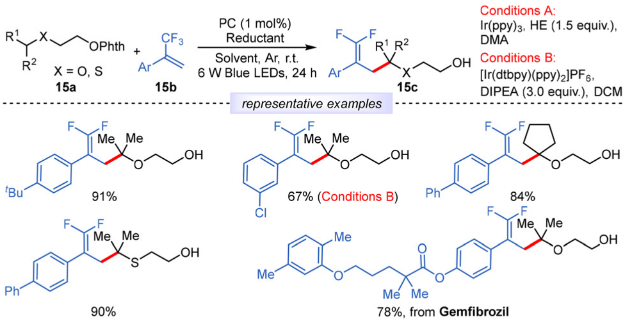


Scheme 16 Photocatalytic synthesis of γ,γ-difluoroallylic ketones and δ,δ-difluoroallylic ketones *via* a desulfurative/defluorinative alkylation process.

cal strategy for the divergent synthesis of *gem*-difluoroalkene-containing sulfamate esters.

As a proficient approach for initiating long-range inert C–H bond, the 1,5-HAT process is also a commonly method for generating alkyl radicals.[36a,39] In the same year, Wang and colleagues subsequently discovered a 1,5-HAT process for synthesizing *gem*-difluoroalkenes in photoredox-catalyzed reactions (Scheme 15).[40] In this transformation, various *N*-alkoxyphthalimides **15a** served as radical precursors to generate alkyl radicals. These radicals then reacted with diverse α-trifluoromethyl arylalkenes **15b** to afford numerous synthetically attractive *gem*-difluoroalkenes **15c** in moderate to excellent yields under optimal conditions. Compared with conventional methods, the reactions proceeded under mild conditions with broad functional group tolerance, including compatibility with a wide range of sensitive and functionalized moieties.

In 2024, Sun' group developed new strategies for synthesizing δ,δ-difluoroallylic ketones and γ,γ-difluoroallylic ketones through a desulfurative/defluorinative alkylation procedure (Scheme 16).[41] They successfully prepared a variety of γ,γ-difluoroallylic ketones **16b** in moderate to high yields *via* the desulfurative *gem*-difluoroallylation of various α-thiol esters **16a**, utilizing [Ir(ppy)$_2$(bpy)]PF$_6$ as the photocatalyst, DABCO as the base, and PPh$_3$ as the sulfur scavenger in DCM. Particularly, the *gem*-difluoroallylation modification of natural products was also successful. Additionally, they unexpectedly disclosed that thioic acids **16c** and α-trifluoromethyl arylalkenes **16d** were also compatible with these strategies. Furthermore, δ,δ-difluoroallylic ketones **16e** were smoothly synthesized under similar conditions, employing [Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ as the photocatalyst, Cs$_2$CO$_3$ as the base, and PPh$_3$ as the sulfur scavenger in a mixed solvent of DCM and H$_2$O.



Scheme 15 Photoredox catalyzed synthesis of *gem*-difluoroalkenes *via* 1,5-hydrogen atom transfer.

2.2 Ru-based photocatalysts

The regioselective cross-coupling of *gem*-difluoroalkene motifs with the C–H bonds of simple arenes remains a challenge.

In 2022, Patureau and co-workers reported a photoredox-catalyzed late-stage defluorinative *gem*-difluoroallylation of (hetero)aryl frameworks using aryl sulfonium salts (**17a**) as radical precursors. The transformation proceeds under visible-light irradiation *via* site-selective direct C(sp^2)–H functionalization, enabling the efficient installation of *gem*-difluoroallyl groups onto structurally complex molecules at a late stage (Scheme 17).[42] They explored a diverse array of substrates, including aryl sulfonium salts **17a** and α-trifluoromethyl arylalkenes **17b**, with particular emphasis on derivatives of two important drugs: flurbiprofen and pyriproxyfen. This process was performed under mild and sustainable conditions using the [Ru(bpy)$_3$](PF$_6$)$_2$/TMEDA system in acetonitrile solvent. This discovery pretty supplemented the existing synthetic technology of fluorine-containing drugs.

There are only few reports on using an *S*-centered radical route to prepare *gem*-difluoroallylsulfones. In 2023, Lei and co-

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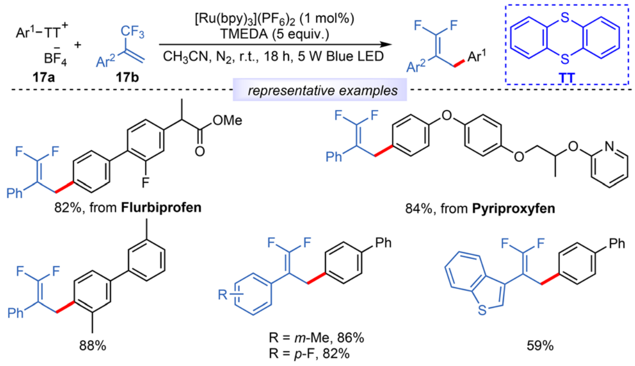
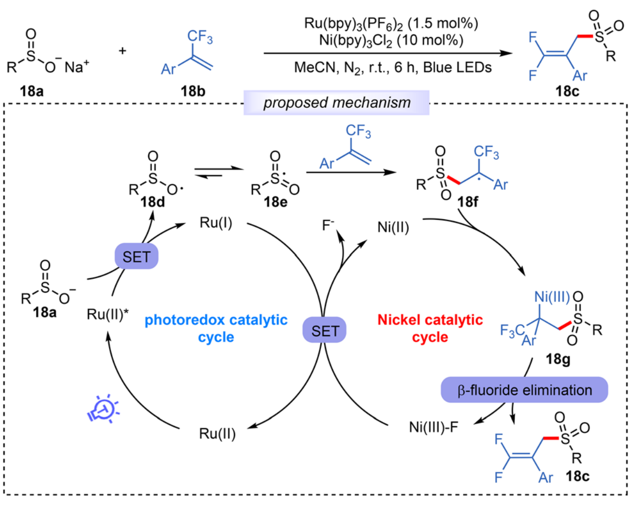


Scheme 17 Late-stage defluorinative *gem*-difluoroallylation of aryl sulfonium salts with α-trifluoromethyl arylalkenes.

workers developed a study for synthesizing a range of *gem*-difluoroallylsulfones **18c** with moderate to good yields through a photo/Ni dual-catalyzed radical defluorinative sulfonylation of α-trifluoromethyl arylalkenes **18b.**[13a] They selected aryl sulfonium salts **18a** as sulfonyl radical precursors for this transformation employing a dual catalytic system comprising photocatalyst Ru(bpy)$_3$(PF$_6$)$_2$ and nickel catalyst Ni(bpy)$_3$Cl$_2$ in MeCN at room temperature under blue LEDs irradiation. A proposed reaction mechanism was depicted in Scheme 18 based on previous reports.[12g,13i,43] First, the Ru(II)* preferentially oxidized sodium sulfinates **18a**, generating the sulfonyl radicals **18e** and Ru(I). The sulfonyl radicals **18e** then added to α-trifluoromethyl arylalkenes **18b** to form benzyl carbon radicals **18f.** This radicals subsequently reacted with Ni(II) to produce alkyl-Ni(III) intermediates **18g**, which further underwent β-fluoride elimination to produce the target products **18c**. The catalytic cycle was ultimately completed through SET-mediated regeneration of both the Ru(II) and Ni(II). To be noted, this dual-catalytic system effectively suppressed the rapid oxygen-mediated side reactions triggered by trace amount of air, preventing the formation of α-trifluoromethyl-β-sulfonyl tertiary alcohol by-product.



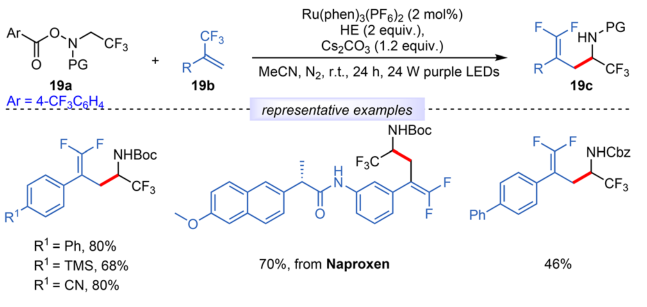
Scheme 18 *gem*-Difluoroallylation of aryl sulfonium salts with α-trifluoromethyl arylalkenes.

The α-CF$_3$ amine motif serves as an effective surrogate for the natural peptide bond [CONH] in peptide mimics, significantly altering physical and biological properties such as cell membrane permeability, lipophilicity, and metabolic stability.[44] In 2023, Chen and colleagues introduced an innovative defluorinative α-C(sp^3)–H alkylation for the synthesis of *gem*-difluoroallylated α-trifluoromethylamines **19c** in good to excellent yields.[45] The reaction employed various *N*-trifluoroethyl hydroxylamine reagents **19a** and diverse α-trifluoromethyl alkenes **19b** in the presence of Ru(phen)$_3$(PF$_6$)$_2$ as photocatalyst, Hantzsch ester (HE) as the reductant, and Cs$_2$CO$_3$ as the base in CH$_3$CN under the irradiation of 24 W purple LEDs (Scheme 19). Furthermore, this protocol was also successfully applied to the late-stage functionalization of complexes, such as bioactive compounds and natural products.

Incorporating fluoroalkenes into the structural framework of trialkylamines is an appealing but uncharted transformation.[13n,45,46] In 2024, Yang *et al.* developed a photocatalytic multicomponent reductive aminoalkylation process for synthesizing fluorinated tertiary aliphatic homoallylamines **20d** that integrated naturally occurring secondary alkylamines **20a**, carbonyl compounds **20b**, and readily available fluoroalkyl-substituted alkenes, such as α-trifluoromethyl alkenes **20c**, using Ru(bpy)$_3$(PF$_6$)$_2$ as the photocatalyst, Hantzsch ester (HE) as the reductant, and propionic acid along with 4 Å MS as the additive in DMSO under irradiation with a 456 nm Kessil lamp at room temperature (Scheme 20).[47] The utility of this method is demonstrated through its broad functional group tolerance, successful derivatization of complex alkylamines, and applications in the synthesis of drug analogues.

3 Organo-photocatalysts

There has been rising attention in the challenging and essential construction of all-carbon quaternary centers. Photoredox-catalyzed *gem*-difluoroallylation of cesium tertiary alkyl oxalates **21a** using 4CzIPN as the photocatalyst in MeCN without requiring base was disclosed by Yuan and colleagues in 2022 (Scheme 21).[48] In this method, oxalates served as activating



Scheme 19 Defluorinative α-C(sp^3)–H alkylation for the synthesis of *gem*-difluoroallylated α-trifluoromethylamines.

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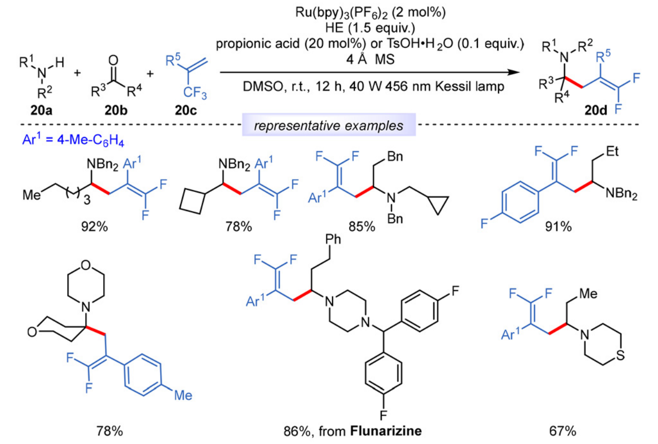
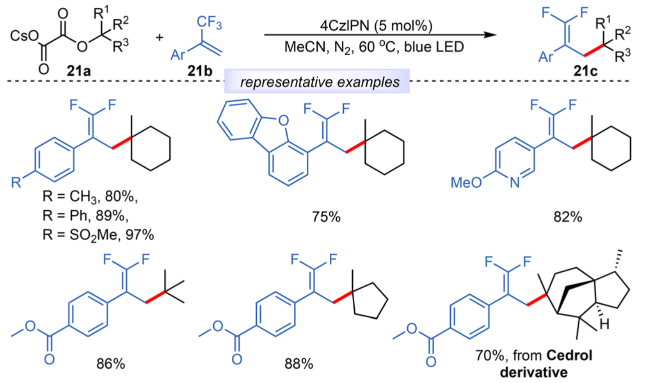
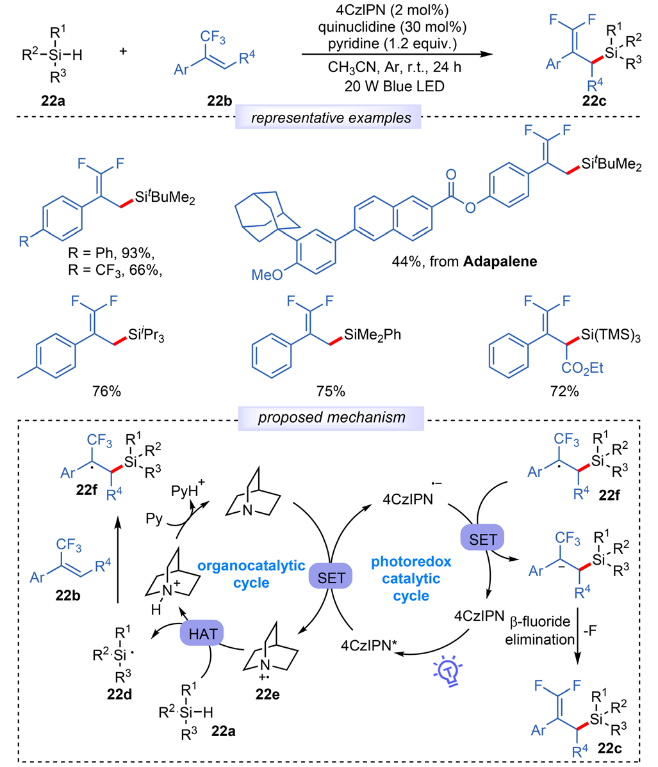


Scheme 20 Photocatalytic multicomponent reductive aminoalkylation process for synthesizing group-rich fluorinated tertiary aliphatic homoallylamines.



Scheme 21 *gem*-Difluoroallylation of cesium tertiary alkyl oxalates to construct all-carbon quaternary centers.



Scheme 22 Allylic defluorinative silylation of α-trifluoromethyl arylalkenes with hydrosilanes.

groups for tertiary alcohols to generate tertiary alkyl radicals, enabling the construction of all-carbon quaternary centers. The transformation demonstrated great functional group tolerability for both cesium tertiary alkyl oxalates **21a** and α-trifluoromethyl arylalkenes **21b**, which has also been successfully applied to late-stage modifications of bioactive molecules.

Organosilicon compounds have numerous applications in organic synthesis,[49] material science,[50] medicinal chemistry.[51] Among them, *gem*-difluoroallylsilanes have recently emerged as a privileged motif, garnering growing attention in chemical research. In 2022, Jing's group presented an environmentally friendly and simple method for photoredox metal-free allylic defluorinative silylation of α-trifluoromethyl arylalkenes **22b** with hydrosilanes **22a** by combining 4CzIPN as a photocatalyst and quinuclidine as the HAT reagent under 20 W blue LED irradiation in CH$_3$CN (Scheme 22).[52] This method provided an alternative approach to prepare *gem*-difluoroallylsilanes, which showed good functional group compatibility in moderate to excellent yields. Notably, the required hydrosilanes – serving as silyl radical precursors – are commercially available and relatively inexpensive. Furthermore, this technique was suitable for individual α-trifluoromethyl arylalkenes with a double bond in the middle position. A feasible mechanism was proposed in Scheme 22. Stern–Volmer analysis revealed that the 4CzIPN* was primarily quenched by quinuclidine. The silyl radical intermediates **22d** were formed when radical cation **22e** abstracted a hydrogen atom from hydrosilanes **22a**. **22d** then added to α-trifluoromethyl arylalkenes **22b**, forming radical intermediates **22f**, which subsequently underwent another SET process and β-fluoride elimination to obtain the target products **22c**.

A simple and versatile photocatalytic method enables the synthesis of unsaturated ketones bearing valuable *gem*-difluoroalkene moieties, which could benefit the pharmaceutical, agrochemical, and material industries. In 2022, Wu and coworkers developed a method to synthesize distal *gem*-difluoroalkenyl ketones **23c** in moderate to excellent yields *via* organophotoredox-catalyzed ring-opening *gem*-difluoroallylation of nonstrained cycloalkanols **23a** with a broad scope of α-trifluoromethyl arylalkenes **23b**, utilizing Mes-2,7-Me$_2$-Acr-Me$^+$ClO$_4^-$ as organophotocatalyst, 2,4,6-collidine and [C$_4$MPr]$^+$PF$_6^-$ in DCM under the irradiation of 30 W blue LEDs lamp (Scheme 23).[53] Notably, this strategy enabled precise control over product chain length through the use of cyclic alcohols with defined ring sizes, providing an efficient and regioselective route to distal *gem*-difluoroalkenyl ketones.

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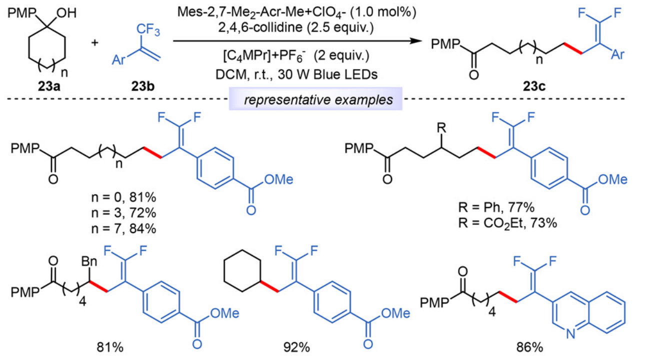
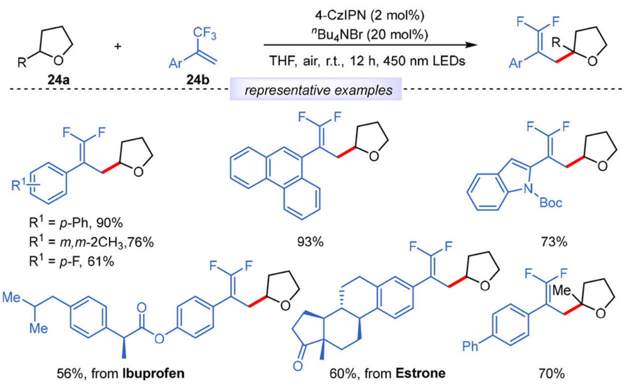


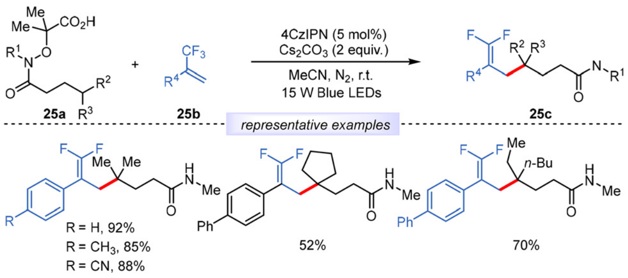
Scheme 23 Ring-opening *gem*-difluoroallylation of nonstrained cycloalkanols with α-trifluoromethyl arylalkenes.

The direct and site-selective α-C(sp^3)–H activation of THF remains challenging owing to its inherent inertness. In 2023, Zhong and colleagues introduced a metal-free and site-selective α-C–H *gem*-difluoroallylation of tetrahydrofuran **24a** (Scheme 24).[54] In this work, various α-trifluoromethyl arylalkenes **24b** were investigated in the presence of 4-CzIPN as a photocatalyst and ^{n}Bu$_4$NBr as a HAT catalyst in THF, under 450 nm LEDs irradiation in an air atmosphere. Overall, substrates containing electron-donating groups showed superior performance compared to those with electron-withdrawing groups. Furthermore, this methodology was practical and also applicable for the late-stage functionalization of several α-trifluoromethyl arylalkenes derived from natural products and pharmaceuticals. Based on the control experiments and mechanistic studies, the photocatalytic production of bromine radicals was critical to the success of the process, as indicated. Moreover, the feature of transition-metal-free aligned with green chemistry principles by avoiding metal contaminant and minimizing environmental impact.

In 2023, Yuan's group depicted a 4CzIPN-catalyzed *gem*-difluoroallylation of carboxylic acids **25a** with α-trifluoromethyl alkenes **25b** *via* 1,5-HAT using Cs_2CO_3 as base, in MeCN at room temperature under 15 W blue LEDs irradiated (Scheme 25).[55] The resulting *gem*-difluoroalkene derivatives **25c** were obtained with good functional group compatibility in moderate to excellent yields. Moreover, this method enabled the visible-light photocatalyzed *gem*-difluoroallylation of unactivated C(sp^3)–H bonds, providing a site-selective approach to introduce *gem*-difluoroallyl groups into aliphatic frameworks.



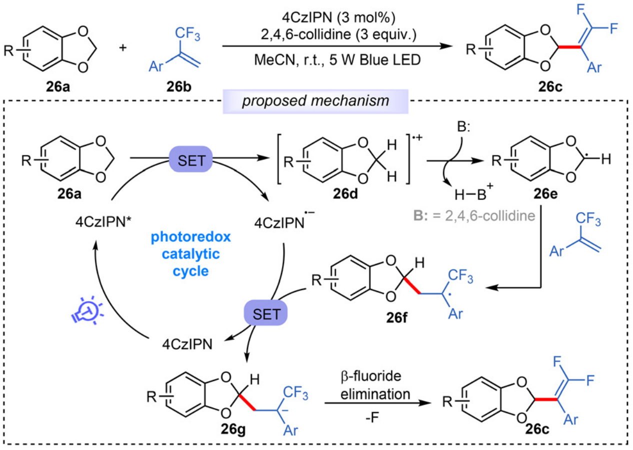
Scheme 24 Site-selective α-C–H *gem*-difluoroallyslation of tetrahydrofuran with α-trifluoromethyl arylalkenes.



Scheme 25 *gem*-Difluoroallylation of carboxylic acid with α-trifluoromethyl alkenes.

In 2023, Zhou *et al.* reported a simple and mild strategy for the photocatalytic mono-*gem*-difuoroallylation of 1,3-benzodioxoles **26a** with various α-trifluoromethyl arylalkenes **26b** in the presence of 4CzIPN and 2,4,6-collidine in MeCN under the irradiation of 5 W blue LED.[56] A proposed mechanism of this transformation was depicted in Scheme 26. The 4CzIPN* oxidized 1,3-benzodioxoles **26a** to produce radical cations **26d**, which subsequently underwent deprotonation to generate the 1,3-benzodioxol-2-yl radicals **26e**. These radicals added to the α-trifluoromethyl arylalkenes **26b** to give intermediate radicals **26f**. Reduction of **26f** by 4CzIPN$^{\bullet-}$ yielded the α-CF_3 carbanions **26g** while regenerating the 4CzIPN catalyst. Finally, β-fluoride elimination of **26g** afforded the target products **26c**. To be noted, in this work the crucial 1,3-benzodioxol-2-yl radicals were formed *via* direct single-electron oxidation of the precursors, rather than through hydrogen atom abstraction pathway.

Fluorinated amino acids (FAAs) are crucial components in organic synthesis and have numerous applications in medic-



Scheme 26 Mono-*gem*-difuoroallylation of 1,3-benzodioxoles with α-trifluoromethyl arylalkenes.

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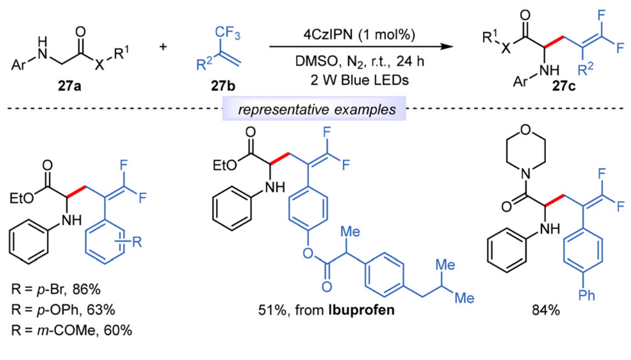
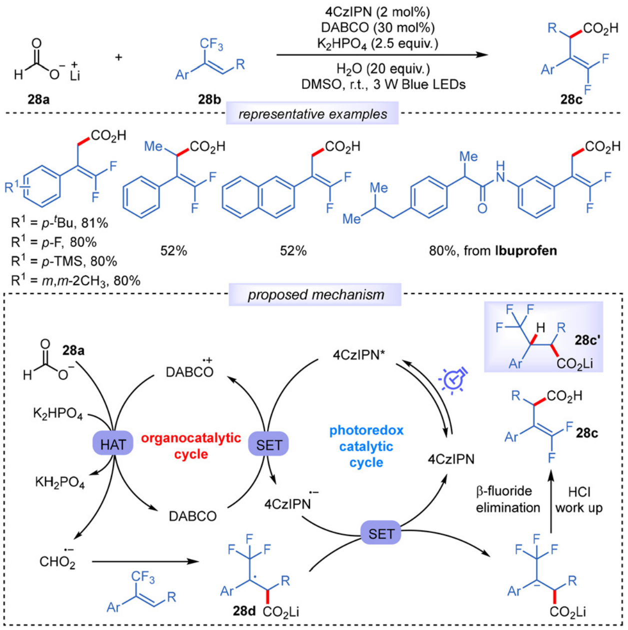
inal and bio-organic chemistry.[4b,57] In 2023, Guo and colleagues disclosed a 4CzIPN-catalyzed, 2 W blue LEDs-driven α-C(sp^3)–H *gem*-difluoroallylation of glycine derivatives and dipeptides **27a** with α-trifluoromethyl alkenes **27b** without any additives in DMSO (Scheme 27).[58] This method exhibited a broad substrate scope and excellent functional group tolerance, allowing the synthesis of diverse fluorine-containing amino acids and dipeptides **27c** in good to excellent yields. Notably, the methodology demonstrated remarkable compatibility with biomolecules, highlighting its potential for biological applications. Additionally, a series of 2-trifluoromethyl 1,3-enynes also exhibited compatibility with this transformation.

In 2023, Zhu and co-workers reported an intriguing monodefluorocarboxylation of diverse α-trifluoromethyl arylalkenes **28b** with lithium formate **28a** to access *gem*-difluorovinylacetic acids **28c** (Scheme 28).[59] This transformation employed a catalytic system consisting of 4CzIPN as the photocatalyst, DABCO as the HAT catalyst, and K_2HPO_4 as the base, with 20 equivalents of H_2O in DMSO, under irradiation with a 3 W blue LEDs at room temperature. The reaction demonstrated excellent tolerance for sterically demanding functional groups, including TMS and vinyl moieties, *ortho*-substituted hindered substrates, and trisubstituted alkenes, as well as complex substrates derived from liquid crystals and natural products. A propose mechanism for the defluorocarboxylation was described in Scheme 28. The $CO_2^{\bullet-}$ radical, generated *via* HAT by the DABCO radical cation, underwent Giese radical addition to the α-trifluoromethyl arylalkenes **28b** to form radicalintermediates **28d**. The target products **28c** were obtained through sequential steps, including: (1) a SET process with $4CzIPN^{\bullet-}$ to regenerate 4CzIPN, and (2) β-fluoride elimination to afford the final products **28c**. They speculated that although H_2O participated in the reaction, no side products **28c′** was detected. This observation suggests that both the reduction of **28d** and the β-fluoride elimination occurred rapidly. In this work, the reactivity of $CO_2^{\bullet-}$ radical anion plays a key role in driving the defluorinative transformation.

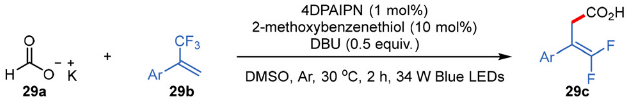
Shortly later, Fu's group reported a similar defluorinative carboxylation of α-trifluoromethyl arylalkenes **29b** that demonstrated good functional group compatibility (Scheme 29).[60] The reaction employed potassium formate **29a** as the $CO_2^{\bullet-}$ precursor under a 34 W LEDs irradiation, with catalytic 4DPAIPN as the photocatalyst, 2-methoxybenzenethiol as the HAT catalyst, and DBU as the base in DMSO at 30 °C. This strategy required only 2 h, providing an efficient alternative approach to synthesize structurally diverse *gem*-difluorovinylacetic acids **29c**.



Scheme 27 α-C(sp^3)–H *gem*-difluoroallylation of glycine derivatives with α-trifluoromethyl alkenes.



Scheme 28 Mono-defluorocarboxylation of multifarious α-trifluoromethyl arylalkenes with lithium formate to access *gem*-difluorovinylacetic acids.



Scheme 29 Defluorinative carboxylation of α-trifluoromethyl arylalkenes with potassium formate.

Current cross-coupling protocols can efficiently create *gem*-difluoroalkenes. However, the construction of multi-fluorinated compounds, such as *gem*-difluoroalkene difluoroacetates found in some pharmaceuticals, under mild conditions remains challenging. In 2023, Chen and co-workers reported a defluorinative difluoroalkylation of α-trifluoromethyl arylalkenes **30b** with bromodifluoro precursors **30a**, which gave a range of difluoromethylene-containing *gem*-difluoroalkenes **30c** mediated by the photoredox catalyst 4CzIPN in DMF under the irradiation of purple LEDs (Scheme 30).[61] Notably, 2-bromo-2,2-difluoroacetamides **30a** could serve as effective difluoroalkylating reagents only when they lacked an N–H bond or when the N–H bond was sterically hindered. Under these conditions, they could be converted into the corresponding *gem*-difluoroalkenes with excellent tolerance of functional groups.

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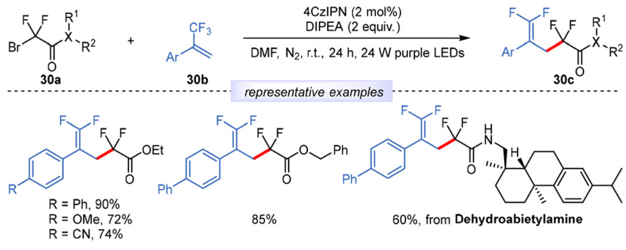
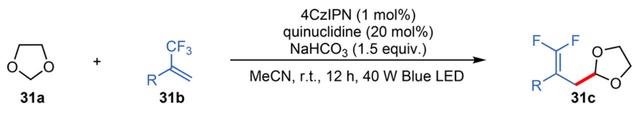


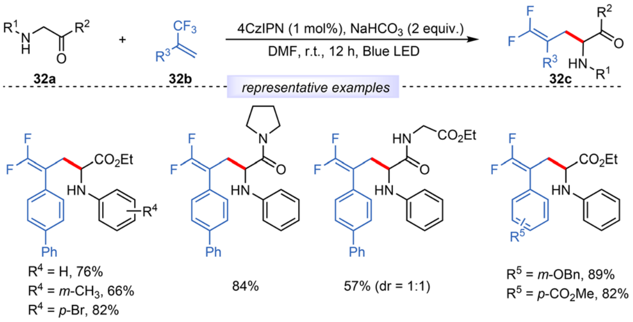
Scheme 30 Defluorinative difluoroalkylation of α-trifluoromethyl arylalkenes with 2-bromo-2,2-difluoroacetates derivatives.

In 2023, Chen and colleagues presented a study on the monomasked formylation of α-trifluoromethyl alkenes **31b** (Scheme 31).[62] They utilized low-priced 1,3-dioxolane **31a** as a masked formyl radical equivalent to provide significant amounts of masked formylated *gem*-difluoroalkenes **31c** in moderate to high yields, through the synergistic combination of 4CzIPN as a catalyst and catalytic quinuclidine as a HAT reagent in MeCN. Moreover, this study disclosed a solvent-dependent switch between mono- and dimasked formylation of α-trifluoromethyl alkenes, enabling by organophotoredox-catalyzed C–F bond activation.

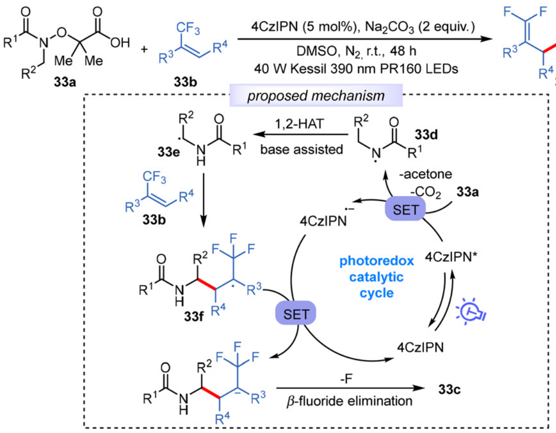
The conversion of glycine into nonproteinogenic amino acids and the modification of glycine-containing peptides can significantly enhance their activity, pharmacokinetics, and pharmacological properties of these compounds compared to their natural counterparts.[63] In 2024, Chen *et al.* described a method for the 4CzIPN-catalyzed defluorinative *gem*-difluoroallylation of glycine derivatives **32a** with α-trifluoromethyl alkenes **32b**. This protocol used $NaHCO_3$ as base and blue LED as a light source, delivering a broad scope of *gem*-difluoroalkenes **32c** in moderate to excellent yields (Scheme 32).[64] Additionally, this transformation utilized readily available starting materials, mild conditions, good functional group compatibility, providing an alternative procedure for the synthesis of alkylated *gem*-difluoroalkenes.



Scheme 31 Monomasked formylation of α-trifluoromethyl alkenes with 1,3-dioxolane.



Scheme 32 Defluorinative *gem*-difluoroallylation of glycine derivatives with α-trifluoromethyl alkenes.



Scheme 33 C(sp^3)–H *gem*-difluoroallylation of amides with α-trifluoromethyl alkenes.

While the 1,5-HAT of *N*-centered radicals is well-established, the 1,2-HAT process has found far fewer synthetic applications, primarily due to its higher energy barrier and the geometric constraints of the three-membered transition state. In 2024, Yuan' group discovered a mild C(sp^3)–H *gem*-difluoroallylation of amides **33a** with α-trifluoromethyl alkenes **33b**, facilitated by a base-assisted formal 1,2-HAT of amidyl radicals (Scheme 33).[65] The proposed mechanism was illustrated in Scheme 33. Upon irradiation with 40 W Kessil 390 nm PR160 LEDs, the 4CzIPN* oxidized **33a** to generate amidyl radicals **33d**. Assisted by Na_2CO_3, an intramolecular formal 1,2-HAT process preferentially occurred, yielding α-amino alkyl radicals **33e**, which then added to α-trifluoromethyl alkenes **33b**, forming the α-trifluoromethyl radical intermediates **33f**. Subsequent reductive quenching of the photocatalyst and β-fluoride elimination gave the desired products **33c**. However, an intermolecular HAT process cannot be entirely excluded. Enantioselective construction of the target products through radical addition remains a formidable challenge. Nevertheless, the reaction manifold may be biased by chiral copper or iron complexes that serve as stereo-directing Lewis-acid catalysts. In addition, this method introduced a novel strategy for generating α-aminoalkyl radicals *via* the reductive quenching cycle of the photocatalyst.

Quinazolin-4(3*H*)-ones constitute a significant class of N-heterocyclic compounds, demonstrating diverse pharmacological activities such as antibacterial, anti-inflammatory, anticancer, and antihypertensive properties.[66] In 2024, Guo *et al.* reported a 4CzIPN-photocatalyzed *gem*-difluoroallylation of spiro-dihydroquinazolinones **34a** using α-trifluoromethyl arylalkenes **34b** (Scheme 34).[67] Notably, α-trifluoromethyl arylalkenes bearing electron-donating groups (EDGs) or weak electron-withdrawing groups (WEWGs) at the *para*-position of the phenyl ring both exhibited excellent reactivity in this *gem*-

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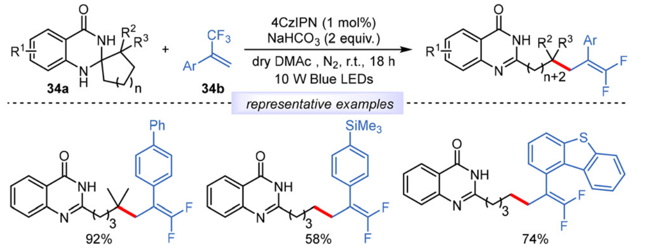
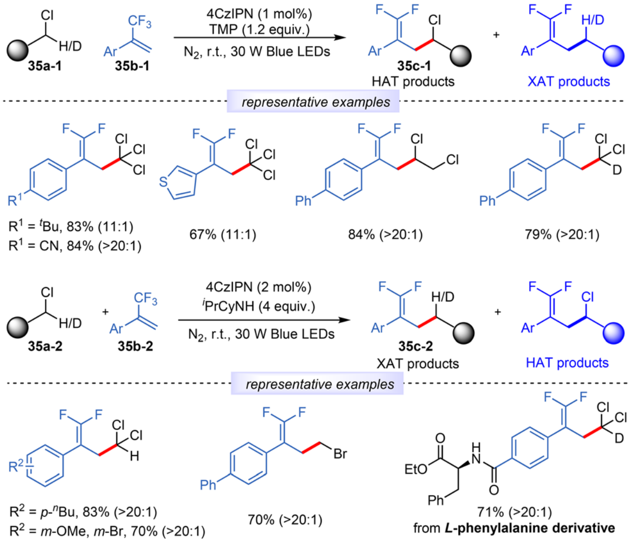


Scheme 34 *gem*-Difluoroallylation of spiro-dihydroquinazolinones using α-trifluoromethyl arylalkenes.

difluoroallylation reaction, affording the desired products in moderate to good yields. This protocol enables the introduction of a fluorine-containing group at the designated position of quinazolin-4(3*H*)-ones. Additionally, it features mild, redox-neutral conditions, excellent atom economy, and good functional group compatibility, highlighting its considerable potential for organic synthesis applications.

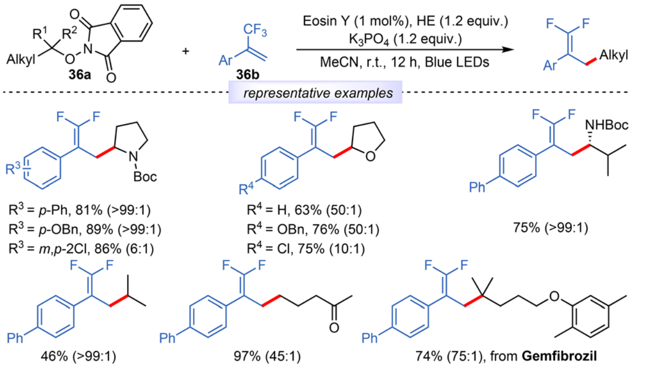
Polychloroalkyl motifs are prevalent in pharmaceuticals, agrochemicals, and natural products, and their unique physicochemical properties have driven growing interest in the selective and efficient synthesis of these structural units.[68] In 2025, Hu' group described a 30 W blue LEDs-driven selective defluorinative alkylation of α-trifluoromethyl arylalkenes **35b** with readily available and inexpensive polychloroalkane feedstocks **35a** as alkyl radical precursors, provided efficient access to a variety of polychloroalkylated *gem*-difluoroalkenes **35c** at room temperature (Scheme 35).[69] When using 1 mol% of 4CzlPN and 1.2 equivalents of TMP in polyhaloalkanes **35a-1**, the reaction enabled selective functionalization of C–H bonds in polychloroalkanes through HAT processes. Alternatively, when using 2 mol% of 4CzlPN and 4 equivalents of ^{i}PrCyNH in polyhaloalkanes **35a-1**, the reaction enabled selective activation of C–X bonds in polychloroalkanes **35a-2** through XAT processes. It is worth noting that the selective functionalization of C–H or C–X bonds in polychloroalkanes was controlled by the addition of an amine, without the need for toxic reagents and oxidants.



Scheme 35 Defluorinative alkylation of α-trifluoromethyl arylalkenes with polychloroalkanes.

Eosin Y is an attractive organic photocatalyst due to its low cost and easy preparation, combined with high photoredox efficiency and strong absorption throughout the visible-light region, enabling effective utilization of a broad range of irradiation wavelengths.[70] Chen and co-workers developed a defluorinative alkylation of α-trifluoromethyl arylalkenes **36b** with *N*-alkoxyphthalimides **36a** using Eosin Y as photocatalyst, Hantzsch ester (HE) as reductant, K_3PO_4 as base under irradiation of blue LEDs in MeCN in 2025 (Scheme 36).[71] This method exhibited excellent chemoselectivity, favoring defluorinative alkylation over competing hydroalkylation pathways, delivered high product yields, and tolerated a broad range of functional groups, establishing a highly effective platform for the synthesis of structurally diverse and bioactive fluorinated compounds.

In 2025, Keyume *et al.* reported a visible-light-induced defluorinative acylation of α-trifluoromethyl arylalkenes **37b** with aromatic carboxylic anhydrides **37a**, providing various γ,γ-difluoropropenyl ketones **37c** under irradiation with a 10 W blue LED at room temperature (Scheme 37).[72] In this reaction, 4CzIPN was employed as the photocatalyst, PPh_3 served as the reductant, and Cs_2CO_3 was used as the base in DMF. When anhydride **37d** bears an electron-withdrawing substituent (*e.g.*, *para*-Cl) on one aryl ring and an electron-donating substituent (*e.g.*, *para*-OMe) on the other, the reaction proceeded exclusively through allylic defluoroacylation, affording product **37e** as the sole product and possible 4-methoxybenzoylation product **37f** was not detected. However, when aryl anhydride **37g** bearing one *meta*-methyl substituent was used as the substrate, a mixture of benzoylation product **37h** and *meta*-methylbenzoylation product **37i** was obtained in a 54 : 46 ratio. Mechanistic studies suggested that reaction selectivity may be influenced by both electronic and steric effects of substituents on unsymmetrical anhydrides, with electron-withdrawing groups tending to facilitate C–O bond cleavage and steric bulk appearing to control regioselective acyl transfer.



Scheme 36 Defluorinative alkylation of α-trifluoromethyl arylalkenes with *N*-alkoxyphthalimides.

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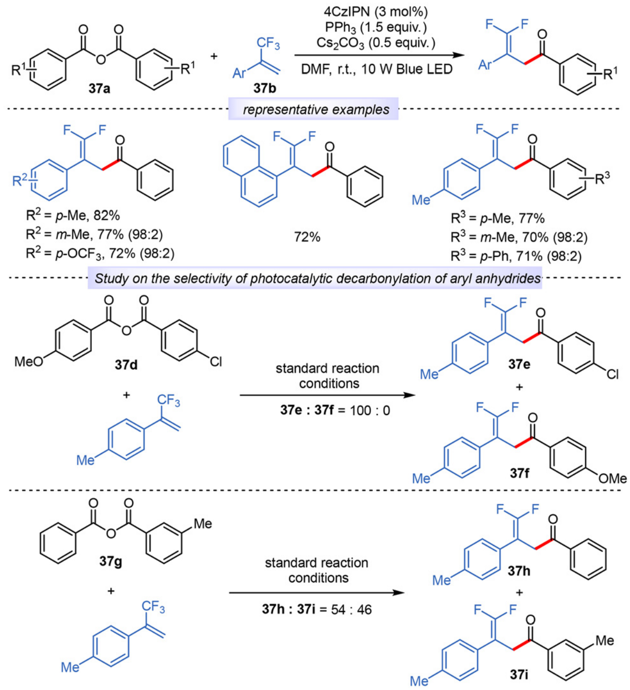
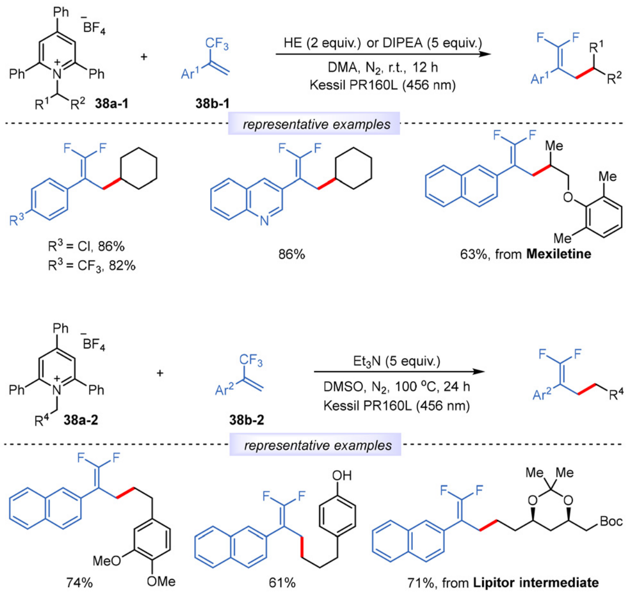


Scheme 37 Defluorinative acylation of α-trifluoromethyl arylalkenes with aromatic carboxylic anhydrides.

4 Reactions with other photoinduced systems

4.1 Photocatalysts-free conditions

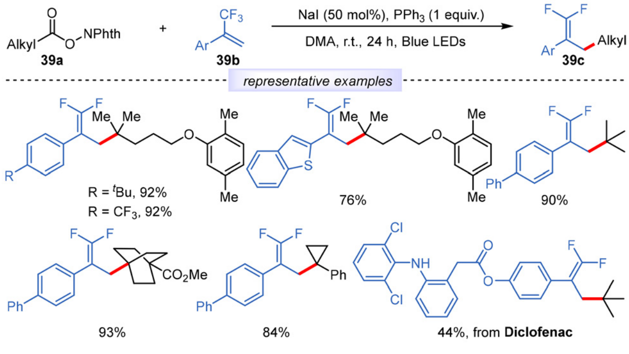
Since the groundbreaking research reported by Watson's group in 2017,[73] great interests have focused on the reactions of Katritzky salts, which can be easily synthesized through a one-step condensation of primary alkylamines with pyrylium salts and efficiently generate alkyl radicals.[74] In 2022, Zhang and colleagues reported a photoinduced, EDA-complex-mediated defluorinative alkylation of α-trifluoromethyl arylalkenes **38b** with katritzky salts **38a** under catalyst- and metal-free conditions (Scheme 38).[75] This approach afforded a sustainable strategy for synthesis of *gem*-difluoroalkenes with a broade substrate scope and excellent functional group compatibility, and suitability for late-stage bioactive molecules and drug derivatives. In this reaction, the electron donor–acceptor (EDA) complex formed between inexpensive organic reductants (electron donor) and Katritzky salts (strong electron acceptor) drives the transformation. When *N*-secondary alkyl Katritzky salts **38a-1** were employed, the reaction typically utilized Hantzsch ester (HE) or DIPEA as the reductant in DMA under blue LEDs irradiation at room temperature. Notably, switching to the more economical reductant Et_3N in DMSO under blue LEDs irradiation at 100 °C, the researchers made a significant observation: *N*-primary alkyl Katritzky salts **38a-2** could successfully participate in this reaction. This method is distinguished by using cheap and easily accessible organic reductants (Hantszch ester or Et_3N), thus enabling catalyst- and metal-free conditions.



Scheme 38 Defluorinative alkylation of α-trifluoromethyl arylalkenes with Katritzky salts.

More recently, transient EDA complexes have played a crucial role in photoinduced organic synthesis by generating radicals without requiring external transition metals or organic dye-based photoredox catalysts. In 2024, Fu's group described a general photoinduced reductive defluorinative decarboxylative alkylation of α-trifluoromethyl arylalkenes **39b** *via* an EDA complex formed between iodide salts and *N*-hydroxyphthalimide esters (redox-active esters, RAEs) **39a** (Scheme 39).[76] These esters were stable and can be easily prepared from the corresponding carboxylic acids.[77] The reaction afforded a variety of *gem*-difluoroalkenes **39c** with broad functional group compatibility.

Aryl and alkyl thianthrenium salts have emerged as significant electrophiles or radical precursors for various reactions mediated by metal or photoredox catalysts. In 2024, Fan and colleagues disclosed a visible-light-promoted defluoroallyla-



Scheme 39 Defluorinative decarboxylative alkylation of α-trifluoromethyl arylalkenes with *N*-hydroxyphthalimide esters (redox-active esters, RAEs).

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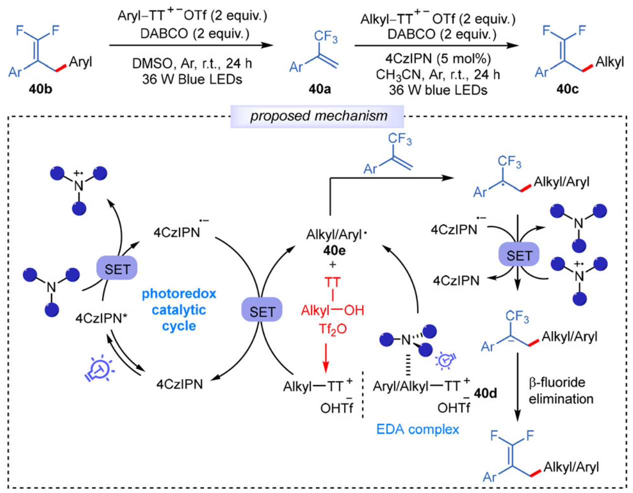
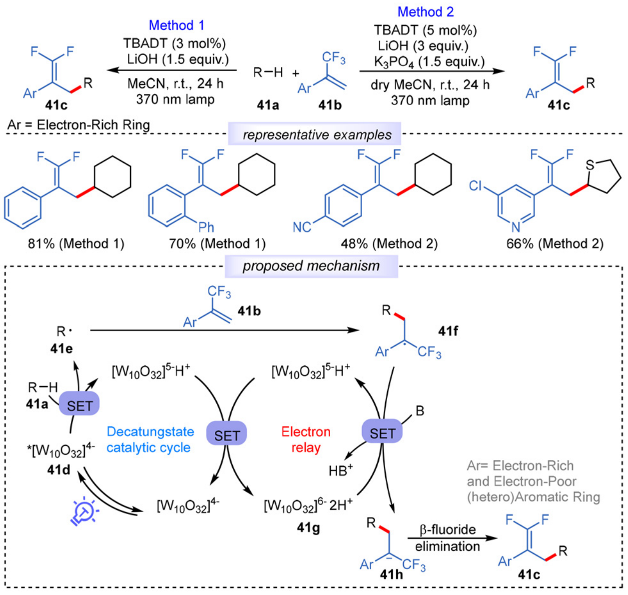
tion procedure involving α-trifluoromethyl arylalkenes **40a** and aryl/alkyl thianthrenium salts, using DABCO as the initiator under 36 W blue LEDs irradiation, providing *gem*-difluoroalkenes with excellent functional group tolerance in moderate to excellent yields.[78] Interestingly, when aryl-substituted thianthrenium salts were used, the desired products **40b** could be obtained in DMSO without adding the photocatalyst 4CzIPN. In contrast, reactions involving alkyl-substituted salts with 5 mol% of the organic photocatalyst 4CzIPN in CH_3CN to obtain the corresponding products **40c**. The proposed mechanism is shown in Scheme 40. Aryl or alkyl thianthrenium salts **40d** interacted with DABCO to form an EDA complex, resulting in the generation of the alkyl or aryl radicals **40e** through a SET triggered by blue LEDs. For alkyl thianthrenium salts, the 4CzIPN photocatalyst could enhanced the efficiency of SET and facilitated the generation of alkyl radicals **40e**. The radicals then underwent a series of similar processes, including addition reaction, single-electron reduction, and β-fluoride elimination, to afford the desired products and furnish the photoredox cycle. This method is notable for employing the inexpensive organic reductant DABCO to generate EDA complexes that facilitate radical formation without the need for an external photocatalyst.

4.2 TBADT as photocatalyst

The direct functionalization of unactivated C(sp^3)–H bonds in alkanes remains a significant challenge in modern synthetic chemistry. In 2024, Martínez-Balart and co-workers developed a photoredox-catalyzed HAT protocol that directly cleaves C(sp^3)–H bond, enabling the defluorinative alkylation of α-trifluoromethyl arylalkenes **41b** using unfunctionalized alkanes **41a** as radical precursors (Scheme 41).[79] Notably, when using α-trifluoromethyl arylalkenes **41b** bearing an electron-poor ring, a stronger basic system comprising LiOH (3 equiv.) and K_3PO_4 (1.5 equiv.) selectively afforded the *gem*-difluoroalkenes over the hydroalkylation products. Based on mechanistic investigations and previous studies of TBADT photocatalysis,[80] the authors proposed the following reaction mechanism: the excited-state decatungstate **41d** facilitated hydrogen atom abstraction from the alkanes **41a**, generating an alkyl radicals **41e**. This radical then added to the α-trifluoromethyl arylalkenes **41b**, forming radical intermediates **41f**. Subsequently, the intermediates **41f** underwent single-electron reduction by the doubly reduced decatungstate **41g**, facilitated by the base, yielding carbanions **41h**, which underwent β-fluoride elimination to produce the *gem*-difluoroalkene products **41c**. Moreover, saturated hydrocarbons, such as gaseous alkanes, were directly employed as alkylating agents without the need for pre-activated radical precursors, enhancing both the step economy and atom economy of this strategy.



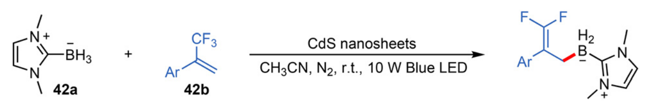
Scheme 40 Defluorinative alkylation/arylation of α-trifluoromethyl arylalkenes with thianthrenium salts.



Scheme 41 Defluorinative alkylation of α-trifluoromethyl arylalkenes with unfunctionalized alkanes.

4.3 Semiconductors as photocatalysts

In 2023, Dai's group reported a heterogeneous photocatalyzed defluorinative *gem*-difluoroallylation of 1,3-dimethylimidazol-2-ylidene borane **42a**, which served as the boryl radical precursor, with several α-trifluoromethyl arylalkenes **42b** using stable CdS nanosheets as catalyst in CH_3CN under the irradiation of a 10 W blue LED (Scheme 42).[81] In this work, the use of ultrathin CdS nanosheets as recoverable heterogeneous photocatalyst with high surface area and efficient light absorption facilitated the photoinduced defluorinative transformation while allowing easy catalyst recovery and reuse.



Scheme 42 Defluorinative *gem*-difluoroallylation of 1,3-dimethylimidazol-2-ylidene borane with α-trifluoromethyl arylalkenes.

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5 Conclusions

In summary, we have summarized recent advances in visible-light-induced defluorinative functionalization of α-trifluoromethyl arylalkenes, enabling streamlined access to diversified fluorinated molecules. By harnessing the power of visible-light photocatalysis, these methods enable mild and efficient radical-mediated allylic defluorination through single-electron transfer (SET) processes, followed by β-fluorine elimination. This strategy provides a sustainable and robust platform for constructing privileged *gem*-difluoroalkene motifs, which are highly valuable as carbonyl bioisosteres in drug discovery. The ongoing development of these photochemical approaches, coupled with deeper mechanistic insights and improved functional group compatibility, has successfully addressed key synthetic challenges. Consequently, it substantially expands the toolbox for accessing diverse and complex fluorinated molecules, thereby opening new avenues for the application of such compounds in medicinal chemistry and related fields.

Author contributions

All authors contributed to the review and editing of the original manuscript.

Conflicts of interest

There are no conflicts of interest to declare.

Data availability

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

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