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REVIEW

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# Photo-induced 1,2-carbohalofunctionalization of C–C multiple bonds *via* ATRA pathway

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Radical vicinal carbohalofunctionalization of C–C multiple bonds *via* atom transfer processes constitutes an efficient method for the construction of halogenated building blocks with complete atom economy *via* radical cleavage of a pre-existing carbon–halogen σ-bond of an atom transfer reagent and their transposition over the π-bond of alkenes and alkynes. This review summarizes the recent advances in the photo-induced version of this class of transformations. A variety of transition-metal complexes, organic dyes, phosphines, amines, phenols and aldehydes were utilized as catalysts for the cleavage of the existing carbon–halogen bond of the corresponding atom transfer reagent in the presence of a light source. Alongside a variety of 1,2-haloalkylation and haloperfluoroalkylation reactions, atom transfer radical addition (ATRA) or cyclization (ATRC) reactions *via* the cleavage of the carbon–halogen bonds of aryl halides are also discussed.

## Introduction

The pervasiveness of carbon–halogen bonds in an extensive variety of organic molecules present in natural products,[1] medicinally active compounds,[2] agrochemicals[3] and molecules with high material importance[4] has encouraged a revitalized interest in synthetic methodologies involving environmentally benign protocols (Fig. 1). Over the past decade, along with transition-metal catalyzed[5] or electophilic[6] carbon–halogen bond forming protocols, vicinal carbo-halo-difunctionalization reactions of carbon–carbon multiple bonds have emerged significantly. Amongst the available methods for α,β-carbo-halo functionalization reactions, atom transfer radical addition (ATRA) onto carbon–carbon multiple bonds has played a remarkable role in the synthesis of halogenated building blocks.[7]

Formally, atom transfer radical addition (ATRA) is the transposition of a pre-existing σ-bond of an atom transfer reagent

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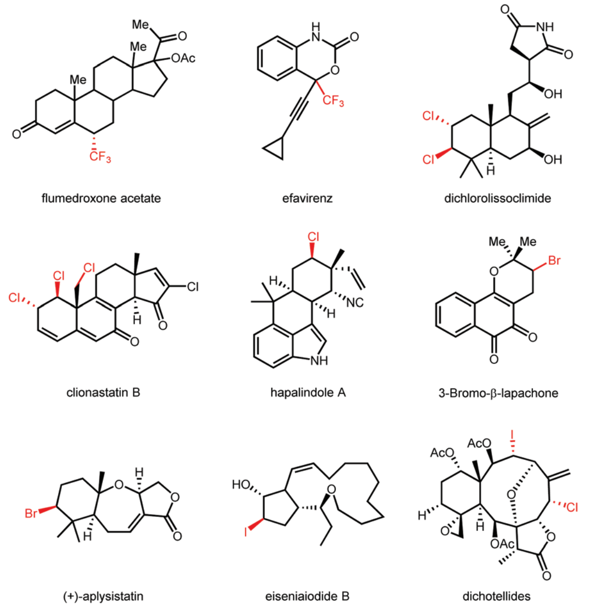

**Fig. 1** Representative examples of halogenated natural products and drug molecules.

across the π bond of carbon–carbon multiple bonds *via* free radical intermediates affording two new sigma bonds, a C–X bond and a C–C bond. In the mid-1900s, Kharasch *et al.* first investigated[8] the ATRA reaction and with time these particular types of reactions have become popular and have found application in both academic and industrial research owing to the mild reaction conditions along with high atom economy, versatility and enhanced levels of chemo-, regio-, and stereoselectivities.

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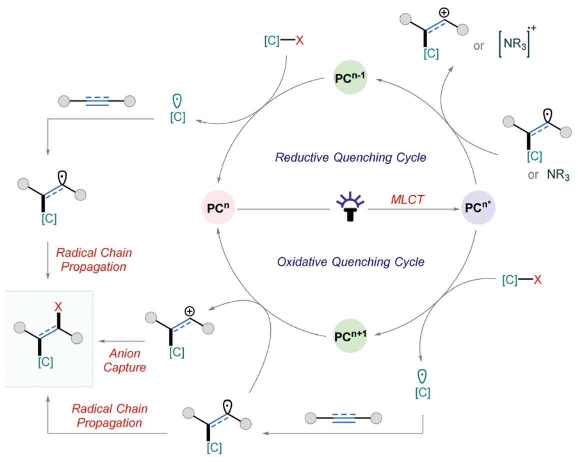
Initially the atom transfer radical processes were limited to the employment of stoichiometric quantities of harmful oxidants,[8] organotin reagents,[9a–d] or organoboron reagents[9e–h] as radical initiators and substrates that do not undergo ready radical polymerization reactions. Later, the use of transition-metal complexes as halogen transfer reagents were found to be more efficient with their ability to catalyse an atom transfer radical process involving a reversible redox pathway.[10] Even though the utilization of stoichiometric or catalytic transition metal complexes was successful for the efficient difunctionalization of C–C multiple bonds following the ATRA-pathway, unfortunately they required harsh conditions and/or toxic reagents.

In this context, employment of visible light mediated catalysts as initiators for ATRA reactions has emerged significantly involving mild reaction conditions and simple operation.

In principle, photoredox catalyzed transformations involve the conversion of photon energy into chemical energy and they proceed *via* radical intermediates.[11] Firstly, absorption of a photon upon irradiation of light results in the excitation of an electron from the metal-centred $t_{2g}$ orbital to the ligand-centred π* orbital. This metal to ligand charge transfer (MLCT) process results in the formation of a species in which the metal centre is oxidized along with the single-electron reduced ligand framework. A photochemically excited catalyst has the outstanding property of being more-oxidizing and more-reducing than the ground-state catalyst. This catalyst photoexcitation process generates a higher-energy electron, which can be expelled from the catalyst π* orbital when the photocatalyst behaves as a reductant. Concurrently, the excitation of a $t_{2g}$ orbital electron gives rise to a lower-energy hole which can accept an electron and the photocatalyst acts as an oxidant. As a result, commonly photo-induced ATRA reactions proceed through a closed cycle or propagation pathway involving the oxidative or reductive quenching cycle where the photo-excited catalyst involves a single electron transfer process (SET) with the atom transfer reagent (Scheme 1).[12]



**Scheme 1** Photo-induced-ATRA-reactions involving a reductive and oxidative quenching cycle.

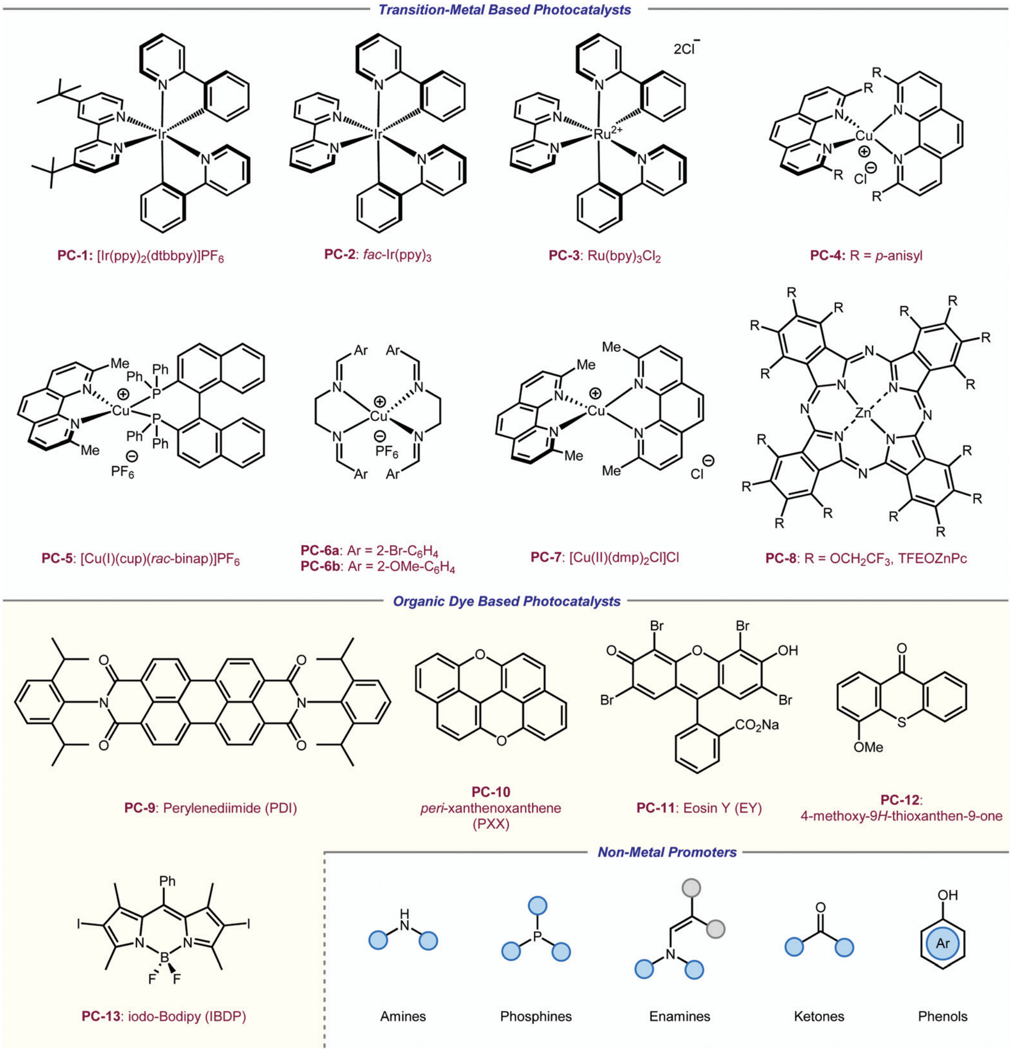


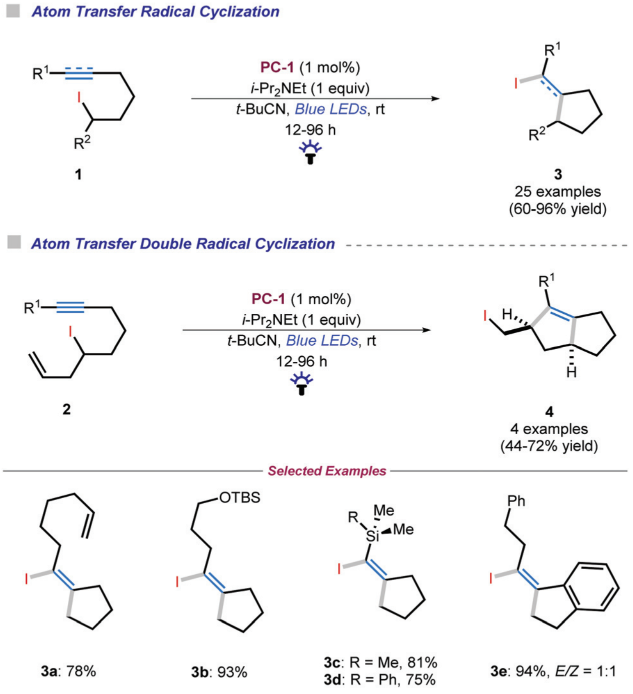
**Fig. 2** Commonly utilized photocatalysts and promoters for the photo-induced-ATRA/ATRC-reactions.

Even though, in 1994, Barton and co-workers reported the first example of photoredox-catalyzed ATRA reaction by utilizing $[Ru(bpy)_3]_2^+$ as a photocatalyst,[13] the field gained attention[14] around 2011 and thereafter a variety of transition-metal complexes and organic dyes have been utilized for ATRA reactions (Fig. 2). The scope of this review is restricted to the recent advances (2017 onwards) in the photo-induced vicinal carbohalofunctionalization reactions involving the ATRA-mechanism. Depending on the nature of photocatalysts used, this minireview is divided into multiple sections.

## Ir- and Ru-based photocatalysts

In 2011, vicinal carbo-halo functionalization of olefins by utilizing iridium based photocatalyst enabled ATRA reaction was first explored by Stephenson *et al.* In successive years, Yao[15a] and Melchiorre[15b] independently explored the ATRA difunctionalization of alkenes involving the cleavage of activated organohalides.

Later in 2017, Martin and co-workers reported the first example of visible light-promoted, *redox-neutral* atom transfer radical cyclization of unactivated alkyl iodides.[16] Irradiation of blue LEDs in the presence of a 1 mol% Ir-based photocatalyst $[Ir(ppy)_2(dtbbpy)]PF_6$ ($E_{red}$ $[Ir^{III}/Ir^{II}] = -1.51$ V *vs.* SCE in MeCN) provided the corresponding vinyl or alkyl halides **3** in good yields (Scheme 2). Employment of a stronger reducing Ir-complex *fac*-$Ir(ppy)_3$ ($E_{red}$ $[Ir^{III}/Ir^{II}] = -2.19$ V *vs.* SCE in MeCN)[12c] resulted in a decrease in yield, whereas a stronger oxidizing Ir-complex $[Ir[dF(CF_3)ppy]_2(dtbbpy)]PF_6$ ($E_{red}$ $[Ir^{III}/Ir^{II}] = -1.37$ V *vs.* SCE in MeCN)[12c] resulted in similar yield. After successful optimization, the substrate scope for this atom transfer radical cyclization (ATRC) process was explored. High functional group tolerance at the alkyne terminus suggested the high chemoselectivity of this intramolecular atom transfer process. Interestingly, secondary alkyl iodides consisting of unsymmetrical substituents resulted in an equi-



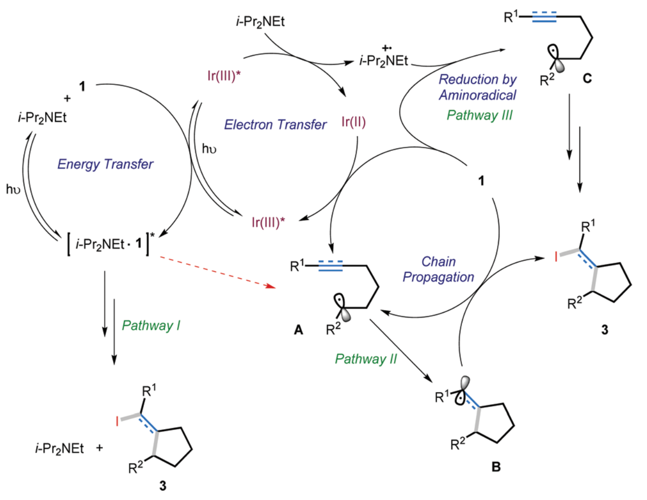
**Scheme 2** Ir-Photocatalyzed ATRA reaction of unactivated alkyl iodides.

molar mixture of *E*/*Z*-isomers of the desired products. Together with alkynes, terminal alkene bearing alkyliodides were also found to be effective for the ATRC process. This strategy was further extended for the synthesis of bicyclic skeletons **4** *via* atom transfer double radical cyclization of substrates containing both alkyne and allyl components.

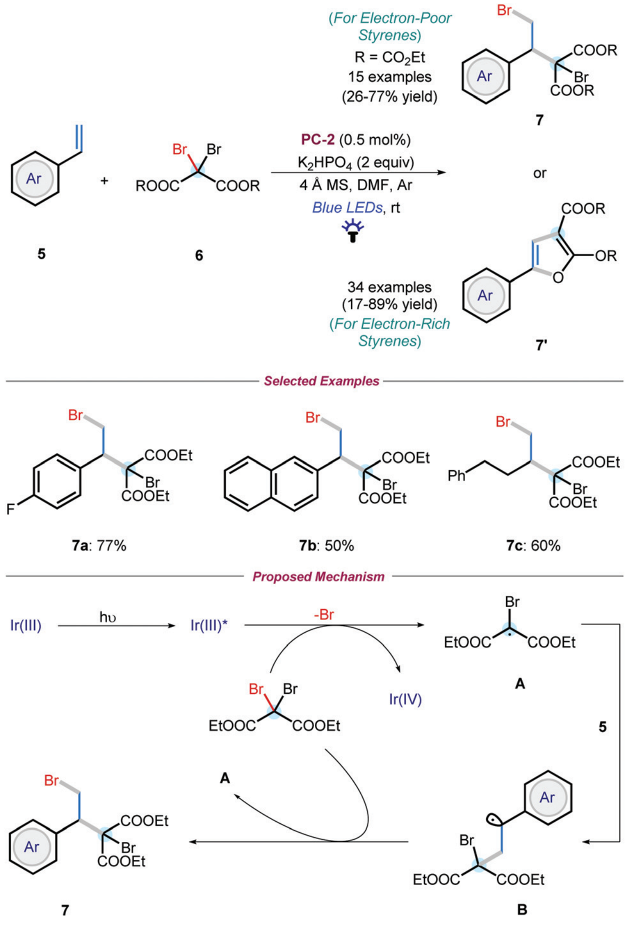
The mechanism of this radical cyclization process involves three possible pathways (Scheme 3). The large energy mismatch (~1 V) between redox potentials of **PC-1** and **1** suggested that an unconventional photocatalytic redox cycle might be involved. The formation of the desired product by employing a stoichiometric amount of an amine in the absence of a photocatalyst with a slower reaction rate suggests the possible involvement of an exciplex under light irradiation (pathway I). In the presence of the photocatalyst, the possibility of a radical-chain propagation pathway (pathway II and III) was supported by quantum yield calculations. Moreover, the authors rationalized that the presence of the photocatalyst probably promotes the exciplex formation *via* energy transfer from the excited triplet state of the Ir-complex.

In the same year, Zhu, Xie and co-workers developed a photocatalytic radical strategy for 1,2-carbohalofunctionalization of alkenes with *gem*-dibromides.[17] After successfully establishing the optimal reaction conditions, a range of electron-poor and weakly electron-rich styrenes were fruitfully transformed into the corresponding 1,3-dibromomalonates. Interestingly, within the same set of reaction conditions, strongly electron-rich styrenes were found to yield 1,2-carboxygenation products involving two successive photocatalytic cycles (Scheme 4).

The excitation of a photocatalyst upon irradiation with blue LEDs followed by single electron transfer (SET) between photo-



**Scheme 3** Mechanism of Ir-photocatalyzed ATRA reaction of unactivated alkyl iodides.



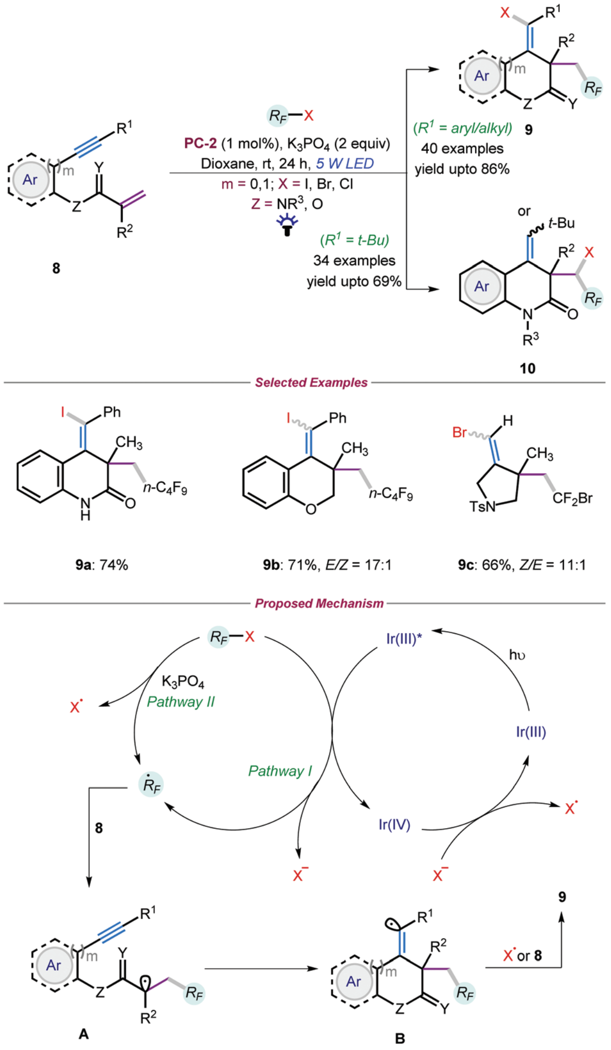
**Scheme 4** Photoredox-ATRA difunctionalization of alkenes with *gem*-di-bromides.

excited Ir(ppy)$_3$* ($E_{red}$*[Ir$^{IV}$/Ir$^{III}$] = −1.73 V *vs.* SCE) and *gem*-dibromomalonate ($E_{red}$ = −1.44 V *vs.* SCE) generates monobromomalonate radical **A** and the Ir(IV) species. Subsequent regioselective addition of radical **A** onto styrene furnishes the benzyl radical **B**. Depending upon the electronic nature of the aromatic substitution on the styrene, radical **B** either undergoes radical chain propagation resulting in the 1,2-carbohalogenated product **7** (for electron poor or weakly electron donating styrene) or can initiate a second photocatalytic cycle resulting in the formation of 1,2-carbooxygenated products **7′** (for strong electron donating styrenes) (Scheme 4).

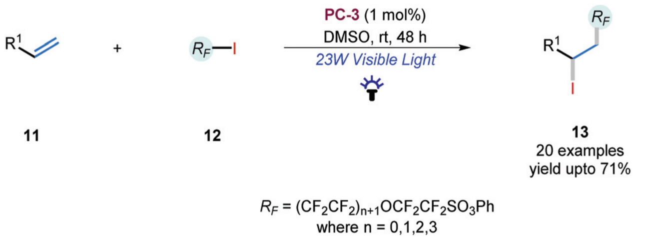
In 2019, Tang and co-workers established a photocatalytic strategy for the synthesis of halo-perfluorinated N-heterocycles *via* atom transfer radical addition and cyclization of 1,*n*-enynes (*n* = 6,7) with perfluoroalkyl halides.[18] The scope of this highly atom economical transformation was explored under Ir-photocatalysis and it was found to be effective in a wide variety of benzene-tethered 1,7-enynes and N-tethered enynes. Both long and short chain fluoroalkyl halides were found compatible for the process. It is noteworthy that *t*-Bu substituted alkynes containing 1,7-enynes yielded α,α-haloperfluorinated-2,4-dihydronquinolin-2(1*H*)-ones following a hydrogen atom transfer (HAT) pathway (Scheme 5).

The reaction proceeds *via* initial oxidative quenching of photoexcited Ir(III) by the fluoroalkyl halide generating a fluoroalkyl radical species. Subsequent regioselective addition of the fluoroalkyl radical species onto the olefinic double bond results in the formation of radical intermediate **A**. Subsequent radical addition onto the alkyne furnishes the vinyl radical **B** with a more stable *E*-configuration which readily undergoes iodine radical capture yielding the desired product with an *E*-configuration. Along with the photoredox generation of the fluoroalkyl radical, the possibility of the involvement of an alternative base-mediated classical fluoroalkyl halide homolysis pathway was also discussed.

In 2019, He *et al.* reported photo-induced atom transfer radical addition of iodo-3-oxaperfluoroalkanesulphonates onto alkenes by utilizing 1 mol% Ru(ppy)$_3$Cl$_2$. A wide variety of alkenes and ATRA reagents were efficient furnishing the desired products in moderate to good yields (Scheme 6).[19]



**Scheme 5** ATRA and ATRC reactions of perfluoroalkl iodides with 1,*n*-enynes.

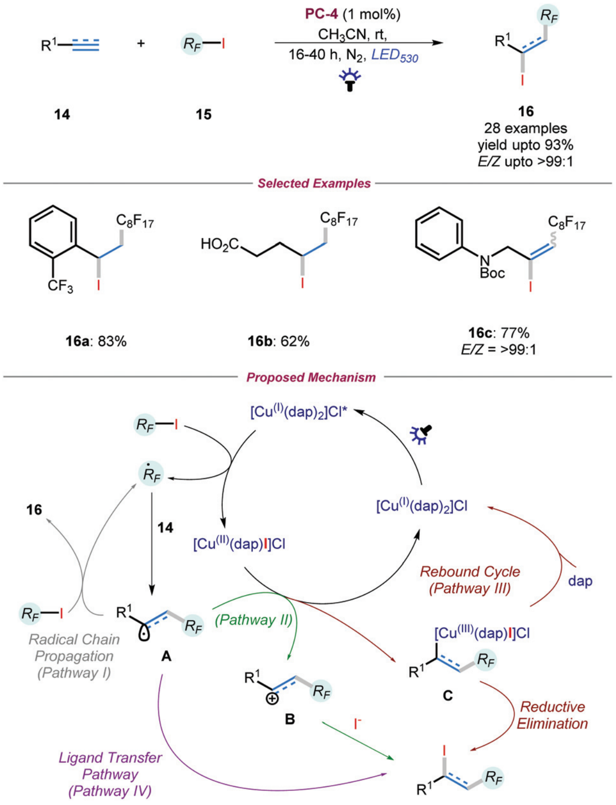


$R_F$ = $(CF_2CF_2)_{n+1}OCF_2CF_2SO_3Ph$
where n = 0,1,2,3

**Scheme 6** Ru-Photocatalyzed ATRA difunctionalization of alkenes.

## Cu-Based photocatalysts

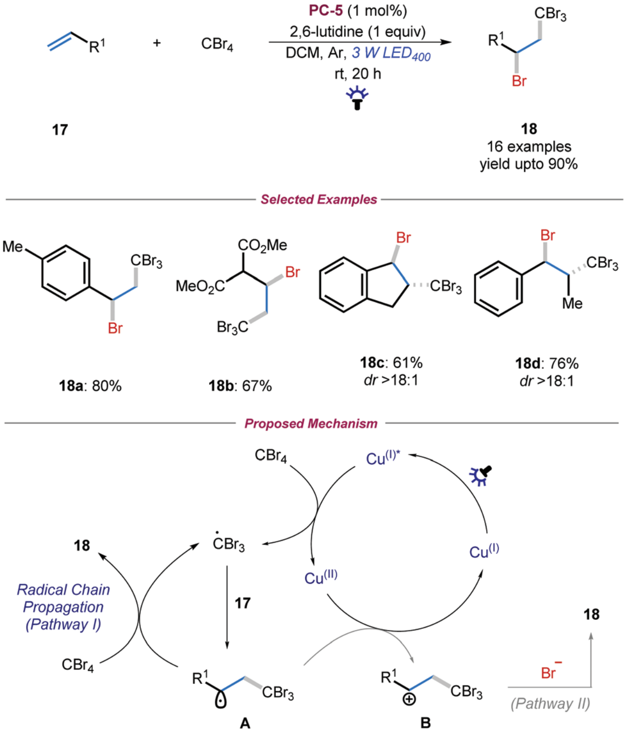
In recent years, due to their high natural abundance, lower cost and lower toxicity, Cu-based photocatalysts have gained admiration and a variety of transformations employing Cu-photocatalysis has been developed.[20a,b] In 2018, Reiser and co-workers reported an elegant photocatalytic approach for atom transfer radical addition of perfluoroalkyliodides to phenyl acetylenes and styrenes by utilizing a Cu-based photocatalyst.[21] After a thorough screening of reaction conditions, the use of 1 mol% [Cu(dap)$_2$]Cl ($E_{red}$[Cu$^{2+}$/Cu$^{+}$*] = −1.43 V *vs.* SCE)[12c] in MeCN upon irradiation with 530 nm visible light was found to be optimum for this difunctionalization process. Interestingly, an analogous reaction employing [Ru(bpy)$_3$]Cl$_2$ and Ir(ppy)$_3$ as photocatalysts was found to be less effective. A wide variety of terminal alkynes and styrenes were found to be suitable for this difunctionalization process with high yield and selectivity (Scheme 7). After a series of mechanistic experiments, the authors expelled the possibility of a radical chain process as employing heating or a radical initiator failed to promote the styrene difunctionalization reaction (pathway I). A second



**Scheme 7** Iodoperfluoroalkylation of C–C multiple bonds under Cu(I)-photocatalysis.

possible pathway was also ruled out (pathway II). The failure of $[Ru(bpy)_3]Cl_2$ as a photocatalyst to promote the reaction encouraged the authors to hypothesize two plausible mechanistic pathways. SET between the photoexcited Cu(I)-complex with the corresponding fluoroalkyl iodide generates fluoroalkyl radicals and Cu(II)-species $[Cu^{II}(dap)I]Cl$. Regioselective addition of fluoroalkyl radicals onto C–C multiple bonds of styrene or acetylene generates the corresponding C-centered radical **A**. In pathway III, radical species **A** follows a rebound cycle where it recombines with the Cu(II)-species forming a Cu(III)-complex which readily undergoes reductive elimination generating the desired 1,2-difunctionalized product along with the regeneration of the catalyst *via* ligand exchange. Alternatively, following pathway IV, trapping of radical **A** *via* iodine transfer from the Cu(II)-species furnishes the desired product with regeneration of the catalyst.

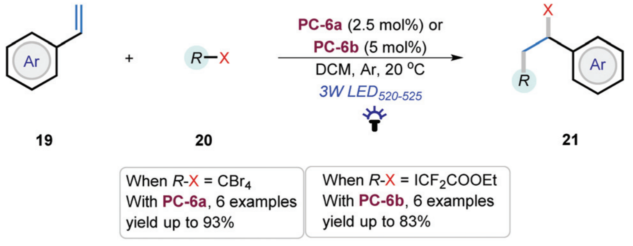
In the same year, Yamaguchi and Itoh explored the atom transfer radical addition of $CBr_4$ onto alkenes by employing Cu-photocatalysis.[22] 1 mol% [Cu(I)(cup)(*rac*-binap)]$PF_6$ upon visible light irradiation was found to be efficient in transforming a wide variety of terminal and internal alkenes to the corresponding tribromomethylated bromoalkanes **18** in good yields (Scheme 8). The transformation initiates by a SET between the photoexcited Cu(I)-species and $CBr_4$ generating tribromomethyl radicals. Subsequent addition of $CBr_3$ radicals onto the alkene forms carbon-centered radical **A** which proceeds *via* either a carbocation-bromide capturing pathway (pathway II) or a chain propagation pathway (pathway I) furnishing the desired product. Based on control experiments, the possibility of the involvement of an alternative reductive elimination pathway is presumed to be less likely for the case of a heteroleptic complex.



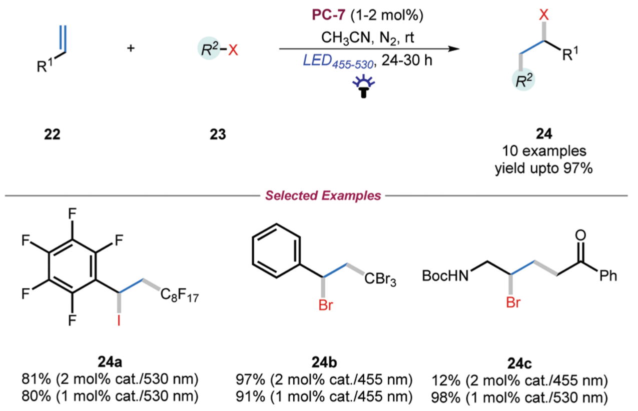
**Scheme 8** Photo-induced ATRA reaction of alkenes with $CBr_4$.

In 2019, J. Peelen and Novák designed and synthesized diimine-based copper(I) complexes and explored their catalytic activity in the photo-induced ATRA difunctionalization reaction of styrenes with $CBr_4$ and $ICF_2COOEt$ (Scheme 9).[23]

In 2019, Reiser and Engl described a similar photo-induced ATRA carbohalodifunctionalization of olefins by utilizing a Cu(II)-complex having a simpler ligand system (Scheme 10). Interestingly, the effectiveness of the Cu(II)-catalytic system during the iodoperfluoroalkylation reaction of styrene was found to be similar to that in an earlier report.[24a] This catalytic system was also found to be effective during the 1,2-carbobromofunctionalization of olefins with the cleavage of the C–Br



**Scheme 9** Cu(I)-Photocatalyzed 1,2-difunctionalization of styrenes.



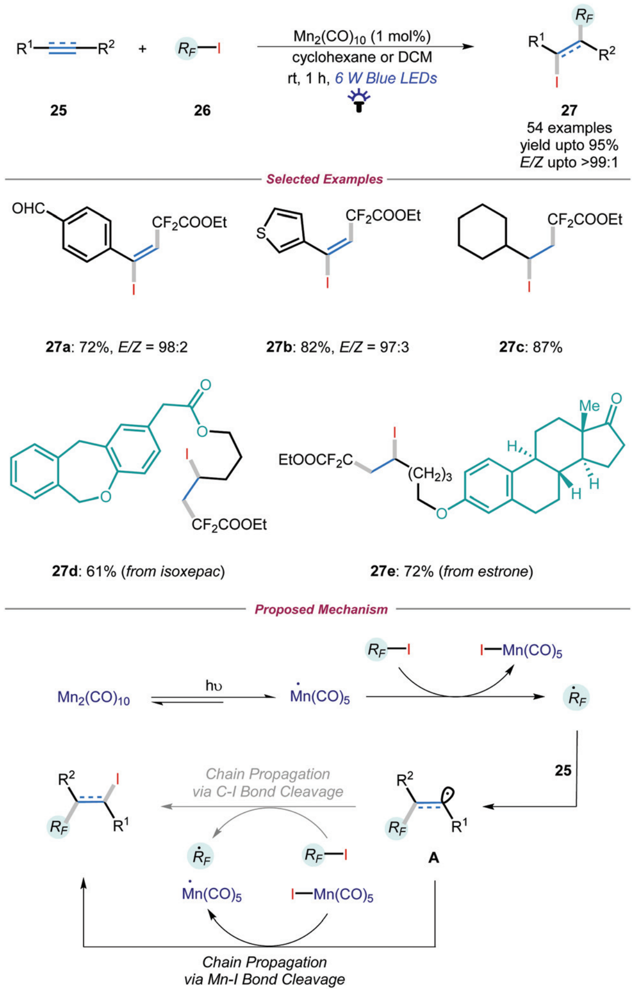
**Scheme 10** Cu(II)-Photocatalyzed ATRA difunctionalization of alkenes.

bonds of divergent ATRA reagents. Based on experimental observations and a previously established mechanism,[24b] the involvement of the Cu(I)-species as an active photocatalytic constituent for both the Cu(I) and Cu(II)-catalyzed transformations was postulated.

## Mn-Based photocatalysts

In 2019, Bi and Zhang explored photo-assisted intermolecular atom transfer radical iodoperfluoroalkylation of unactivated alkenes and alkynes by utilizing a Mn-catalyst.[25] Thorough screening of divergent catalysts and reaction conditions, the authors achieved the optimized conditions by employing 10 mol% $Mn_2(CO)_{10}$ in cyclohexane upon irradiation of blue LEDs. To establish the generality of the transformation, a wide variety of internal alkynes and olefins were transformed into the corresponding perfluoroalkylated vinyl or alkyl iodides **27** in good yields (Scheme 11). Changing the solvent to DCM, the scope of divergent long chain fluoroalkyl iodides was explored. Furthermore, efficient late stage functionalization of biologically relevant complex molecules containing alkene and alkynes verified the high selectivity of this ATRA process.

After a series of control experiments, the plausible mechanism was proposed. Upon visible light irradiation, the homolysis of $Mn_2(CO)_{10}$ generates $Mn(CO)_5$ radicals which upon iodine capture from the perfluoroalkyl iodide form perfluoroalkyl radicals and $IMn(CO)_5$. Addition of perfluoroalkyl radicals onto C–C multiple bonds generates carbon centered radical species **A** which can undergo iodine transfer *via* radical chain propagation by the C–I bond cleavage of a second molecule of the perfluoroalkyl iodide or can undergo iodine transfer from $IMn(CO)_5$ yielding the final product. Moreover, the comparative bond dissociation energies suggest that the iodine transfer *via* the cleavage of the carbon–iodine bond of $R_FI$ is more favorable (BDE = 49 kcal mol$^{-1}$) over the cleavage of the Mn–I bond of $IMn(CO)_5$ (BDE = 67 kcal mol$^{-1}$).

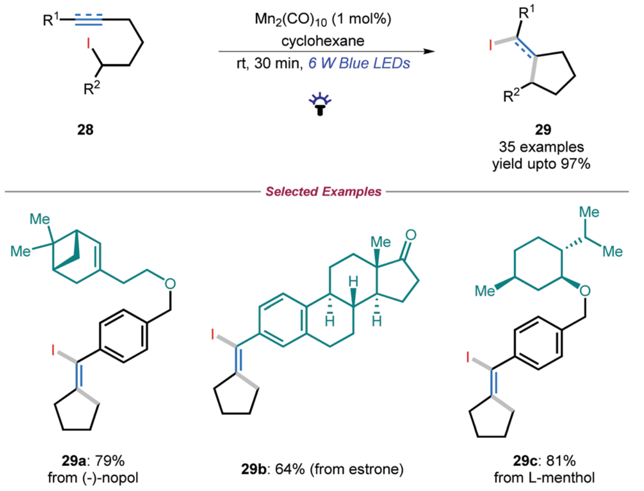


**Scheme 11** Mn-Photocatalyzed iodofluoroalkylation of unactivated alkenes and alkynes.

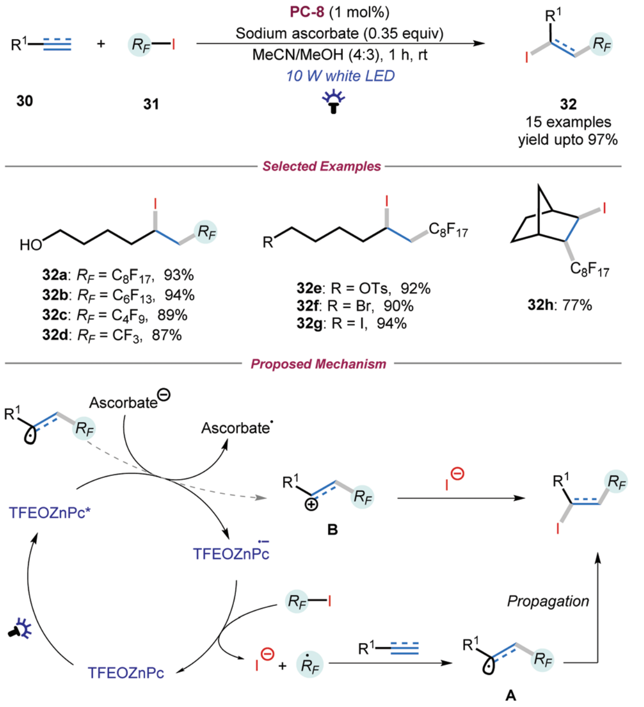
Continuing their exploration of visible-light-induced Mn-catalyzed atom transfer radical addition/cyclization reactions, Zhang and co-workers reported intramolecular radical cyclization of unactivated alkyl iodides **28**, a very similar transformation to Martin's report of Ir-photocatalyzed ATRC reaction discussed earlier (Scheme 2).[26] The use of a cheap catalyst and a broad substrate scope made this methodology more economical and applicable. Along with a broad substrate scope, the synthetic utility of this efficient difunctionalization process was demonstrated by late stage modification of complex natural molecules with high efficiency. A similar mechanism described earlier accounts for the transformation (Scheme 12).

## Zn-Based photocatalysts

In 2017, Shibata and co-workers demonstrated an elegant photo-induced atom transfer radical addition of perfluoroalkyl iodides onto alkenes efficiently catalyzed by trifluoroethoxy-coated phthalocyanine.[27] Initial screening of reaction conditions revealed the employment of 1 mol% catalyst along with 0.35 equiv. sodium ascorbate upon irradiation with a white LED as optimum for this difunctionalization process



**Scheme 12** Mn-Catalyzed ATRC reaction of unactivated alkyl iodides.



**Scheme 13** Photo-induced iodoperfluoroalkylation of alkenes and alkynes catalyzed by a Zn-complex.

(Scheme 13). A wide variety of terminal and internal alkenes were found to be tolerated providing the desired products in good yields. Alongside alkenes, perfluoroalkylation of terminal alkynes could also be achieved employing this strategy. The proposed mechanism involves electron transfer from sodium ascorbate to the photoexcited catalyst generating photocatalyst radical anions. This photocatalyst radical anions generate fluoroalkyl radicals upon reacting with fluoroalkyl iodide. Subsequent addition of fluoroalkyl radicals onto C–C multiple bonds generates intermediate **A** which yields the final difunctionalized product by following either a radical chain propagation pathway or a carbocation pathway.

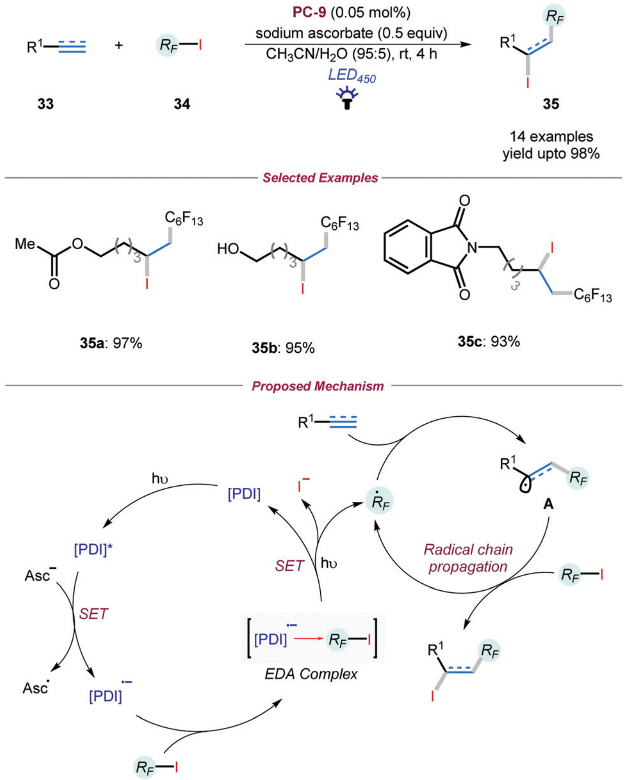
## Organic dye as photocatalysts

Alongside transition-metal photocatalysts, the use of non-metal organic dyes as metal-free alternatives in visible-light mediated transformations has been established.[28] In 2019, Prato's group discovered ATRA reactions of perfluoroalkyl iodides with olefins prompted by the photochemical activity of the organic dye perylenediimide (PDI).[29] Employment of PDI in very low quantity (0.05 mol%) was fruitful in catalyzing the transformation upon photo-irradiation (Scheme 15). After establishing the optimized conditions, the scope of a wide range of olefins and perfluoroalkyl iodides was investigated and a high functional group tolerance justifying the generality of the transformation was observed. The reaction of iodopentafluorobenzene failed under the standard conditions. Alongside alkenes, terminal alkynes were also found to be tolerated providing an *E*/*Z*-mixture of the corresponding vinyl iodide in good yield.

Investigating the role of the photocatalyst PDI in this process, the authors observed no ground-state association between the perylene diimide and the radical source. According to the Rehm–Weller equation, PDI is a strong oxidant in the excited state ($E_{\text{Red}}$ of PDI*/PDI$^{\bullet-}$ = +1.97 V). Thus, reductive quenching of PDI* in the presence of sodium ascorbate generating radical anions of PDI is postulated. This PDI radical anion possibly undergoes aggregation with the corresponding perfluoroalkyl iodide generating an electron donor–acceptor (EDA) complex. Photoinduced single electron transfer (SET) from electron rich radical anions to electron deficient perfluoroalkyl iodide generates perfluoroalkyl radicals with the reconstruction of PDI. Subsequent addition of the fluoroalkyl radical onto carbon–carbon multiple bonds and radical chain propagation provide the final product (Scheme 14).

Afterwards, a similar PDI-photocatalyzed ATRA reaction was explored efficiently under a continuous flow synthesis strategy upon irradiation with blue light (Scheme 15). The use of PDI and 450 nm irradiation along with triethylamine instead of the earlier used sodium ascorbate was found suitable providing the desired product in excellent yield.[30] Interestingly, during the screening of irradiation wavelengths it was observed that the irradiation at 422 nm or a shorter wavelength can furnish the desired ATRA product following a halogen-bonded electron donor acceptor (EDA) complex formation. More screening confirmed that the use of 405 nm purple light irradiation is optimum for the transformation along with 20 mol% $NEt_3$. Alongside a broad substrate scope, this highly efficient continuous flow iodoperfluoroalkylation strategy was employed for the construction of a key intermediate in the synthesis of the breast cancer drug fulvestrant.

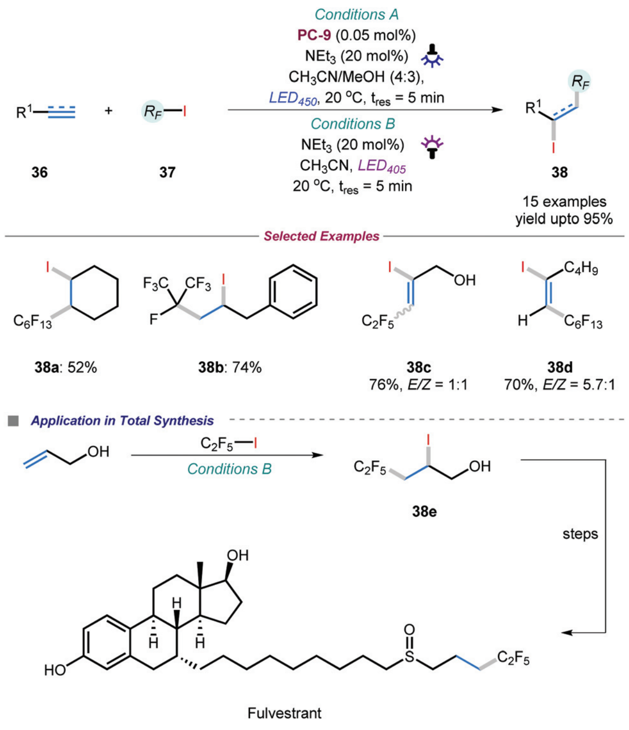
Recently Dilman and co-workers reported an elegant photo-induced ATRA reaction between an olefin and iododifluoro-



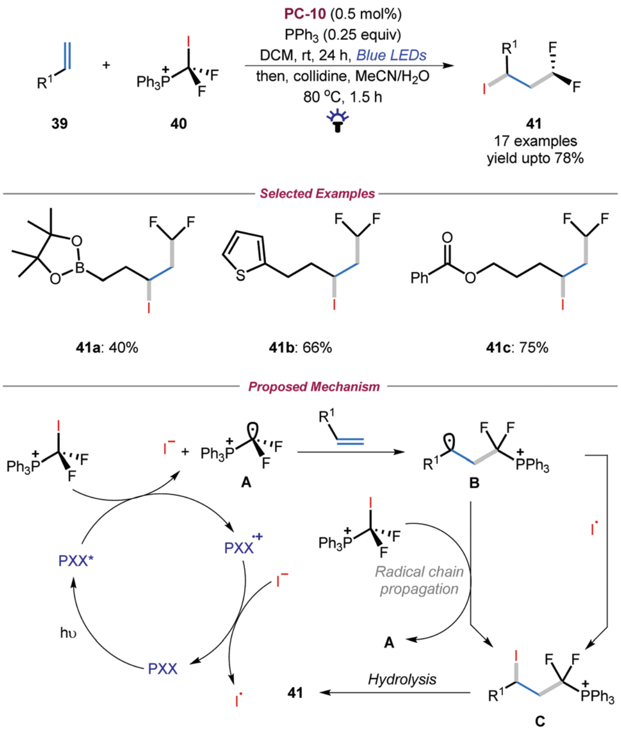
**Scheme 14** PDI-promoted 1,2-carbohalofunctionalization of C–C multiple bonds.

methylphosphonium salt by utilizing organic dye *peri*-xanthenoxanthene as the photocatalyst.[31a] This efficient protocol was found feasible for a wide variety of terminal alkenes. The presence of functional groups such as alkyl iodides, esters, MEM- and THP-protected hydroxy groups, aldehyde and nitrile groups, and pinacolboranes were found to be tolerated under this photocatalytic transformation (Scheme 16). The plausible mechanism involves the reduction of the phosphonium salt by the photoexcited catalyst (−2.0 V *vs.* SCE)[31b] generating difluorinated phosphonium-substituted radical cation **A**. Subsequent addition of **A** onto the alkene constructs the carbon-centered radical species **B**, which can combine with the iodine radical generated by the SET between the iodide ion and the radical cation of the photocatalyst. Alternatively, **B** can also undergo radical chain propagation yielding the final product along with the regeneration of **A**. Subsequent hydrolysis of the intermediate phosphonium salt furnishes the final product.

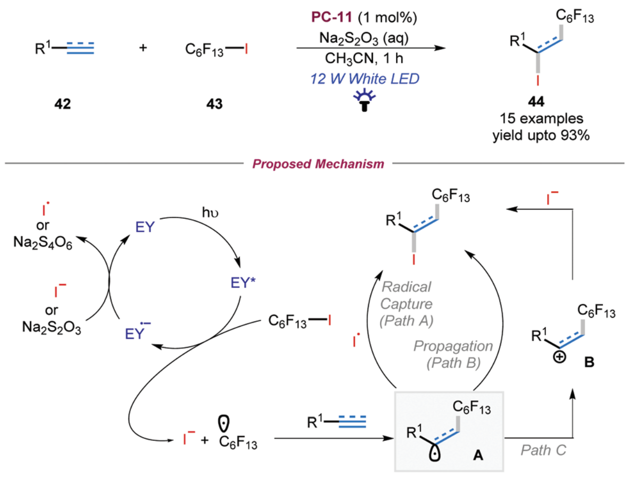
In 2017 Yajima and Ikegami demonstrated photo-induced atom transfer radical addition of perfluoroalkyl iodides onto terminal alkenes and alkynes catalyzed by organic dye Eosin Y (EY).[32] After a thorough screening of photocatalysts and the nature of irradiation, 1 mol% EY upon irradiation with a 12 W white LED was established to be the best condition for this efficient photocatalytic process (Scheme 17). Employing the optimized conditions, a variety of terminal alkenes and alkynes were transformed efficiently. Terminal alkynes were found to provide a mixture of *E* and *Z*-isomers of the desired



**Scheme 15** Photo-induced iodoperfluoroalkylation *via* a continuous flow process.



**Scheme 16** Light-promoted iododifluoromethylation of olefins *via* (phosphonio)difluoromethyl radical cations.

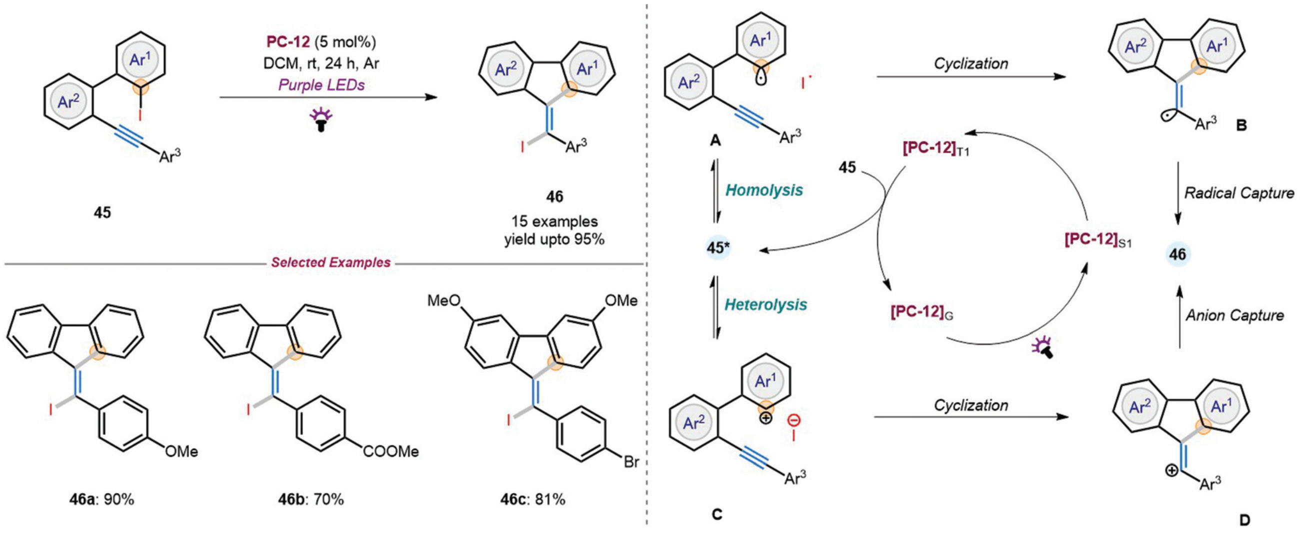


**Scheme 17** Eosin Y promoted iodoperfluoroalkylation of olefins and alkynes.

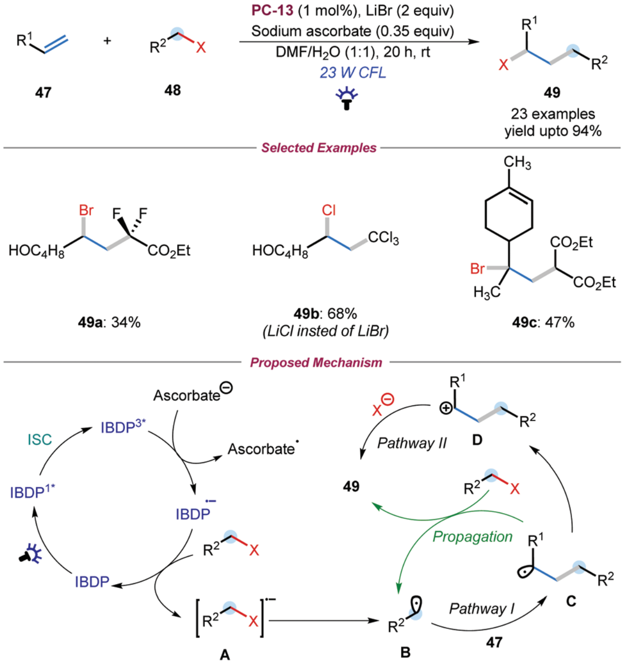
vinyl iodides. To figure out the underlying mechanism, the authors performed photoluminescence quenching experiments and found that the photoluminescence of excited EY is quenched by perfluoroalkyl iodide suggesting the involvement of an oxidative quenching pathway. Initial SET between photoexcited EY and perfluoroalkyl iodide generates perfluoroalkyl radicals which upon subsequent regioselective addition onto the carbon–carbon multiple bonds generate radical species **A**. Radical **A** can form the final compounds by following any of the (a) radical chain propagation, (b) carbocation formation and iodide capture and (c) iodine radical capture pathways. Disruption in the progress of the reaction upon removal of continuous irradiation rules out the involvement of the radical chain propagation pathway. The hydroxyperfluoroalkylated product was not observed during the transformation suggesting the non-involvement of the carbocation pathway.

In 2019, Guo and group investigated a visible light-induced intramolecular atom transfer radical addition of alkynes involving the cleavage of C($sp^2$)–I bonds with complete atom-economy. The use of 5 mol% thioxanthone as a photosensitizer upon irradiation with a purple LED was found be optimum for this ATRA process.[33] With the optimized conditions, a variety of substrates having unsubstituted or electron donating group substituted aromatic rings ($Ar^1$ and $Ar^2$) were found to be effective. Both electron-donating and electron-withdrawing functional group bearing aromatic rings in the alkyne terminus ($Ar^3$) also underwent smooth transformation into the corresponding vinyl iodides in good yields (Scheme 18).

Among a series of control experiments, addition of 5 equiv. of TEMPO was found to be interesting where strong inhibition was observed but not complete inhibition, suggesting the involvement of a non-radical pathway alternative to the radical pathway. Upon irradiation, PC-12 undergoes an n–π* transition to its singlet excited state and relaxes to its first singlet excited state, PC-$12_{S1}$. Subsequent intersystem crossing (ISC) generates the first triplet excited state, PC-$12_{T1}$. Energy transfer from PC-$12_{T1}$ to the substrate forms triplet **45*** which further proceeds either *via* a radical or ionic pathway. The reversible homolysis of the C($sp^2$)–I bond of **45*** generates intermediate **A** which upon successive intramolecular radical addition and recombination with iodine radicals furnishes the desired product **46**. On the other hand, the ionic pathway involves reversible heterolytic C–I bond cleavage generating cationic intermediate **C** and iodide anions. Subsequent addition of carbon–carbon triple bonds leads to cyclization yielding the cyclized alkenyl cation **D** which in the last step recombines with iodide anions providing the desired vinyl iodide. Incorporation of bromine in the final product upon addition of the bromide source tetrabutylammonium bromide supported the postulated ionic pathway.



**Scheme 18** Photo-induced ATRC reaction *via* C($sp^2$)–I bond cleavage.

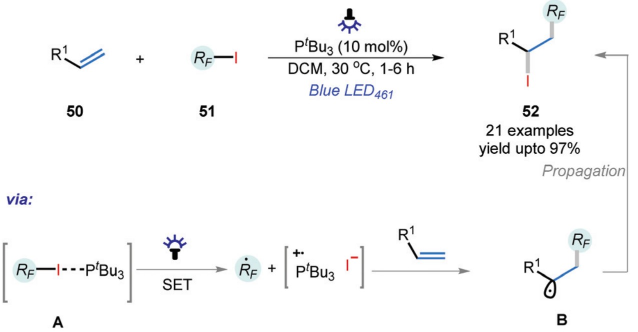


**Scheme 19** Photocatalytic ATRA reaction promoted by iodo-Bodipy and sodium ascorbate.

In 2017, Ceroni and Cozzi reported photo-induced ATRA reaction of alkenes with activated haloalkanes by using iodo-Bodipy dye as an energy transfer agent (Scheme 19). 1 mol% photocatalyst along with sodium ascorbate upon irradiation with a 23 W CFL was efficient for the 1,2-haloalkylation of a variety of alkenes.[34] Haloalkyl pyridines also participated in the ATRA process effectively. Reduction of the photocatalyst by sodium ascorbate generates [Bodipy]$^{\bullet-}$ (reduction potential: −1 to −1.54 V *vs.* SCE)[35] which converts the corresponding haloalkyl reagent (−0.5 to −1.5 V *vs.* SCE)[36] to the haloalkyl radical anion species **A** which generates the C-centered radical **B**. Subsequent addition of **B** onto the alkene forms a new radical species **C** which constructs the final product by following either the chain propagation (pathway I) or oxidation/halide ion capture pathway (pathway II).

## Phosphine, amine, phenol and aldehyde as promoters

In addition to metal complexes and organic dyes as photocatalysts, a variety of protocols have been developed employing metal-free catalysts/promoters involving phosphines, amines *etc.*, where these mediators activate the carbon–halogen bond to be broken. In 2019, in a seminal work, Czekelius and co-workers reported photo-induced atom transfer radical addition of perfluoroalkyl iodides onto alkenes involving C–I activation by a phosphine catalyst (Scheme 20). Screening of multiple phosphines revealed that 10% tri-*tert*-butylphosphine is the best choice of catalyst upon irradiation with a blue LED of 461 nm. A series of terminal and internal olefins having divergent functional groups were found to be suitable for this difunctionalization process. Along with simple trifluoromethyl iodide, various long chain fluoroalkyl iodides also efficiently took part in this ATRA reaction. Based on a series of mechanistic experiments, the initial formation of adduct **A** *via* interactions of an electron-donating Lewis base (phosphine) and a halo-perfluoroalkane was proposed. Subsequent SET leads to the generation of perfluoroalkyl radicals which undergo addition and chain propagation furnishing the final product.[37a]

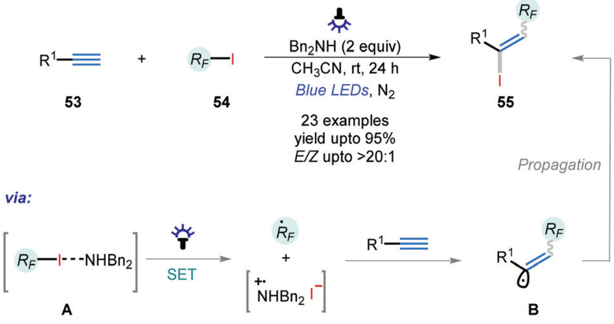


**Scheme 20** Photo-induced ATRA reaction catalyzed by phosphine.

Moreover, a considerable increase in the UV-absorption spectra of $n\mathrm{Bu}_3\mathrm{P}$, $t\mathrm{Bu}_3\mathrm{P}$, and $(\mathrm{MeO})_3\mathrm{P}$ in the presence of perfluoroalkyliodides attracted the attention of the authors for detailed mechanistic exploration of the homolytic cleavage of perfluoroalkyl iodides mediated by the phosphines involved in the photo-induced ATRA reaction.[37b]

In 2017, Yu and co-workers reported a photo-mediated atom transfer iodoperfluoroalkylation of alkynes promoted by the noncovalent halogen-bonding interaction between an amine and perfluoroalkyl iodides.[38] 2 equiv. of $\mathrm{Bn_2NH}$ upon blue LED irradiation were found to be efficient in transforming a wide range of terminal alkynes into the corresponding perfluoroalkylated vinyl iodides **55** in good yields. Starting from trifluoromethyl iodide, a series of different long-chain perfluoroalkyl iodides were efficient in this ATRA process. The underlying mechanism involves initial photo-assisted homolytic cleavage of the C–I bond in halogen bonded amine-perfluoroalkyl iodide conjugate **A** generating the perfluoroalkyl radical. Successive addition of perfluoroalkyl radicals onto the alkyne followed by radical chain propagation yields the final vinyl iodide (Scheme 21).

In 2019, Yajima and group explored photo-assisted-ATRA reaction of unactivated olefins and alkynes with perfluoroalkyl iodides jointly catalyzed by an *in situ* generated enamine species and free amine. 10 mol% aldehyde along with pyrrolidine was found to efficiently catalyze the iodoperfluoroalkylation reaction upon irradiation with visible light (23 W CFL).[39] Employing the optimized conditions, the scope of a variety of perfluoroalkyl iodides and olefins/alkynes was explored and a high functional group tolerance was achieved. Interestingly, reaction with preformed enamine in the absence of a free



**Scheme 21** Photo-induced ATRA reaction catalyzed by an amine.

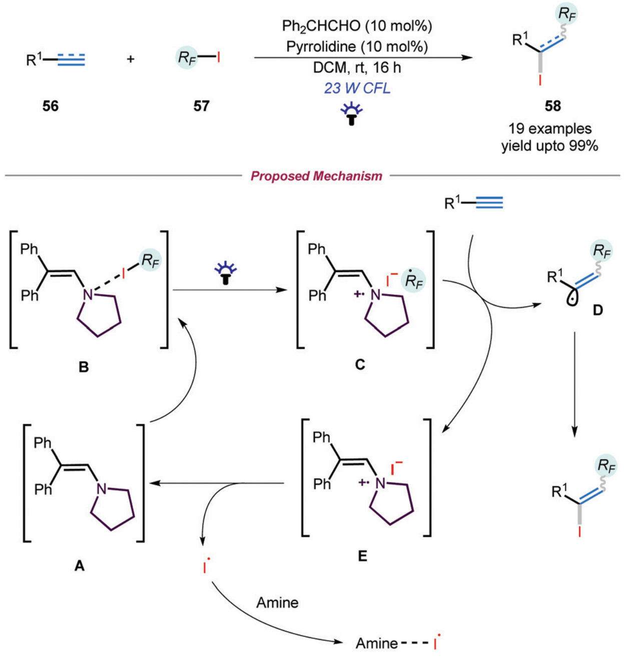
amine did not proceed efficiently but the addition of a free amine improved the yield suggesting the role of the free amine in catalyzing the reaction (Scheme 22).

The plausible mechanism explains the formation of an EDA complex **B** between the *in situ* formed enamine **A** and perfluoroalkyl iodide. Upon irradiation of light, the EDA complex generates a fluoroalkyl radical. Addition of the fluoroalkyl radical onto the alkene/alkyne forms the radical intermediate **D** and amine radical cation **E**. Upon reaction with the iodide anion, **E** results an iodine radical and regenerates the enamine. The iodine radical combines with the free amine generating a iodide radical–amine complex. Intermediate **D** undergoes iodine transfer either from the iodide radical–amine species or starting fluoroalkyl iodide constructing the final product.

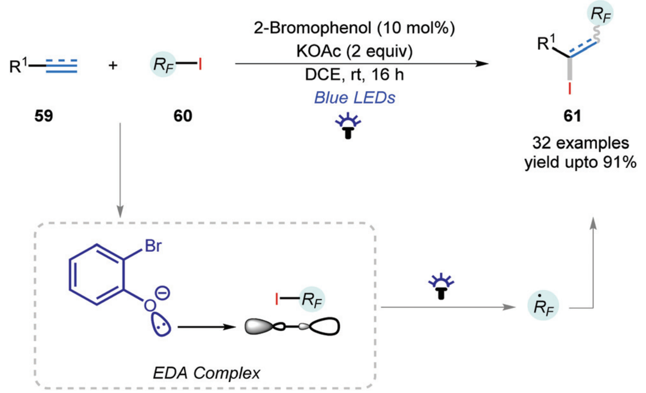
In 2019, He and co-workers reported visible light induced atom transfer radical addition of fluoroalkyl iodides onto alkenes and alkynes by employing 2-bromophenol as a photocatalyst. The reaction proceeds *via* initial formation of an EDA complex between 2-bromophenol and fluoroalkyl iodide in the presence of a base. Upon irradiation with blue LEDs, the EDA complex generates a fluoroalkyl radical species. Regioselective addition of the fluoroalkyl radical onto the C–C multiple bonds followed by radical chain propagation yields the final 1,2-difunctionalized product. A wide variety of terminal alkenes, alkynes and fluoroalkyl iodides were found to be efficient for the transformation dictating the high functional group tolerance (Scheme 23).[40]

Later in 2020, the same He research group reported a similar 1,2-iodofluoroalkylation reaction of alkenes and alkynes promoted by non-covalent interactions between acetone and fluoroalkyl iodides in the presence of visible light (Scheme 24). Formation of an EDA complex between the fluoroalkyl iodide and acetone and generation of fluoroalkyl radicals upon irradiation with blue LEDs are proposed to be involved in this 1,2-carbohalodifunctionalization process.[41]

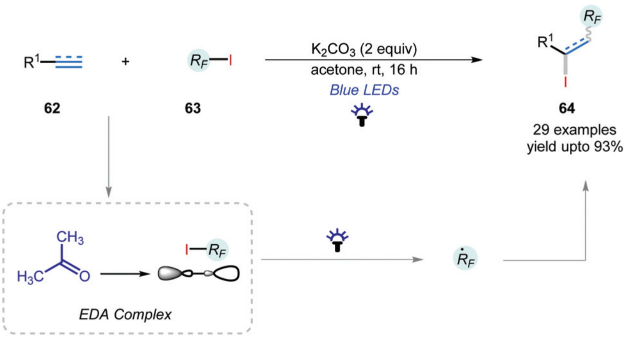
In 2019, Wang and Yuan established an efficient photo-induced protocol for the atom transfer radical addition of aryl



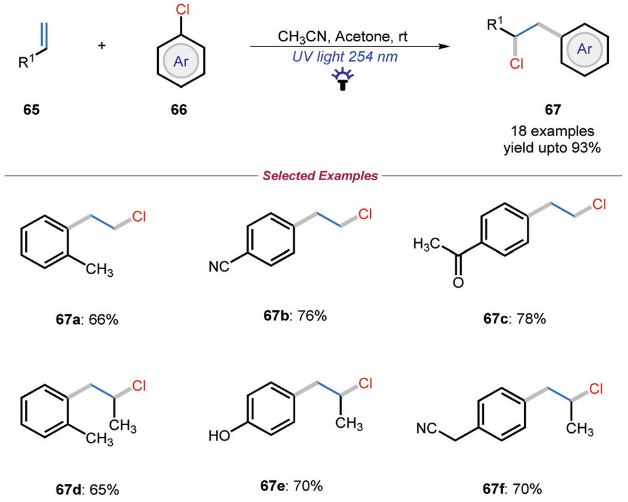
**Scheme 22** Photo-induced ATRA reaction jointly catalyzed by an amine and *in situ* generated enamine.



**Scheme 23** Photo-induced ATRA reaction catalyzed by 2-bromophenol.



**Scheme 24** Base mediated, photo-induced 1,2-difunctionalization of alkenes and alkynes.



**Scheme 25** Photo-induced chloride atom transfer radical addition onto alkenes.

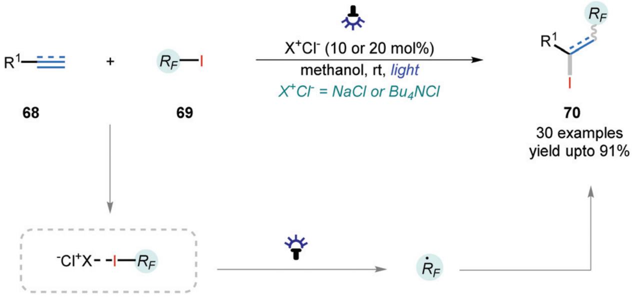
chlorides onto alkenes (Scheme 25). Upon irradiation with 254 nm UV light at room temperature, aryl chloride generates the corresponding aryl and chloride radicals *via* homolysis of the C(sp$^2$)–Cl bond. Subsequent regioselective addition of aryl radicals onto the alkene generates alkyl radicals which upon chloride radical capture furnish the final product.[42]

## Miscellaneous types

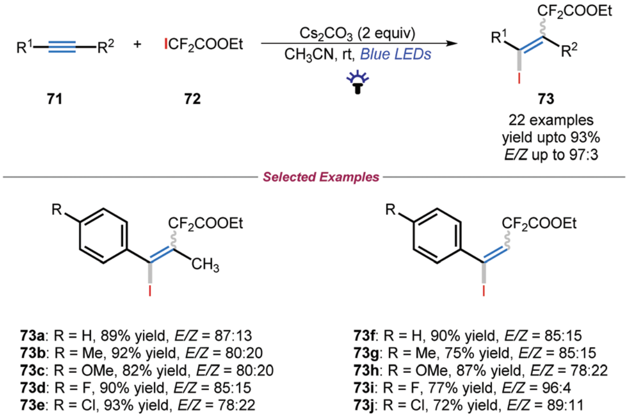
In 2018, Vincent and co-workers explored the role of halogen bonding during the light-mediated iodoperfluoroalkylation of alkenes and alkynes catalyzed by chloride ions. Catalytic NaCl or $Bu_4NCl$ in deoxygenated methanol upon irradiation with low intensity UVA (low pressure Hg lamp, 6 W, 365 nm) was found to be efficient for the ATRA process. The generation of perfluoroalkyl radicals *via* halogen bond promoted photolysis of perfluoroalkyl iodide was hypothesized to be the key step of this difunctionalization process (Scheme 26).[43]

In 2019, Fan *et al.* reported an efficient photo-induced, base-mediated iodofluoroalkylation of alkynes following an atom transfer radical addition pathway (Scheme 27).[44] Initial exploration revealed that 1 equiv. $Cs_2CO_3$ upon irradiation with a blue LED can effectively catalyse the ATRA process. Employing these conditions, a variety of internal and terminal alkynes having aryl, heteroaryl and alkyl substituents were successfully transformed into the corresponding fluoroalkylated vinyl iodides with good *E*/*Z*-ratios. Importantly, during the transformations of the unsymmetrically substituted internal alkynes, the final products were obtained as single regioisomers.

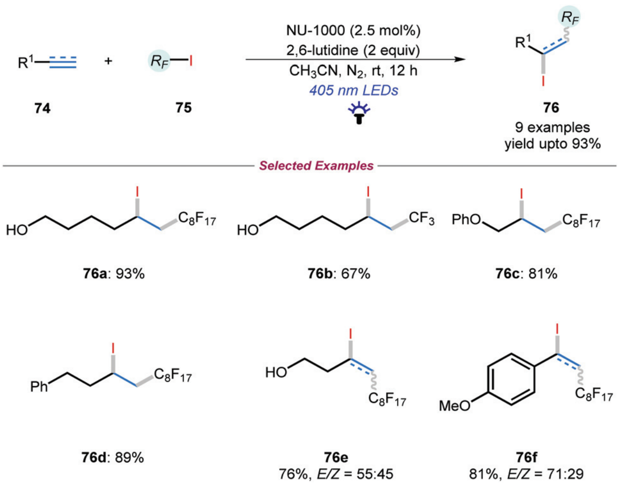
In 2018, Zhang *et al.* reported pyrene-based metal organic framework (MOF) catalyzed photo-induced atom transfer radical addition of perfluoroalkyl iodides onto olefins and alkynes. Upon irradiation with 405 nm LEDs onto NOU-1000, an ATRA difunctionalized iodoalkylated product was obtained in a heterogeneous mode. Applying this strategy, a series of terminal alkenes were successfully transformed. Alongside alkenes, alkynes were also found to be tolerated during this transformation (Scheme 28).[45]



**Scheme 26** Halogen bonding promoted ATRA addition of perfluoroalkyl iodides.



**Scheme 27** Base mediated iodoperfluoroalkylation of acetylenes promoted by visible light.



**Scheme 28** MOF-catalyzed photo-mediated ATRA reaction of perfluoroalkyl iodides with C–C alkenes and alkynes.

## Conclusions

The 1,2-carbohalofunctionalization of alkenes and alkynes is an efficient means for the construction of organohalides in a highly regioselective and atom economical fashion. This review summarizes the recent advancements in the photo-induced atom transfer radical addition and cyclization processes involving the transposition of an atom transfer reagent *via* photocatalytic radical cleavage of a pre-existing carbon–halogen σ-bond over the π-bond of alkenes and alkynes. Upon irradiation of light, a variety of transition metal complexes, organic dyes and non-metal promoters were found to be efficient catalytic systems. Alongside ATRA processes involving activated carbon–halogen bonds, a number of protocols involving non-activated carbon–halogen bonds have been developed. A large number of literature reports of 1,2-haloperfluoroalkylation of alkenes and alkynes have been reported suggesting the importance of this field. While these developments have left a solid foundation for the field, asymmetric variants of these transformations are yet to be explored. We strongly believe that photo-induced ATRA/ATRC transformations catalyzed or promoted by organic dyes and *in situ* generated EDA complexes will serve as a high in demand and important asset to synthetic chemistry due to their wide applicability, low-cost and easy availability. We anticipate that this review will provide collective details about the progress of the field and encourage researchers for newer discoveries.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

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