VISIBLE-LIGHT-INDUCED SYNTHESIS OF PHOSPHORYLATED COMPOUNDS

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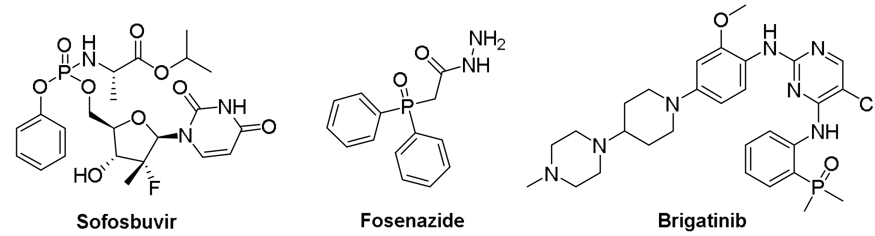
Abstract. *Organophosphine compounds have shown good potential in the field of biomedicine, organic synthesis, pesticides, and functional materials. Meanwhile, visible-light-induced organic reactions are characterized by mild reaction conditions, simple reaction operations, and good functional group compatibility, which are in line with the implementation of green and sustainable chemistry. This minireview is aimed at summarizing recent advances in synthesizing organophosphine compounds under visible-light-induced homogeneous systems and heterogeneous systems (mainly from 2018 to 2022).*

Contents

1. Introduction

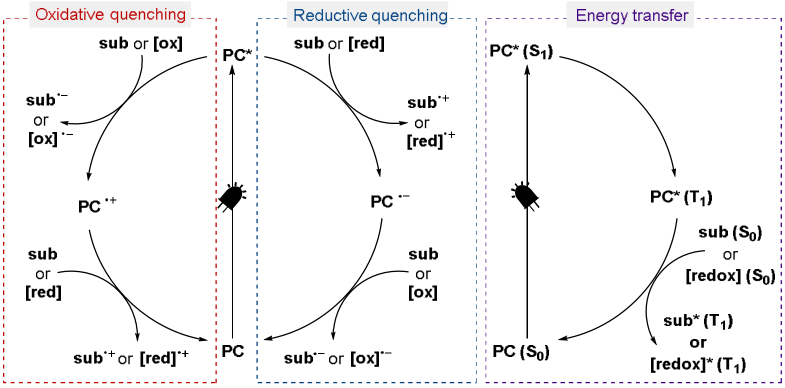
Nobel laureate Richard Kuhn pointed out that "Without phosphorus, there is no life". Phosphorus plays a vital role in life activities.[1] For example, adenosine triphosphate is the most direct energy source in living organisms; RNA or DNA are formed *via* the connection of phosphodiester bonds for ribonucleotides or deoxyribonucleotides; the basic skeleton of biological cell membranes is a phospholipid bilayer, which maintains cell metabolism. Due to the unique properties of phosphorus-containing compounds, they show good potential in the field of biomedicine, organic synthesis, pesticides, functional materials, *etc.*[2-4] For example, organophosphine pharmaceuticals such as Sofosbuvir, Fosenazide, and Brigatinib (Scheme 1),[5-6] organophosphine catalyst,[7] phosphine ligands,[8-10] organophosphine pesticides and functional materials[11-13] have been successfully developed and widely applied.



Scheme 1. Examples of organophosphine pharmaceuticals.

On the other hand, sunlight is an abundant, eco-friendly, and renewable energy source, which contains 52% infrared light, 43% visible light, and 5% ultraviolet light.[14] In the 1900s, Ciamician first proposed the concept of photochemistry, which is able to convert light energy into chemical energy.[15] Since the pioneering works reported by MacMillan, Yoon, and Stephenson in 2008 and 2009,[16-18] the past decade has witnessed a great renaissance of photochemistry. Especially, visible-light-induced organic synthesis provides a clean, eco-friendly, and convenient strategy for modern synthetic chemistry.[19-20]

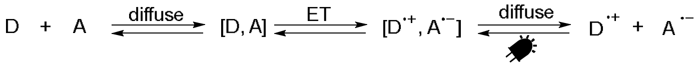
Generally, photocatalytic reactions are followed by one of the following mechanisms: electron transfer (**ET**) and energy transfer (**EnT**).[21] As shown in Scheme 2, the mechanism of **ET** includes two pathways: oxidative quenching and reductive quenching. In the oxidative quenching catalytic cycle, the excited state of photocatalyst (**PC***) is quenched by an electron acceptor, like substrate (**sub**) or oxidant (**[ox]**) in the reaction system, generating oxidized photocatalyst ($\mathbf{PC}^{\bullet+}$); while in the reductive quenching catalytic cycle, **PC*** is quenched by an electron donor, like substrate **sub** or reductant (**[red]**) in the reaction system, generating reduced photocatalyst ($\mathbf{PC}^{\bullet-}$). Then, the redox activities of $\mathbf{PC}^{\bullet+}$ and $\mathbf{PC}^{\bullet-}$ species in the catalytic cycle are responsible for catalyst turnover. Meanwhile, in the energy transfer (**EnT**) process, the ground state photocatalyst $\mathbf{PC(S_0)}$ absorbs energy to generate an excited singlet photocatalyst $\mathbf{PC^*(S_1)}$, which undergoes vibrational relaxation or nonradiative intersystem crossing to obtain a triplet photocatalyst $\mathbf{PC^*(T_1)}$. The triplet photocatalysts $\mathbf{PC^*(T_1)}$ return to ground state photocatalyst $\mathbf{PC(S_0)}$ *via* directly providing energy to the substrate **sub** or redox agent (**[redox]**), generating active intermediates such as triplet substrates.



PC = photoredox catalyst; sub = substrate; [ox] = oxidant; [red] = reductant; [redox] = reductant or oxidant

Scheme 2. General mechanism of photoredox catalytic reactions.

However, another specific and important property of the electron transfer process, namely the Electron Donor-Acceptor (EDA) process, should be noted. The EDA complexes could be formed between suitable electron donor molecules and electron acceptor molecules, which were also called "charge-transfer complexes" (Scheme 3).[22] The intramolecular electron transfer in EDA complexes provides a new strategy to generate some active radical species furnishing photocatalyst-free photochemical processes.



D = electron donor; A = electron acceptor; ET = electron transfer

Scheme 3. The intramolecular charge transfer in electron donor-acceptor complex.

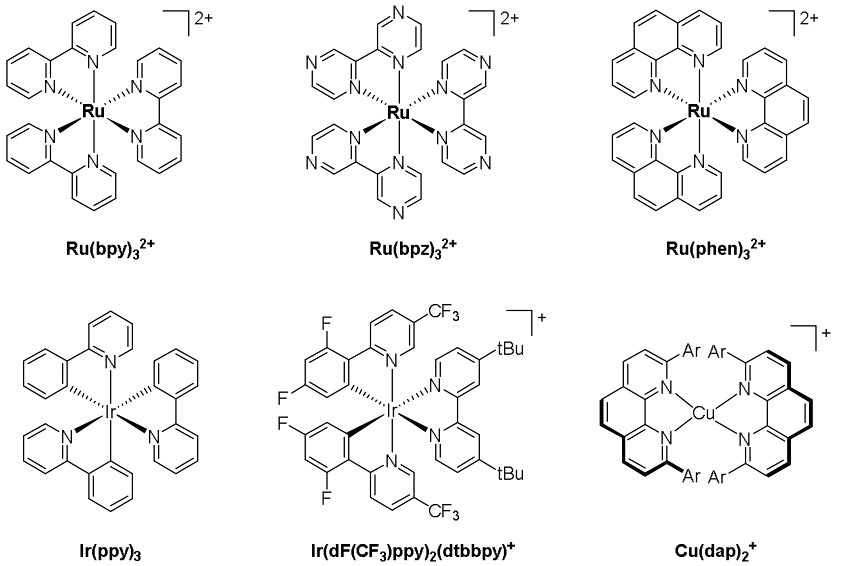
Although many methods have been developed for the synthesis of organophosphine compounds in the past decades,[23-40] most of the strategies inevitably require high temperatures or a large amount of transition metal reagents, leading to harsh reaction conditions or metal-contamination issues. In contrast, visible-light-induced synthesis of organophosphine compounds is generally carried out at room temperature with good functional group compatibility. The reported photocatalytic procedure for the synthesis of organophosphine compounds could be roughly divided into two catalogs: (1) homogeneous photocatalytic systems; (2) heterogeneous photocatalytic systems. In homogeneous photocatalytic systems, the photocatalyst can be dissolved in a solvent, generally showing high efficiency, but the catalyst cannot be recycled. In contrast, heterogeneous photocatalysts are insoluble in the solvent. In a typical heterogeneous reaction system, the organic reaction happens on the surface of the photocatalyst. Therefore, the reaction rate of heterogenous reaction is relatively slower than the corresponding homogeneous reaction system. However, considering the concept of green chemistry, the recyclability of heterogeneous catalysts makes the heterogeneous catalytic system sustainable and attractive. Herein, we summarize recent advances in the visible-light-induced synthesis of organophosphine compounds *via* the formation of C–P bonds (mainly from 2018 to 2022).

2. Homogeneous photocatalytic phosphorylation reactions

In this section, we summarize the visible-light-induced phosphorylation reactions according to different types of homogeneous photocatalytic systems including (i) transition metal complex-photocatalyzed phosphorylation reactions; (ii) organic dyes-photocatalyzed phosphorylation reactions; (iii) photocatalyst-free phosphorylation reactions.

2.1. Transition metal complex-photocatalyzed phosphorylation reactions

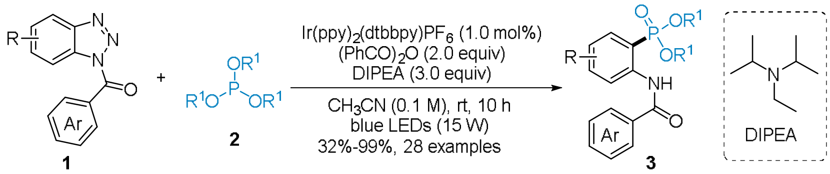
In the recent ten years, the commercialized transition metal complex photocatalysts, as depicted in Scheme 4, have been shown to exhibit high efficiency in numerous photocatalytic syntheses. However, most of them are the complex of iridium and ruthenium, which are rare and expensive.



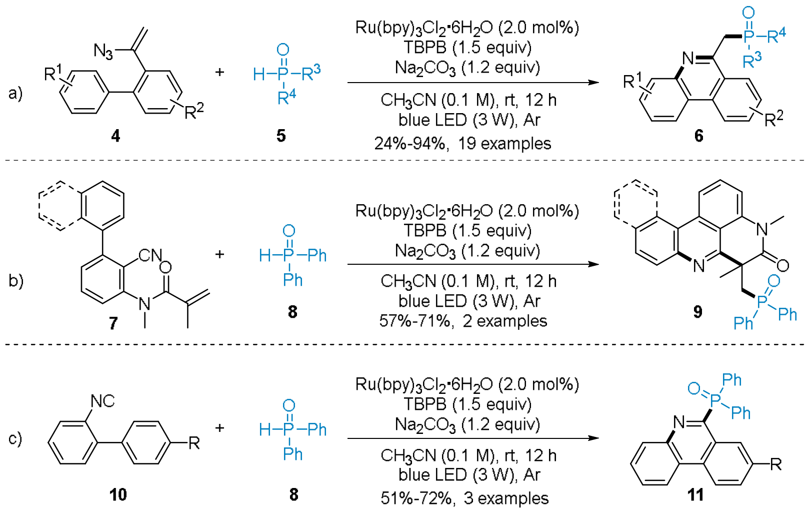
Scheme 4. Several commercialized transition metal complex photocatalysts.

In 2018, the group of Xia and Yang[41] reported the reaction of benzotriazoles **1** with trialkyl(aryl) phosphites **2** to obtain phosphorylated compounds **3** *via* denitrogenating process under the irradiation of blue LEDs, using a catalytic amount of [Ir(ppy)$_2$(dtbbpy)]PF$_6$ as a photocatalyst (Scheme 5). Compared with the previous methodologies, this strategy allowed the formal phosphorylation of aromatic C(sp^2)–H bonds in good to excellent yields under milder reaction conditions, simpler operations, and better tolerance with various functional groups. At the same time, the authors proved the formation of aryl radicals through control experiments. The aryl radical anion intermediate generated from the denitrogenation of benzotriazoles was supported by the byproduct *N*-phenylbenzamide, which was produced from the corresponding aryl radical anion intermediate through the abstracting of a hydrogen atom and proton.

In the same year, the Yang group[42] also developed a strategy for the denitrogenation and tandem phosphorylation cyclization of vinyl azides **4** with a commercially available phosphorylation reagent **5** to construct C–P bonds and C–N bonds, utilizing Ru(bpy)$_3$Cl$_2$·6H$_2$O as the photocatalyst, Na$_2$CO$_3$ as the base, *tert*-butyl peroxybenzoate (TBPB) as the oxidant, and CH_3CN as the solvent under irradiation of blue LED at room temperature (Scheme 6a). It is worth mentioning that this mild and efficient protocol was not only suitable for synthesizing phosphorus phenanthridines **6** but could also be applied to the radical addition reaction of phosphine reagents **8** with biaryl cyanides **7** (Scheme 6b) and isocyanides **10** (Scheme 6c), to give polyphenyl (pyrido[4,3,2-*gh*]phenanthridin-6-yl) phosphorus derivatives **9** and phosphorylated phenanthridines **11**.



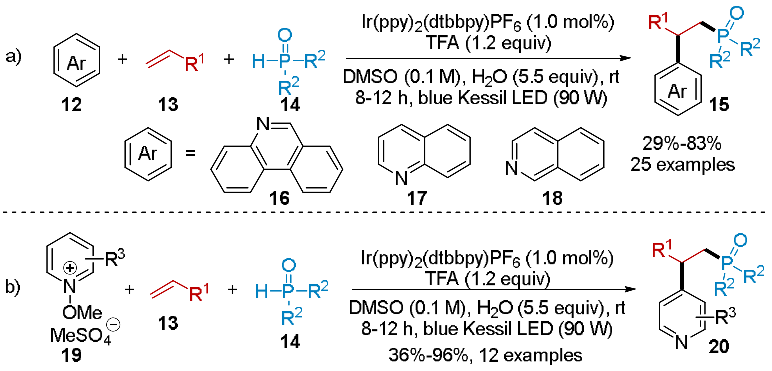
Scheme 5. Denitrogenative phosphorylation of benzotriazoles.



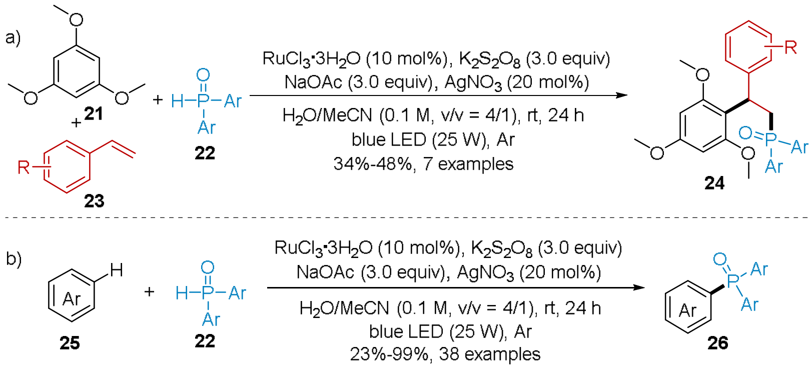
Scheme 6. Phosphorylation of *N*-heterocycles.

Although multicomponent reactions can realize one-pot multi-bond construction with a good step economy, they can be challenging processes due to possible low regioselectivity and poor compatibility of functional groups, However, in 2019, the Nagib group[43] achieved a three-component reaction of aromatic heterocyclic compounds **12** (phenanthridines **16**, quinolines **17**, isoquinolines **18**, and pyridine nitrogen oxides **19**), alkenes **13** and phosphine reagents **14**, realized alkene difunctionalization under the irradiation of visible light (Scheme 7). Mechanistic studies demonstrated that electrophilic phosphine radicals generated by the irradiation of blue light were selectively added to alkenes to produce nucleophilic C-centred radicals, which then reacted with electrophilic aromatic heterocyclic compounds to obtain the target products **15** and **20**. Compared with the two-component strategies, this method allowed the difunctionalization of alkenes *via* visible-light-induced polarity-reversing radical cascade to construct vicinal C–C and C–P bonds with the characteristics of simple and eco-friendly operations.

In a similar way, the Liang group[44] also developed a difunctionalization strategy of alkene under blue light irradiation, utilizing $RuCl_3·3H_2O$ as a photocatalyst (Scheme 8a). This three-component reaction of 1,3,5-trimethoxybenzene **21**, diarylphosphine oxide **22**, and styrene **23** permitted the phosphorylation and aromatization of alkene in water, constructing the C–C bond and C–P bond in one step. Although this strategy showed a limited substrate scope and moderate yields for the difunctionalization of alkenes to get target products **24**, the reaction system used water as a solvent, which had the unique advantage to develop green organic synthesis methodology and green chemistry under safe and environmentally friendly conditions. Meanwhile, the optimal reaction conditions were also applicable to the phosphorylation of C(sp^2)–H bond of aromatic compounds and heterocyclic compounds **25**, producing triarylphosphine oxide **26** (Scheme 8b).



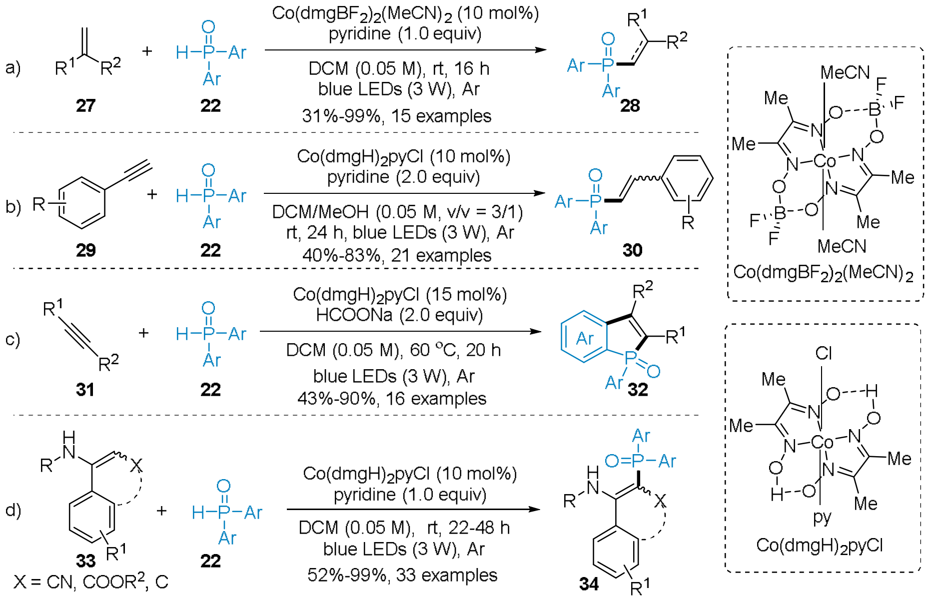
Scheme 7. Phosphorylation and arylation of alkenes.



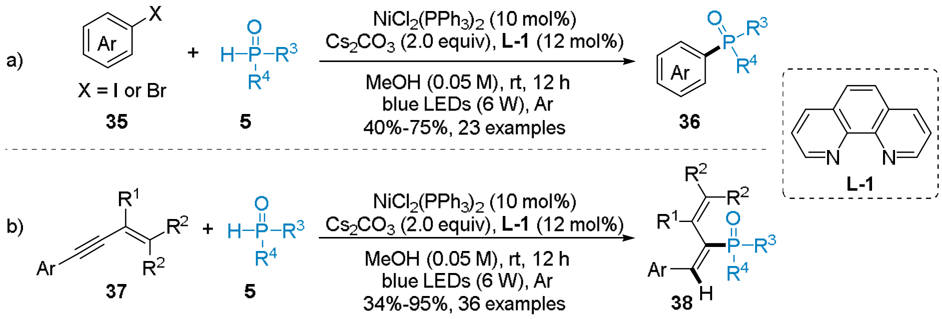
Scheme 8. Phosphorylation and aromatization of styrene.

Since cobalt is a cheap, readily available, and earth-abundant element, in 2019 the Wu group[45] used cobaloxime as a photocatalyst to synthesize alkenylphosphine oxides **28**, **30**, and **32** *via* the reaction of diarylphosphine oxide **22** and compounds **27**, **29**, and **31** containing an unsaturated carbon-carbon bond under visible light irradiation (Scheme 9a-c). Although the reaction conditions did not require an external oxidant, the selectivities of the products were poor. For example, the phosphorylated olefins contained a small amount of phosphorylated hydrogenated products and mixed products of *Z*/*E* configuration. Therefore, in 2020, the same group[46] employed $Co(dmgH)_2pyCl$ as a photocatalyst, realizing the direct C(sp^2)–H phosphorylation of enamine and enamide **33** (Scheme 9d). Noteworthy, this method could lead to diverse β-phosphinoyl products **34** in good stereoselectivity and good to excellent yields. Due to the effect of intramolecular hydrogen bonds, the *Z*/*E* mixture of acyclic enamines could be transformed into a purified *Z*-product with good stereoselectivity and reactivity under standard reaction conditions, which is beneficial for drug synthesis.

In 2021, the group of Zhu and Hou[47] developed a visible-light-induced nickel-catalyzed cross-coupling of aryl halides **35** and phosphine reagents **5** to generate the phosphorylated aryl compounds **36** (Scheme 10a). Additionally, this strategy also allowed a stereoselective and regioselective *cis*-hydrophosphorylation reaction of the internal alkyne of 1,3-enynes **37** to generate *cis*-phosphorylated 1,3-dibutene products **38** in good isolated yields (Scheme 10b)[48]. Mechanistic studies demonstrated that the direct radical addition of phosphine radicals to alkynes can be excluded. The *in situ* formed nickel(II)-phosphorus species could migrate into the internal alkyne of the 1,3-enynes to afford vinyl nickel species. Finally, various phosphorylated 1,3-dibutene **38** were obtained by protonation.



Scheme 9. Phosphorylation of unsaturated carbon–carbon bond.

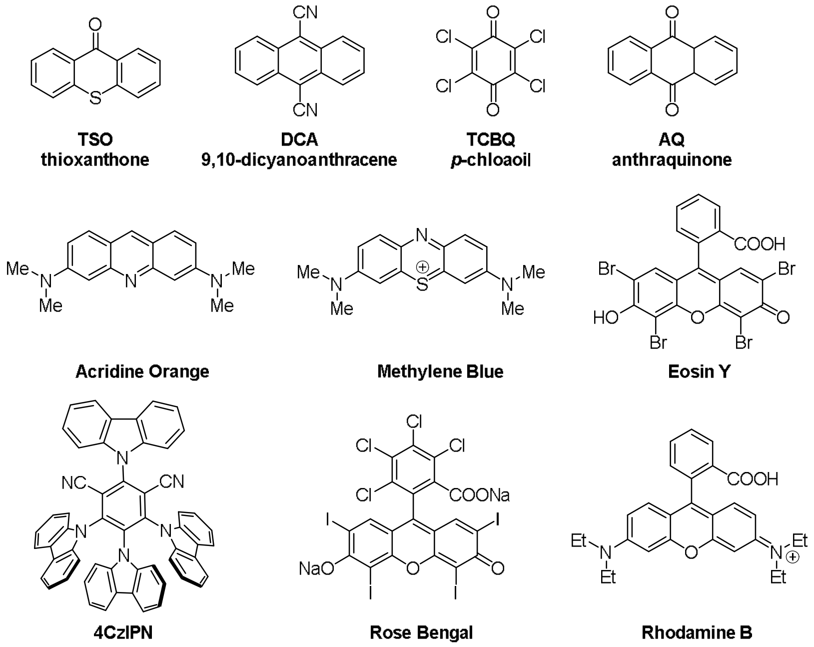


Scheme 10. Phosphorylation of aryl halides and alkynes.

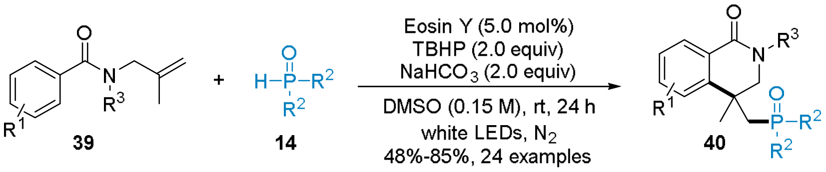
2.2. Phosphorylation reactions catalyzed by organic photocatalysts

Compared with transition metal complex photocatalysts, organic photocatalysts (Scheme 11) usually are economical and easily available. Additionally, the metal contamination issues could be avoided in those metal-free organic photocatalytic systems, which possess greater advantages in industrial applications.

In 2019, the group of Chen and Yu reported a visible-light-promoted radical phosphorylation/cyclization of *N*-allylbenzamides **39** *via* reacting with phosphine reagents **14** to generate phosphoryl-substituted dihydroisoquinolones **40** in dimethyl sulfoxide (DMSO), using Eosin Y as a photocatalyst, $NaHCO_3$ as base, and *tert*-butyl hydroperoxide (TBHP) as oxidant (Scheme 12).[49] This reaction featured a wide range of substrates with simple operation and mild conditions. This is the first photocatalytic example of the transition-metal-free synthesis of phosphoryl-substituted dihydroisoquinolones **40** under mild conditions.



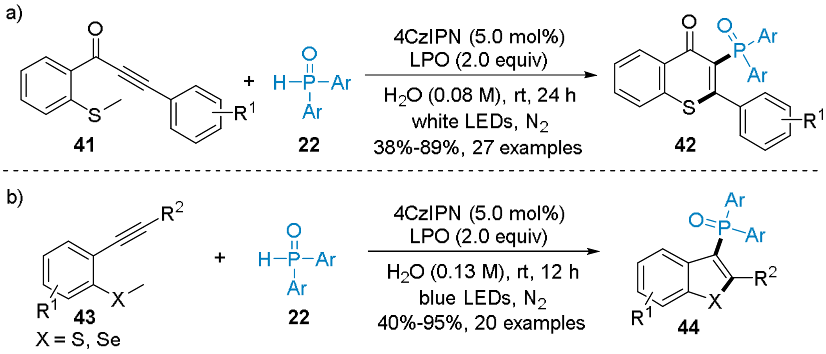
Scheme 11. Several commercial organic photocatalysts.



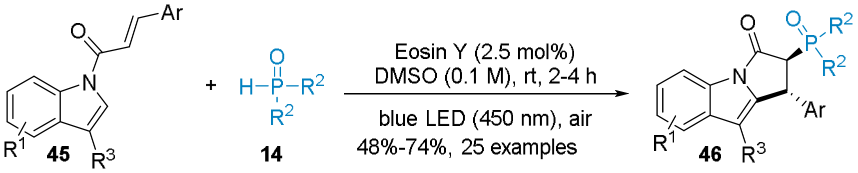
Scheme 12. Phosphorylation and cyclization of *N*-allylbenzamides.

Later on, the same group used a similar strategy to synthesize phosphorylated thioflavones **42** (Scheme 13a)[50] and benzothiophenes or benzoselenophene **44** (Scheme 13b)[51] *via* a phosphorylation/cyclization protocol catalyzed by 2,4,5,6-tetra(9*H*-carbazol-9-yl)isophthalonitrile (4CzIPN), utilizing methylthiolated alkynones **41**, methyl(2-(phenylethynyl)phenyl)-sulfanes or -selanes **43** and phosphine oxides **22** as raw materials. These systems used lauroyl peroxide (LPO) as the oxidant and water as the green solvent to develop the metal-free green and sustainable photocatalytic systems at room temperature. Meanwhile, the reaction conditions were also suitable for synthesizing other phosphorylated *N*-heterocycles, including phosphorylated oxindole, phosphorylated quinoline-2,4(1*H*,3*H*)-dione, and phosphorylated benzothiazole, demonstrating that this protocol had good substrate compatibility. This group developed a promising, environmentally friendly, efficient, and versatile strategy to generate phosphorylated compounds.

In 2020, the Akondi group[52] synthesized 2-phosphinoyl-3*H*-pyrrolo[1,2,*a*]indoles **46** *via* a visible-light-induced Eosin Y-catalyzed procedure (Scheme 14). The controlled experiments demonstrated that the excited state of eosin Y was quenched by phosphine reagent **14** under the induction of visible light, generating phosphine-centered radicals. Then the phosphine-centered radicals underwent radical addition with alkenes of **45** to produce carbon-centered radicals, which underwent radical addition again with the α-position of indole. Finally, the target product **46** was obtained by deprotonation. This strategy presented good chemoselectivity and diastereoisomeric selectivity in simple operation and mild reaction conditions.

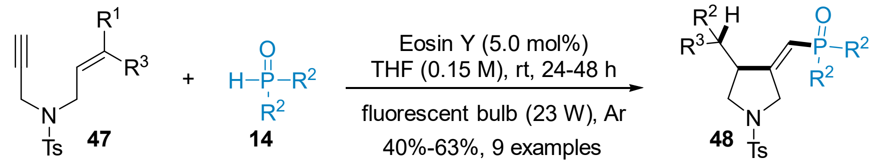


Scheme 13. The synthesis of phosphorylated thioflavones and benzothiophenes.



Scheme 14. The synthesis of 2-phosphinoyl-3*H*-pyrrolo[1,2,*a*]indoles.

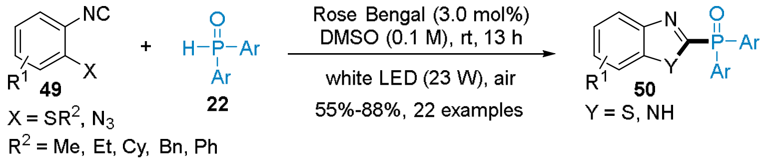
In 2020, the Zhu group[53] developed a methodology to synthesize phosphorylated five-membered *N*-heterocyclic **48** through the intramolecular radical tandem cyclization of 1,6-enynes **47** and diarylphosphine oxide **14** without additives bases and oxidants, utilizing eosin Y as a photocatalyst (Scheme 15). Different from previous reports, the excited state photocatalyst was quenched by diarylphosphine oxide **14** *via* direct hydrogen atom transfer (HAT) to generate the corresponding phosphine-centered radical, which then participated in the next radical addition of intramolecular tandem cyclization.



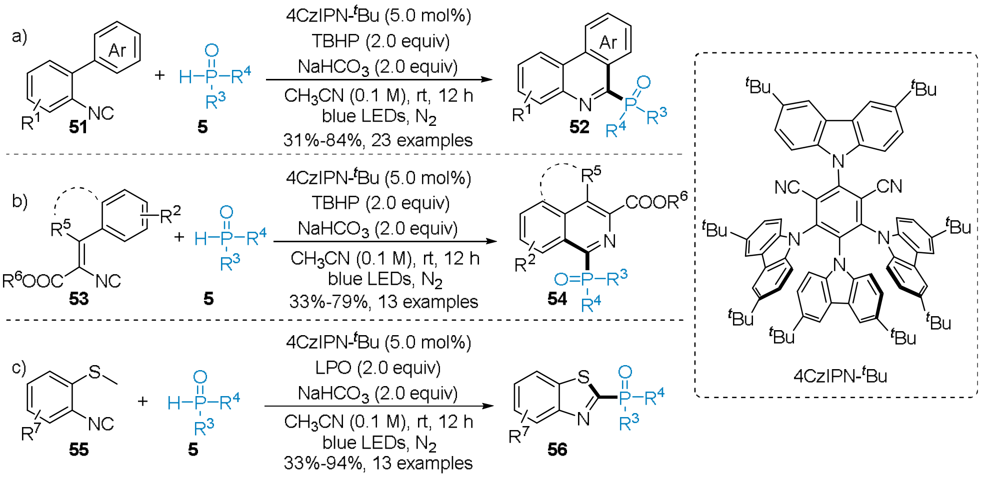
Scheme 15. Phosphorylation cyclization of 1,6-enynes.

Isocyanides are important organic intermediates, which can be transformed into a variety of heterocyclic compounds like phenanthridine, quinolinone, quinoxaline, indole, etc., but most of the reports required external transition-metal or peroxide oxidants. In 2020, the group of Yang and Feng[54] developed a method to synthesize phosphorylated benzothiazoles and benzimidazoles **50** catalyzed by Rose Bengal under the irradiation of visible light, using 2-isocyanoaryl thioethers or 2-isocyanoaryl azides **49** and diarylphosphine oxides **22** as substrates (Scheme 16). This method simultaneously constructed the C–S bond (or C–N bond) and C–P bond in moderate to good yields with eco-friendly and novel reaction conditions.

Subsequently, the group of Chen and Yu[55] reported a strategy to generate phosphine radicals, utilizing 2,4,5,6-tetrakis(3,6-di-*tert*-butyl-9*H*-carbazol-9-yl)isophthalonitrile (4CzIPN-^{t}Bu) as a photocatalyst. Isocyanides **51**, **53** and **55** reacted with diarylphosphine oxides **5** to synthesize phosphorylated phenanthridines **52**, isoquinolines **54**, and benzothiazoles **56** in the presence of bases and peroxides (Scheme 17). It was proposed that phosphine radicals were obtained *via* a process of proton-coupled electron transfer (PCET): the diarylphosphine oxide and the excited state photocatalyst underwent electron transfer (ET), accompanying proton transfer (PT) from tautomer hydroxydiphenylphophine of diarylphosphine oxide to base. The density functional theory (DFT) calculations demonstrated that the synergistic pathway of PCET possessed lower activation energies than the pathways of individual ET and PT processes, which was more unfavorable for this reaction.

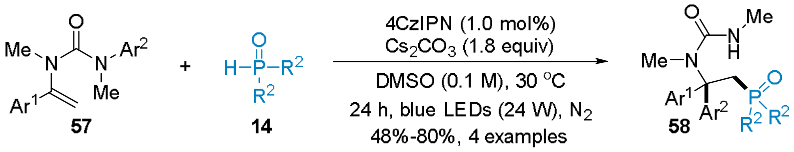


Scheme 16. The synthesis of phosphorylated benzothiazoles and benzoimidazoles.



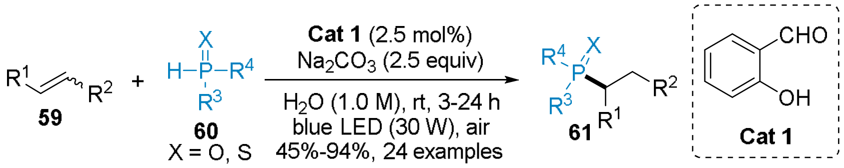
Scheme 17. Phosphorylation of *N*-heterocycles.

In 2020, the Clayden group[56] reported a strategy for the difunctionalization of the carbon-carbon double bond of vinyl ureas **57** *via* a visible-light-induced radical-polar crossover mechanism of vinyl ureas **57** and phosphine reagents **14** to generate phosphorylated products **58** (Scheme 18). The phosphine radical generated by the photocatalytic ring was added to the double bond and then reduced by the photocatalyst to generate a carbanion, which then underwent a Truce-Smiles rearrangement to construct a C–C bond, realizing the difunctionalization of the alkene. Additionally, the Truce-Smiles rearrangement under the reaction conditions was not limited by the electronic properties of the migrating aryl groups, even electron-rich aryl groups also can obtain bifunctionalized alkenyl urea in moderate yields.



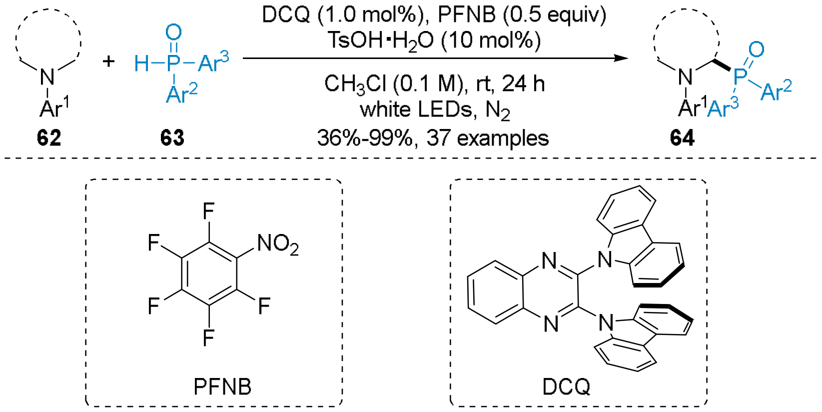
Scheme 18. Phosphorylation of vinyl ureas.

In 2021, the Li group[57] reported a hydrophosphinylation reaction of inactivated alkenes **59** induced by visible light irradiation in air and water (Scheme 19). Interestingly, this reaction did not require typical organic dye photocatalysts, as a common and cheap organic small molecule salicylaldehyde (**Cat 1**) was used as a photocatalyst. In basic aqueous, deprotonated salicylaldehyde exhibited visible light absorption, which can replace organic dye photocatalysts to complete the photocatalytic cycle. Meanwhile, this strategy can also use diphenylphosphine sulfides **60** as a phosphine reagent to obtain hydrophosphinylated compounds **61** under mild conditions, broadening the scope of the substrate.



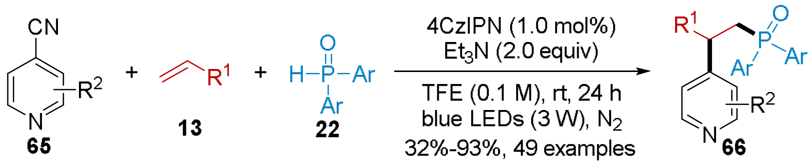
Scheme 19. Hydrophosphinylation for unactivated alkenes.

The Xu group[58] reported the D-A fluorescent molecule DCQ as a photocatalyst for the direct phosphorylation of *N*-heterocycles **62** C(sp^3)–H bonds under mild and metal-free conditions (Scheme 20). This strategy had a wide range of substrate scopes, whether the substrate was a five-membered small ring or a multi-membered macrocycle. Meanwhile, diverse substrated diarylphosphine oxides **63** were also compatible with this reaction system. The phosphorylated products **64** can be obtained in moderate to excellent yields. The controlled experiments indicated that the reaction underwent three processes: single electron transfer (SET), hydrogen atom transfer (HAT), and proton coupling-electron transfer (PCET).



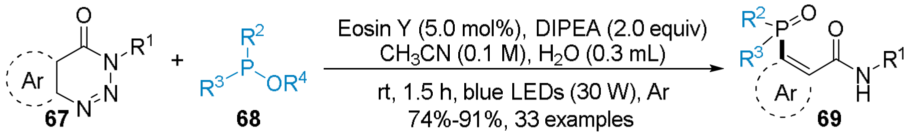
Scheme 20. Phosphorylation of *N*-heterocycles C(sp^3)–H bonds.

The bifunctionalization of alkenes is an important synthetic strategy with simple operation and a high step economy. In 2021, the Shen group[59] developed a three-component synthesis strategy catalyzed by 4CzIPN, using alkene **13**, 4-cyanopyridine **65**, and diarylphosphine oxide **22** as raw materials, generating phosphorylation and aromatization products **66** (Scheme 21). This methodology constructed the C–C bond and C–P bond *via* a one-step reaction. Noteworthy, the triethylamine in the reaction system was both a single electron transfer (SET) reagent and a hydrogen atom transfer (HAT) reagent.



Scheme 21. Phosphorylation and aromatization of alkenes

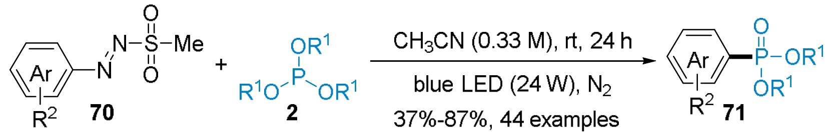
In 2021, the Tang group[60] developed an efficient denitrogenation phosphorylation from benzotriazinones **67** and phosphine reagents **68** under metal-free and visible-light-induced conditions, producing target compound **69** in good to excellent yields (Scheme 22). Interestingly, the gram-scale reaction can be purified by simple extraction and recrystallization, avoiding tedious, complicated, and high-cost chromatographic purification, which further promoted the industrial application of this method.



Scheme 22. Denitrogenative phosphorylation of benzotriazinones.

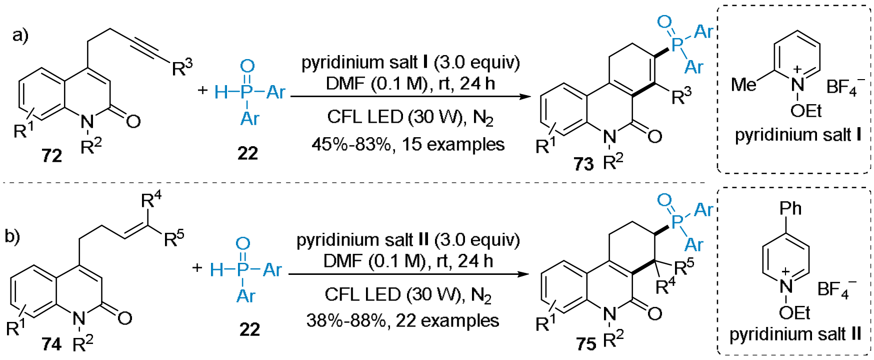
2.3. Phosphorylation reactions in photocatalyst-free condition

In 2019, the group of Qiu and Protti[61] developed a visible-light-induced strategy for synthesizing (hetero)aryl phosphonates **71** without photocatalysts (Scheme 23). Arylazo sulfones **70** reacted with triaryl or trialkyl phosphites **2** in CH_3CN for 24 h to obtain the target products **71** in moderate to good yields. Additionally, this protocol had good functional group compatibility. Compared with Sandmeyer-type phosphorylation reactions, electron-rich arenes and (hetero)aromatics also showed good compatibility under these reaction conditions.



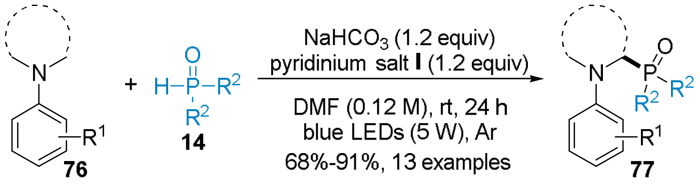
Scheme 23. Phosphorylation of arylazo sulfones.

In 2021, the Hong group[62] designed a methodology to produce phosphorylated dihydro- or tetrahydrophenanthridin6(5*H*)-ones **73** and **75** from substrates of quinolinone-containing compounds **72** and **74** under the irradiation of visible light (Scheme 24). The mechanism studies indicated that the structure of quinolinone-containing compounds **72** and **74** could absorb light energy to generate an excited state and then undergo single electron transfer (SET) with the added pyridinium salt to generate ethoxy radicals. Ethoxy radicals interacted with diarylphosphine oxides **22** *via* hydrogen atom transfer (HAT) to produce phosphine-centered radicals, followed by radical addition and radical addition cyclization to obtain products in moderate to good yields. This strategy constructed the C–C bond and C–P bond in one step with multiple processes, including SET, HAT, radical addition, and radical addition cyclization, under mild reaction conditions without photocatalysts.



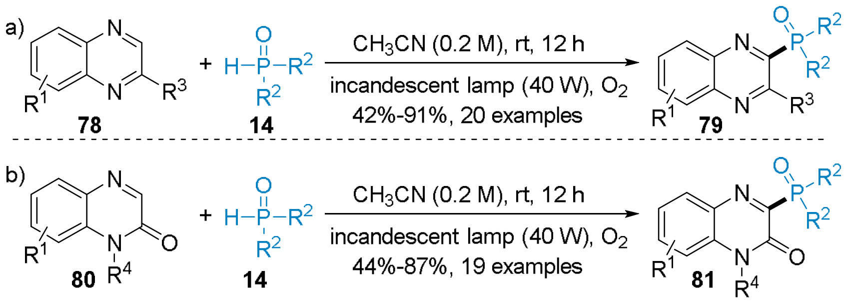
Scheme 24. Phosphorylation of quinolinone-containing compounds.

The Lakhdar group[63] reported a metal-free, photocatalyst-free synthetic strategy for the visible-light-induced α-phosphorylation of *N*-aryl tertiary amines **76** (Scheme 25). The controlled experiments demonstrated that *N*-aryl tertiary amines **76** were electron donors and pyridinium tetrafluoroborate was an electron acceptor, the combination of two compounds formed an important electron donor-acceptor (EDA) complex, which underwent a single electron transfer (SET) and hydrogen atom transfer (HAT) to generate imide cations. Finally, imide cations reacted with the tautomer of diarylphosphine oxide **14** *via* nucleophilic addition reaction to obtain phosphorylated products **77**.



Scheme 25. α-Phosphorylation of *N*-aryl tertiary amines.

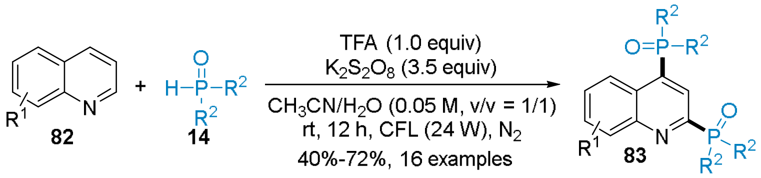
In 2020, the Adimurthy group[64] developed a strategy for the synthesis of phosphorylated quinoxalines **79** (Scheme 26a) and phosphorylated quinoxalin-2(1*H*)-ones **81** (Scheme 26b) under the atmosphere of oxygen and irradiation of visible light without external photocatalysts. Besides the broad substrate scopes of quinoxaline **78** and quinoxalin-2(1*H*)-ones **80**, various phosphine reagents **14** including *H*-phosphonates and diarylphosphine oxides can also afford phosphorylated products in good yields. Additionally, quinoxalin-2(1*H*)-ones **80** possessed higher reactivity than quinoxaline **78** under these mild and simple reaction conditions.



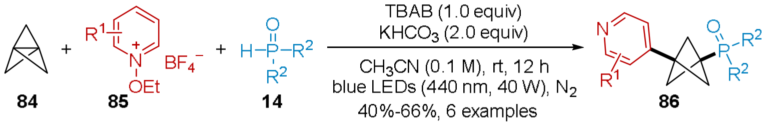
Scheme 26. Phosphorylation of quinoxalines and quinoxalin-2(1*H*)-ones.

In 2020, the Wang group[65] developed a visible-light-induced method to produce diphosphorylated quinoline compounds **83** without external photocatalysts, utilizing quinolines **82** and phosphine oxides **14** as raw materials, the mixture of acetonitrile and water as solvents, and an equivalent amount of trifluoroacetic acid (TFA) and oxidant ($K_2S_2O_8$) as additives (Scheme 27). Interestingly, this strategy enabled the simultaneous phosphorylation of quinolines **82** at C-2 and C-4 positions to obtain diphosphorylated quinolines **83**. Unfortunately, this is a stoichiometric process, in which an equivalent amount of acid and an excess amount of oxidant were required. Meanwhile, *H*-phosphonate compounds were not suitable for this reaction system.

In 2021, the Hong group[66] developed a photocatalyst-free three-component phosphorylative pyridylation protocol of [1,1,1]propane **84** (Scheme 28). The reaction mechanism proposed that tetrabutylammonium bromide (TBAB) was a HAT reagent for phosphine oxides **14** to produce a phosphine-centered radical, which was then added to [1,1,1]propane **84**, generating a carbon-centered radical. Finally, the carbon radical was added to the pyridinium salt **85** to obtain the target product **86**. This strategy was unprecedented to realize the phosphorylation of [1,1,1]propane **84** in a three-component coupling under catalyst-free and mild conditions.

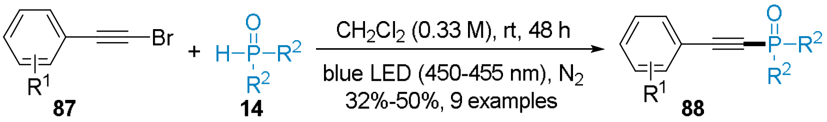


Scheme 27. The synthesis of diphosphorylated quinoline compounds.



Scheme 28. Phosphorylative pyridylation of [1,1,1]propane.

The Meng group[67] designed a C(*sp*)-P bond formation strategy to obtain alkynylphosphine oxides **88** promoted by visible light without external catalysts or oxidants (Scheme 29). Unlike the classical radical addition of phosphine-centered radicals and alkynes, this method did not obtain phosphorylated styrene products or benzophosphole oxide compounds[45]. The homolytic cleavage of bromoalkynes **87** under visible light irradiation generates alkynyl radicals and bromine radicals. Then bromine radicals abstract the hydrogen atom of diarylphosphine oxides **14** to afford phosphine-centered radicals *via* a HAT process. Finally, the coupling of alkynyl radical and phosphine radical gave the corresponding alkynylphosphine oxides **88**.



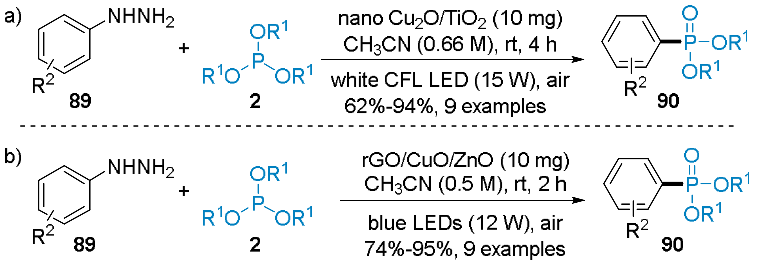
Scheme 29. The synthesis of alkynylphosphine oxides.

3. Visible-light-induced phosphorylation in heterogeneous systems

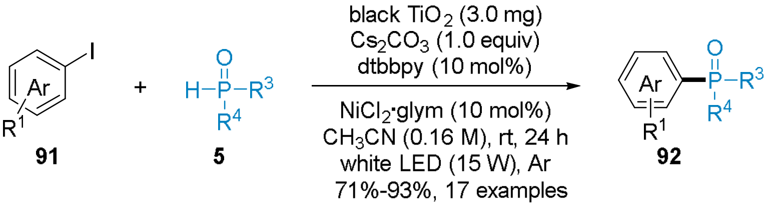
Heterogeneous catalysts are insoluble in the reaction solvent, so the reaction rate can be relatively slow. However, considering the problems of environmental pollution and green chemistry, heterogeneous catalysts possess stable catalytic activity and can be recycled many times, which is environmentally friendly and economical. Therefore, the development and application of heterogeneous catalysts have always been hot research topics.[68] Recently, heterogeneous photocatalytic strategies have been applied in carbon dioxide reduction, and photocatalytic splitting of water to produce hydrogen and oxygen,[69-72] while the application of heterogeneous photocatalytic systems for organic synthesis is still in its infancy.[73-75] We herein summarized the recent examples of the heterogeneous photocatalytic synthesis of organophosphine compounds.

In 2018, the Hosseini-Sarvari group[76] developed a heterogeneous visible-light-induced strategy to construct an aromatic C–P bond using arylhydrazines **89** and trialkyl phosphonates **2** as raw materials (Scheme 30a). In this reaction, Cu_2O/TiO_2 nanoparticles were used as inexpensive and recyclable photocatalysts and air was used as an oxidant to synthesize the target product **90** without external additives such as base and ligand. Compared with the previously reported homogeneous photocatalytic system,[77] this heterogeneous photocatalyst can be reused up to 6 times without a significant change in yield. Subsequently, the same group[78] continued to develop a ternary recyclable nanophotocatalyst (rGO/CuO/ZnO) to synthesize aryl phosphonate derivatives **90** from arylhydrazines **89** and trialkyl phosphonate **2** without external additives (Scheme 30b). This is the first example of a ternary hybrid nanomaterial as a heterogeneous photocatalyst for organic reactions, which possessed the advantages of fast reaction rate, high catalyst stability, and good recyclability up to 6 times.

In 2020, the Hosseini-Sarvari group[79] designed a dual catalytic system using black nano-TiO_2 as a photocatalyst and nickel(II) as a co-catalyst to achieve phosphorylation of aryl iodide **91** from commercially available phosphine reagent **5** under the irradiation of visible light, processing broad substrate scopes in good to excellent yields (Scheme 31). The gram-scale experiment, sunlight experiment, and reusability test under the optimized reaction conditions showed excellent practical application. The controlled experiments demonstrated that black nano-TiO_2 played a vital role in the generation of phosphine-centered radicals, which would participate in the next catalytic cycle of nickel(II) to obtain the phosphorylated product **92**.



Scheme 30. The synthesis of aryl phosphonate derivative.



Scheme 31. Phosphorylation of aryl iodide.

The group of Yang and Xu[80] designed two-dimensional covalent organic frameworks (2D-COFs), which were further utilized as a heterogenous photocatalyst for the reaction of isocyanides **93** and diarylphosphine oxides **8** to synthesize phosphorylated phenanthridines **94** in moderate to good yields *via* a visible-light-induced tandem radical addition-cyclization sequence (Scheme 32). This strategy is characterized by mild reaction conditions with good functional group compatibility. Various radicals including aryl, alkyl, trifluoromethyl, phosphoryl radicals, and phenylthio were suitable in this reaction system. Noteworthy, this heterogeneous 2D-COFs photocatalyst showed good recyclability (up to 6 times).

4. Conclusions

Phosphorylated *N*-heterocycles play significant roles in the development of active pharmaceutical molecules, pesticides, natural products, and functional materials. Meanwhile, visible-light-induced phosphorylation reactions have been demonstrated as environmentally friendly and efficient strategies for the synthesis of phosphorylated heterocycles. In this minireview, we have summarized recent advances in visible-light-induced phosphorylation reactions (mainly from 2018 to 2022) by homogeneous systems and heterogeneous systems. These visible-light-induced phosphorylation reactions were carried out at room temperature with characteristics of mild, good functional group compatibility and simple operations. Particularly, heterogeneous photocatalyst in visible-light-induced phosphorylation is still rare. We believe the heterogeneous photocatalytic strategies will draw more attention from the community due to their stability and recyclability.

Acknowledgments

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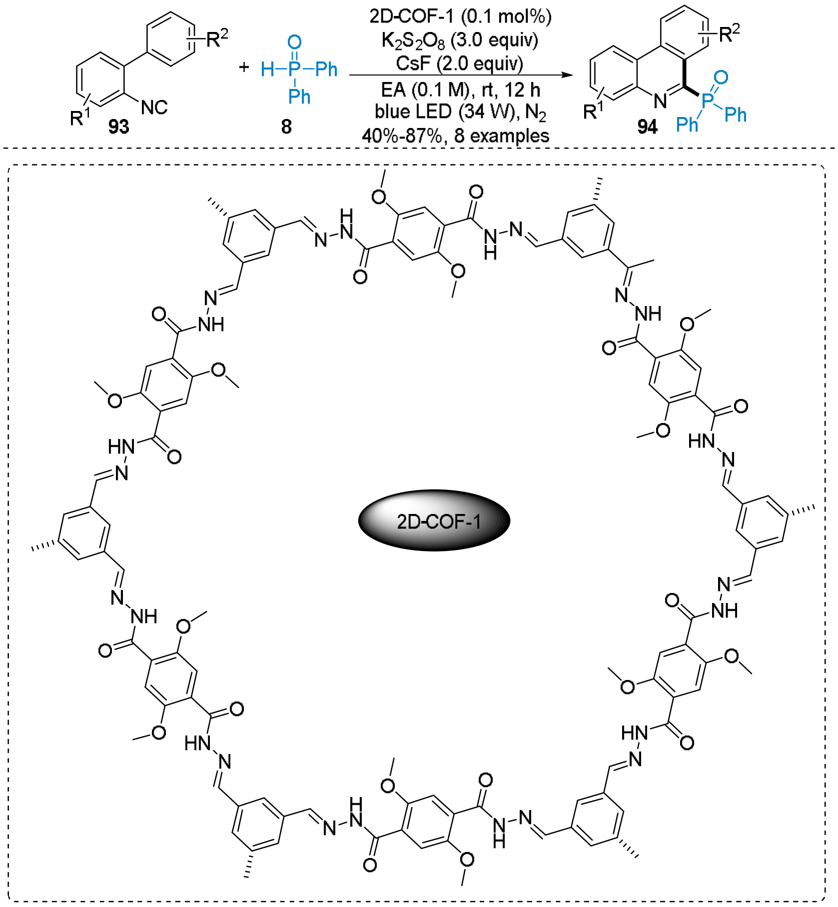

Scheme 32. The synthesis of phosphorylated phenanthridines.

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