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The Merger of Photoredox and Cobalt Catalysis

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Abstract

In the last decade, synthetic chemists have discovered the outstanding generality and potential of visible-light-driven photoredox catalysis, which converts visible light into chemical energy and realizes numerous transformations of small molecules. The current state-of-the-art strategy in photoredox catalysis, combining photoredox and transition-metal catalysis, has received considerable attention in organometallic chemistry. In parallel to the rapid development of nickel/photoredox and copper/photoredox catalysis, cobalt/photoredox catalysis has emerged as a distinct new option in this area. This short review covers the general strategy, characteristics compared to other metallaphotoredox systems, and future perspectives of cobalt/photoredox catalysis. To the best of our knowledge, this is the first review encompassing the general combination of cobalt catalysis and photoredox catalysis in synthetic chemistry.

Keywords: photoredox catalysis; cobalt; dehydrogenation; dual catalysis; metallaphotoredox catalysis

Merger of 3d-metal catalysis and photoredox catalysis

Photochemistry historically represents a vital part of synthetic chemistry. Although direct excitation of organic compounds by UV light has long been mainstream in synthetic photochemistry [1], visible-light-driven photoreactions have recently started to flourish as a safer and more user-friendly alternative. This renaissance in photochemistry relies on the emergence of photoredox catalysts [2-7]. In general, a photoredox catalyst absorbs visible light and reaches its **excited state** (see Glossary) with a lifetime that is typically > 100 ns. The photocatalyst in its excited state serves as a one-electron oxidant or reductant that enables the transfer of one electron between the catalyst and the organic substrates. Thus, photoredox catalysts are suitable for generating radicals from stable organic molecules and have contributed to recent development of radical-mediated transformations [8-10]. Following its success in radical-mediated transformations, the application of a photoredox phenomenon in transition-metal-catalyzed reactions, the so-called metallaphotoredox catalysis [11-15], has attracted the interest of researchers in both photochemistry and organometallic chemistry.

A pioneering contribution by Sanford and colleagues employed an organopalladium [16] complex generated *in situ*, that allows the formation of C–C bonds *via* organometallic complexes that reside in unusually high **oxidation states**. This pioneering work has quickly been extended by a study into other metals as potential partners in metallaphotoredox chemistry, and this merger has been established for 3d, 4d, and 5d metal catalysts. Among these, 3d metals such as cobalt, nickel, and copper are particularly appealing because they are more earth abundant than to 4d or 5d metals. Moreover, several mechanistic studies have indicated the involvement of one-electron redox

processes in the thermal catalytic cycle [17-19], as well as the feasibility of controlling their **redox potential** by a judicious choice of ancillary ligands. These aspects promise potential for their compatibility with photoredox catalysis, which operates under mild conditions, provides facile access to radical intermediates, and is characterized by a rich choice of redox potentials for one-electron transfers (Figure 1A).

Indeed, nickel/photoredox [20-22] and copper/photoredox [23, 24] cooperative systems have evolved rapidly, showcasing their potential in challenging C–C- [25-29] or C–heteroatom- [30-35] bond-forming reactions as well as highly enantioselective transformations (Figure 1B, right) [36-38]. Since the primary discoveries on metallaphotoredox catalysis was analogous to cross-coupling-type reactions previously catalyzed by palladium (Suzuki–Miyaura, Buchwald–Hartwig, etc.), studies on nickel or copper (which are established alternatives for palladium catalysts in thermal cross-coupling reactions) have dominated the area, while the potential of other first row transition metals including cobalt was largely unexplored. On the other hand, the merger of photoredox catalysis with cobalt catalysis has a long history in inorganic chemistry (Figure 1B, left). The reduction of protons into molecular hydrogen is an indispensable transformation in **artificial photosynthesis** and, in that context, the combination of visible-light-driven photocatalysts and cobalt complexes has been intensively studied [39]. In addition, early contributions on **biomimetic chemistry** regarding vitamin B12 and its model compounds under photochemical conditions [40, 41] should also be regarded as pioneering work in cobalt/photoredox cooperative catalysis. Despite these precedents and recent developments in cobalt/photoredox cooperative catalysis, to the best of our knowledge there is still no review that focuses on this topic from the

perspective of synthetic chemistry. This review aims to cover recent examples (typically those reported between 2014 and 2019) on the merger of cobalt and photoredox catalysis, focusing on (1) dehydrogenative transformations (cross-coupling hydrogen evolution and acceptorless dehydrogenation), and (2) C–C- or C–heteroatom-bond-forming reactions in which organocobalt intermediates presumably play a vital role (e.g., hydrofunctionalization of alkenes, cycloaddition of alkynes, allylation/deallylation, and reactions using stoichiometric oxidant or reductant). Despite the diversity of these precedents, they all share the general mechanistic strategies depicted in Figure 1C: The reduction of the cobalt catalyst by the reduced photocatalyst is responsible for low-valent cobalt or cobalt-hydride-mediated transformations. On the other hand, one-electron oxidation of a cobalt complex would provide a high-valent cobalt complex that could subsequently mediate an oxidative transformation.

Cross-coupling hydrogen evolution (CCHE)

The oxidative functionalization of C–H bonds to C–C or C–heteroatom bonds represents a desirable method for streamlining multistep syntheses of complex molecules, as it avoids the pre-functionalization steps that are usually associated with the preparation of reaction partners in classical cross-coupling reactions [42, 43]. Early examples of such transformations are based on the use of equimolar amounts of chemical oxidants, which is not ideal with respect to sustainability, safety, and functional-group tolerance. On the other hand, oxidative couplings that occur under the concomitant evolution of hydrogen gas (cross-coupling hydrogen evolution; CCHE) have emerged as a more advanced technology in this context [44-48]. While the proof-of-concept study on CCHE employed a heterogeneous graphene-supported ruthenium oxide nanocomposite for the hydrogen

evolution [49], it was quickly demonstrated that cobaloxime derivatives are able to play the same role under homogeneous conditions (*vide infra*).

An early example of the intermolecular formation of C–C bonds by CCHE was reported by Wu and colleagues who introduced a combination of the organophotocatalyst eosin Y and $Co(dmgH)_2Cl_2$ for the noble-metal-free CCHE between tetrahydroisoquinolines and indoles (Figure 2A) [50]. In their proposed catalytic cycle, photoexcited eosin Y is responsible for the one-electron oxidation of amines, while the second oxidation of the α-aminoalkyl radical intermediate is mediated by the cobaloxime cocatalyst. This successive two-electron oxidation leads to the formation of an iminium intermediate, which leads to the formation of a new C–C bond upon reaction with a nucleophile. Finally, molecular hydrogen is generated by the two-electron reduction of cobaloxime followed by protonolysis. Through the similar photochemical oxidation of substrates, dehydrogenative functionalization of amino acids [51] and isochromanes [52] were also possible. Furthermore, Luo and Wu and colleagues reported an asymmetric variant of the dehydrogenative coupling assisted by a chiral amine catalyst [53].

Cobaloxime/photoredox cooperative catalysis has been proven to be generally applicable to synthetically valuable C–C bond-forming reactions including synthesis of heterocycles [54], oxidative Heck [55, 56], and Minisci-type [57, 58] reactions. Notably, the catalytic dehydrogenative formation of C–C bonds was also extended to provide access to more complex molecular scaffolds: Lei and colleagues reported the dehydrogenative coupling between styrene derivatives and alkynes, which affords multisubstituted naphthalene rings in a single step (Figure 2B) [59]. The high oxidation potential of an excited Acr^+-

Mes organophotocatalyst enables the oxidation of styrene derivatives. Then, the addition of alkynes to the resulting radical cation is responsible for the formation of the first C–C bond. The second C–C bond formation occurs by an intramolecular Friedel–Crafts-type reaction, followed by an aromatization through the release of two protons and an electron. This aromatization is facilitated by the simultaneous formation of cobalt hydride, whose protonation results in the release of hydrogen gas and the regeneration of the cobaloxime catalyst. Consecutive formations of C–C and C–N bonds were also demonstrated in the similar reaction design for the preparation of 3,4-dihydroisoquinoline derivatives [60] or isoquinoline derivatives [61].

Since CCHE realizes oxidative transformations in the absence of chemical oxidants, its advantage is evident for the construction of C–heteroatom bonds, for which the starting materials or products are susceptible to undesirable oxidation. Lei and colleagues have demonstrated the intramolecular C–H thiolation of aromatic thioamides using a combined cobaloxime/photoredox catalytic system (Figure 2C) [62]. The products were obtained in lower yield when chemical oxidants were used, presumably because thioamides readily decompose by these reagents. From a mechanistic perspective, the one-electron oxidation of a thioamide by the excited $Ru(bpy)_3^{2+}$ photoredox catalyst provides access to a thiyl radical, which undergoes addition to an aromatic ring. The oxidation of the resulting radical intermediate by the reduced cobaloxime affords the benzothiazole product, while hydrogen gas is released by protonolysis of the cobalt hydride. The authors proposed that precise tuning of the proton transfer steps by basic additives contributes to high catalytic turnovers.

Wu and Tung and colleagues reported another impressive example of CCHE, i.e., the C–H amination and hydroxylation of benzene (Figure 2D) [63]. The UV-light-driven, highly oxidizing photocatalyst $QuCN^+$ oxidizes benzene to afford a benzene radical cation. The addition of a heteroatom nucleophile to the intermediate and release of a proton delivers a cyclohexadienyl radical intermediate, which is presumably oxidized by the reduced cobaloxime to afford the products with a new C–N or C–O bond. Protonation of the resulting cobalt hydride regenerates the cobaloxime cocatalyst under concomitant release of hydrogen gas. It is proposed that overoxidation of the products is inhibited by a rapid electron back transfer between the product and the photocatalyst. Other challenging dehydrogenative bond-forming reactions (e.g., C–N [64-66]; C–O [64, 67-69]; C–P [70-72]; C–S [62, 73]; and C–Si [74]) by CCHE have also been reported, providing further evidence for the versatility of this strategy to construct C–heteroatom bonds.

Acceptorless dehydrogenation

Desaturation of a C–C or C–heteroatom single bond to a double bond is a fundamental process for the preparation of fine chemicals and other industrial applications. Among these transformations, acceptorless dehydrogenation is considered to be ideal because chemical oxidants are not required, and useful hydrogen gas is the sole byproduct [48]. However, catalytic acceptorless dehydrogenation under thermal conditions generally requires high reaction temperatures because the release of hydrogen gas together with the desaturation is thermodynamically unfavorable in terms of enthalpy.

In order to realize the acceptorless dehydrogenation of alkanes under milder conditions, Sorensen and colleagues have employed a cooperative base-metal catalytic system that consists of a tetra-*n*-butylammonium decatungstate photocatalyst and cobaloxime (Figure

3A) [75]. Notably, the acceptorless dehydrogenation of unactivated alkanes proceeds at room temperature under irradiation with UV light. The authors proposed that the excited decatungstate photocatalyst abstracts a hydrogen atom from the alkane, which affords a radical intermediate and the partially hydrogenated photocatalyst. Then, a second hydrogen-atom transfers from the radical intermediate to the cobaloxime affords an alkene and cobalt hydride. The release of hydrogen gas by the reaction between the reduced photocatalyst and the cobalt hydride regenerates the two base-metal catalysts. The same cooperative base-metal catalysts are also applicable to the dehydroformylation of aliphatic aldehydes (Figure 3B) [76]. In this case, the photochemical cleavage of the C–H bond is followed by a decarbonylation, which leads to an sp^3-hybridized carbon-centered radical. This radical intermediate engages with the cobaloxime catalyst to afford an alkene and molecular hydrogen.

Li and colleagues have demonstrated that the merger of a photoredox catalyst and a cobaloxime catalyst is a viable strategy for the acceptorless dehydrogenation of partially saturated *N*-heterocycles (Figure 3C) [77]. The catalytic dehydrogenation provides access to valuable *N*-heteroarenes such as quinolines, quinoxalines, indoles, and thiazoles, and thus represents broad substrate generality due to exceptionally mild reaction conditions (under irradiation with visible light at room temperature). The photoredox catalyst $Ru(bpy)_3^{2+}$ facilitates the one-electron oxidation of saturated amines, which allows the generation of an α-aminoalkyl radical intermediate. Subsequent electron transfer from the radical intermediate to the photochemically reduced cobaloxime affords cobalt hydride. The ensuing protonolysis of cobalt hydride results in the formation of molecular hydrogen and the regeneration of the cobaloxime catalyst. This chemistry was later proven to be

compatible with aqueous reaction media [78]. It should also be noted here that similar cooperative catalysis can facilitate the dehydrogenative coupling of two *N*-heterocycles by finely tuning the reaction conditions [79]. In addition to C–N bond, N–N bond was able to be desaturated to afford azobenzene derivatives by cobaloxime/photoredox system [80].

An interesting extension of the catalytic acceptorless dehydrogenation is the decarboxylative desaturation of carboxylic acids. According to the report by Ritter and colleagues, the combination of the photocatalyst $Ir[dF(CF_3)ppy]_2(dtbpy)PF_6$ and a cobaloxime cocatalyst provided a general system that converts aliphatic carboxylic acids into alkenes (Figure 3D) [81]. In the proposed reaction mechanism, single-electron oxidation of a carboxylate by the photoredox catalyst affords an alkyl radical via decarboxylation. Engagement of the radical with the reduced cobaloxime mediates the formation of an alkene, which is followed by the release of hydrogen gas from cobalt hydride. The net transformation can be accomplished under stoichiometric additive-free conditions, which is appealing for the conversion of abundant fatty acids into industrially valuable α-olefins. Tunge and Cartwright have reported a relevant dehydrogenation of amino acids into enamides using a combination of cobaloxime and an organophotocatalyst, thus demonstrating the generality of such combinations for acceptorless dehydrogenations [82]. Larionov and colleagues have reported a catalytic decarboxylative dehydrogenation under enzyme-compatible conditions, which allowed the direct transformation of esters into alkenes [83].

Hydrofunctionalization of alkenes

Considering that cobalt hydride species derived from cobaloximes can be readily generated and are compatible with a series of reaction conditions (*vide supra*), it is reasonable to assume that cobalt-hydride-mediated transformations should be possible by using cobalt/photoredox catalysis. Considering that cobalt hydride is responsible for the Drago–Mukaiyama hydration and related hydrofunctionalizations of alkenes [84], the cobalt/photoredox approach found applications in the hydrofunctionalization of alkenes using photochemically generated cobalt hydride species.

Rovis and Thullen have reported the hydroaminoalkylation of conjugated dienes using a dual catalyst system consisting of a cobalt diphosphine complex and the photocatalyst $Ir[dF(CF_3)ppy]_2(dtbpy)PF_6$ (Figure 4A) [85]. From a mechanistic perspective, the one-electron reduction of the Co^{II} complex generates Co^{I} *in situ*, which is subsequently protonated to afford the cobalt hydride. Its insertion into conjugated dienes generates π-allylcobalt species. On the other hand, amines are oxidized by the excited photocatalyst to furnish nucleophilic α-aminoalkyl radicals. The photoredox-mediated reduction of the organocobalt complex, followed by an addition of the α-aminoalkyl radical affords a new C–C bond and regenerates the low-valent cobalt complex. Conjugated dienes with electron-withdrawing groups generally furnish the hydroalkylated products in good yield, and the authors unambiguously confirmed that cobalt catalysis is indispensable to achieve high product yields. This system is also applicable to the transformation of aliphatic amines or simple conjugated dienes without functional groups. The transformation also allows the construction of quaternary carbon atoms, which might be facilitated by sterically less hindered nature of the α-aminoalkyl radicals.

Another application for photochemically-generated cobalt hydrides has been disclosed by König and colleagues, who reported the isomerization of terminal alkenes into internal alkenes using a combination of cobalt acetylacetonate and 4CzIPN (Figure 4B) [86]. The excited organophotocatalyst was quenched using a Hantzsch ester, and the electron transfer from the reduced photocatalyst generates a Co^{I} complex. A subsequent protonation affords a cobalt hydride, which serves as a catalyst for the isomerization of alkenes [87]. In the proposed mechanism, the insertion of cobalt hydride into terminal alkenes affords an alkylcobalt intermediate. A subsequent β-hydride elimination, which might be accelerated by visible light, affords thermodynamically more favorable internal alkenes and regenerates the cobalt hydride. The combined catalytic system was applied to the isomerization of hydrocarbons and natural-product derivatives, affording the internal alkenes in high yield. It is worthwhile noting that sequential (or "chain-walking") isomerization is also possible with this system.

The cobalt-catalyzed hydrofunctionalization was successfully applied to C–C bond forming reaction by Maji and coworkers who reported reductive hydroalkenylation of electron deficient alkenes (Figure 4C) [88]. In their mechanistic hypothesis, cobalt hydride which was obtained by protonation of Co^{I} inserts to electron deficient alkene. Insertion of an alkyne is followed by the release of the hydroalkenylated product and reductive regeneration of the Co^{I} catalyst.

Collins and colleagues proposed distinct access to cobalt hydride and application to hydroalkynylation of alkynes [89]. This report represents prospects of the cobalt/photoredox system for hydrofunctionalization of alkynes.

Cycloaddition of alkynes

The cobalt-catalyzed cycloaddition of alkynes has been studied mainly relying on the well-defined low-valent cobalt catalysts [90-92]. Inspired by these precedents, the application of photochemically generated low-valent cobalt complexes for the cycloaddition of alkynes has attracted attention in the merger of cobalt and photoredox catalysis. A pioneering contribution has been made by Rovis and Ruhl, who have employed a combination of $CoBr_2(PCy_3)_3$ and $Ir[dF(CF_3)ppy]_2(dtbpy)PF_6$ for the [2+2+2] cyclotrimerization of diynes and alkynes (Figure 5A) [93]. The catalytic system contains catalytic amounts of an organic amine, which most likely serves as a reductant for the initial generation of a low-valent cobalt catalyst. In the proposed catalytic cycle, a low-valent cobalt(0) complex, generated by a photoredox-mediated reaction, enables the oxidative cyclization of alkynes. The scope of this cyclotrimerization includes aliphatic alkynes, diynes with different tethers, and internal alkynes. The authors insightfully applied the catalytic system to the photolithographic modification of a polymer surface, given that the light-driven reaction provides spatial control over the reaction. This “light-gated” control might be due to sophisticated electron-transfer steps between the organocobalt intermediate and the photocatalyst. This light-gated strategy was also effective in controlling the molecular weight in polymer syntheses, meaning that temporal control of the reaction is possible [94]. Interestingly, a relevant [2+2+2] cycloaddition

was later achieved in the absence of a photoredox catalyst [95]. In that case, the organocobalt intermediate absorbs visible light and is involved in electron-transfer steps.

Zhao and Wu and colleagues have demonstrated another application of photoredox-induced low-valent cobalt catalysis, in which the cycloaddition of alkynes and carbon dioxide affords oxygen-containing heterocycles (Figure 5B) [96]. Although poorly functional-group-tolerant organometallic reductants are often required to incorporate carbon dioxide into organic molecules, an organic amine can be used here as a mild stoichiometric reductant. The amine is oxidized by the excited photocatalyst $Ir(ppy)_2(dtbpy)PF_6$, and an electron transfer from the reduced photocatalyst to a cobalt diphosphine complex affords a low-valent Co^I complex. This cobalt complex mediates the oxidative cycloaddition of alkynes and carbon dioxide. A subsequent migration of the acetyl group and a transmetallation with zinc bromide releases a tricyclic intermediate that eventually cyclizes to afford γ-hydroxybutenolides, and the low-valent cobalt complex is regenerated by a photoredox-mediated reduction. The scope of the reaction includes multisubstituted five-membered heterocycles with cyclopropyl groups, electron-rich or -deficient arenes, and sterically hindered acyl groups. The same catalytic system mediates the cycloaddition with other substituted alkynes to afford coumarin derivatives and substituted cinnamic acid derivatives. These results indicate that photochemically induced low-valent cobalt catalysis exhibits reasonable functional-group tolerance and can be considered as a useful option in synthetic chemistry.

Allylation and deallylation

Transition-metal-catalyzed allylic substitution reactions constitute an intensively investigated area in synthetic organometallic chemistry. Among all conceivable metal catalysts, noble group 9 metals such as rhodium [97] and iridium [98-100] represent a privileged class of catalysts due to their intrinsic tendency to afford synthetically versatile branched products. On the other hand, cobalt-mediated allylic substitution reactions have received less attention, despite the abundance of cobalt salts in the earth's crust and the intrinsic similarity between cobalt, rhodium, and iridium. Active catalysts for allylic substitution reactions are often low-valent group 9 metals such as Rh^{I} or Ir^{I}, and therefore, their low-valent congener Co^{I} should serve as a potent catalyst for allylation reactions, as suggested by recent thermal reactions [101, 102].

Gryko and coworkers have reported an insightful combination of a titanium oxide photocatalyst and vitamin B12 for the deallylation of phenol derivatives (Figure 6A) [103]. The authors proposed that a low-valent cobalt complex, generated *in situ* by electron transfer from the titanium photocatalyst to vitamin B12, serves as the active species in the catalytic cycle. The resulting low-valent cobalamine is highly nucleophilic, and its addition to the substrate results in the formation of an allylcobalt intermediate and the release of the deallylated arenols. A subsequent protonation and reduction of the allylcobalamine regenerates the low-valent cobalamine catalyst. A subsequent treatment with hydrochloric acid is desirable as enol ethers are the major byproducts in this reaction, which might be derived from the isomerization of the double bond of the allyl group. The deallylation proceeds in high yield for sterically hindered 2,4,6-methylphenol or phenols with electron-withdrawing groups and a deallylation to afford an aliphatic alcohol is also possible. Unfortunately, the transfer of the allyl group to other nucleophiles was not

accomplished in this catalytic system, possibly due to the limited electrophilicity of the allylcobalamine intermediate.

More recently, Kojima and Matsunaga and colleagues have reported the organophotoredox-promoted regioselective allylation of active methylene nucleophiles (Figure 6B) [104]. The authors employed a Co^{II} diphosphine complex as the catalyst precursor and generated a low-valent cobalt complex *in situ* by electron transfer from the 4CzIPN organophotocatalyst in the presence of an organic amine. The oxidative addition of allylic electrophiles to the generated Co^{I} complex affords a π-allylcobalt intermediate. A nucleophilic addition of a soft carbon nucleophile to the electrophilic π-allylcobalt species induces the formation of a C–C bond and regenerates the Co^{I} catalyst. The reaction afforded branched allylic substitution products in high regioselectivity, suggesting a similarity between the cobalt-catalyzed method and rhodium- or iridium-catalyzed allylation reactions. In addition, the catalytic allylation was successfully expanded to the regioselective substitution of an allyl sulfone. Considering that substitution of allyl sulfones is challenging for rhodium- or iridium-based catalysts, this report is the first example of the superiority of cobalt catalysts compared to established Rh- and Ir-based catalytic systems.

Reactions using stoichiometric oxidant or reductant

Metallaphotoredox catalysis enables the use of environmentally benign oxidant instead of stoichiometric transition metals such as copper or silver salts. Rueping and coworkers elegantly demonstrated the photoredox-enabled aerobic oxidative C–H functionalization with rhodium catalysis [105]. Inspired by the precedent, Sundararaju and colleagues

reported a C–H activation/oxidative cycloaddition of alkynes using a merger of Co^{II} catalysis and eosin Y under aerobic conditions (Figure 7A) [106]. It is proposed that after the irreversible, turnover limiting C–H bond cleavage, successive coordination of an alkyne, migratory insertion, and reductive elimination affords the product along with the release of Co^{I} catalyst. Finally, the photoredox-mediated electron transfer regenerates Co^{III} using molecular oxygen as an oxidant. Terminal alkenes are also able to involve in the relevant oxidative C–H alkylation while the turnover limiting step in this reaction was not the C–H bond cleavage [107]. These combinations represent rare examples of cobalt/photoredox catalysis in the presence of an oxidant, and serve as a starting point for the combination of high-valent cobalt-catalyzed C–H bond functionalizations with photoredox catalysis [108].

Cobalt/photoredox dual system allows the use of milder and more tractable reagents for net reductive transformations. Lloret-Fillol and coworkers reported reduction of ketones and aldehydes catalyzed by dual cobalt catalysis and photocatalysis using triethylamine or *N*,*N*-diisopropylethylamine as a reductant (Scheme 7B) [109]. Interestingly, photochemically generated Co^{II} hydride reduces the carbonyl compounds either via stepwise single electron transfer/hydrogen atom transfer mechanism or via hydride transfer mechanism. The excited copper-based photoredox catalyst is reductively quenched by amines and transfers an electron to the polydentate cobalt catalyst.

Casitas and Lloret-Fillol and colleagues applied virtually the same combination of cobalt and photoredox catalysis for reduction of unactivated alkyl chlorides (Figure 7C) [110]. This transformation clearly demonstrates the advantage of metallaphotoredox chemistry

because unactivated alkyl chlorides are known to be inert toward conventional photoredox catalysis. In this case a respective polydentate nickel complex was studied in detail, and the mechanism of cobalt/photoredox catalysis for dechlorination is proposed in Figure 7C assuming that the two metal catalysts should work in similar mechanisms. Oxidative addition of an alkyl chloride to low valent metal complex affords alkyl metal intermediate. On the other hand, photoredox catalyst is reduced by amines assisted by visible light. Single electron transfer from the reduced photoredox catalyst to the alkyl metal intermediate prompts homolysis of the metal-carbon bond, and an alkyl radical is formed and the low valent metal complex is regenerated. The alkyl radical undergoes intramolecular addition to the tethered alkene and the cyclized product is obtained.

Concluding remarks

Although the merger of cobalt catalysis and photoredox catalysis has previously been a focus in inorganic chemistry, it is now clear that cobalt/photoredox cooperative catalysis also constitutes an innovative technology in synthetic chemistry. While nickel/photoredox or copper/photoredox system are useful for cross-coupling-type reactions which were previously catalyzed by palladium, cobalt/photoredox catalysis provides new options to dehydrogenative transformations and reactions which were efficiently catalyzed by noble group 9 metals such as branch-selective allylic alkylation. Since cobalt can exist in a variety of oxidation states (e.g., 0, I, II, and III) and engage both in one-electron transfers and two-electron mediated bond forming processes, its combination with photoredox catalysis validates numerous reaction pathways that were not accessible in thermal transformations. Rational control of the reaction pathways is thus essential for productive transformations, and more mechanistic studies as well as the variety of established ligands

and photoredox catalysts would help us establish practical reaction conditions. In addition, employment of other photocatalysts [111-113] or combination with hydrogen atom transfer catalyst [114-117] are promising strategies for functionalization of less reactive small molecules, and should expand the scope of cobalt/photoredox catalysis. Since several more tasks (enantioselectivitive reactions, comparison with thermal reactions, merger with Co-catalyzed C-H functionalizations [118-120] and mechanistic understanding; see Outstanding Questions for details) remain to be addressed, cobalt/photoredox dual catalysis continues to deserve intense attention in synthetic community as a worthwhile challenge in metallaphotoredox chemistry.

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Glossary

Artificial photosynthesis: an artificial photochemical process which enables synthesis of an energy carrying molecule (for example, molecular hydrogen) from an abundant molecule (for example, water) toward green production of chemical fuel.

Biomimetic chemistry: an area of chemistry which aims to mimic highly efficient chemical phenomena in biological system by rational design and application of artificial molecules or chemical methods

Excited state: a higher energy state of a molecule or a system in quantum chemistry compared to its original, thermally stable state (or "ground state"), typically accessed by an absorption of a photon

Oxidation state: a formal degree of oxidation of a specific atom in a molecule calculated by its formal charge and covalent bonds, which is informative for simplified interpretation of electrophilicity and potential reactivity of the atom

Redox potential: a measure in electrochemistry which quantitatively describes the voltage required for electron transfer from the specific molecule to an electrode: comparison of the values between different chemical species helps predict the feasibility of an electron transfer between the two

Disclaimer Statement

The authors declare no competing financial interest.

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Figure Captions.

Figure 1. Merger of 3d-metal Catalysis and Photoredox Catalysis. (A) 3d-metal catalysts and photoredox catalysts are compatible in nature. (B) Cobalt/photoredox cooperative catalysis is an emerging technology in organic synthesis. (C) Representative mechanisms in cobalt/photoredox catalysis. Abbreviations: PC, photoredox catalyst; A, electron acceptor; D, electron donor.

Figure 2. Cobalt/Photoredox-catalyzed Cross-coupling Hydrogen Evolution (CCHE). (A) A representative CCHE between amines and nucleophiles. (B) CCHE for the construction of naphthalenes *via* the formation of two C–C bonds. (C) CCHE enables an oxidative transformation of thioamides. (D) Direct formation of phenols from benzene by CCHE. Abbreviations: LED, light-emitting diode; PMP, 4-methoxyphenyl.

Figure 3. Cobalt/Photoredox-Catalyzed Acceptorless Dehydrogenation. (A) Dehydrogenation of unreactive alkanes. (B) Dehydroformylation of aldehydes *via* a dehydrogenation. (C) Dehydrogenation of *N*-heterocycles provides *N*-heteroarenes. (D) Application of the catalytic system to the conversion of carboxylic acids into alkenes. Abbreviations: Py, pyridine; M.S., molecular sieves; DME, 1,2-dimethoxyethane.

Figure 4. Hydrofunctionalization of Alkenes by Cobalt/Photoredox Cooperative Catalysis. (A) Hydroaminoalkylation of dienes by merging cobalt catalysis and radical chemistry. (B) A photochemically generated cobalt hydride mediates the catalytic isomerization of alkenes. Abbreviations: acac, acetylacetonate; DMF, *N*,*N*-dimethylformamide.

Figure 5. Cycloaddition of Alkynes mediated by Cobalt/Photoredox Dual Catalysis. (A) Visible-light-gated [2+2+2] cycloaddition. (B) Low-valent cobalt catalysis enables the capture of CO_2 by cycloaddition. Abbreviations: CFL, compact fluorescent lightbulb; Cy, cyclohexyl; Ts, *p*-toluenesulfonyl.

Figure 6. Allylation and deallylation by Cobalt/Photoredox Dual Catalysis. (A) Photochemically activated Vitamin B12 mediates the deallylation of phenols. (B) Low-valent cobalt-catalyzed allylation exhibits high regioselectivity. Abbreviations: B, branched isomer; L: linear isomer; dppp, 1,3-diphenylphosphinopropane.

Figure 7. Reactions using stoichiometric oxidant or reductant. (A) Photoredox-enabled aerobic oxidative C–H bond alkenylation/cyclization. (B) Cobalt-catalyzed reduction of carbonyls via net hydride transfer. (C) Reductive dechlorination/cyclization by low-valent cobalt catalyst. Abbreviations: TFE, 2,2,2-trifluoroethanol; E, ethoxycarbonyl.

Figures.

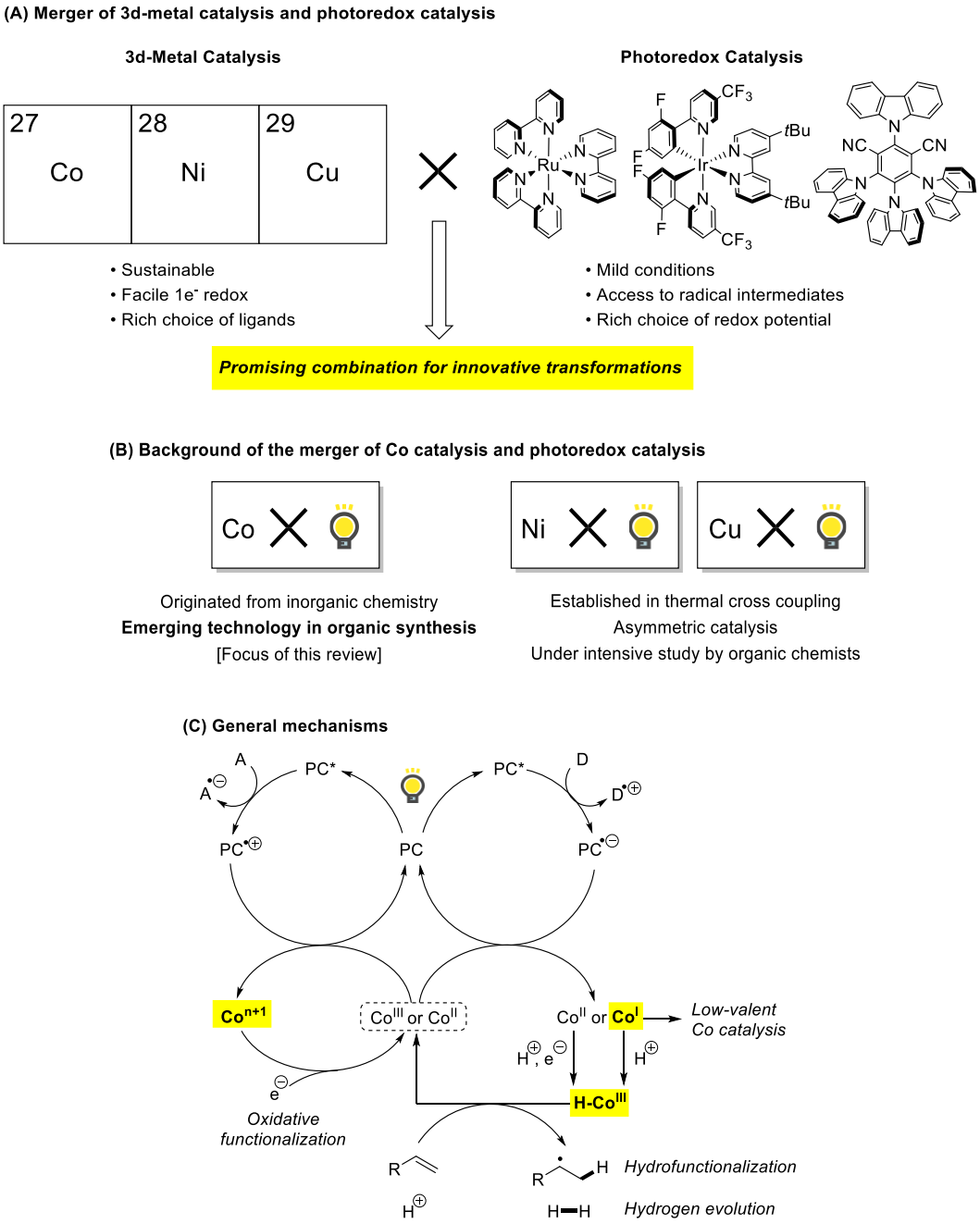


Figure 1.

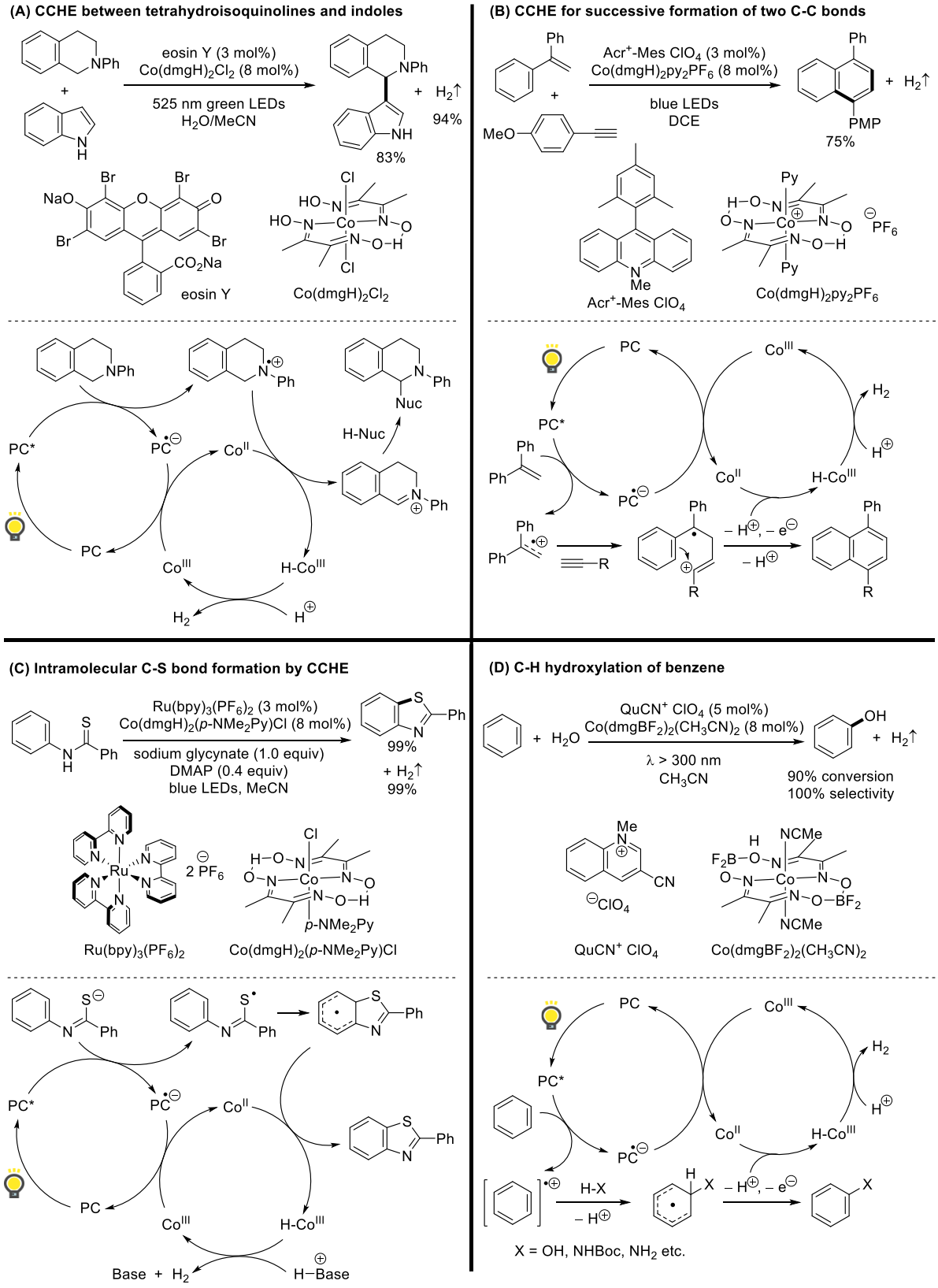

(A) CCHE between tetrahydroisoquinolines and indoles
eosin Y (3 mol%)
Co(dmgH)2Cl2 (8 mol%)
525 nm green LEDs
H2O/MeCN
83%
94%
eosin Y
Co(dmgH)2Cl2
(B) CCHE for successive formation of two C-C bonds
Acr+-Mes ClO4 (3 mol%)
Co(dmgH)2py2PF6 (8 mol%)
blue LEDs
DCE
75%
Acr+-Mes ClO4
Co(dmgH)2py2PF6
(C) Intramolecular C-S bond formation by CCHE
Ru(bpy)3(PF6)2 (3 mol%)
Co(dmgH)2(p-NMe2Py)Cl (8 mol%)
sodium glycynate (1.0 equiv)
DMAP (0.4 equiv)
blue LEDs, MeCN
99%
99%
Ru(bpy)3(PF6)2
Co(dmgH)2(p-NMe2Py)Cl
(D) C-H hydroxylation of benzene
QuCN+ ClO4 (5 mol%)
Co(dmgBF2)2(CH3CN)2 (8 mol%)
λ > 300 nm
CH3CN
90% conversion
100% selectivity
QuCN+ ClO4
Co(dmgBF2)2(CH3CN)2
X = OH, NHBoc, NH2 etc.

Figure 2.

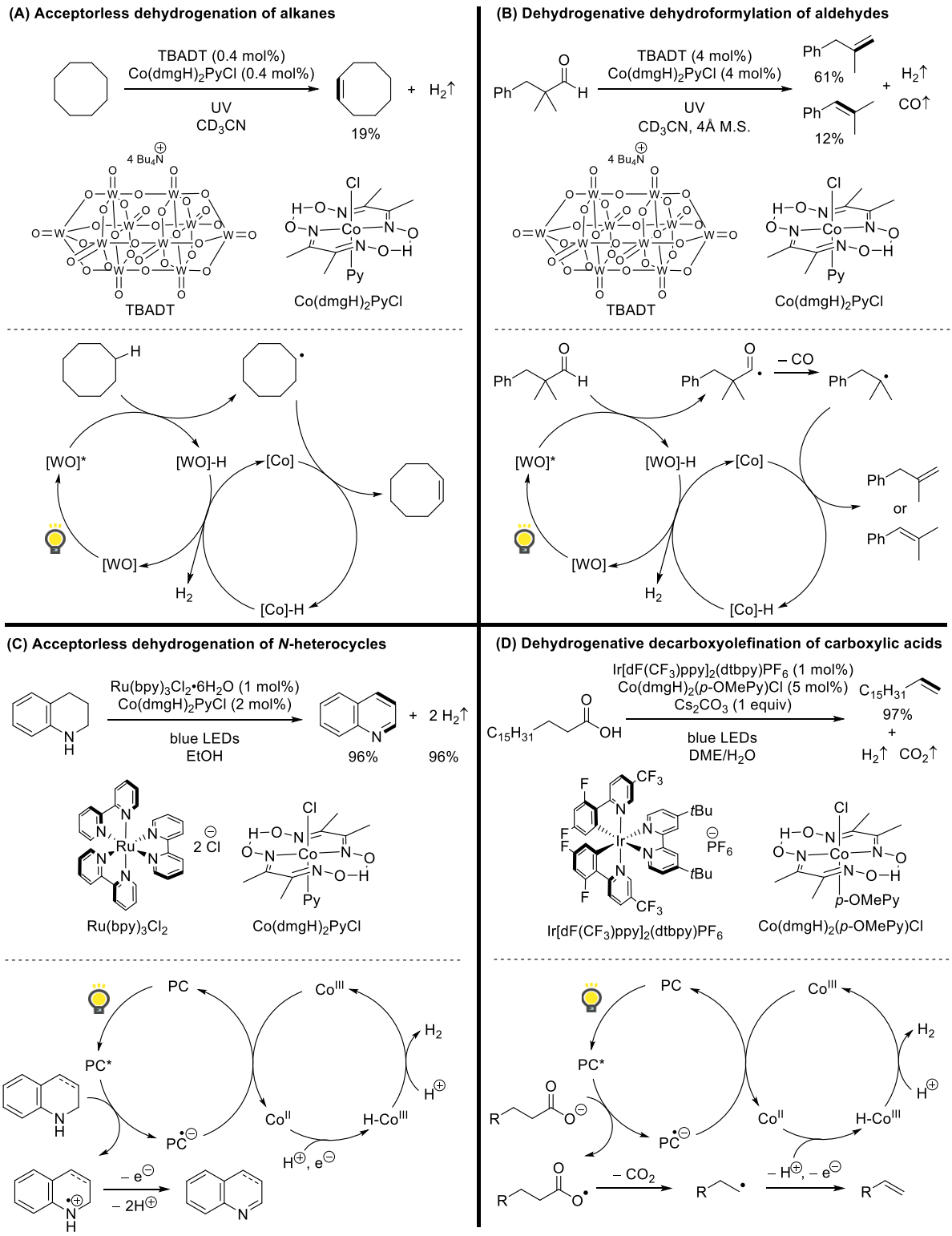
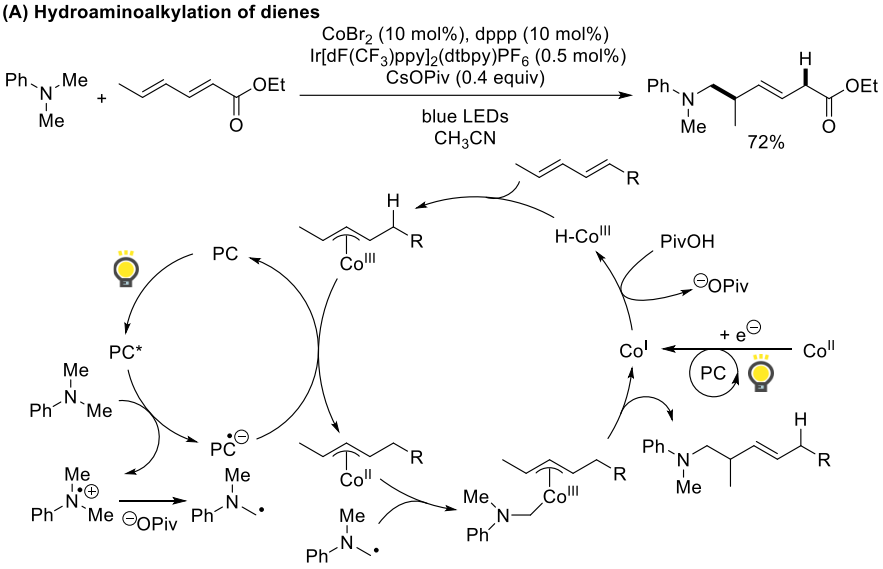
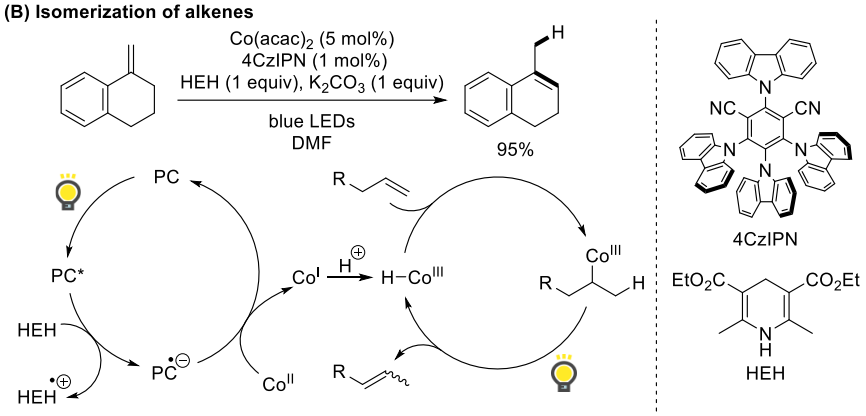

(A) Acceptorless dehydrogenation of alkanes
TBADT (0.4 mol%)
Co(dmgH)2PyCl (0.4 mol%)
UV
CD3CN
19%
+ H2↑
4 Bu4N
TBADT
Co(dmgH)2PyCl
[WO]*
[WO]-H
[Co]
[WO]
H2
[Co]-H
(B) Dehydrogenative dehydroformylation of aldehydes
TBADT (4 mol%)
Co(dmgH)2PyCl (4 mol%)
UV
CD3CN, 4Å M.S.
61%
12%
H2↑
CO↑
– CO
or
(C) Acceptorless dehydrogenation of N-heterocycles
Ru(bpy)3Cl2•6H2O (1 mol%)
Co(dmgH)2PyCl (2 mol%)
blue LEDs
EtOH
96%
96%
+ 2 H2↑
2 Cl
Ru(bpy)3Cl2
Co(dmgH)2PyCl
PC
PC*
PC•⊖
CoIII
CoII
H-CoIII
H2
H⊕, e⊖
– e⊖
– 2H⊕
(D) Dehydrogenative decarboxylefination of carboxylic acids
Ir[dF(CF3)ppy]2(dtbpy)PF6 (1 mol%)
Co(dmgH)2(p-OMePy)Cl (5 mol%)
Cs2CO3 (1 equiv)
blue LEDs
DME/H2O
97%
+
H2↑ CO2↑
Ir[dF(CF3)ppy]2(dtbpy)PF6
Co(dmgH)2(p-OMePy)Cl
– CO2
– H⊕, – e⊖

Figure 3.

(A) Hydroaminoalkylation of dienes



(B) Isomerization of alkenes



(C) Hydroalkenylation of alkenes

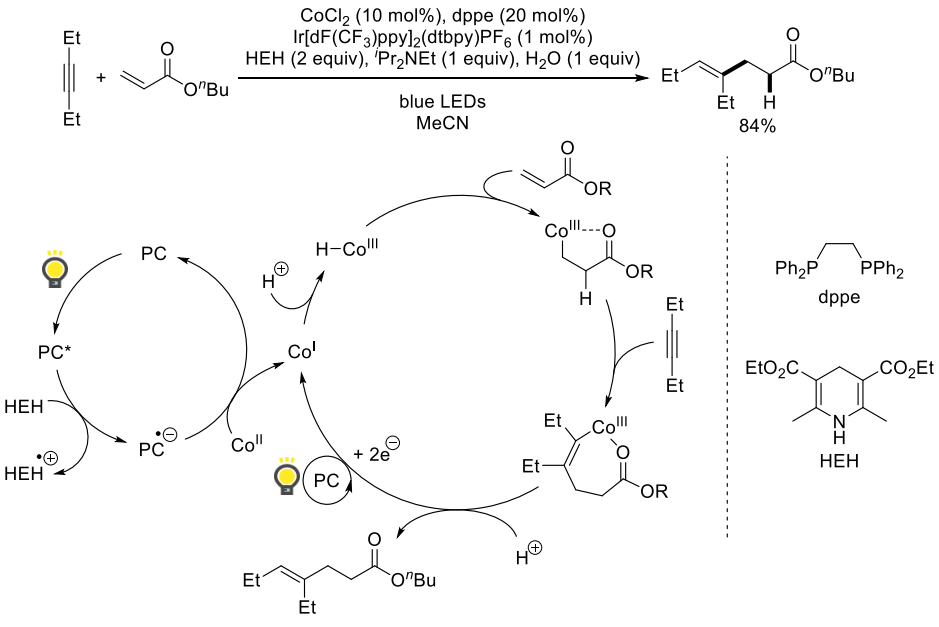


Figure 4.

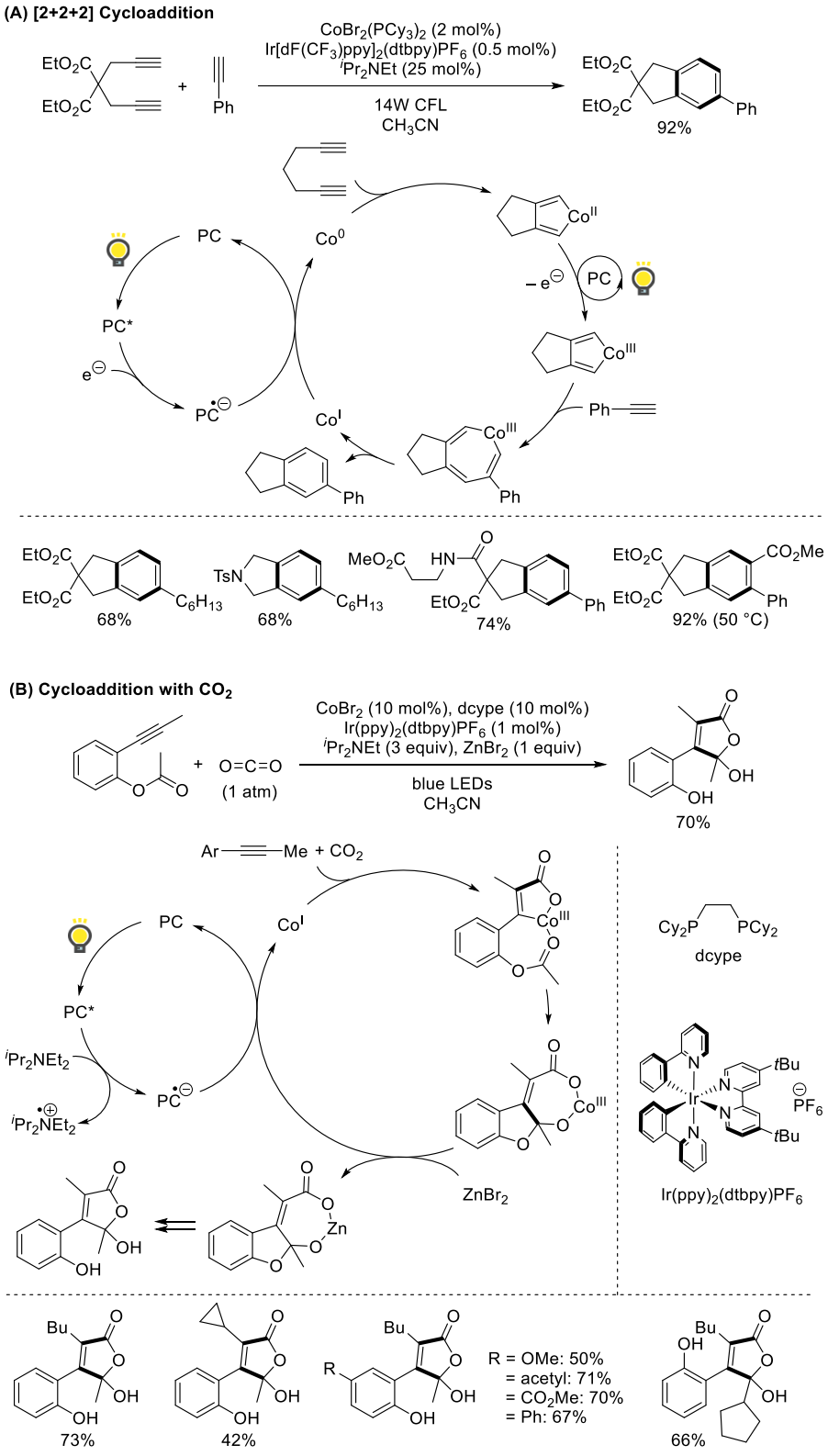

(A) [2+2+2] Cycloaddition
CoBr2(PCy3)2 (2 mol%)
Ir[dF(CF3)ppy]2(dtbpy)PF6 (0.5 mol%)
iPr2NEt (25 mol%)
14W CFL
CH3CN
92%
PC
PC*
Co0
CoII
CoIII
CoI
68%
68%
74%
92% (50 °C)
(B) Cycloaddition with CO2
CoBr2 (10 mol%), dcype (10 mol%)
Ir(ppy)2(dtbpy)PF6 (1 mol%)
iPr2NEt (3 equiv), ZnBr2 (1 equiv)
blue LEDs
CH3CN
(1 atm)
70%
ZnBr2
dcype
Ir(ppy)2(dtbpy)PF6
73%
42%
R = OMe: 50%
= acetyl: 71%
= CO2Me: 70%
= Ph: 67%
66%

Figure 5.

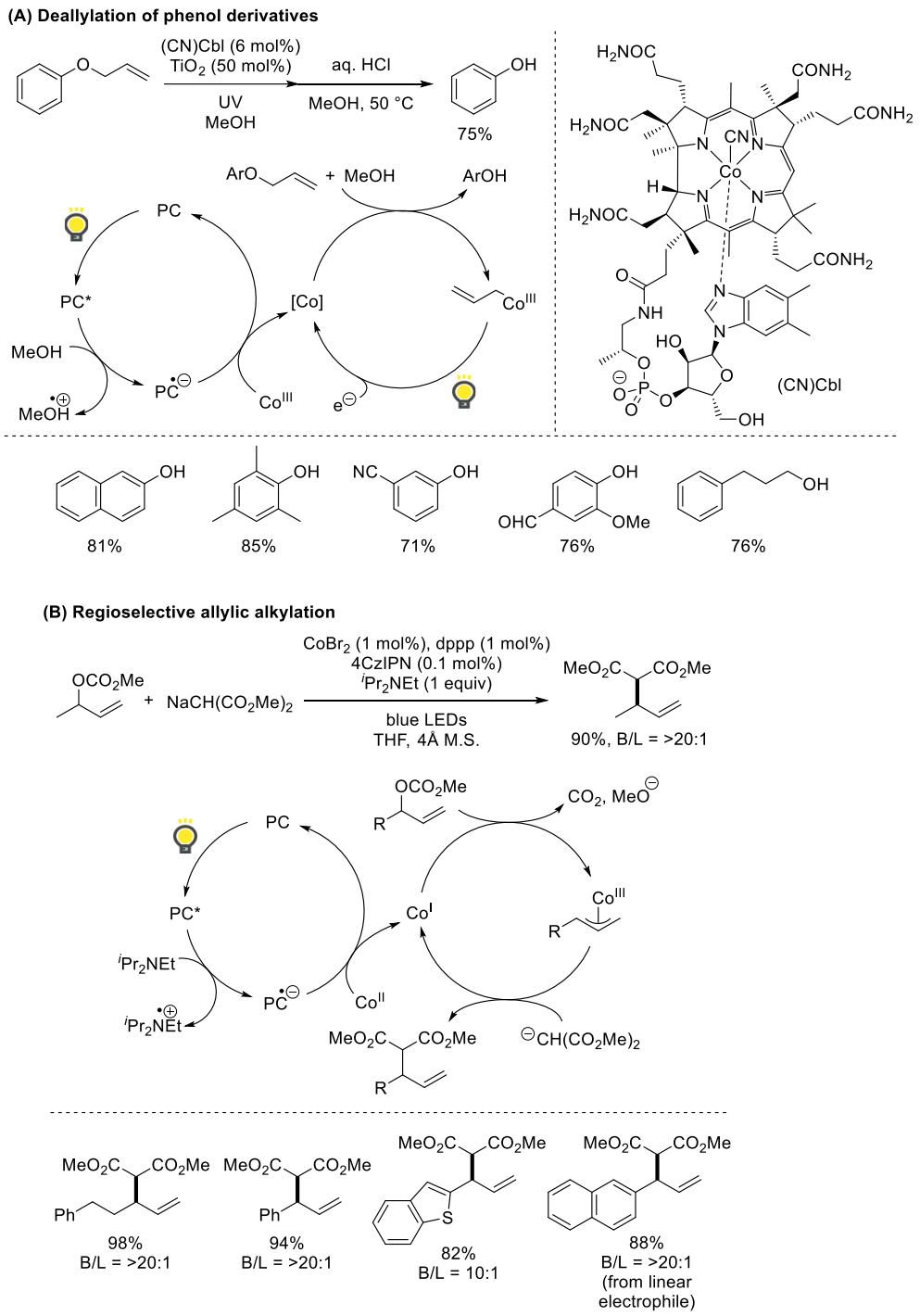

(A) Deallylation of phenol derivatives
(CN)Cbl (6 mol%)
TiO2 (50 mol%)
UV
MeOH
aq. HCl
MeOH, 50 °C
75%
ArO
+ MeOH
ArOH
PC
PC*
MeOH
MeOH
PC
Co^III
[Co]
Co^III
e
H2NOC
CONH2
CN
Co
H
NH
HO
(CN)Cbl
OH
81%
85%
71%
76%
76%
(B) Regioselective allylic alkylation
OCO2Me
+ NaCH(CO2Me)2
CoBr2 (1 mol%), dppp (1 mol%)
4CzIPN (0.1 mol%)
iPr2NEt (1 equiv)
blue LEDs
THF, 4Å M.S.
MeO2C
CO2Me
90%, B/L = >20:1
CO2, MeO
Co^I
Co^III
Co^II
iPr2NEt
CH(CO2Me)2
Ph
S
98%
B/L = >20:1
94%
B/L = >20:1
82%
B/L = 10:1
88%
B/L = >20:1
(from linear
electrophile)

Figure 6.

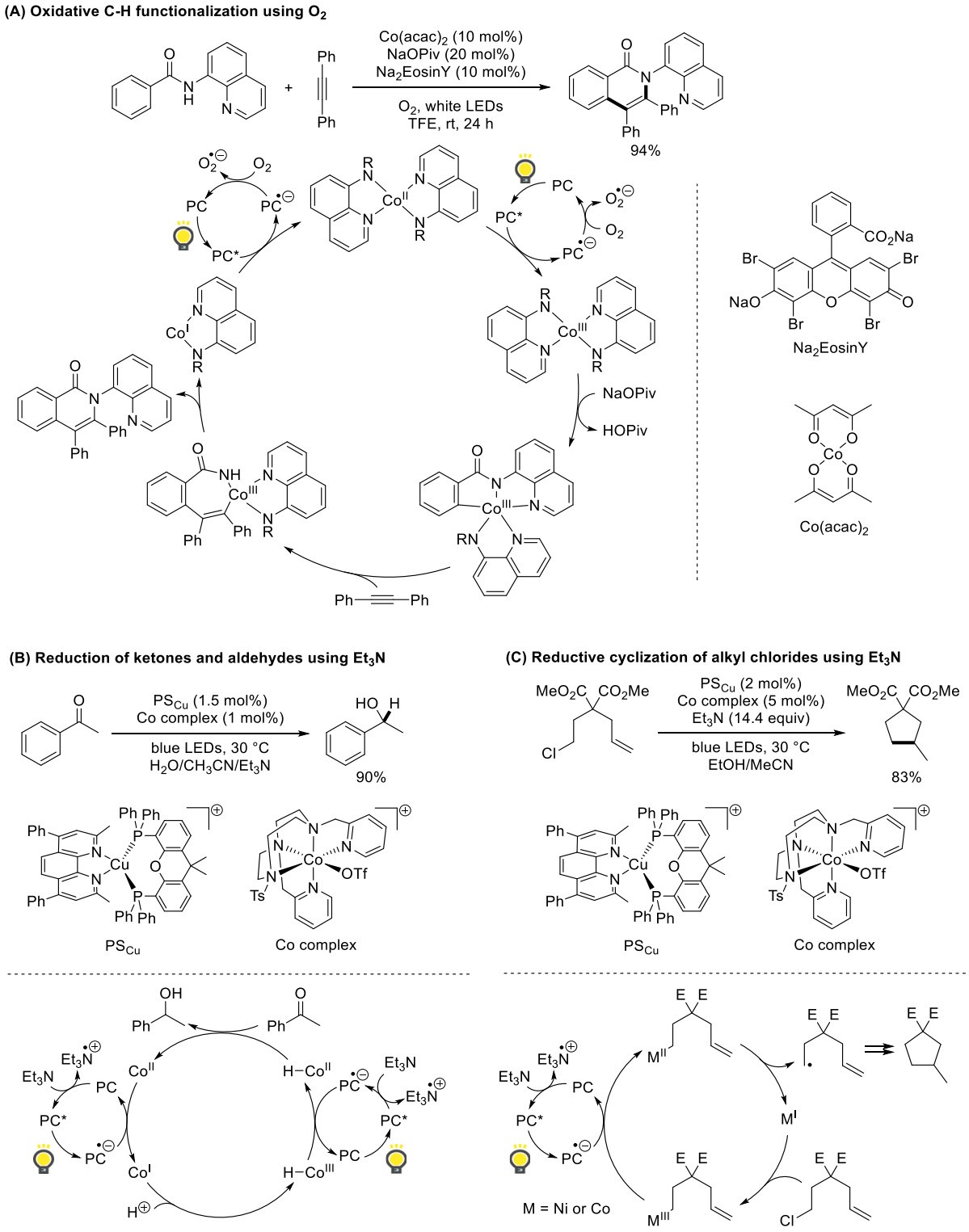

(A) Oxidative C-H functionalization using O2
Co(acac)2 (10 mol%)
NaOPiv (20 mol%)
Na2EosinY (10 mol%)
O2, white LEDs
TFE, rt, 24 h
94%
NaOPiv
HOPiv
Na2EosinY
Co(acac)2
(B) Reduction of ketones and aldehydes using Et3N
PSCu (1.5 mol%)
Co complex (1 mol%)
blue LEDs, 30 °C
H2O/CH3CN/Et3N
90%
PSCu
Co complex
(C) Reductive cyclization of alkyl chlorides using Et3N
PSCu (2 mol%)
Co complex (5 mol%)
Et3N (14.4 equiv)
blue LEDs, 30 °C
EtOH/MeCN
83%
PSCu
Co complex
M = Ni or Co

Figure 7.