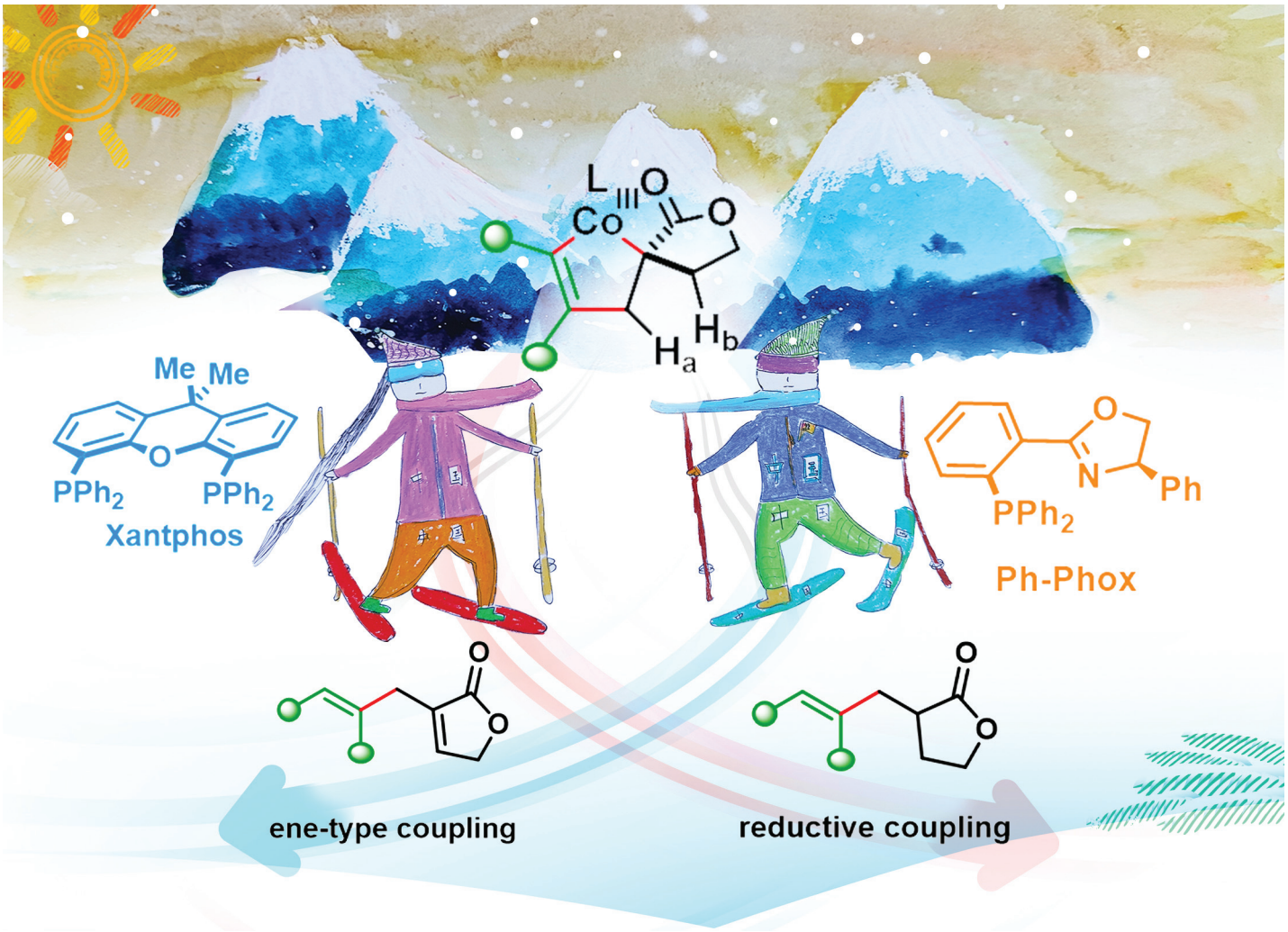

Showcasing research from Professor Ji-Bao Xia's laboratory, State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou, China.

Regio- and stereoselective divergent cross-coupling of alkynes and disubstituted alkenes *via* photoredox cobalt dual catalysis

Ligand-controlled ene-type or reductive coupling of alkynes and *gem*-disubstituted alkenes has been developed by photoredox cobalt dual catalysis. Stereodefined 1,4-dienes or trisubstituted alkenes are obtained by choosing different ligands from the same intermediate.

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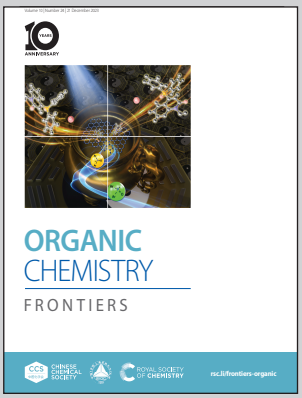

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Regio- and stereoselective divergent cross-coupling of alkynes and disubstituted alkenes *via* photoredox cobalt dual catalysis†

Shi-Qi Zhang,[a,e] Yan-Lin Li,[a] Kun Cui,[a] Chen Chen,[a,e] Zheng-Yang Gu,[c] Hu He*[d] and Ji-Bao Xia*[a,b]

Achieving divergent synthesis from the same substrates quickly to generate different products remains an attractive objective in synthetic chemistry and the medicinal industry. Here, we report a discovery of highly selective divergent cross-coupling of alkynes and disubstituted alkenes by merging visible light photoredox and cobalt catalysis. Under otherwise identical conditions, the use of either a hemilabile P,N-ligand or a strong bidentate diphosphine ligand leads to ene-type coupling or reductive coupling of alkynes and Tulipalin A, producing stereodefined 1,4-diene or trisubstituted alkene products, respectively. The approaches feature considerable advantages for the straightforward synthesis of stereodefined multiple substituted alkenes, such as easily available substrates, low catalyst loading of an organophotocatalyst, excellent regio- and stereoselectivity, good functional group tolerance, and mild reaction conditions. Reasonable catalytic reaction pathways from the same cobaltacyclopentene intermediate have been proposed.

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Introduction

As essential constituents, 2-furanones (butyrolactones) have been found in over 5800 natural compounds and drug molecules and possess diverse biological activities such as anthelmintic, antiviral, antifungal, and anticancer activities (Scheme 1A).[1] Many methods have been developed to access butyrolactones, including the widely used intramolecular esterification or selective oxidation of furan derivatives.[2] Tulipalin A, α-methylene-γ-butyrolactone (MBL), is a structurally simple and commercially available sesquiterpene lactone present in bulb scales of tulips with antibacterial and antitumor properties.[3] Bearing an exo-methylene group at the α-position of lactone, Tulipalin A is considered as a cyclic analog of methyl methacrylate (MMA). Thus, it has been broadly used as a naturally originating vinyl monomer for the synthesis of biocompatible and biodegradable polymers.[4] In addition, Tulipalin A has been used as a reactant in organic synthesis, such as a Michael acceptor or an electron-deficient olefin.[5] However, it is rarely used as an efficient coupling partner in transition-metal-catalyzed cross-coupling reactions. It is suspected that the use of Tulipalin A as a simple synthon to couple with other easily accessed materials would be a straightforward and modular approach to access complex targets containing 2-furanone frameworks.

Transition-metal-catalyzed intermolecular cross-coupling of alkynes and alkenes provides a highly atom- and step-economical route to form C–C bonds with easily accessed materials in organic synthesis.[6] The main challenge of this reaction is the control of its chemo-, regio- and stereoselectivities because diverse products can be obtained *via* a common intermediate **A** of metallacyclopentene generated from oxidative cyclometallation of alkynes and alkenes (Scheme 1B). To minimize the steric strain and reduce the regioisomeric products, less hindered monosubstituted alkenes (α-alkenes) have been mainly used as the substrates. For instance, Ru[7]- or Co-catalyzed[8] ene-type coupling of alkynes and monosubstituted alkyl alkenes produced 1,4-dienes as the favored products *via* exocyclic β-hydride elimination followed by reductive elimination (path a). Through endocyclic β-hydride elimination followed

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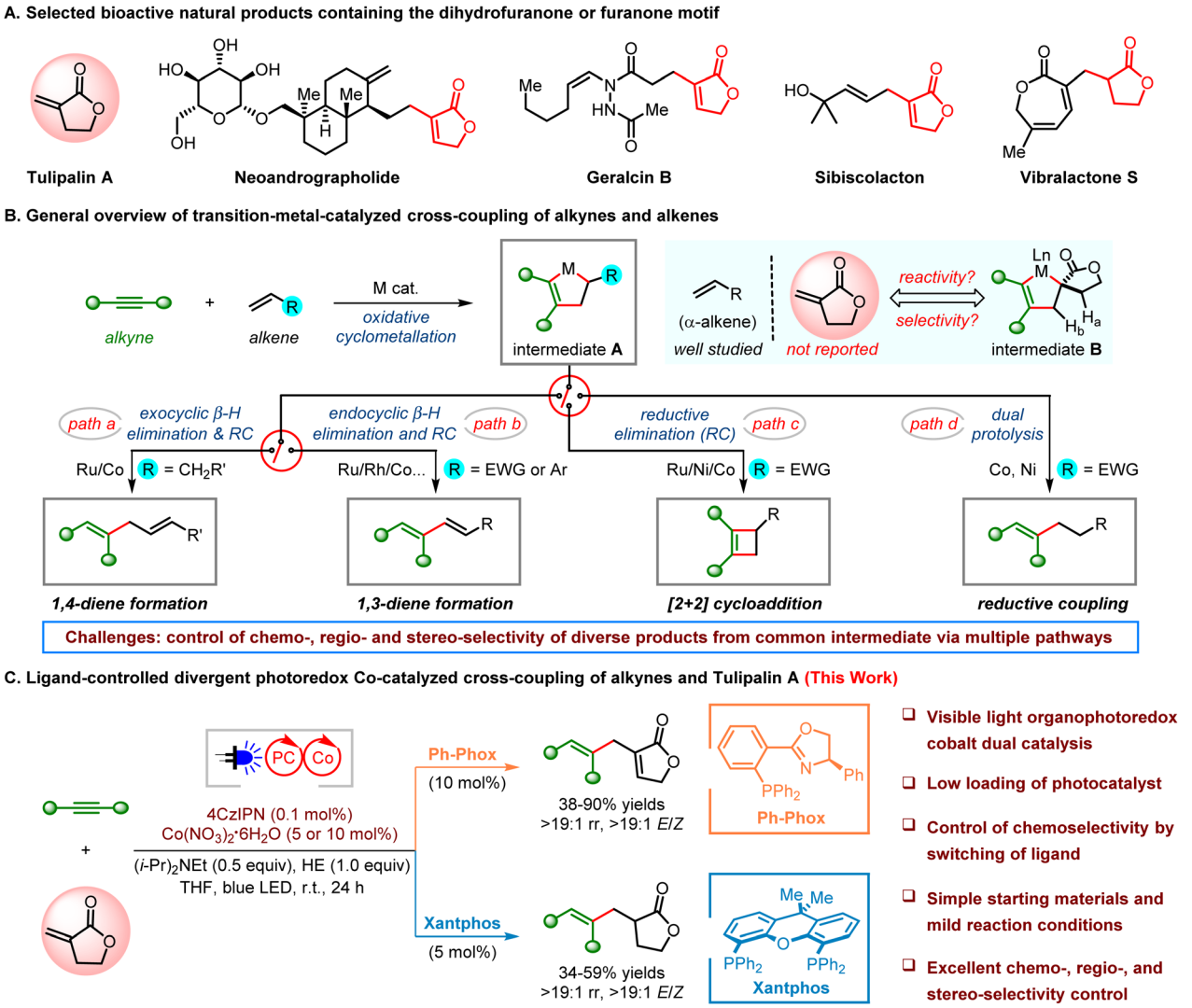


Scheme 1 Transition-metal-catalyzed selective cross-coupling of alkynes and alkenes.

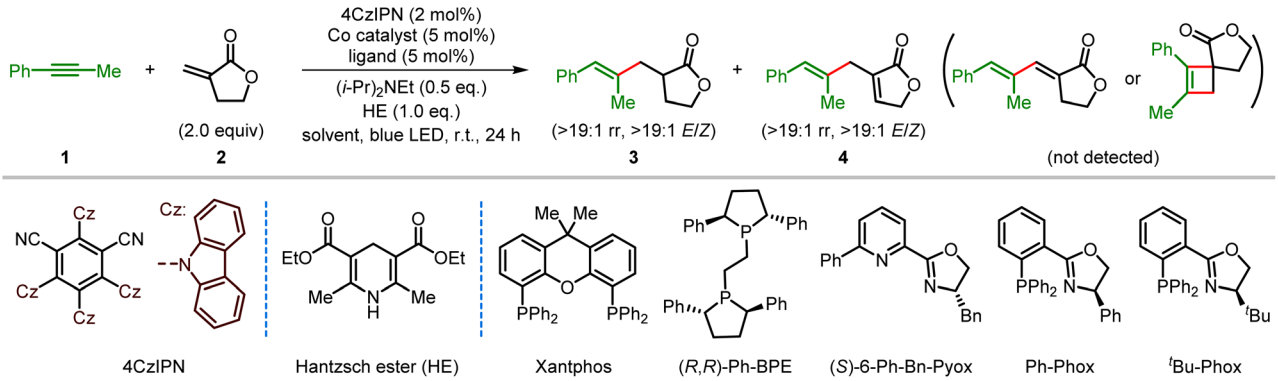
by reductive elimination, 1,3-dienes were obtained using styrenes[9] (Co catalysis) or electron-deficient alkenes (Ni,[10] Rh,[11] Ru[12] or Pd[13] catalysis) as the coupling partners since exocyclic β-hydride does not exist in intermediate **A** (path b). Interestingly, cyclobutenes were favored by coupling monosubstituted electron-deficient alkenes under cobalt catalysis *via* [2 + 2]-cyclization through direct C–C bond reductive elimination of **A** (path c).[14] In addition, Co- or Ni-catalyzed cross-coupling of alkynes and electron-deficient alkenes easily produces multi-substituted alkenes as the reductive coupling products under reducing conditions (path d).[15] Recently, a few elegant examples have been reported other than monosubstituted alkenes. Well-designed multi-substituted alkenes containing a directing group were found to be efficient coupling partners in Ru-catalyzed ene-type coupling with silyl alkynes, or propargyl or homopropargyl alcohols.[16] Symmetrical cyclic alkenes have also been used in Rh- or Co-catalyzed ene-type alkyne/alkene couplings.[17] On the other hand, few examples of Co-catalyzed reductive coupling of alkynes and simple electron-deficient internal alkenes have been reported.[18] We questioned whether simple Tulipalin A could be used as a versatile *gem*-disubstituted alkene to couple with alkynes, providing a direct and concise route to 2-furanone-containing stereodefined alkene targets. Two challenges have been considered in this reaction. First, a crowded spirocyclic metallacyclopentene **B** should be generated, which may cause a strong steric effect. Second, selective control of the coupling product will be attractive but difficult because intermediate **B** could possibly undergo either of the following reaction pathways, exocyclic β-H_a or endocyclic β-H_b elimination, direct reductive elimination, or reductive coupling. Photocatalysis has captured the imagination of both synthetic and medicinal chemists and has become an attractive tool in green synthesis.[19] In particular, photoredox metal dual catalysis has been proved to be a powerful strategy in the synthesis of complex targets under mild reaction conditions.[20,21] Herein, we reported for the first time a photoredox Co-catalyzed regio- and stereoselective ene-type coupling of alkynes and Tulipalin A, a *gem*-disubstituted

alkene, producing 2-furanone-containing 1,4-dienes with excellent control of geometry (Scheme 1C). Moreover, the reductive coupling of alkynes and *gem*-disubstituted alkenes has also be achieved, affording stereodefined trisubstituted alkenes using a different ligand under otherwise identical conditions.

Results and discussion

We started our research by investigating the cross-coupling of unsymmetrical 1-phenyl-1-propyne (**1**) and Tulipalin A (**2**) *via* visible light photoredox cobalt dual catalysis (Table 1). Initially, using the commercially available $CoCl_2$ as the catalyst, Xantphos as the ligand, and 2,4,5,6-tetrakis(carbazol-9-yl)-1,3-dicyanobenzene (4CzIPN) as the organic photocatalyst,[22] the anticipated reductive coupling reaction occurred smoothly, affording the trisubstituted alkene product **3** in 65% yield with >19 : 1 regioselectivity (rr) and >19 : 1 *E*/*Z* stereoselectivity using Hantzsch ester (HE) as an organic reducing reagent in tetrahydrofuran (THF) under 5 W blue LED irradiation (Table 1, entry 1). After extensive screening of a variety of cobalt catalysts, an improved yield was obtained with Co$(NO_3)_2{\cdot}6H_2O$ as the metal catalyst (Table 1, entry 2, also see Table S1 in the ESI†). To our surprise, the ene-type coupling product 1,4-diene **4** was also obtained in 5% yield under these typical reductive coupling conditions. Interestingly, the cross-coupling reaction afforded skipped diene **4** as the major product when *N*,*N*-dimethylformamide (DMF) was used as the solvent, indicating that the reductive coupling or ene-type coupling reaction might be possibly controlled by changing the reaction conditions (Table 1, entry 3). Since one chiral center exist in product **3**, various chiral ligands were then tested to achieve an enantioselective reductive coupling reaction. Unfortunately, low enantioselectivity control was observed with a wide range of chiral phosphine or nitrogen ligands (Table 1, entries 4 and 5; for details see Table S2 in the ESI†). To our delight, the 1,4-diene product **4** was obtained as the major product in 66% yield with >19 : 1 regioselectivity and >19 : 1 *E*/*Z* stereoselectivity when Ph-Phox was used as the ligand under otherwise identical conditions (Table 1, entry 6). The ligand plays an important role in the reaction. No reaction occurred with the structurally similar ^{t}Bu-Phox as the ligand, but dppp gave a similar yield of **4** (Table 1, entries 7 and 8). The yield of product **4** was further increased to 86% after detailed optimizations of the ratio of substrates, the catalyst loadings of the cobalt catalyst and photocatalyst and the amount of HE (Table 1, entries 9–12). Notably, an excellent yield was still maintained when the

Table 1 Summary of the effects of reaction parameters on the reaction efficiency[a]



Entry	Co catalyst	Ligand	Solvent	Yield of **3** [b] (%)	ee of **3** [c] (%)	Yield of **4** [b] (%)
1	$CoCl_2$	Xantphos	THF	65	—	Trace
2	Co$(NO_3)_2{\cdot}6H_2O$	Xantphos	THF	68 (59)	—	5
3	Co$(NO_3)_2{\cdot}6H_2O$	Xantphos	DMF	29	—	46
4	Co$(NO_3)_2{\cdot}6H_2O$	(*R*,*R*)-Ph-BPE	THF	17	5	<5
5	Co$(NO_3)_2{\cdot}6H_2O$	(*S*)-6-Ph-Bn-Pyox	THF	11	12	Trace
6	Co$(NO_3)_2{\cdot}6H_2O$	Ph-Phox	THF	5	—	66
7	Co$(NO_3)_2{\cdot}6H_2O$	^{t}Bu-Phox	THF	0	—	0
8	Co$(NO_3)_2{\cdot}6H_2O$	dppp	THF	Trace	—	62
9[d]	Co$(NO_3)_2{\cdot}6H_2O$	Ph-Phox	THF	5	—	82
10[d,e]	Co$(NO_3)_2{\cdot}6H_2O$	Ph-Phox	THF	<5	—	79
11[d,e,f]	Co$(NO_3)_2{\cdot}6H_2O$	Ph-Phox	THF	<5	—	86 (81)
12[d,e,f,g]	Co$(NO_3)_2{\cdot}6H_2O$	Ph-Phox	THF	<5	—	38
13[d,e]	No Co catalyst	No ligand	THF	0	—	0
14[d,e,f,h]	Co$(NO_3)_2{\cdot}6H_2O$	Ph-Phox	THF	0	—	0

[a] Reaction conditions: **1** (0.2 mmol), **2** (2.0 equiv.), Co catalyst (5 mol%), ligand (5 mol%), 4CzIPN (2 mol%), (*i*-Pr)$_2$NEt (0.5 equiv.), HE (1.0 equiv.), solvent (3.0 mL), 5 W blue LED, r.t., 24 h, unless otherwise noted. [b] Determined by GC with dodecane as an internal standard, and isolated yield is shown in parentheses. [c] Determined by chiral HPLC analysis. [d] With **2** (3.0 equiv.). [e] With 4CzIPN (0.1 mol%). [f] With Co$(NO_3)_2{\cdot}6H_2O$ (10 mol%) and Ph-Phox (10 mol%). [g] With HE (0.5 equiv.). [h] Without light.

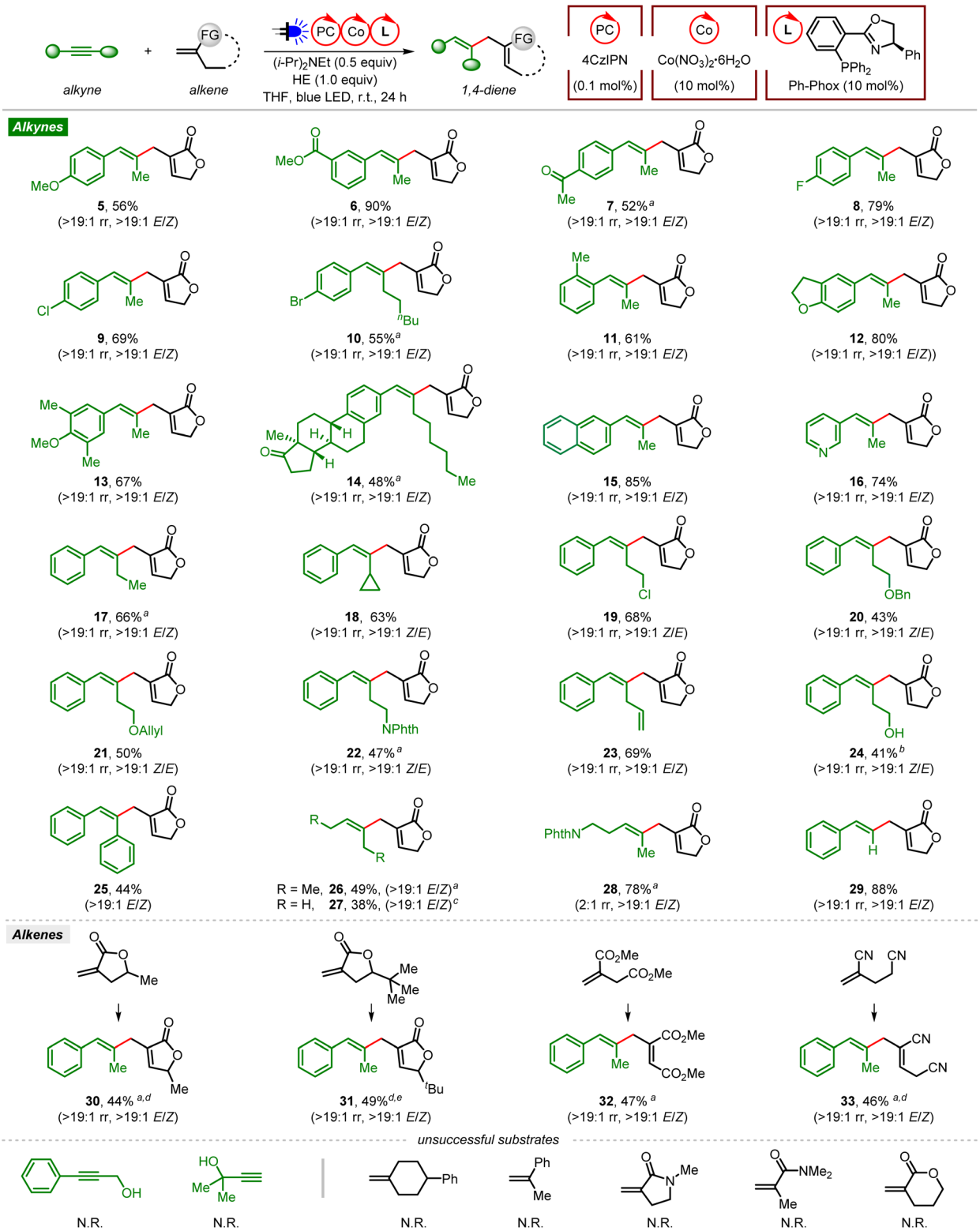


Fig. 1 Reaction scope of organophotoredox Co-catalyzed ene-type coupling of alkynes and alkenes. Reaction conditions: alkyne (0.2 mmol), alkene (3.0 equiv.), 4CzIPN (0.1 mol%), $Co(NO_3)_2{\cdot}6H_2O$ (10 mol%), Ph-Phox (10 mol%), $(i\text{-}Pr)_2NEt$ (0.5 equiv.), HE (1.0 equiv.), THF (3.0 mL), 5 W blue LED, r.t., 24 h, isolated yield, unless otherwise noted. [a] With 4CzIPN (2 mol%). [b] With TMS-protected homopropargylic alcohol as the substrate. [c] With 2-butyne (50 equiv., 1 mL, 10 M solution in THF). [d] With DMF as the solvent. [e] With 4CzIPN-Br (2 mol%) as the photocatalyst.

catalyst loading of 4CzIPN was decreased to 0.1%. It should be noted that the 1,3-diene or cyclobutene product was not observed under the tested conditions. Finally, control experiments demonstrate that no reductive coupling or ene-type coupling product was observed in the absence of a cobalt catalyst, ligand, photocatalyst, or light, which means that they are all required for the progression of the current cross-coupling reactions (Table 1, entries 13 and 14, also see Table S8 in the ESI†).

With the optimized reaction conditions in hand, we first examined the generality of the ene-type coupling of alkynes and *gem*-disubstituted alkenes leading to 1,4-dienes *via* visible light organophotoredox cobalt dual catalysis (Fig. 1). In general, excellent regio- (>19 : 1 rr) and stereoselectivities (>19 : 1 *E*/*Z* or *Z*/*E*) were obtained. Coupling of aryl alkyl alkynes and Tulipalin A produced the desired products **5–7** in 52–90% yields, tolerating electron-donating (OMe) and electron-withdrawing (CO_2Me, Ac) groups at the *meta*- or *para*-position of the aryl ring. Halide (F, Cl, Br) groups are also tolerated to give the corresponding 1,4-dienes in good yields (**8–10**). Aryl methyl alkynes bearing a bulky *ortho*-methyl group on the aryl ring (**11**) or a multi-substituted aryl substituent reacted smoothly, indicating good steric compatibility in this transformation (**12** and **13**). The alkyne derived from a natural steroid was a suitable coupling partner (**14**), demonstrating the utility of this reaction for the late-stage functionalization of complex molecules. In addition, an internal alkyne containing a naphthalene or pyridine group was also compatible, generating the corresponding product **15** or **16** in a good yield with excellent regio- and stereoselectivity.

Besides, ene-type coupling of Tulipalin A and terminal alkyl group (ethyl or cyclopropyl) substituted phenylacetylene also occurred smoothly, giving the desired products **17** and **18.** A variety of functional groups on the alkyl chain of the phenyl alkyl alkynes, such as halogen (Cl), ether (OBn, OAllyl), imide (Phth, phthalimide), and terminal alkene, were well tolerated, leading to the corresponding products in moderate to good yields (**19–23**). Notably, the free alcohol product **24** was obtained when trimethylsilyl (TMS)-protected homopropargylic alcohol was used as the substrate, with the removal of the TMS protecting group during isolation using flash column chromatography on silica gel.

Next, we tested symmetrical internal alkynes, such as diphenylethyne, 3-hexyne and 2-butyne, in this cross-coupling reaction. They reacted smoothly with Tulipalin A, affording the corresponding products in moderate yields (**25–27**). When the unsymmetrical dialkyl alkyne PhthN-substituted 2-pentyne was used as the substrate, 1,4-diene **28** was obtained in 78% yield albeit with low regioselectivity (2 : 1 rr). Notably, the terminal alkyne phenylacetylene was also proved to be a suitable coupling partner in this reaction, producing **29** in a good yield with excellent regio- and stereoselectivity. However, no reaction occurred with internal or terminal propargylic alcohol under the standard conditions. Then the scope of *gem*-disubstituted alkenes was explored. The *O*-alpha alkyl (methyl and *tert*-butyl) substituted Tulipalin A analogs were successfully employed as the substrates, affording the desired products in moderate yields with excellent regio- and stereoselectivities (**30** and **31**). Linear alpha-alkyl substituted acrylate and acrylonitrile were also suitable coupling partners, leading to functionalized 1,4-

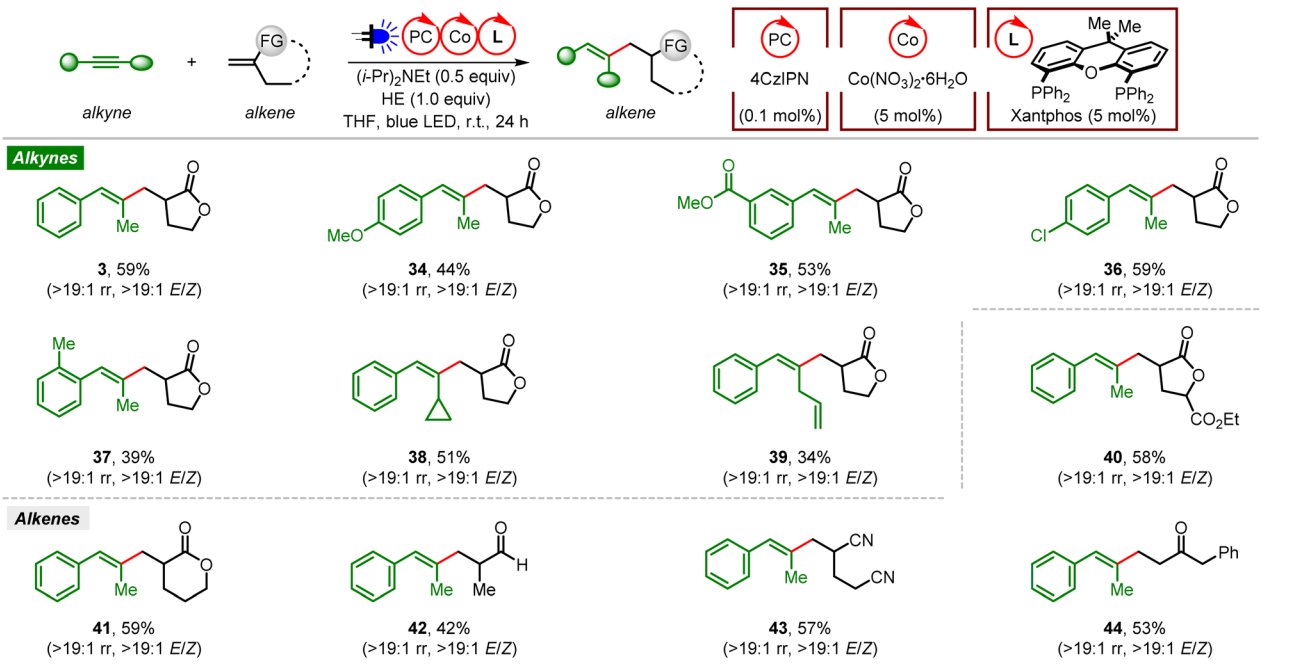


Fig. 2 Reaction scope of organophotoredox Co-catalyzed reductive coupling of alkynes and alkenes. Reaction conditions: alkyne (0.2 mmol), alkene (3.0 equiv.), 4CzIPN (0.1 mol%), $Co(NO_3)_2{\cdot}6H_2O$ (5 mol%), Ph-Phox (5 mol%), $(i\text{-}Pr)_2NEt$ (0.5 equiv.), HE (1.0 equiv.), THF (3 mL), 5 W blue LED, r.t., 24 h, isolated yield.

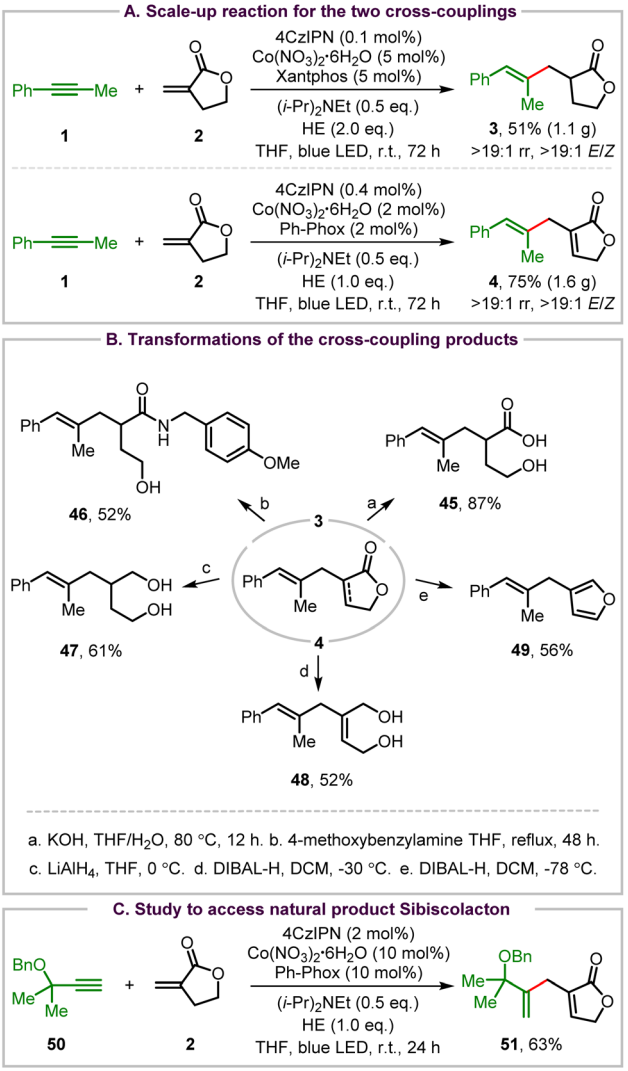
dienes with excellent regio- and stereoselectivities (**32** and **33**). A variety of other *gem*-disubstituted alkenes have also been investigated in this ene-type coupling, such as 1,1-dialkyl substituted ethene, α-methylstyrene, cyclic or linear acrylamide, and 2-methylene-5-pentanolide. Unfortunately, no desired product was observed with these substrates.

We then examined the scope of organophotoredox Co-catalyzed reductive coupling of alkynes and *gem*-disubstituted alkenes (Fig. 2). Generally, stereodefined trisubstituted alkenes were obtained with excellent regio- (>19 : 1 rr) and stereoselectivities (>19 : 1 *E*/*Z*). A variety of unsymmetrical aryl alkyl alkynes bearing diverse functional groups (*p*-OMe, *m*-COOMe, *p*-Cl, and *o*-Me) on different sites of the phenyl ring were found to be efficient coupling partners, affording the desired reductive coupling products in moderate yields (**34**–**37**). Similar to the ene-type coupling reaction, reductive coupling of a cyclopropane-containing alkyne and Tulipalin A produced the corresponding product **38** without ring-opening of cyclopropane. Moreover, a terminal alkene on the side alkyl chain of a phenyl alkyl alkyne was also tolerated in this reductive coupling reaction (**39**).

On the other hand, various *gem*-disubstituted alkenes were tested with 1-phenylpropyne under these conditions. Reductive coupling of alkynes with analogs of Tulipalin A or 2-methylene-5-pentanolide proved to be successful, affording the corresponding products in good yields (**40** and **41**). Methacrolein and linear alpha-alkyl substituted acrylonitrile were also compatible in this reaction (**42** and **43**). Furthermore, reductive coupling of 1-phenylpropyne and a simple vinyl ketone also occurred smoothly, leading to the desired product **44** in a moderate yield. Unfortunately, no reductive coupling occurred with 1,1-dialkyl substituted ethene, α-methylstyrene, or cyclic or linear acrylamide either.

A variety of synthetic transformations have been carried out to demonstrate the synthetic uses of the two organophotoredox Co-catalyzed cross-coupling reactions (Scheme 2). First, scale-up reactions of both cross-couplings were performed for the synthesis of **3** and **4** (Scheme 2A). The scale-up reductive coupling reaction produced the stereodefined trisubstituted alkene **3** in 51% yield with >19 : 1 regioselectivity and >19 : 1 *E*/*Z* stereoselectivity under the standard conditions. The scale-up ene-type coupling reaction also occurred smoothly, affording the desired product **4** in 75% yield without any loss of regio- and enantioselectivity control using 2 mol% Co $(NO_3)_2{\cdot}6H_2O$/Ph-Phox as the catalyst with a slight increase of the catalyst loading of 4CzIPN (0.4 mol%).

Then, selective transformations of the reductive coupling and ene-type coupling products were investigated. Hydrolysis of the reductive coupling product **3** provided γ-hydroxy carboxylic acid **45** in an excellent yield (Scheme 2Ba). And aminolysis of **3** with 4-methoxybenzylamine afforded γ-hydroxy amide **46** in a moderate yield with incomplete conversion of **3** (Scheme 2Bb). Next, reduction of the 2-furanone group of the ene-type coupling product **4** with $LiAlH_4$ afforded alkene-containing 1,4-diol **47** in 61% yield (Scheme 2Bc). However, reduction of 2-furanone of **4** with DIBAL-H at −30 °C generated

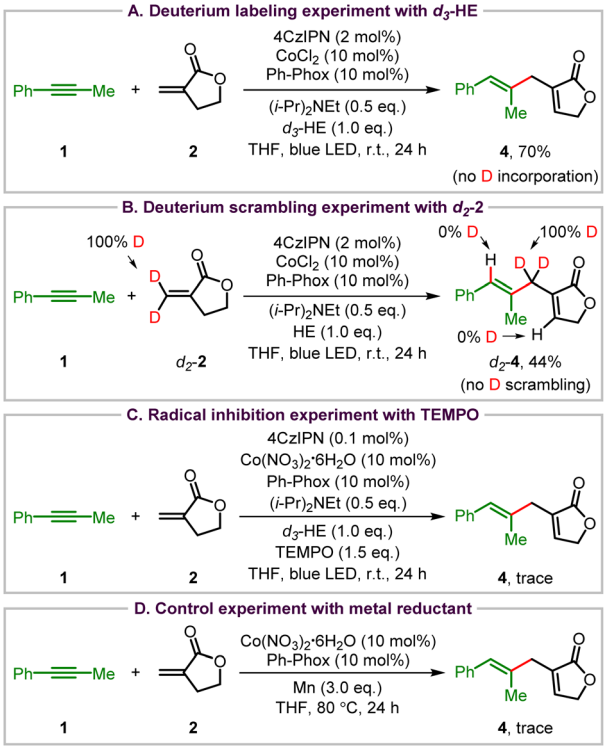


Scheme 2 Synthetic applications.

allylic diol **48** in 52% yield (Scheme 2Bd). Interestingly, a reductive isomerization of **4** took place, leading to furan-containing trisubstituted alkene **49** in 56% yield when the reaction was performed with DIBAL-H at −78 °C (Scheme 2Be).

Although 2-methyl-3-butyn-2-ol failed to produce the ene-type coupling product, its benzyl-protected derivative **50** was further tested for coupling with Tulipalin A to access the natural product sibiscolacton (Scheme 1A).[23] Interestingly but unfortunately, selective ene-type coupling at the internal sp carbon of this terminal alkyne occurred smoothly, leading to product **51** in 63% yield (Scheme 2C). This result also indicates that the regioselectivity control of an alkyne is determined by both the electronic and steric effect of the substituents.

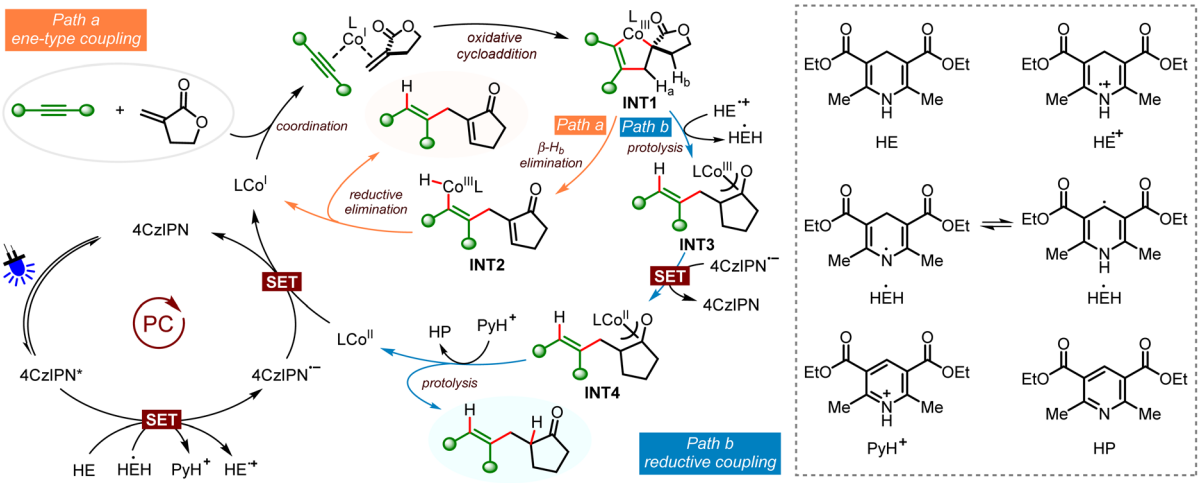
To explore the reaction mechanism of this visible light organophotoredox Co-catalyzed cross-coupling reaction, a range of control experiments were conducted (Scheme 3). First, deuterium labeling experiments were carried out using d_3-HE with $CoCl_2$ as the catalyst to exclude the influence of



Scheme 3 Control experiments and mechanistic studies.

water in $Co(NO_3)_2·6H_2O$ under the standard conditions. The 1,4-diene **4** was obtained without any deuterium atom incorporation in the presence of d_3-HE, indicating that HE does not provide the hydrogen atom in the ene-type coupling reaction (Scheme 3A). When d_2-Tulipalin A (d_2-**2**) was used as the coupling partner, there was no deuterium atom scrambling, with deuterium totally maintained at the methylene carbon of the Tulipalin A motif (Scheme 3B). These results demonstrate that the transfer of the allylic C–H of Tulipalin A to the alkyne triple bond might take place in this reaction. Then a radical inhibition experiment was also carried out with 2,2,6,6-tetramethylpiperidinyloxy (TEMPO) as the radical trapping reagent. Although the radical trapping product was not observed, the ene-type reaction was indeed suppressed, revealing that some free radical intermediates might exist in this reaction (Scheme 3C). Finally, Co-catalyzed cross-coupling of **1** and **2** was carried out using excess amounts of manganese powder as the reductant. A trace amount of **4** was observed, which indicates the high efficiency of the photoredox cobalt dual catalytic system (Scheme 3D).

Based on the control experiments and previous reports, we have proposed the possible catalytic cycles of the two coupling reactions (Scheme 4). With coupling of Tulipalin A as the example, upon irradiation with blue LED light, single electron oxidation of HE [$E^{ox}_{1/2}$ (HE/HE$^{\bullet+}$) = +0.51 V *vs.* Fc^+/Fc in MeCN][24] with photoexcited 4CzIPN* produces HE$^{\bullet+}$ and 4CzIPN$^{\bullet-}$[$E^{red}_{1/2}$(4CzIPN*/4CzIPN$^{\bullet-}$) = +1.43 V *vs.* SCE in MeCN].[22] Next, reduction of the ligand coordinated Co(II) complex [$E^{red}_{1/2}$ (Co^{II}/Co^{I}) = −0.75 V *vs.* SCE in MeCN][21c] with 4CzIPN$^{\bullet-}$ [$E^{red}_{1/2}$ (4CzIPN/4CzIPN$^{\bullet-}$) = −1.24 V *vs.* SCE in MeCN][25] affords the low valent Co(I) species and regenerates 4CzIPN. Then coordination of the alkyne and Tulipalin A to the Co(I) species followed by oxidative cyclization gives the crowded spirocyclic cobaltacyclopentene **INT 1**, which is the common intermediate of the two cross-couplings. The selective control of the ene-type coupling or reductive coupling is achieved by using different ligands. Using hemilabile Ph-Phox as the ligand, the alkenyl Co^{III}–H species **INT 2** is formed by exocyclic β-H_b elimination (Path a). The following reductive elimination affords the 1,4-diene product and regenerates the Co^{I} catalyst. The 1,3-diene product from endocyclic β-hydride elimination is not observed, probably due to cobalt and β-H_a is not in a *syn* coplanar arrangement. It is supposed that β-H_b elimination is much faster than β-H_a elimination in the spirocyclic cobaltacyclopentene **INT 1**. On the other hand, when Xantphos is used as the ligand, protolysis of **INT 1** with HE$^{\bullet+}$ takes place, generating HEH$^{\bullet}$[21c] and the α-carbonyl alkyl Co^{III}



Scheme 4 The proposed reaction pathway.

species **INT 3**, which can be stabilized by the isomerized cobalt enolate (Path b). Next, the strong electron donor HEH$^{\bullet}$ (E^{ox} = −1.13 V *vs.* SCE) can also donate a radical to 4CzIPN*, leading to 4CzIPN$^{\bullet-}$ and the pyridinium ion PyH^{+}.[26] Furthermore, single electron reduction of Co^{III} species **INT 3** with 4CzIPN$^{\bullet-}$ affords Co^{II} species **INT 4** [$E^{red}_{1/2}$ (Co^{III}/Co^{II}) = −0.51 V *vs.* Fc^{+}/Fc] and 4CzIPN.[27] Finally, protonation of the alkyl Co(II) species **INT 4** with PyH^{+} produces a stereodefined alkene as the reductive coupling product and HP as the by-product. It is surprising and interesting that the β-hydride elimination occurs efficiently under this photoredox reductive conditions in the presence of a suitable ligand.

Conclusions

In summary, we reported here the first general method of ligand-controlled ene-type or reductive coupling of alkynes and *gem*-disubstituted alkenes *via* visible light organophotoredox cobalt dual catalysis. Using the natural product Tulipalin A and other *gem*-disubstituted alkenes to couple with internal or terminal alkynes, functionalized 1,4-dienes have been obtained *via* ene-type coupling in moderate to good yields with excellent chemo-, regio-, and stereoselectivities using a PHOX ligand. Similarly, stereodefined trisubstituted alkenes were synthesized *via* reductive coupling with Xantphos as the ligand under otherwise similar conditions. Notably, as low as a thousandth of a commercially available organic photocatalyst has been used to efficiently catalyze the two coupling reactions. In general, this study shows that coupling of alkynes with multi-substituted alkenes is much difficult compared to well-studied monosubstituted alkenes.

Conflicts of interest

There are no conflicts to declare.

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