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Photo-Induced Decarboxylative Heck-Type Coupling of Unactivated Aliphatic Acids and Terminal Alkenes in the Absence of Sacrificial Hydrogen Acceptors

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ABSTRACT: 1,2-Disubstituted alkenes such as vinyl arenes, vinyl silanes, and vinyl boronates are among the most versatile building blocks that can be found in every sector of chemical science. We herein report a noble-metal-free method of accessing such olefins through a photo-induced decarboxylative Heck-type coupling using alkyl carboxylic acids, one of the most ubiquitous building blocks, as the feedstocks. This transformation was achieved in the absence of external oxidants through the synergistic combination of an organo photoredox catalyst and a cobaloxime catalyst, with H_2 and CO_2 as the only by-products. Both control experiments and DFT calculations supported a radical-based mechanism which eventually led to the development of a selective three-component coupling of aliphatic carboxylic acids, acrylates and vinyl arenes. More than 90 olefins across a wide range of functionalities were effectively synthesized with this simple protocol.

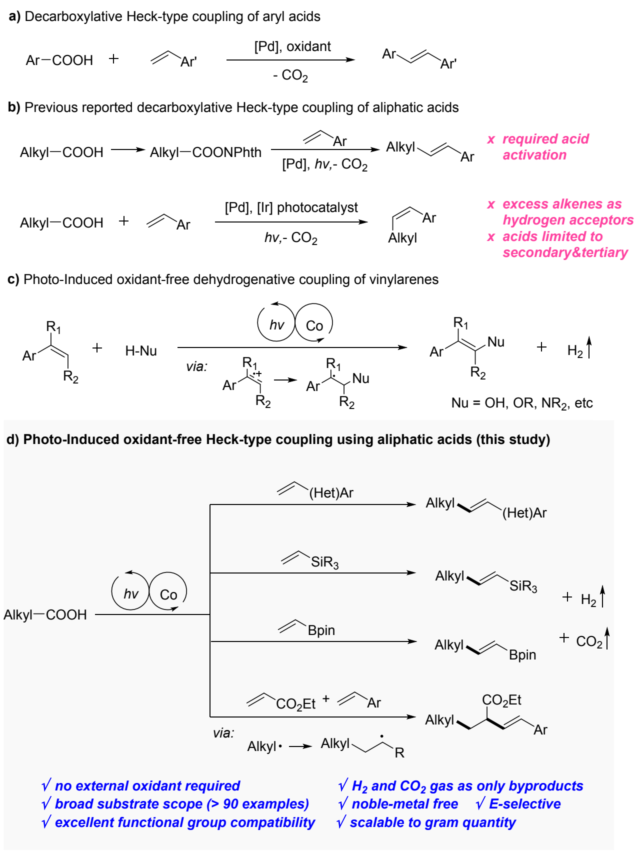
INTRODUCTION

The Mizoroki-Heck reaction, which allows coupling of olefins with organohalides, is among the most powerful methods for the synthesis of substituted alkenes.[1] However, compared to organohalides, carboxylic acids are more naturally abundant and readily available, inexpensive, non-toxic and more stable, representing exceptionally useful feedstocks for coupling reactions. Although many reports on transition-metal-catalyzed decarboxylative Heck-type coupling of carboxylic acids have been published since the pioneering study in 2002 by Myers et. al.,[2] the reported scope was mainly limited to aryl carboxylic acids (Scheme 1a) due to the inaccessibility and instability of alkyl metallic intermediates derived from aliphatic acids.[3] The need to overcome this restriction is further underscored by the limited success of Heck coupling using aliphatic halides, especially the substrates possessing hydrogen at the β position to the halide atom.[4]

Photocatalysis has witnessed dramatic developments over the past decade which have enabled previously inaccessible synthetic transformations.[5] For instance, alkyl radicals can be easily accessed from aliphatic carboxylic acids or their derivatives by a photoredox-mediated single-electron-transfer (SET) and CO_2-extrusion mechanism.[6] Recently, Fu[7] and Glorius[8] have achieved photo-induced Pd-catalyzed decarboxylative Heck-type coupling of redox-active esters in a redox-neutral manner (Scheme 1b). However, the Heck-type coupling of unactivated aliphatic acids involves loss of two electrons and two protons, hence requiring stoichiometric oxidants which is an obstruction for large-scale production. The Shang and Na group has employed excess vinyl arenes as the hydrogen acceptor to achieve the first decarboxylative Heck-type coupling of unactivated aliphatic acids through the merger of an Ir photoredox catalyst and a Pd catalyst (Scheme 1b).[9] Nonetheless, a stoichiometric amount of alkene hydrogenation side products was generated which could complicate the purification afterwards, and the substrate scope was limited to certain secondary/tertiary aliphatic carboxylic acids and vinyl arenes. As a consequence, a method for decarboxylative Heck-coupling of unactivated aliphatic acids, that does not require stoichiometric additives and can be applied to a broad range of substrate patterns, is highly attractive and desirable.

In this context, we were attracted by the cobaloxime catalysts due to their intriguing properties: i) cobalt as an earth-abundant transition-metal catalyst; ii) associated rich radical chemistry;[10] iii) excellent proton reduction reactivity;[11] iv) broad functional group tolerance; v) privileged in merging with photoredox catalysis.[11-14] The radical chemistry involving cobaloximes has attracted much attention since the early 1960s.[15] The unique ability of these complexes to form alkyl cobalt derivatives, in combination with the ease of homolysis of the C–Co bonds under visible-light-irradiation to form alkyl radicals, has led to the development of various transformations, including an efficient cobaloxime-catalyzed intramolecular Heck coupling of alkyl halides and alkenes, which avoided the β-elimination problem encountered in Pd-catalysis.[10c] More recently, Wu and Lei have developed external oxidant-free cross-dehydrogenative-coupling reactions through the synergistic merging of a photoredox catalyst and a cooperative cobaloxime catalyst as the proton reduction catalyst (Scheme 1c).[12-14] Chemical waste from the use of oxidants was therefore avoided with hydrogen gas as the sole byproduct, and many oxidant-sensitive functionalities could be tolerated. However, the reaction patterns for this type of transformations remain limited.[16] We herein report that through the merging of an organo acridinium photocatalyst and a cobaloxime catalyst, the decarboxylative Heck-type coupling of alkyl carboxylic acids with vinyl arenes or heteroarenes proceeded efficiently in the presence of a catalytic amount of base under blue LED irradiation. This protocol was applicable to various commercially available vinyl silanes and vinyl boronates, which represents the first example of Heck-type coupling of alkyl partners with vinyl silanes and vinyl boronates. A radical mechanism was proposed based on control experiments and DFT calculations, which led to the development of a selective three-component coupling of aliphatic carboxylic acids, acrylates, and vinyl arenes (Scheme 1d). In addition, this strategy exhibits broad scope across a range of both carboxylic acid (primary, secondary, and tertiary) and olefin (from electron-poor to electron-rich) coupling partners, tolerating extremely broad functionalities, and is distinguished by its noble-metal-free character and the absence of harmful by-products.

Scheme 1. Decarboxylative Heck-Type Coupling

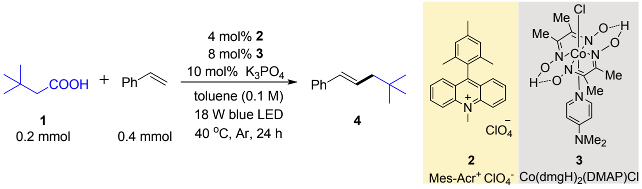


Bpin = boronic acid pinacol ester.

RESULTS AND DISCUSSION

Reaction Optimization. Our study was initiated by an investigation of 3,3-dimethyl-butanoic acid (**1**) and styrene as model substrates for the decarboxylative Heck-type coupling in the presence of a photoredox catalyst and a cobaloxime catalyst under blue LED irradiation. After extensive evaluation (Table 1 and Tables S1-S9), we established that the combination of acridinium **2** (4 mol%), Co(dmgH)$_2$(DMAP)Cl **3** (8 mol%), and K$_3$PO$_4$ (10 mol%) in toluene (0.1 M) at 40 ˚C was optimal, affording disubstituted alkene **4** in 82% isolated yield with an *E*/*Z* ratio of 15:1 (Table 1, entry 1). It was noted that the reaction system did not require any external oxidant, and H$_2$ and CO$_2$ constituted the only by-products (Figure S16), which rendered this decarboxylative coupling highly sustainable. The possibility of styrene serving as hydrogen acceptor was ruled out as ethylbenzene was not detected. The acridinium perchlorate (**2**) was the only effective photocatalyst and no reaction occurred with other photocatalysts including common Ru/Ir metallic catalysts (Table 1, entry 2) or other organophotocatalysts (Table S4). Co(dmgH)$_2$PyCl and Co(dmgH)$_2$(4-COOMePy)Cl were less effective than cobaloxime **3** (Table 1, entries 3 and 4). Switching reaction solvent from toluene to MeCN or PhCF$_3$ produced product **4** in much lower yields (entries 5 and 6). A survey of inorganic and organic bases (Table 1, entries 7-9, and Table S2) revealed that K$_3$PO$_4$ was the best choice. The amount of base was crucial, as an increased loading of K$_3$PO$_4$ led to lower yield of the product (Table 1, entry 10). The coupling proceeded more slowly at ambient temperature (entry 11). Good yield of product **4** could also be obtained when styrene was employed as the limiting reagent with 2 equiv of acid **1** (entry 12), demonstrating the practicality of this protocol for functionalization of an alkene which is of particular value. No product was detected in the absence of photocatalyst **2**, cobaloxime **3**, K$_3$PO$_4$, or light, demonstrating the need for all these components (entry 13). It is important to note that replacement of the cobaloxime catalyst with stoichiometric amounts of oxidants such as O$_2$, Na$_2$S$_2$O$_8$, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), MnO$_2$, or di-tert-butyl peroxide (DTBP) gave no desired product **4** (Table S10), highlighting the unique nature of the photoredox/cobalt dual catalytic system.

Table 1. Selected Optimization Results



entry	deviation	yield^a (*E*/*Z*)^b
1	no	83, 82^c (15:1)
2	Ru(bpy)$_3$Cl$_2$•6H$_2$O or [Ru(bpz)$_3$][PF$_6$]$_2$ or Ir(dF-CF$_3$ppy)$_2$(dtbbpy)PF$_6$ instead of **2**	0
3	Co(dmgH)$_2$PyCl instead of **3**	81 (13:1)
4	Co(dmgH)$_2$(4-COOMePy)Cl instead of **3**	65 (15:1)
5	MeCN as solvent	12 (13:1)
6	PhCF$_3$ as solvent	61 (15:1)
7	10 mol % Na$_3$PO$_4$ as base	68 (13:1)
8	10 mol % Cs$_2$CO$_3$ as base	28 (11:1)
9	10 mol % TBA-OH as base	20 (12:1)
10	30 mol % K$_3$PO$_4$ as base	47 (15:1)
11	r.t. instead of 40 ˚C	56 (15:1)
12	0.4 mmol **1**, 0.2 mmol styrene, 36 h	83 (15:1)
13	without **2** or **3** or K$_3$PO$_4$ or light	0

^{a}Yields were determined from the crude ^{1}H NMR spectra using 1,3,5-trimethoxybenzene as an internal standard. ^{b}*E*/*Z* ratios were determined by GC analysis of the crude mixtures. ^{c}Isolated yield.

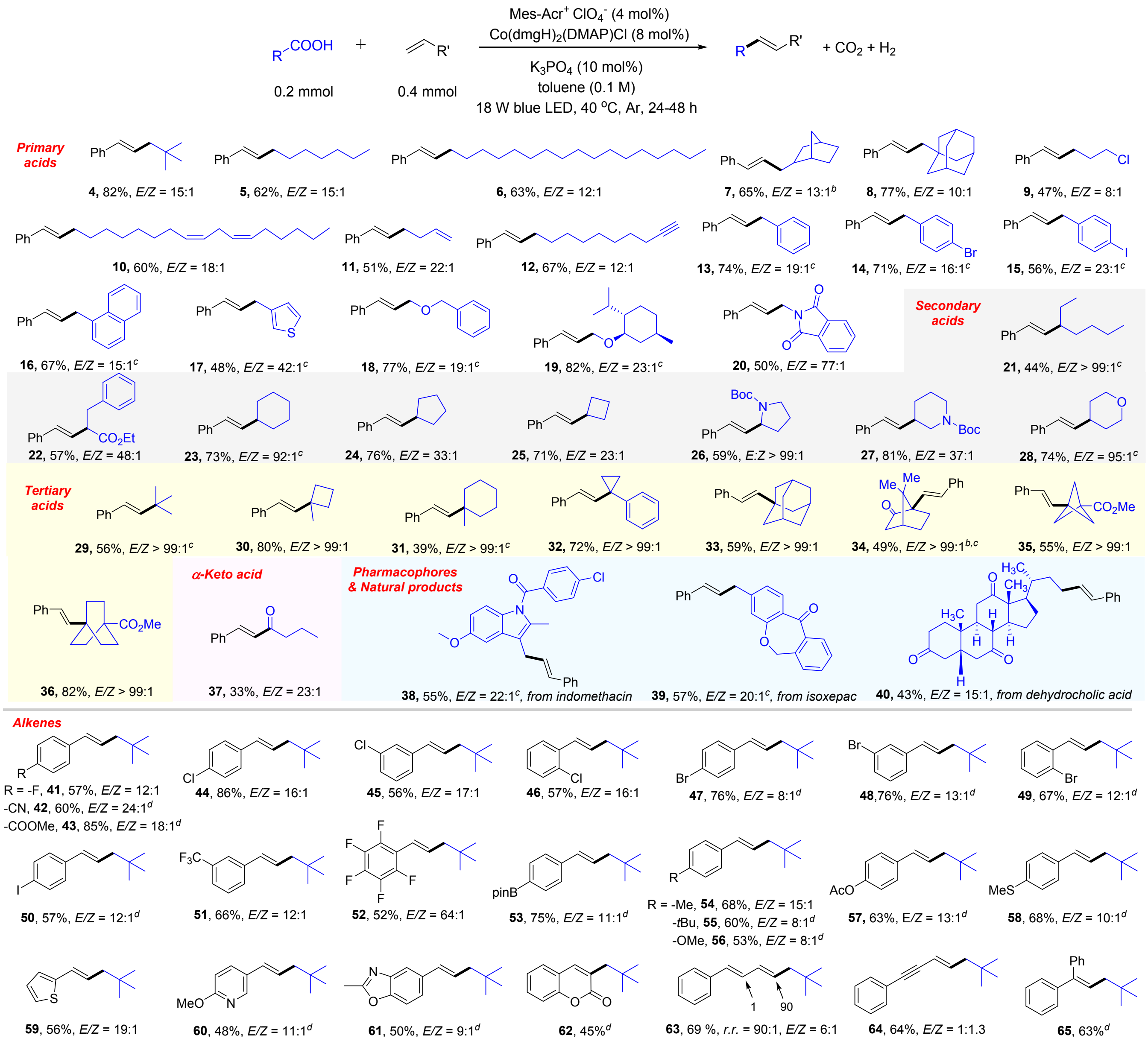
Scope of Decarboxylative Heck-Type Coupling with Vinyl Arenes or Heteroarenes. A remarkably broad scope of aliphatic acids were effective under the optimal conditions and provided disubstituted olefins from styrene in moderate to good yields with generally excellent *E*/*Z* selectivity (Scheme 2). Primary carboxylic acids representing some of the most readily available feedstocks, such as steric acid (**6**) and linoleic acid (**10**), participated in smooth decarboxylative coupling (**4-20**). Notably, some sensitive functionalities in conventional Heck coupling reactions, including alkyl chlorides (**9**), alkenes (**10**, **11**), alkynes (**12**), aryl bromides (**14**) and aryl iodides (**15**) were well-tolerated, leading to products without olefin isomerization or dehalogenation. Phenylacetic acids and 3-thiopheneacetic acids were found to be competent substrates for the coupling protocol (**13-17**). α-Alkoxy acids (**18**, **19**) and α-amino acids (**20**) were also suitable substrates, generating allyl ether and allylamine derivatives. It is worth mentioning that both primary aliphatic carboxylic acids and α-alkoxy aliphatic acids reacted poorly under the catalytic conditions defined by Shang and Na.[9]

Secondary alkyl carboxylic acids, either acyclic (**21**, **22**), or cyclic with varying ring sizes (**23-25**), and heterocycles (**26-28**) were all viable coupling partners. Remarkably, a number of tertiary alkyl carboxylic acids could be employed to access alkene products with quaternary carbon centers in exclusive *E* configuration. The reactions proceeded well with pivalic acid and methyl or phenyl substituted cyclic carboxylic acids (**29**-**32**). Bridged systems such as adamantane (**33**), bicyclo[2.2.1]heptanone (**34**), bicyclo[1.1.1]pentane (**35**) or bicyclo[2.2.2]octane (**36**) formed the desired products efficiently. *α*-Keto acids could be exploited to directly synthesize enone compounds (**37**), albeit in lower yield.

Our method also provides a convenient protocol to pursue late-stage modification of bioactive molecules, as more than 450 marketed drugs possessed the carboxylic acid moiety.[17] The decarboxylative vinylation of complex natural products and drug molecules proceeded highly chemoselectively, as demonstrated by the reactions of indomethacin (**38**), isoxepac (**39**), and dehydrocholic acid (**40**).

The generality of this decarboxylative Heck-type coupling with respect to the vinyl arene component was subsequently investigated (Scheme 2). Electron-deficient (**41**-**53**) and electron-rich (**54**-**58**) styrene derivatives possessing *ortho*-, *meta*-, or *para*-substituents were all found to be efficient to provide the corresponding disubstituted alkene products in moderate to good yields. A wide range of functionalities, including aryl fluorides, chlorides, bromides, iodides, nitriles, esters, trifluoromethyl compounds, pentafluoro arenes, boronic esters, ethers, and thioethers were tolerated. Decarboxylative coupling of acid **1** with vinyl heteroarenes such as thiophenes, pyridines, benzoxazoles, and coumarins led to products (**59-62**) with moderate yields and good selectivity. 1,3-Dienes, which were not amenable substrates for light-mediated Pd-catalyzed Heck reactions,[4c,7] delivered the desired product **63** with excellent regioselectivity and moderate *E*/*Z* selectivity. Notably, identical results were obtained regardless of whether (*E*)-1,3-diene or (*Z*)-1,3-diene was used. Enynes were also suitable substrates for the decarboxylative coupling, even though the *E*/*Z* selectivity of product **64** was diminished. 1,1-Diphenylethylene reacted smoothly to deliver product **65** in good yield. However, *β*-substituted vinyl arenes and aliphatic alkenes gave very low yields (<10%).

Scheme 2. Scope of Decarboxylative Heck-Type Coupling of Aliphatic Carboxylic Acids with Vinyl Arenes or Hetereoarenes[a]

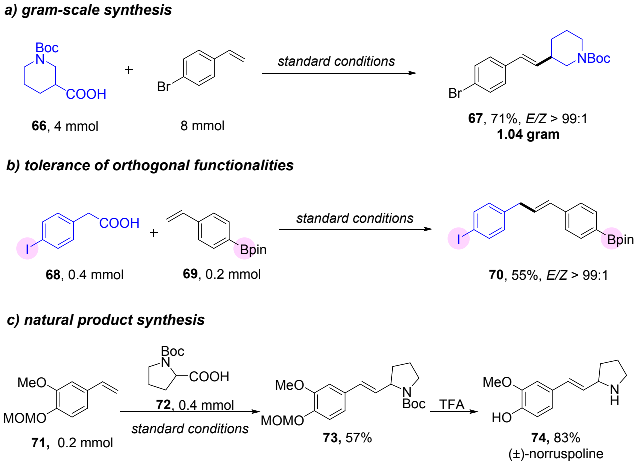


4, 82%, *E/Z* = 15:1
5, 62%, *E/Z* = 15:1
6, 63%, *E/Z* = 12:1
7, 65%, *E/Z* = 13:1[b]
8, 77%, *E/Z* = 10:1
9, 47%, *E/Z* = 8:1
10, 60%, *E/Z* = 18:1
11, 51%, *E/Z* = 22:1
12, 67%, *E/Z* = 12:1
13, 74%, *E/Z* = 19:1[c]
14, 71%, *E/Z* = 16:1[c]
15, 56%, *E/Z* = 23:1[c]
16, 67%, *E/Z* = 15:1[c]
17, 48%, *E/Z* = 42:1[c]
18, 77%, *E/Z* = 19:1[c]
19, 82%, *E/Z* = 23:1[c]
20, 50%, *E/Z* = 77:1
21, 44%, *E/Z* > 99:1[c]
22, 57%, *E/Z* = 48:1
23, 73%, *E/Z* = 92:1[c]
24, 76%, *E/Z* = 33:1
25, 71%, *E/Z* = 23:1
26, 59%, *E:Z* > 99:1
27, 81%, *E/Z* = 37:1
28, 74%, *E/Z* = 95:1[c]
29, 56%, *E/Z* > 99:1[c]
30, 80%, *E/Z* > 99:1
31, 39%, *E/Z* > 99:1[c]
32, 72%, *E/Z* > 99:1
33, 59%, *E/Z* > 99:1
34, 49%, *E/Z* > 99:1[b,c]
35, 55%, *E/Z* > 99:1
36, 82%, *E/Z* > 99:1
37, 33%, *E/Z* = 23:1
38, 55%, *E/Z* = 22:1[c], *from indomethacin*
39, 57%, *E/Z* = 20:1[c], *from isoxepac*
40, 43%, *E/Z* = 15:1, *from dehydrocholic acid*
R = -F, **41**, 57%, *E/Z* = 12:1
-CN, **42**, 60%, *E/Z* = 24:1[d]
-COOMe, **43**, 85%, *E/Z* = 18:1[d]
44, 86%, *E/Z* = 16:1
45, 56%, *E/Z* = 17:1
46, 57%, *E/Z* = 16:1
47, 76%, *E/Z* = 8:1[d]
48,76%, *E/Z* = 13:1[d]
49, 67%, *E/Z* = 12:1[d]
50, 57%, *E/Z* = 12:1[d]
51, 66%, *E/Z* = 12:1
52, 52%, *E/Z* = 64:1
53, 75%, *E/Z* = 11:1[d]
R = -Me, **54**, 68%, *E/Z* = 15:1
-*t*Bu, **55**, 60%, *E/Z* = 8:1[d]
-OMe, **56**, 53%, *E/Z* = 8:1[d]
57, 63%, *E/Z* = 13:1[d]
58, 68%, *E/Z* = 10:1[d]
59, 56%, *E/Z* = 19:1
60, 48%, *E/Z* = 11:1[d]
61, 50%, *E/Z* = 9:1[d]
62, 45%[d]
63, 69 %, *r.r.* = 90:1, *E/Z* = 6:1
64, 64%, *E/Z* = 1:1.3
65, 63%[d]

[a] Isolated yields. *E*/*Z* ratios were determined by GC analysis of the crude reaction mixtures. [b] d.r. > 20:1. [c] Alkene (1 mmol, 5 equiv) was applied. [d] 3,3-Dimethylbutanoic acid (0.4 mmol) and alkene (0.2 mmol) were used.

Synthetic Applications. The synthetic utility of this decarboxylative Heck-type coupling with vinyl arenes was demonstrated by scaling-up to gram quantities (Scheme 3a). The compatibility with aryl halides and aryl boronic esters allowed further orthogonal functional group manipulation (Scheme 3b). Its potential application to natural product synthesis was illustrated by a concise synthesis of (±)-norruspoline (**74**) (Scheme 3c).

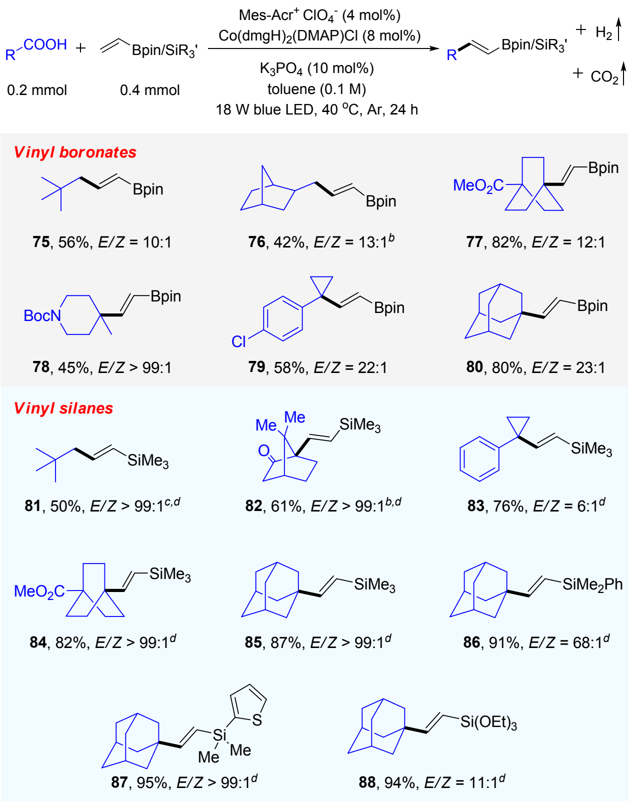
Scheme 3. Synthetic Applications of Decarboxylative Heck-Type Coupling with Vinyl Arenes[a]



[a]Standard conditions: 4 mol% **2**, 8 mol% **3**, 10 mol% K_3PO_4, in toluene (0.1 M), under argon and 18 W blue LED irradiation, 24-48 h. Boc = tert-butyloxycarbonyl, MOM = methoxymethyl.

Decarboxylative Heck-Type Coupling for the Preparation of Vinyl Silanes and Vinyl Boronates. Vinyl silanes and vinyl boronates are indispensable nucleophiles in organic synthesis due to their stability, non-toxicity and synthetic versatility.[18] They are widely applied in Hiyama or Suzuki cross-couplings, and can also be transformed into a variety of other functional groups, including halides, ketones, amines, and etc. There are three distinctive methods for the synthesis of 1,2-disubstituted vinyl silanes and vinyl boronates: 1) hydrosilylation or hydroboration of alkynes,[19] which normally requires multistep synthesis to prepare the alkyne starting materials; 2) olefin metathesis,[20] where the reactivity and selectivity really depend on substituent patterns; 3) Heck-type couplings, that can be complicated by unwanted Hiyama or Suzuki-Miyaura couplings. There are only a few conditions that could offer the Heck products,[21] and they are typically limited in scope and frequently suffered from poor selectivity,[21d,f] competitive side reactions,[21d-f] and use of special reagents.[21a,b] A literature survey indicated that only sp^2-sp^2 coupling has been achieved in Heck coupling of organohalides with vinyl silanes or vinyl boronates.[21c,22] A method to realize selective sp^3-sp^2 Heck-type coupling with commercially available vinyl silanes and vinyl boranes is therefore highly demanded. We were delighted to find out that our decarboxylative Heck protocol worked effectively to produce a wide range of disubstituted vinyl boronates (**75-80**) and vinyl silanes (**81-88**) in moderate to excellent yields (Scheme 4), which represents the first example of sp^3-sp^2 Heck-type coupling with vinyl silanes and vinyl boronates. Notably, tertiary alkyl carboxylic acids were the most effective substrates that participated in this transformation, and the generated products are not easily accessible by other methods, such as olefin metathesis, due to the steric hindrance.[23]

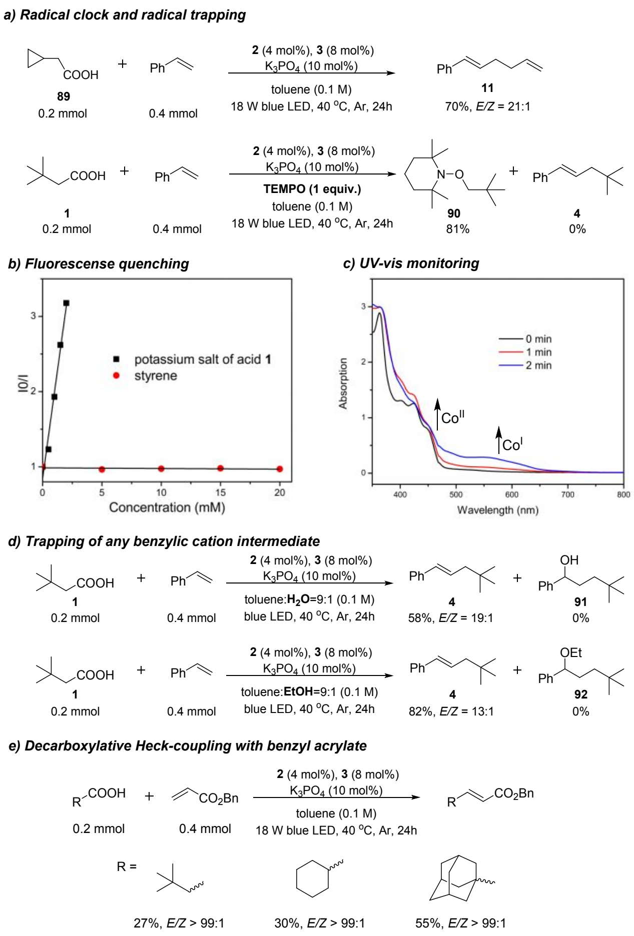
Scheme 4. Decarboxylative Heck-Type Coupling of Aliphatic Carboxylic Acids with Vinyl Silanes and Vinyl Boronates[a]



[a]Isolated yields. *E*/*Z* ratios were determined by GC analysis of the crude reaction mixtures. [b]d.r. > 20:1. [c]The reaction was conducted in toluene-d8 and yield was determined by ^1H NMR using dibromomethane as the internal standard. [d]5 equiv alkene was used.

Supporting Evidences for Mechanistic Elucidation. To reveal more hints for the mechanism of the aforementioned transformation, the formation of alkyl radicals from carboxylic acids was first evidenced by radical clock and radical trapping experiments (Scheme 5a). A series of Stern-Volmer fluorescence quenching studies were performed. As illustrated in Scheme 5b, the emission intensity of the excited state of photosensitizer **2** was weakened in the presence of the potassium salt of acid **1**, consistent with linear Stern-Volmer behavior. In contrast, emission quenching of the excited state of **2** by styrene was not observed. A UV-Vis monitoring study of the reaction mixture revealed that two absorption bands at 440−500 nm and 550−650 nm quickly appeared upon light irradiation (Scheme 5c), which was in agreement with the formation of Co^{II} and Co^{I} intermediates, respectively.[11a,b] These species have been widely identified as intermediates in cobaloxime-mediated radical reactions[10] and hydrogen evolution processes.[11] Previous studies on dehydrogenative coupling via merging photoredox and cobalt catalysis generally proposed a SET process between cobalt and the radical intermediate to form carbocation species, which was followed by loss of proton to deliver products.[12-14] However, attempted to trap any benzylic cation species using water or EtOH failed to give any alcohol (**91**) or ether (**92**) (Scheme 5d), indicating that a benzylic cation intermediate may not be involved.[24] Good reactivity with electron-deficient styrenes (e.g. **52**) also suggested that a mechanism involving the generation of a benzylic cation intermediate was unlikely. This was further supported by the successful decarboxylative coupling with electron-deficient benzyl acrylate (Scheme 5e), although the reaction efficiency varied among different acids.[25]

Scheme 5. Control Experiments for Mechanistic Investigation


a) Radical clock and radical trapping

b) Fluorescense quenching

c) UV-vis monitoring

d) Trapping of any benzylic cation intermediate

e) Decarboxylative Heck-coupling with benzyl acrylate

Yields were determined from the crude ^{1}H NMR spectra using 1,3,5-trimethoxybenzene as an internal standard. *E*/*Z* ratios were determined by GC analysis of the crude mixtures. Bn = benzyl.

A tentative mechanism was proposed in light of all the experimental data (Figure 1). Excitation of the photocatalyst **2** with blue light will generate the excited state Mes-Acr^{+}* ($E_{1/2}^{red}$ = +2.06 V vs SCE).[26] A SET from the carboxylate[27] derived from the carboxylic acid and base to the highly oxidizing excited state Mes-Acr^{+}* delivers an alkyl radical R• upon extrusion of CO_2. Subsequent addition of the alkyl radical R• to styrene will furnish a more stable benzylic radical intermediate **I**.[28] The reduced photosensitizer Mes-Acr• can be oxidized by the Co^{III} catalyst **3** to complete the photoredox catalytic cycle.[14d,29] On the cobalt side, Co^{II} can reversibly capture benzylic radical **I** to form a Co^{III} intermediate **II**,[30] which will readily deliver the alkene product and a Co^{III}–H intermediate via homolytic cleavage of the Co–C bond and subsequent β-hydrogen abstraction by Co^{II} under blue light irradiation.[30] The Co^{III}–H then may react with another proton or another molecule of Co^{III}–H to release H_2 and regenerate Co^{III} catalyst **3**.[11] Alkaline conditions have been reported to convert the putative hydridocobaloxime to a Co^{I} species,[10c,31] the reverse reaction of Co^{I} protonation, even at pH 7.5.[32] The base utilized for acid deprotonation inevitably drives the equilibrium from Co^{III}–H to Co^{I}.[10] This explains the presence of Co^{I} during the reaction process and highlights the importance of using the correct amount of an appropriate base for the success of this transformation.[12] Even though another reaction pathway involving the capture of the alkyl radical R• by the Co^{II} species followed by carbocobaltalation to give intermediate **II** may be also possible (Figure S17), density functional theory (DFT) calculations indicated this pathway was unlikely as the relative free energy barrier was too high (46 kcal/mol, Figure S21).

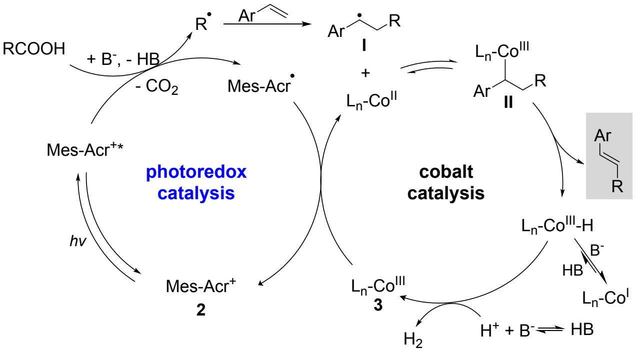
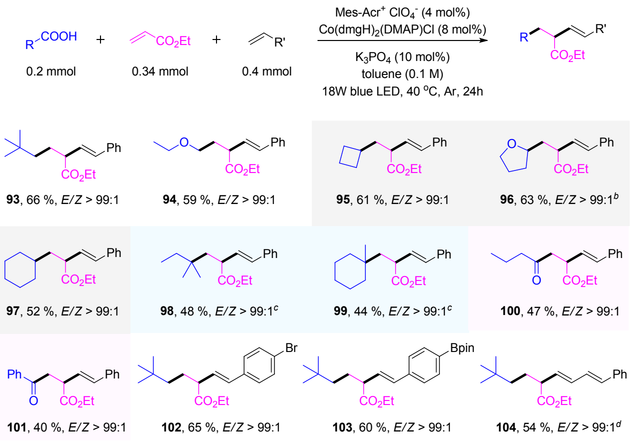


Figure 1. Plausible mechanism.

Selective Three-Component Coupling. The multicomponent reactions play a privileged role in organic synthesis as it enables direct construction of molecules with a high level of complexity and diversity. Even though significant progress has recently been achieved in the area of photoredox chemistry,[5] development of photo-promoted multicomponent reactions is still in its infancy.[33] The limited success of decarboxylative Heck-coupling with acrylates (Scheme 5e) and the radical nature of this coupling inspired us to seek for a possible photo-mediated cascade process. We speculated that the nucleophilic alkyl radicals derived from aliphatic acids could preferentially react with electron-deficient acrylates, while the newly formed α-acyl radical was relatively electrophilic and could selectively couple with vinyl arenes to furnish the catalytic cycle. To our delight, the decarboxylative Heck-coupling protocol was efficient for the selective coupling of aliphatic acids, acrylates, and vinyl arenes, affording densely functionalized vinyl arenes in a highly selective manner, which would be difficult to access by other methods (Scheme 6). Primary (**93**, **94**), secondary (**95-97**), tertiary (**98**, **99**) and α-keto (**100**, **101**) carboxylic acids were all effective substrates and led to products in good yields with exclusive *E* configuration. Good tolerance of functional groups such as the aryl bromide (**102**) and boronic ester (**103**) provided handles for further molecular manipulation. The use of a diene substrate was also feasible to deliver the coupling product **104** smoothly. This method represents a novel mode of the photo-induced cascade reaction based on the unique property of the photoredox/cobalt dual catalysis.

Scheme 6. Selective Three-Component Coupling of Aliphatic Carboxylic Acids, Acrylates and Vinyl arenes[a]



[a]Isolated yields. *E*/*Z* ratios were determined by GC analysis of the crude

reaction mixtures. [b]d.r. = 2:1. [c]1.3 equiv ethyl acrylate was used. [d]1 equiv diene was used.

CONCLUSION

In conclusion, we have demonstrated that alkyl carboxylic acids, which represent inexpensive and widely available sources of carbon frameworks, can be directly used to synthesize Heck-type products. An extremely broad scope of substrates is accommodated to give products in an external oxidant-free manner via the synergistic merger of an organo photoredox catalyst and a cobaloxime catalyst in the presence of a catalytic amount of base under blue LED irradiation. Some of the synthesized alkenes such as the vinyl silanes and vinyl boronates bearing a tertiary alkyl substituent, and the three-component coupling products are difficult to access by other means. The key to the success relies on the unique proton/electron accepting ability of the cobaloxime catalyst, which is beyond the capacity of conventional oxidants. This dual-catalysis protocol features merits such as widely available feedstocks, absence of both noble-metal and harmful by-products, which will likely find broad applications in the synthesis of valuable disubstituted alkenes and late-stage functionalization of pharmacophores.

ASSOCIATED CONTENT

Supporting Information

This material is available free of charge via the Internet at http://pubs.acs.org.

Experimental procedures and characterization data for all products, additional comments on mechanism, computational details, Figures S1-S26 and Tables S1-S11

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Notes

The authors declare no competing financial interests.

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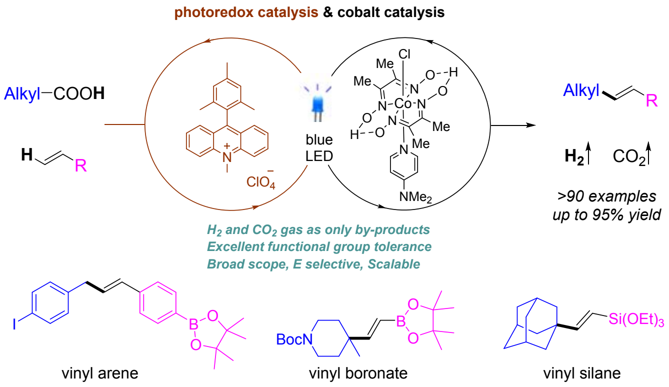

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