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Iron-Facilitated Oxidative Radical Decarboxylative Cross-Coupling between α-Oxocarboxylic Acids and Acrylic Acids: An Approach to α,β-Unsaturated Carbonyls

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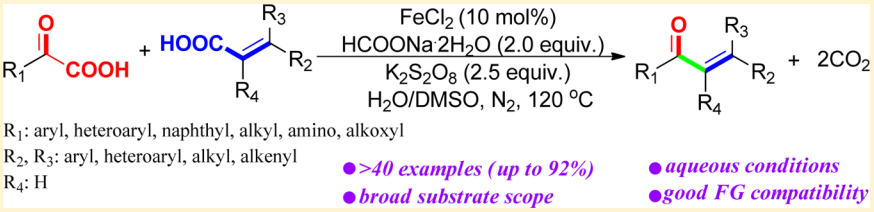
Supporting Information



ABSTRACT: The first Fe-facilitated decarboxylative cross-coupling reaction between α-oxocarboxylic acids and acrylic acids in aqueous solution has been developed. This transformation is characterized by its wide substrate scope and good functional group compatibility utilizing inexpensive and easily accessible reagents, thus providing an efficient and expeditious approach to an important class of α,β-unsaturated carbonyls frequently found in bioactive compounds. The synthetic potential of the coupled products is also demonstrated in subsequent functionalization reactions. Preliminary mechanism studies suggest that a free radical pathway is involved in this process: the generation of an acyl radical from α-oxocarboxylic acid via the excision of carbon dioxide followed by the addition of an acyl radical to the α-position of the double bond in acrylic acid then delivers the α,β-unsaturated carbonyl adduct through the extrusion of another carbon dioxide.

INTRODUCTION

Transition-metal-catalyzed decarboxylative coupling reactions have attracted much attention in the past decade due to their potential advantages, such as high selectivity, efficiency, and convenience as well as the nontoxic byproduct (CO_2). Thus far, notable progress has been made in the area of decarboxylative couplings for various C−C bond and C−heteroatom bond forming reactions.[1] However, examples involving a decarboxylative coupling reaction between carboxylic acids remain much underdeveloped:[2] almost all of these reactions are restricted to Pd-catalyzed decarboxylative hetero- or homocouplings between aromatic carboxylic acids. Herein, we report the first example of a decarboxylative cross-coupling reaction between α-oxocarboxylic acids and acrylic acids to α,β-unsaturated carbonyl compounds facilitated by an iron catalyst through the extrusion of two molecules of CO_2 in aqueous media (Scheme 1).

α,β-Unsaturated carbonyls are a particularly important class of naturally occurring and manmade compounds that display extraordinary and interesting pharmaceutical and biological properties, including anticancer, antioxidant, antimicrobial, anti-inflammatory, antianginal, antimutagenic, antihepatotoxic, antimalarial, antimitotic, and antiallergic activities (Scheme 2).[3]Also, this class of compounds is extremely attractive as intermediates both in the synthesis of various heterocycles[4] and in functional materials.[5] Because of the important applications of α,β-unsaturated carbonyls in biology, medicine, and materials science, considerable efforts have been made to develop various synthetic approaches for their synthesis.[6−12] Traditionally, α,β-unsaturated ketones are mainly prepared by aldol condensation (Claisen−Schmidt condensation) between ketones and aldehydes.[7] Unfortunately, this process often requires relatively strong basic reaction conditions, which place limitations on the use of functional groups that are sensitive to bases. Accordingly, the development of methods to overcome this limitation would be of significant importance. In 2000, Müller reported Sonogashira coupling of electron-deficient aryl halides with aryl 1-propargyl alcohols for the synthesis of α,β-unsaturated ketones, even though the reaction required the use of an expensive palladium catalyst combined with a cocatalyst.[8] Later on, the groups of Beller and Skrydstrup and Feng developed a very efficient access to α,β-unsaturated ketones through Pd-catalyzed carbonylative Heck coupling[9] of aryl halides/boronic acids with styrenes and carbonylative addition[10] of aryl halides to arylalkynes in the presence of CO; however, the requirement for high CO pressure and/or the presence of halide anions make this reaction environmentally unfavorable. Recently, Su and Lei independently achieved the Pd-catalyzed C−H olefination of (hetero)arenes/aryl carboxylic acids with saturated ketones in the presence of a stoichiometric amount of Ag_2CO_3 assisted by a phosphine ligand[11] and the copper-catalyzed oxidative coupling of styrenes with aromatic aldehydes using TBHP as the oxidant[12] for the preparation of

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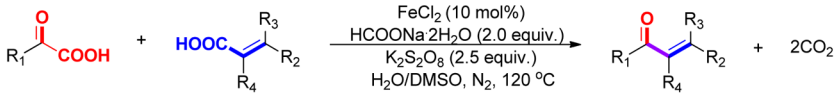
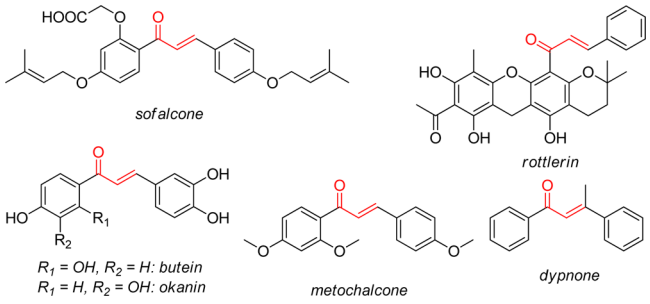
Scheme 1. Decarboxylative Cross-Coupling Reaction between Carboxylic Acids To Form α,β-Unsaturated Carbonyls



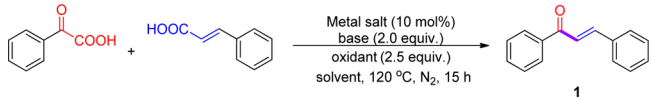
√ Inexpensive and easily available reagents
√ Runs in aqueous conditions
√ Wide substrate scope
√ The generation of innocuous by-product CO_2
√ Compatible with various functional groups, including halides, carboxyl, amido, hydroxyl and formyl group

Scheme 2. Biological Significance of α,β-Unsaturated Carbonyl-Containing Compounds



α,β-unsaturated ketones, respectively. Despite formidable advances, most methods suffer from one or more limitations including poor substrate scope, limited functional group tolerance, the use of stoichiometric toxic reagents, and/or the high cost of the catalytic system. Therefore, the development of a general, green, and practical synthetic route toward α,β-unsaturated carbonyls is highly desirable and remains a challenge. Toward this goal, we present an efficient and general protocol for the synthesis of α,β-unsaturated carbonyl compounds from carboxylic acids using a cheap iron catalyst (Scheme 1). To the best of our knowledge, this work demonstrates the first construction of α,β-unsaturated carbonyl scaffolds via the decarboxylative cross-coupling between -oxocarboxylic acids and acrylic acids. The present method is characterized by its broad substrate scope, high functional group compatibility, and the formation of innocuous byproduct CO_2. The generality of this approach is also demonstrated by synthesizing an exemplary set of α,β-unsaturated carbonyl compounds (>40 examples). Moreover, from a practical and sustainable chemistry standpoint, the use of easily available and stable materials and aqueous solvent represent additional benefits. Finally, the preliminary mechanistic studies seem to support a free radical mechanism.

Table 1. Initial Studies toward Decarboxylative Cross-Coupling Reaction between Carboxylic Acids[a]



1

entry	metal source	oxidant	base	solvent (v/v)	yield (%)
1	$AgNO_3$	$K_2S_2O_8$	–	DMSO/H_2O (1/1)	23
2	$AgNO_3$	$K_2S_2O_8$	HCOONa·$2H_2O$	DMSO/H_2O (1/1)	41
3	$AgNO_3$	$K_2S_2O_8$	NaOAc	DMSO/H_2O (1/1)	32
4	$AgNO_3$	$K_2S_2O_8$	Cs_2CO_3	DMSO/H_2O (1/1)	28
5	$AgNO_3$	$K_2S_2O_8$	pyridine	DMSO/H_2O (1/1)	26
6	Ag_2CO_3	$K_2S_2O_8$	HCOONa·$2H_2O$	DMSO/H_2O (1/1)	43
7	CuO	$K_2S_2O_8$	HCOONa·$2H_2O$	DMSO/H_2O (1/1)	34
8	CuCl	$K_2S_2O_8$	HCOONa·$2H_2O$	DMSO/H_2O (1/1)	trace
9	$FeCl_2$	$K_2S_2O_8$	HCOONa·$2H_2O$	DMSO/H_2O (1/1)	54
10	$Ni(OAc)_2$	$K_2S_2O_8$	HCOONa·$2H_2O$	DMSO/H_2O (1/1)	40
11	$FeCl_2$	$K_2S_2O_8$	HCOONa·$2H_2O$	CH_3CN/H_2O (1/1)	25
12	$FeCl_2$	$K_2S_2O_8$	HCOONa·$2H_2O$	DMSO	41
13	$FeCl_2$	$K_2S_2O_8$	HCOONa·$2H_2O$	H_2O	48
14	$FeCl_2$	$K_2S_2O_8$	HCOONa·$2H_2O$	CH_3CN	<5
15	$FeCl_2$	$K_2S_2O_8$	HCOONa·$2H_2O$	DMSO/H_2O (5/15)	69
16	$FeCl_2$	$K_2S_2O_8$	HCOONa·$2H_2O$	DMSO/H_2O (3/17)	83
17	$FeCl_2$	$K_2S_2O_8$	HCOONa·$2H_2O$	DMSO/H_2O (2/18)	76
18	$FeCl_2$	$Na_2S_2O_8$	HCOONa·$2H_2O$	DMSO/H_2O (3/17)	75
19	$FeCl_2$	TBHP	HCOONa·$2H_2O$	DMSO/H_2O (3/17)	0
20	$FeCl_2$	H_2O_2	HCOONa·$2H_2O$	DMSO/H_2O (3/17)	0
21	$FeCl_2$	–	HCOONa·$2H_2O$	DMSO/H_2O (3/17)	0
22	–	$K_2S_2O_8$	HCOONa·$2H_2O$	DMSO/H_2O (3/17)	21

[a]Reaction conditions: benzoylformic acid (0.5 mmol, 1 equiv), cinnamic acid (1.0 mmol, 2 equiv), catalyst (10 mol %), base (2.0 equiv), oxidant (2.5 equiv), solvent (2.0 mL), 120 °C, N_2, 15 h.

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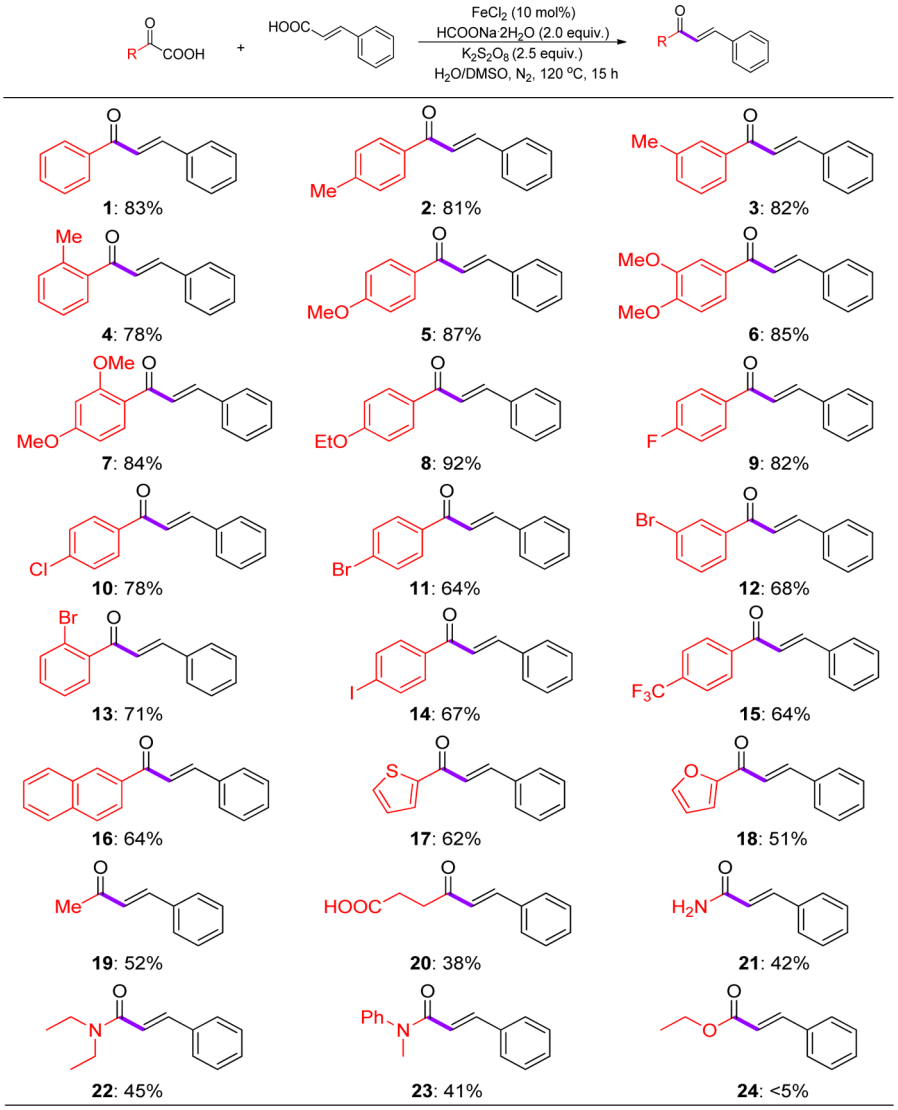
Table 2. Scope of the α-Oxocarboxylic Acids Coupling Component[a]



[a]Reaction conditions: α-oxocarboxylic acid (0.5 mmol, 1 equiv), cinnamic acid (1.0 mmol, 2 equiv), $FeCl_2$ (10 mol %), $HCOONa·2H_2O$ (2.0 equiv), $K_2S_2O_8$ (2.5 equiv), H_2O (1.7 mL), DMSO (0.3 mL), 120 °C, N_2, 15 h.

RESULTS AND DISCUSSION

Optimization of the Reaction Conditions. Our investigation started with the reaction of benzoylformic acid with cinnamic acid using 10 mol % $AgNO_3$ along with 2.5 equiv of $K_2S_2O_8$ in DMSO/H_2O at 120 °C for 15 h. To our delight, the desired chalcone product **1** was obtained in 23% yield under these conditions (Table 1, entry 1). The efficiency of this decarboxylation protocol was improved by adding bases to the reaction mixture, with $HCOONa·2H_2O$ proving to be optimal (Table 1, entries 2−5). Moreover, evaluation of other metal salts revealed that $FeCl_2$ was the best choice (Table 1, entries 6−10). Subsequently, we investigated the influence of the solvent. When other solvents, such as DMSO, H_2O, and CH_3CN, were employed instead of DMSO/H_2O, a low or moderate of the desired product was obtained (Table 1, entries 11−14). In addition, it was observed that varying the ratio of DMSO to H_2O also had an effect on the yield of **1** (Table 1, entries 15−17). The best results (83%) were achieved when the volume ratio of H_2O and DMSO was 17:3. The choice of oxidant was also found to have a dramatic effect on the yield. Among the oxidants tested, $K_2S_2O_8$ afforded the best result (Table 1, entries 18−20). Control experiments showed that no conversion to **1** occurred in the absence of $K_2S_2O_8$ (Table 1, entry 21), while, in the absence of $FeCl_2$, a much lower background reaction was observed (Table 1, entry 22, 21% yield).

Scope of the α-Oxocarboxylic Acid in the Decarboxylative Cross-Coupling Reaction. With the optimized reaction conditions in hand, we sought to examine the scope and generality of the reaction between various α-oxocarboxylic acids and cinnamic acid, and the results are summarized in Table 2. A series of electron-rich and -poor benzoylformic acids readily undergo decarboxylative coupling with cinnamic acid, delivering the corresponding products in 64−92% yield. For example, benzoylformic acid derivatives with electron-donating substituents (Me, MeO, EtO) afforded the desired α,β-unsaturated ketones in yields ranging from 78% to 92% (**2**−**8**), while benzoylformic acid derivatives bearing electron-withdrawing substituents (F, Cl, Br, I, CF_3) provided the desired α,β-unsaturated ketones in yields ranging from 64% to

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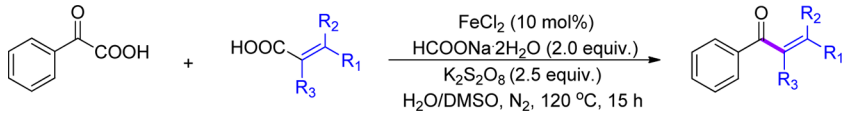
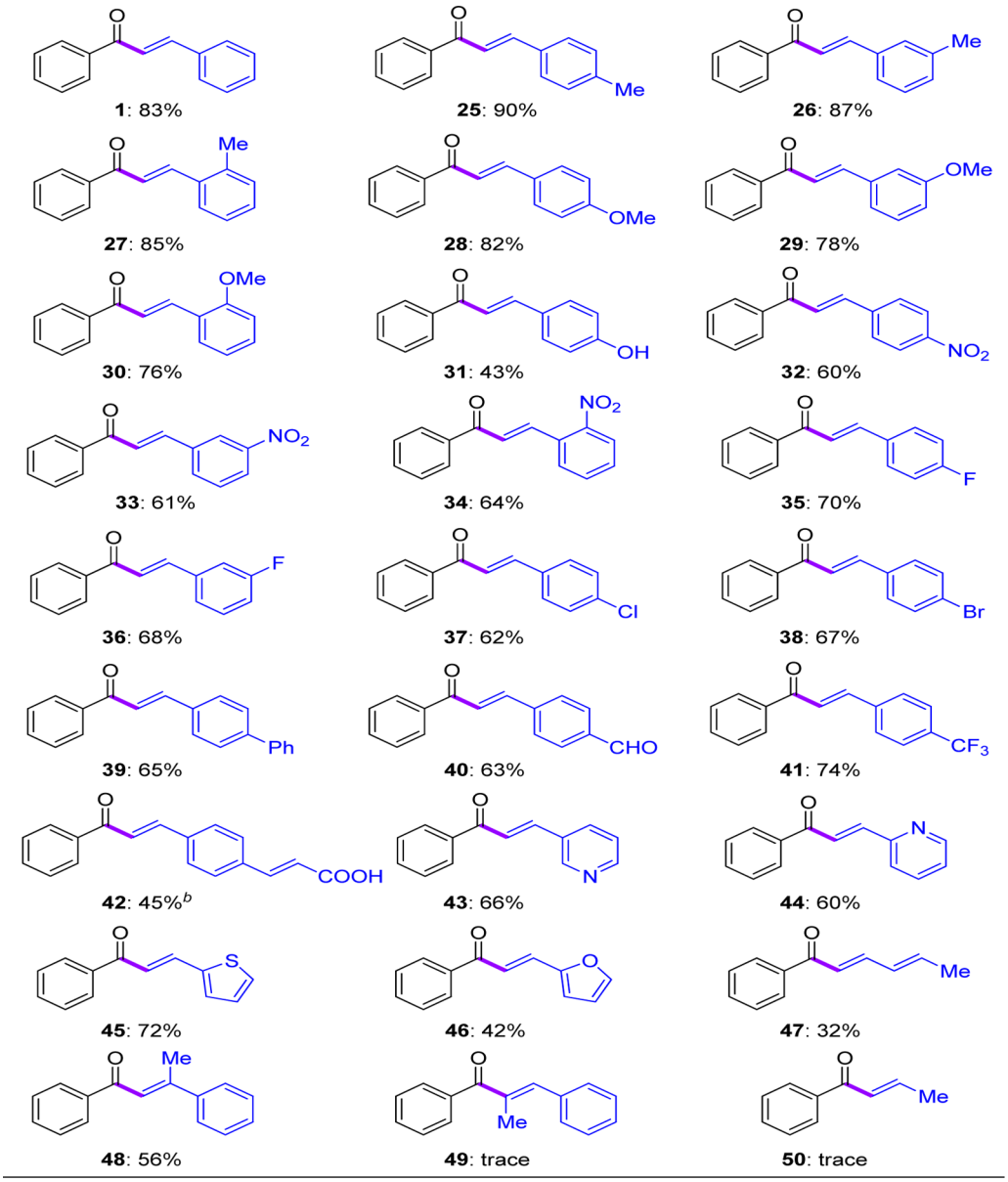
Table 3. Scope of the Acrylic Acids Coupling Component[a]





[a]Reaction conditions: benzoylformic acid (0.5 mmol, 1 equiv), acrylic acid (2.0 mmol, 4 equiv), $FeCl_2$ (10 mol %), $HCOONa{\cdot}2H_2O$ (2.0 equiv), $K_2S_2O_8$ (2.5 equiv), H_2O (1.0 mL), DMSO (3.0 mL), 120 °C, N_2, 15 h. [b]DMSO (4.0 mL).

82% (**9**–**15**). It is noteworthy that benzoylformic acid bearing the same substituents at different positions on the phenyl ring had little influence on the efficiency of the reaction (**2**–**4**, **11**–**13**). A naphthyl oxocarboxylic acid also efficiently reacted with cinnamic acid, giving the product **16** in 64% yield. Importantly, heterocyclic α-keto acids were also productive reaction partners in this transformation (**17** and **18**, 62% and 51% yield). Interestingly, aliphatic α-keto acids also underwent the decarboxylation to give the corresponding products **19** and **20** in 52% and 38% yield, respectively. In addition, oxamic acids were also compatible, albeit affording a lower yield (**21**–**23**, 41–45% yield). Control reactions have established that no amine acyl exchange occurred between oxamic acid and cinnamic acid in only a H_2O/DMSO system or in the absence of an oxidant (see the Supporting Information). 2-Ethoxy-2-oxoacetic acid reacted to afford a much lower yield of the desired product (**24**, <5% yield). It is noteworthy that the halogen groups and carboxyl group in the product are useful handles for further synthetic functionalization.

Scope of the Acrylic Acid in the Decarboxylative Cross-Coupling Reaction. Subsequently, we explored the scope of the reaction between a variety of acrylic acids and benzoylformic acid. As can be seen in Table 3, a wide range of cinnamic acids, with either electron-donating or -withdrawing functional groups on the aromatic ring, were compatible with this transformation. Decarboxylation of electron-rich cinnamic

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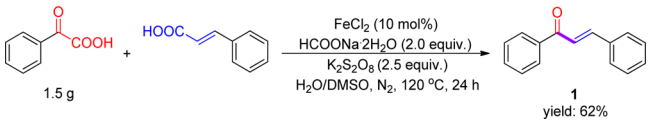
acids gave the corresponding products in 43−90% yield (**25**−**31**), whereas electron-poor cinnamic acids underwent the decarboxylation to afford the desired products in 60−74% yield (**32**−**41**). Notably, the variety of substituents including fluoro, chloro, bromo, trifluoromethyl, methoxyl, hydroxyl, and nitro were well tolerated in these cross-coupling reactions, thus offering potential applications for further synthetic elaboration. Particularly noteworthy was that 4-formylcinnamic acid provided the product **40** in 63% yield. This is particularly important, since aldehydes are susceptible to oxidation in the presence of $K_2S_2O_8$ as the oxidant. Moreover, 1,4-phenylenediacrylic acid only afforded monofunctionalization product **42** in 45% yield, and the attempted difunctionalization reaction was unsuccessful. Gratifyingly, the arene ring is not limited to benzene rings. Decarboxylation of pyridyl, thiophen-2-yl, and furan-2-yl substituted acrylic acid proceeded to give the corresponding products in synthetically useful yields (**43**−**46**, 42−72% yield). Interestingly, a conjugated dienoic acid also underwent the decarboxylative cross-coupling reaction to give the product **47** in 32% yield. In addition, β-disubstituted acrylic acid was also a viable substrate for this reaction, delivering the desired product **48** in 56% yield. The present protocol is not without limitations. The α-substituted acrylic acid such as α-methylcinnamic acid is not amenable to this procedure (**49**), which is presumably due to the increased steric hindrance of the α-position in acrylic acid. Crotonic acid, which is a substrate with a monoalkyl substituent at the β-position of acrylic acid, was scarcely productive, and the attempted reaction provided only a trace amount of the desired product **50**. Also, butenedioic acid gave a complex reaction mixture.

Demonstration of the Scalability of the Decarboxylative Coupling. To demonstrate the preparative practicality of this new decarboxylative cross-coupling process, we performed the reaction on a gram scale. Reaction of 1.5 g (10 mmol) of benzoylformic acid with 2.0 equiv cinnamic acid (**2a**) under the standard reaction conditions generated **1** (1.29 g) in 62% yield (Scheme 3).

Scheme 3. Gram-Scale Reaction with Benzoylformic Acid



Mechanistic Studies. In order to gain insight into the mechanism of the decarboxylative cross-coupling process, several control experiments were carried out. First, when the radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) was added to the reaction mixture, only a trace amount of **1** was observed by GC-MS (Scheme 4a), whereas in the presence of hydroquinone the reaction was completely inhibited and the corresponding radical adducts were detected by GC-MS (Scheme 4b; for details, see the Supporting Information). The results indicate that the transformation proceeds via a free-radical pathway. Subsequently, almost all of the cinnamic acid remained intact when only cinnamic acid was heated under the standard reaction conditions (Scheme 4c). The reaction failed to give the desired product **1** when benzoylformic acid was treated with styrene under the standard conditions (Scheme 4d). These results described above suggest that the initial protodecarboxylation and the following acylation processes might not be involved in the reaction mechanism.

Finally, to probe the nature of the iron cation, the reaction between 2-oxo-2-(*p*-tolyl)acetic acid and cinnamic acid with $FeCl_2$ or $FeCl_3$ as the precatalyst was investigated. The results are shown in Scheme 4e. Using $FeCl_2$ as the catalyst precursor, the reaction provided the desired product **2** in 81% yield. The reaction using $FeCl_3$ as the catalyst precursor afforded a 77% yield of **2**. The similar results show that Fe(III) might be involved in the catalytic cycle for this decarboxylative cross-coupling reaction.

Proposed Mechanism. On the basis of the observed experimental results and previous literature,[13] a plausible mechanism is proposed in Scheme 5. First, the acyl radical **II** is generated from α-oxocarboxylates **I** via an oxidative radical decarboxylative process in the presence of $FeCl_2$ and $K_2S_2O_8$. Moreover, it is also likely that **I** is activated by $K_2S_2O_8$ to produce intermediate **II** (Table 1, entry 22). Subsequently, addition of the benzoyl radical to the double bond of acrylic acid **III** produces the alkyl radical **IV**. Finally, under the reaction conditions, the intermediate **IV** would undergo β-elimination to give the desired product **V** along with the release of CO_2.

As mentioned above, it turned out that the $FeCl_2/K_2S_2O_8/HCOONa{\cdot}2H_2O$ system is useful to the decarboxylative cross-coupling reaction between α-oxocarboxylic acids and acrylic acids in $DMSO/H_2O$. Interestingly, the present method uses stable, cheap, and readily available carboxylic acids as starting materials and exhibits a broader substrate scope and more excellent functional group tolerance than the classical aldol condensation for the synthesis of α,β-unsaturated carbonyls. The present decarboxylation proceeds via a free-radical pathway. In addition, all the reagents (α-oxocarboxylic acids, acrylic acids, $K_2S_2O_8$, and $HCOONa{\cdot}2H_2O$) are used as received without further purification.

CONCLUSION

In summary, we have developed the first Fe-facilitated decarboxylative cross-coupling reaction between α-oxocarboxylic acids and acrylic acids in aqueous solution. This decarboxylative cross-coupling reaction is not only general and efficient but also functional group compatible. Moreover, this transformation could also be conducted on gram-scale, and the synthetic utilities of these decarboxylation products have been showcased in synthetically useful functionalization reactions. In addition, radical-trapping experiments indicated that this transformation proceeded through a free-radical process. In view of the broad substrate scope, excellent functional group compatibility, ready availability of materials, and formation of innocuous byproduct CO_2, the present protocol provides a important complement for the synthesis of the highly valuable enone functionality and should find some applications in organic synthesis.

EXPERIMENTAL SECTION

General Comments. All commercially available compounds were purchased from commercial suppliers and used without further purification unless otherwise noted. All solvents were purified according to the method of Grubbs.[14] All kinds of substituted α-aryketo acids were prepared from oxidation of corresponding methyl ketones with SeO_2 according to the reported procedure.[15] ^1H NMR and ^{13}C NMR spectra were recorded at 400 and 101 MHz in $CDCl_3$ or DMSO-d_6 using TMS as the internal standard. Column chromatography was performed on 200−300 mesh silica gel. Thin-layer chromatography (TLC) was performed on Silicycle 250 mm silica gel F-254 plates. Multiplicities are indicated as s (singlet), d

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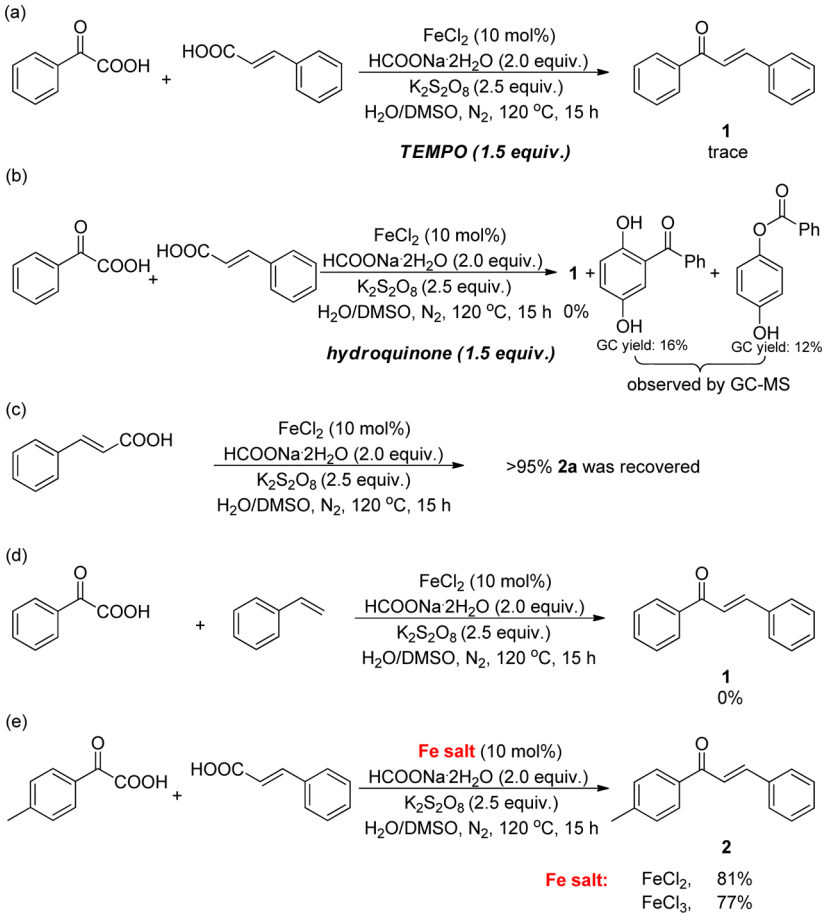
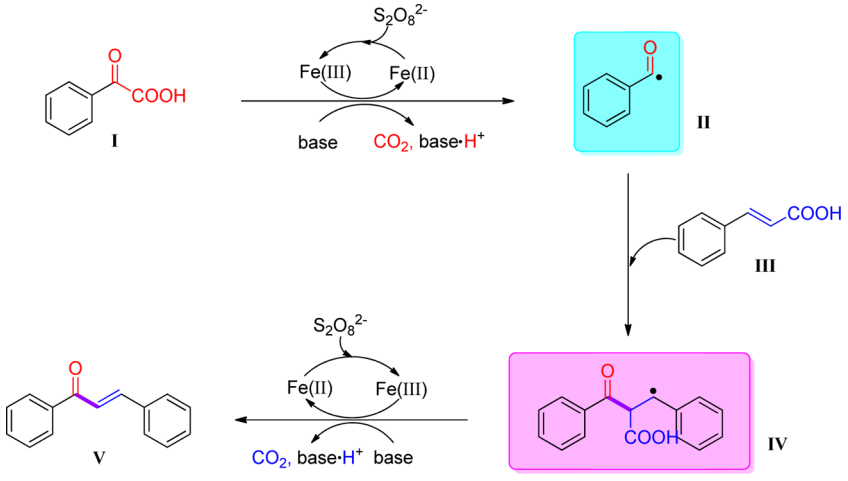
Scheme 4. Control Experiments



Scheme 5. Proposed Mechanism



(doublet), t (triplet), q (quartet), and m (multiplet), and coupling constants (J) are reported in hertz.

Typical Procedure for the Decarboxylative Cross-Coupling Reaction between Various α-Oxocarboxylic Acids and Cinnamic Acid. To a 20 mL Schlenk tube was added α-oxocarboxylic acids (0.5 mmol, 1.0 equiv), cinnamic acid (148 mg, 1.0 mmol, 2.0 equiv), $K_2S_2O_8$ (337.5 mg, 1.25 mmol), $HCOONa{\cdot}2H_2O$ (104 mg, 1.0 mmol), and $FeCl_2$ (6.3 mg, 0.05 mmol). The tube was evacuated and backfilled with N_2 three times. H_2O (1.7 mL) and DMSO (0.3 mL) were added. The reaction mixture was stirred at 120 °C for 15 h. Upon completion, the resulting mixture was dilute by EtOAc and washed with H_2O. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The resulting residue was purified by column chromatography on silica gel to give the desired product α,β-unsaturated carbonyls.

General Procedure for the Decarboxylative Cross-Coupling Reaction between Benzoylformic Acid and Various Acrylic Acids. To a 20 mL Schlenk tube was added benzoylformic acid (75 mg, 0.5 mmol, 1.0 equiv), acrylic acids (2.0 mmol, 4.0 equiv), $K_2S_2O_8$ (337.5 mg, 1.25 mmol), $HCOONa{\cdot}2H_2O$ (104 mg, 1.0 mmol), and $FeCl_2$ (6.3 mg, 0.05 mmol). The tube was evacuated and backfilled with N_2 three times. H_2O (1.0 mL) and DMSO (3.0 mL) were added. The reaction mixture was stirred at 120 °C for 15 h. Upon completion, the resulting mixture was diluted by EtOAc and washed with H_2O.

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The organic phase was separated, dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The resulting residue was purified by column chromatography on silica gel to give the desired product α,β-unsaturated carbonyls.

(*E*)-Chalcone (1):[9b] By following the typical procedure, the product was isolated as a yellow solid, 86.3 mg (83%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 56−58 °C (lit.[9b] mp = 55−57 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40−7.42 (m, 3 H), 7.48−7.60 (m, 4 H), 7.63−7.65 (m, 2 H), 7.81 (d, J = 16.0 Hz, 1 H), 8.01−8.03 (m, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 122.1, 128.4, 128.5, 128.7, 129.0, 130.6, 132.8, 134.9, 138.2, 144.9, 190.6 ppm. Anal. Calcd for $C_{15}H_{12}O$ Elemental Analysis: C, 86.51; H, 5.81. Found: C, 86.47; H, 5.83.

(*E*)-3-Phenyl-1-(*p*-tolyl)prop-2-en-1-one (2):[9b] By following the typical procedure, the product was isolated as a pale yellow solid, 89.9 mg (81%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 48−50 °C (lit.[9b] mp = 47−49 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.31 (s, 3 H), 7.18 (d, J = 8.0 Hz, 2 H), 7.29−7.30 (m, 3 H), 7.43 (d, J = 16.0 Hz, 1 H), 7.51−7.54 (m, 2 H), 7.70 (d, J = 16.0 Hz, 1 H), 7.84 (d, J = 8.0 Hz, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 21.7, 122.1, 128.5, 128.7, 129.0, 129.4, 130.5, 135.0, 135.7, 143.7, 144.4, 190.0 ppm. Anal. Calcd for $C_{16}H_{14}O$ Elemental Analysis: C, 86.45; H, 6.35. Found: C, 86.56; H, 6.23.

(*E*)-3-Phenyl-1-(*m*-tolyl)prop-2-en-1-one (3):[12] By following the typical procedure, the product was isolated as a pale yellow solid, 91.0 mg (82%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 60−62 °C (lit.[17a] mp = 59−60 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.43 (s, 3 H), 7.38−7.42 (m, 5 H), 7.52 (d, J = 16.0 Hz, 1 H), 7.63−7.65 (m, 2 H), 7.78−7.83 (m, 3 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 21.5, 122.3, 125.8, 128.4, 128.5, 129.0, 129.1, 130.5, 133.6, 135.0, 138.3, 138.5, 144.7, 190.7 ppm. Anal. Calcd for $C_{16}H_{14}O$ Elemental Analysis: C, 86.45; H, 6.35. Found: C, 86.37; H, 6.48.

(*E*)-3-Phenyl-1-(*o*-tolyl)prop-2-en-1-one (4):[9b] By following the typical procedure, the product was isolated as a pale yellow oil, 86.6 mg (78%), flash chromatography (petroleum ether/ethyl acetate, 30/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.37 (s, 3 H), 7.06 (d, J = 16.0 Hz, 1 H), 7.17−7.21 (m, 2 H), 7.28−7.43 (m, 6 H), 7.49−7.49 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 21.2, 125.5, 126.8, 128.1, 128.5, 129.0, 130.5, 130.7, 131.4, 134.6, 137.0, 139.1, 146.0, 196.6 ppm; LRMS: m/z calcd for $C_{16}H_{14}O$ (M+H): 223, found: 223.

(*E*)-1-(4-Methoxyphenyl)-3-phenylprop-2-en-1-one (5):[9b] By following the typical procedure, the product was isolated as a pale yellow colorless solid, 103.5 mg (87%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 104−106 °C (lit.[9b] mp = 94−96 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.88 (s, 3 H), 6.96−7.00 (m, 2 H), 7.40−7.42 (m, 3 H), 7.55 (d, J = 16.0 Hz, 1 H), 7.63−7.65 (m, 2 H), 7.80 (d, J = 16.0 Hz, 1 H), 8.04 (d, J = 8.0 Hz, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 55.5, 113.9, 121.9, 128.4, 129.0, 130.4, 130.9, 131.1, 135.1, 143.7, 144.0, 190.0 ppm. Anal. Calcd for $C_{16}H_{14}O_2$ Elemental Analysis: C, 80.65; H, 5.92. Found: C, 80.89; H, 5.75.

(*E*)-1-(3,4-Dimethoxyphenyl)-3-phenylprop-2-en-1-one (6):[9d] By following the typical procedure, the product was isolated as a yellow oil, 113.9 mg (85%), flash chromatography (petroleum ether/ethyl acetate, 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.85 (s, 3H), 3.86 (s, 3 H), 6.81 (d, J = 8.0 Hz, 1 H), 7.30−7.32 (m, 3 H), 7.46 (d, J = 16.0 Hz, 1 H), 7.53−7.55 (m, 3 H), 7.59 (dd, J = 2.0 Hz, 2.0 Hz, 1 H), 7.70 (d, J = 12.0 Hz, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 56.0, 56.1, 110.0, 110.8, 121.6, 123.1, 128.4, 128.9, 130.4, 131.3, 135.1, 144.0, 149.2, 153.3, 188.5 ppm; LRMS: m/z calcd for $C_{17}H_{16}O_3$ (M + H): 269, found: 269.

(*E*)-1-(2,4-Dimethoxyphenyl)-3-phenylprop-2-en-1-one (7):[9d] By following the typical procedure, the product was isolated as a pale yellow solid, 112.6 mg (84%), flash chromatography (petroleum ether/ethyl acetate, 10/1), mp = 76−79 °C (lit.[17b] mp = 80.5−81 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.76 (s, 3H), 3.80 (s, 3 H), 6.40 (d, J = 2.4 Hz, 1 H), 6.46 (dd, J = 2.0 Hz, 2.4 Hz, 1 H), 7.26−7.32 (m, 3 H), 7.43 (d, J = 16.0 Hz, 1 H), 7.45−7.51 (m, 2 H), 7.59 (d, J = 16.0 Hz, 1 H), 7.67 (d, J = 8.0 Hz, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 55.6, 55.8, 98.6, 105.3, 122.2, 127.2, 128.3, 128.9, 130.0, 132.9, 135.5, 142.0, 160.5, 164.2, 190.5 ppm. Anal. Calcd for $C_{17}H_{16}O_3$ Elemental Analysis: C, 76.10; H, 6.01. Found: C, 76.02; H, 6.16.

(*E*)-1-(4-Ethoxyphenyl)-3-phenylprop-2-en-1-one (8):[9b] By following the typical procedure, the product was isolated as a colorless solid, 115.9 mg (92%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 67−69 °C (lit.[9b] mp = 67−69 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.45 (t, J = 8.0 Hz, 3 H), 4.12 (q, J = 8.0 Hz, 2 H), 6.97 (d, J = 8.0 Hz, 2 H), 7.40−7.42 (m, 3 H), 7.55 (d, J = 16.0 Hz, 1 H), 7.63−7.65 (m, 2 H), 7.80 (d, J = 16.0 Hz, 1 H), 8.04 (d, J = 12.0 Hz, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 14.7, 63.8, 114.3, 121.9, 128.4, 129.0, 130.3, 130.8, 130.9, 135.1, 143.9, 162.9, 188.7 ppm. Anal. Calcd for $C_{17}H_{16}O_2$ Elemental Analysis: C, 80.93; H, 6.39. Found: C, 80.90; H, 6.41.

(*E*)-1-(4-Fluorophenyl)-3-phenylprop-2-en-1-one (9):[9b] By following the typical procedure, the product was isolated as a pale yellow solid, 92.7 mg (82%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 72−74 °C (lit.[9b] mp = 71−73 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.06−7.10 (m, 2 H), 7.32−7.33 (m, 3 H), 7.41 (d, J = 16.0 Hz, 1 H), 7.53−7.56 (m, 2 H), 7.72 (d, J = 16.0 Hz, 1 H), 7.85−7.98 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 115.8 (d, J = 22.0 Hz), 121.6, 128.5, 129.0, 130.7, 131.1(d, J = 9.0 Hz), 134.5 (d, J = 3.0 Hz), 134.8, 145.1, 165.6 (d, J = 253.0 Hz), 190.0 ppm. Anal. Calcd for $C_{15}H_{11}FO$ Elemental Analysis: C, 79.63; H, 4.90. Found: C, 79.76; H, 4.82.

(*E*)-1-(4-Chlorophenyl)-3-phenylprop-2-en-1-one (10):[9b] By following the typical procedure, the product was isolated as a pale yellow solid, 94.4 mg (78%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 84−86 °C (lit.[9b] mp = 83−85 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30−7.32 (m, 3 H), 7.35−7.40 (m, 3 H), 7.52−7.54 (m, 2 H), 7.71 (d, J = 16.0 Hz, 1 H), 7.85 (d, J = 8.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 121.5, 128.6, 128.9, 129.0, 130.0, 130.8, 134.7, 136.5, 139.2, 145.4, 189.1 ppm. Anal. Calcd for $C_{15}H_{11}ClO$ Elemental Analysis: C, 74.23; H, 4.57. Found: C, 74.42; H, 4.48.

(*E*)-1-(4-Bromophenyl)-3-phenylprop-2-en-1-one (11):[9b] By following the typical procedure, the product was isolated as a pale yellow solid, 91.5 mg (64%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 98−100 °C (lit.[9b] mp = 90−92 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.31−7.33 (m, 3 H), 7.38 (d, J = 12.0 Hz, 1 H),7.52−7.55 (m, 4 H), 7.72 (d, J = 12.0 Hz, 1 H), 7.79 (d, J = 8.0 Hz, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 121.4, 127.9, 128.6, 129.0, 130.1, 130.8, 132.0, 134.7, 136.9, 145.4, 189.3 ppm. Anal. Calcd for $C_{15}H_{11}BrO$ Elemental Analysis: C, 62.74; H, 3.86. Found: C, 62.94; H, 3.73.

(*E*)-1-(3-Bromophenyl)-3-phenylprop-2-en-1-one (12):[16a] By following the typical procedure, the product was isolated as a pale yellow solid, 97.2 mg (68%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 92−94 °C (lit.[17a] mp = 92−94 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29 (t, J = 8.0 Hz, 1 H), 7.33−7.39 (m, 4 H), 7.55−7.57 (m, 2 H), 7.62 (dd, J = 4.0 Hz, 4.0 Hz, 1 H), 7.73(d, J = 16.0 Hz, 1 H), 7.85 (d, J = 8.0 Hz, 1 H), 8.05 (s, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 121.4, 123.0, 127.0, 128.6, 129.1, 130.2, 130.9, 131.5, 134.6, 135.6, 140.0, 145.7, 189.0 ppm. Anal. Calcd for $C_{15}H_{11}BrO$ Elemental Analysis: C, 62.74; H, 3.86. Found: C, 62.60; H, 3.92.

(*E*)-1-(2-Bromophenyl)-3-phenylprop-2-en-1-one (13):[16b] By following the typical procedure, the product was isolated as a pale yellow oil, 101.5 mg (71%), flash chromatography (petroleum ether/ethyl acetate, 30/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.37 (s, 3 H), 7.10 (d, J = 16.0 Hz, 1 H), 7.31−7.45 (m, 7 H), 7.54−7.57 (m, 2 H), 7.64 (d, J = 8.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 119.5, 126.2, 127.4, 128.6, 129.0, 129.2, 131.0, 131.4, 133.5, 134.4, 141.2, 146.7, 194.8 ppm; LRMS: m/z calcd for $C_{15}H_{11}BrO$ (M + H): 288, found: 288.

(*E*)-1-(4-Iodophenyl)-3-phenylprop-2-en-1-one (14):[16c] By following the typical procedure, the product was isolated as a colorless solid, 111.9 mg (67%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 112−114 °C (lit.[17a] mp = 112−113 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42−7.48 (m, 4 H), 7.63−7.66 (m, 2

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H),7.72−7.75 (m, 2 H), 7.82 (d, J = 16.0 Hz, 1 H), 7.85−7.88 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 100.7, 121.4, 128.6, 129.0, 130.0, 130.8, 134.7, 137.5, 138.0, 145.5, 189.7 ppm. Anal. Calcd for $C_{15}H_{11}IO$ Elemental Analysis: C, 53.92; H, 3.32. Found: C, 53.78; H, 3.41.

(*E*)-3-Phenyl-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (15):[9b] By following the typical procedure, the product was isolated as colorless solid, 88.3 mg (64%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 114−116 °C (lit.[9b] mp = 114−116 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44−7.51 (m, 4 H), 7.65−7.67 (m, 2 H),7.78 (d, J = 12.0 Hz, 1 H), 7.84 (d, J = 16.0 Hz, 1 H), 8.11 (d, J = 8.0 Hz, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 121.6, 123.7 (d, J = 271.0 Hz), 125.7 (q, J = 2.0 Hz), 128.6, 128.8, 129.0, 131.0, 134.1 (d, J = 32.0 Hz), 134.5, 146.2, 189.7 ppm. Anal. Calcd for $C_{16}H_{11}F_3O$ Elemental Analysis: C, 69.56; H, 4.01. Found: C, 69.72; H, 3.93.

(*E*)-1-(Naphthalen-2-yl)-3-phenylprop-2-en-1-one (16):[12] By following the typical procedure, the product was isolated as a pale yellow solid, 82.6 mg (64%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 106−108 °C (lit.[17c] mp = 105 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41−7.44 (m, 3 H), 7.54−7.61 (m, 2 H), 7.66−7.70 (m, 3 H), 7.85−7.93 (m, 3 H), 7.98 (d, J = 8.0 Hz, 1 H), 8.10 (dd, J = 4.0 Hz, 4.0 Hz, 1 H), 8.52 (s, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 122.1, 124.5, 126.8, 127.9, 128.4, 128.5, 128.6, 129.0, 129.6, 130.0, 130.6, 132.6, 135.0, 135.5, 135.6, 144.8, 190.3 ppm. Anal. Calcd for $C_{19}H_{14}O$ Elemental Analysis: C, 88.34; H, 5.46. Found: C, 88.61; H, 5.28.

(*E*)-3-Phenyl-1-(thiophen-2-yl)prop-2-en-1-one (17):[12] By following the typical procedure, the product was isolated as a pale yellow solid, 66.3 mg (62%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 82−84 °C (lit.[17d] mp = 82−83 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.16−7.18 (m, 1 H), 7.40−7.44 (m, 4 H), 7.62−7.65 (m, 2 H), 7.67 (dd, J = 0.8 Hz, 0.8 Hz, 1 H), 7.83−7.87 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 121.6, 128.3, 128.5, 129.0, 130.6, 131.9, 134.0, 134.7, 144.1, 145.6, 182.1 ppm. Anal. Calcd for $C_{13}H_{10}OS$ Elemental Analysis: C, 72.87; H, 4.70. Found: C, 72.95; H, 4.64.

(*E*)-1-(Furan-2-yl)-3-phenylprop-2-en-1-one (18):[16d] By following the typical procedure, the product was isolated as a yellow oil, 50.1 mg (51%), flash chromatography (petroleum ether/ethyl acetate, 30/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.60 (dd, J = 1.6 Hz, 1.6 Hz, 1 H), 7.34 (d, J = 4.0 Hz, 1 H), 7.40−7.48 (m, 4 H), 7.64−7.66 (m, 3 H), 7.88 (d, J = 16.0 Hz, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 112.6, 117.6, 121.2, 128.6, 129.0, 130.6, 134.7, 144.0, 146.6, 153.7, 178.0 ppm; LRMS: m/z calcd for $C_{13}H_{10}O_2$ (M + H), 199; found, 199.

(*E*)-4-Phenylbut-3-en-2-one (19):[16e] By following the typical procedure, the product was isolated as a yellow solid, 38.0 mg (52%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 40−42 °C (lit.[17e] mp = 40−41 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.37 (s, 3 H), 6.70 (d, J = 20.0 Hz, 1 H), 7.37−7.39 (m, 3 H), 7.48−7.54 (m, 3 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 27.5, 127.1, 128.3, 129.0, 130.5, 134.4, 143.4, 198.4 ppm. Anal. Calcd for $C_{10}H_{10}O$ Elemental Analysis: C, 82.16; H, 6.89. Found: C, 82.32; H, 6.74.

(*E*)-4-Oxo-6-phenylhex-5-enoic acid (20). By following the typical procedure, the product was isolated as a colorless solid, 38.8 mg (38%), flash chromatography (petroleum ether/ethyl acetate, 1/1), mp = 124−126 °C (lit.[17o] mp = 124−126 °C); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 2.47 (t, J = 8.0 Hz, 2 H), 2.92 (t, J = 8.0 Hz, 2 H), 3.72 (brs, 1 H), 6.92 (d, J = 16.0 Hz, 1 H), 7.43−7.44 (m, 3 H), 7.62 (d, J = 16.0 Hz, 1 H), 7.71−7.73 (m, 2 H); ^{13}C {^{1}H} NMR (DMSO-d_6, 101 MHz) δ 122.1, 124.5, 126.8, 127.9, 128.4, 128.5, 128.6, 129.0, 129.6, 130.0, 130.6, 132.6, 135.0, 135.5, 135.6, 144.8, 190.3 ppm. Anal. Calcd for $C_{12}H_{12}O_3$ Elemental Analysis: C, 70.57; H, 5.92. Found: C, 70.51; H, 5.95.

Cinnamamide (21):[16f] By following the typical procedure, the product was isolated as a colorless solid, flash chromatography (petroleum ether/ethyl acetate, 1/1), 30.9 mg (42%), mp = 144−147 °C (lit.[16f] mp = 148−150 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.84 (brs, 1 H), 5.98 (brs, 1 H), 6.43 (d, J = 16.0 Hz, 1 H), 7.29−7.30 (m, 3 H), 7.43−7.46 (m, 2 H), 7.57 (d, J = 16.0 Hz, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 119.7, 128.0, 128.9, 130.0, 134.5, 142.5, 168.1 ppm. Anal. Calcd for C_9H_9NO Elemental Analysis: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.62; H, 6.20; N, 9.48.

***N*,*N*-Diethylcinnamamide (22):**[16g] By following the typical procedure, the product was isolated as a colorless solid, 45.7 mg (45%), flash chromatography (petroleum ether/ethyl acetate, 2/1), mp = 61−63 °C (lit.[17f] mp = 60−62 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.19−1.26 (m, 6 H), 3.48−3.50 (m, 5 H), 6.83 (d, J = 16.0 Hz, 1 H), 7.32−7.39 (m, 3 H), 7.52−7.54 (m, 2 H), 7.72 (d, J = 12.0 Hz, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 13.3, 15.1, 41.1, 42.3, 117.8, 127.8, 128.8, 129.5, 135.5, 142.3, 165.7 ppm. Anal. Calcd for $C_{13}H_{17}NO$ Elemental Analysis: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.94; H, 8.48; N, 6.73.

***N*-Methyl-*N*-phenylcinnamamide (23):**[16h] By following the typical procedure, the product was isolated as a colorless solid, 52.7 mg (41%), flash chromatography (petroleum ether/ethyl acetate, 3/1), mp = 66−69 °C (lit.[17g] mp = 67−68 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.41 (s, 3 H), 6.37 (d, J = 16.0 Hz, 1 H), 7.22−7.38 (m, 8 H), 7.44 (t, J = 8.0 Hz, 2 H), 7.68 (d, J = 16.0 Hz, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 37.6, 118.8, 127.3, 127.6, 127.9, 128.7, 129.5, 129.7, 13.5.2, 141.7, 143.6, 166.2 ppm. Anal. Calcd for $C_{16}H_{15}NO$ Elemental Analysis: C, 80.98; H, 6.37; N, 5.90. Found: C, 81.14; H, 6.44; N, 5.76.

(*E*)-1-Phenyl-3-(*p*-tolyl)prop-2-en-1-one (25):[17h] By following the general procedure, the product was isolated as a pale yellow solid, 99.9 mg (90%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 96−98 °C (lit.[17h] mp = 96−97.5 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.24 (t, J = 8.0 Hz, 2 H), 7.47−7.58 (m, 6 H), 7.80 (d, J = 16.0 Hz, 1 H), 8.00−8.03 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 21.6, 121.1, 128.4, 128.5, 128.6, 129.7, 132.2, 132.7, 138.4, 141.1, 145.0, 190.7 ppm. Anal. Calcd for $C_{16}H_{14}O$ Elemental Analysis: C, 86.45; H, 6.35. Found: C, 86.31; H, 6.43.

(*E*)-1-Phenyl-3-(*m*-tolyl)prop-2-en-1-one (26):[6c] By following the general procedure, the product was isolated as a pale yellow solid, 96.6 mg (87%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 62−64 °C (lit.[6c] mp = 59−61 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.39 (s, 3 H), 7.23 (t, J = 8.0 Hz, 1 H), 7.30 (t, J = 8.0 Hz, 1 H), 7.43−7.59 (m, 6 H), 7.78 (d, J = 16.0 Hz, 1 H), 8.01−8.03 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 121.9, 125.8, 128.5, 128.6, 128.9, 129.1, 131.5, 132.8, 134.9, 138.3, 138.7, 145.1, 190.6 ppm. Anal. Calcd for $C_{16}H_{14}O$ Elemental Analysis: C, 86.45; H, 6.35. Found: C, 86.59; H, 6.28.

(*E*)-1-Phenyl-3-(*o*-tolyl)prop-2-en-1-one (27):[16i] By following the general procedure, the product was isolated as a pale yellow oil, 94.4 mg (85%), flash chromatography (petroleum ether/ethyl acetate, 30/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.46 (s, 3 H), 7.21−7.31 (m, 3 H), 7.44−7.51 (m, 3 H), 7.57 (t, J = 8.0 Hz, 1 H), 7.69 (d, J = 8.0 Hz, 1 H), 8.03 (d, J = 8.0 Hz, 2 H), 8.12 (d, J = 16.0 Hz, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 19.9, 123.1, 126.4, 126.5, 128.6, 128.7, 130.3, 131.0, 132.9, 133.9, 138.3, 138.4, 142.5, 190.5 ppm; LRMS: m/z calcd for $C_{16}H_{14}O$ (M + H), 223; found, 223.

(*E*)-3-(4-Methoxyphenyl)-1-phenylprop-2-en-1-one (28):[17h] By following the general procedure, the product was isolated as a yellow solid, 97.6 mg (82%), flash chromatography (petroleum ether/ethyl acetate, 10/1), mp = 74−76 °C (lit.[17h] mp = 71−76 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.84 (s, 3 H), 6.93 (d, J = 8.0 Hz, 2 H), 7.41 (d, J = 16.0 Hz, 1 H), 7.49 (d, J = 8.0 Hz, 2 H), 7.55−7.61 (m, 3 H), 7.79 (d, J = 12.0 Hz, 1 H), 8.00−8.02 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 55.4, 114.5, 119.8, 127.6, 128.4, 128.6, 130.3, 132.6, 138.5, 144.7, 161.7, 190.6 ppm. Anal. Calcd for $C_{16}H_{14}O_2$ Elemental Analysis: C, 80.65; H, 5.92. Found: C, 80.81; H, 5.84.

(*E*)-3-(3-Methoxyphenyl)-1-phenylprop-2-en-1-one (29):[6c] By following the general procedure, the product was isolated as a pale yellow solid, 92.8 mg (78%), flash chromatography (petroleum ether/ethyl acetate, 20/1), mp = 50−52 °C (lit.[6c] mp = 62−63 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.76 (s, 3 H), 6.88 (dd, J = 4.0 Hz, 4.0 Hz, 1 H), 7.07 (s, 1 H), 7.14−7.17 (m, 1 H), 7.24 (t, J = 8.0 Hz, 1 H), 7.40−7.44 (m, 3 H), 7.50 (t, J = 8.0 Hz, 1 H), 7.68 (d, J = 16.0 Hz, 1 H), 7.92−7.94 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 55.4, 113.5, 116.3, 121.1, 122.4, 128.5, 128.7, 130.0, 132.8, 136.3, 138.2,

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144.8, 160.0, 190.6 ppm. Anal. Calcd for $C_{16}H_{14}O_2$ Elemental Analysis: C, 80.65; H, 5.92. Found: C, 80.52; H, 5.98.

(*E*)-3-(2-Methoxyphenyl)-1-phenylprop-2-en-1-one (30):[6c] By following the general procedure, the product was isolated as a pale yellow oil, 90.4 mg (76%), flash chromatography (petroleum ether/ethyl acetate, 20/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.91 (s, 3 H), 6.94 (d, J = 8.0 Hz, 1 H), 6.99 (t, J = 8.0 Hz, 1 H), 7.36−7.40 (m, 1 H), 7.49 (t, J = 8.0 Hz, 2 H), 7.55−7.64 (m, 3 H), 8.01−8.03 (m, 2 H), 8.12 (d, J = 16.0 Hz, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 55.6, 111.3, 120.8, 122.9, 123.9, 128.5, 128.6, 129.3, 131.8, 132.6, 138.5, 140.5, 158.8, 191.2 ppm; LRMS: m/z calcd for $C_{16}H_{14}O_2$ (M + H), 239; found, 239.

(*E*)-3-(4-Hydroxyphenyl)-1-phenylprop-2-en-1-one (31):[16j] By following the general procedure, the product was isolated as a yellow solid, 48.2 mg (43%), flash chromatography (hexane/acetone, 3/1), mp = 184−186 °C (lit.[16j] mp = 187−188 °C); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 6.85 (d, J = 8.0 Hz, 2 H), 7.57 (t, J = 8.0 Hz, 2 H), 7.64−7.68 (m, 1 H), 7.73 (dd, J = 4.0 Hz, 8.0 Hz, 4 H), 8.11−8.14 (m, 2 H), 10.12 (brs, 1 H); ^{13}C {^{1}H} NMR (DMSO-d_6, 101 MHz) δ 116.3, 118.9, 126.2, 128.8, 129.2, 131.5, 133.3, 138.4, 145.0, 160.0, 189.5 ppm. Anal. Calcd for $C_{15}H_{12}O_2$ Elemental Analysis: C, 80.34; H, 5.39. Found: C, 80.29; H, 5.43.

(*E*)-3-(4-Nitrophenyl)-1-phenylprop-2-en-1-one (32):[8b] By following the general procedure, the product was isolated as a yellow solid, 75.6 mg (60%), flash chromatography (petroleum ether/ethyl acetate, 10/1), mp = 162−164 °C (lit.[8b] mp = 163−164 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54 (t, J = 8.0 Hz, 2 H), 7.62−7.67 (m, 2 H), 7.79−7.83 (m, 3 H), 8.03−8.05 (m, 2 H), 8.29 (d, J = 8.0 Hz, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 124.3, 125.7, 128.6, 128.9, 129.0, 133.4, 137.6, 141.1, 141.5, 148.6, 189.7 ppm. Anal. Calcd for $C_{15}H_{11}NO_3$ Elemental Analysis: C, 71.14; H, 4.38; N, 5.53. Found: C, 71.32; H, 4.41; N, 5.41.

(*E*)-3-(3-Nitrophenyl)-1-phenylprop-2-en-1-one (33):[17i] By following the general procedure, the product was isolated as a pale yellow solid, 77.2 mg (61%), flash chromatography (petroleum ether/ethyl acetate, 10/1), mp = 142−144 °C (lit.[17j] mp = 140−142 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54 (t, J = 8.0 Hz, 2 H), 7.61−7.68 (m, 3 H), 7.84 (d, J = 16.0 Hz, 1 H), 7.93 (d, J = 8.0 Hz, 1 H), 8.04−8.07 (m, 2 H), 8.27 (dd, J = 4.0 Hz, 4.0 Hz, 1 H), 8.52−8.53 (m, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 122.4, 124.6, 124.7, 128.6, 128.8, 130.1, 130.3, 133.3, 134.4, 136.7, 141.7, 148.8, 189.7 ppm. Anal. Calcd for $C_{15}H_{11}NO_3$ Elemental Analysis: C, 71.14; H, 4.38; N, 5.53. Found: C, 71.08; H, 4.42; N, 5.50.

(*E*)-3-(2-Nitrophenyl)-1-phenylprop-2-en-1-one (34):[16k] By following the general procedure, the product was isolated as a pale yellow solid, 81.0 mg (64%), flash chromatography (petroleum ether/ethyl acetate, 10/1), mp = 112−114 °C (lit.[17k] mp = 111−113 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.32 (d, J = 12.0 Hz, 1 H), 7.50−7.63 (m, 4 H), 7.68−7.78 (m, 2 H), 8.01−8.03 (m, 2 H), 8.08 (d, J = 8.0 Hz, 1 H), 8.14 (d, J = 16.0 Hz, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 125.0, 127.4, 128.7, 128.8, 129.3, 130.4, 131.4, 133.2, 133.6, 137.4, 140.3, 148.6, 190.6 ppm. Anal. Calcd for $C_{15}H_{11}NO_3$ Elemental Analysis: C, 71.14; H, 4.38; N, 5.53. Found: C, 71.02; H, 4.45; N, 5.48.

(*E*)-3-(4-Fluorophenyl)-1-phenylprop-2-en-1-one (35):[17l] By following the general procedure, the product was isolated as a colorless solid, 79.1 mg (70%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 83−85 °C (lit.[17l] mp = 83−84 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.11 (t, J = 8.0 Hz, 2 H), 7.44−7.53 (m, 3 H), 7.58−7.66 (m, 3 H), 7.78 (d, J = 16.0 Hz, 1 H), 8.01−8.03 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 116.1 (d, J = 22.0 Hz), 121.8 (d, J = 3.0 Hz), 128.5, 128.7, 130.4 (d, J = 8.0 Hz), 131.2, 132.9, 138.1, 143.5, 164.1 (d, J = 251.0 Hz), 190.4 ppm. Anal. Calcd for $C_{15}H_{11}FO$ Elemental Analysis: C, 79.63; H, 4.90. Found: C, 79.78; H, 4.84.

(*E*)-3-(3-Fluorophenyl)-1-phenylprop-2-en-1-one (36). By following the general procedure, the product was isolated as a colorless solid, 76.8 mg (68%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 86−88 °C (lit.[17m] mp = 87−89 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34−7.40 (m, 2 H), 7.50−7.55 (m, 4 H), 7.58−7.64 (m, 2 H), 7.74 (d, J = 16.0 Hz, 1 H), 8.01−8.04 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 123.3, 126.8, 127.9, 128.6, 128.7, 130.2, 130.4, 133.1, 135.0, 136.8, 137.9, 143.1, 190.1 ppm. Anal. Calcd for $C_{15}H_{11}FO$ Elemental Analysis: C, 79.63; H, 4.90. Found: C, 79.58; H, 4.95.

(*E*)-3-(4-Chlorophenyl)-1-phenylprop-2-en-1-one (37):[17h] By following the general procedure, the product was isolated as a pale yellow solid, 75.0 mg (62%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 113−115 °C (lit.[17h] mp = 113.5−115.5 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.31 (d, J = 8.0 Hz, 2 H), 7.43 (t, J = 16.0 Hz, 1 H), 7.49−7.54 (m, 3 H), 7.68 (d, J = 16.0 Hz, 1 H), 7.93−7.95 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 121.4, 127.5, 127.7, 128.2, 128.6, 131.9, 132.4, 135.4, 137.0, 142.3, 189.2 ppm. Anal. Calcd for $C_{15}H_{11}ClO$ Elemental Analysis: C, 74.23; H, 4.57. Found: C, 74.39; H, 4.48.

(*E*)-3-(4-Bromophenyl)-1-phenylprop-2-en-1-one (38):[16l] By following the general procedure, the product was isolated as a colorless solid, 95.8 mg (67%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 122−124 °C (lit.[16l] mp = 127−128 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.49−7.62 (m, 8 H), 7.74 (d, J = 16.0 Hz, 1 H), 8.00−8.03 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 122.6, 124.8, 128.5, 128.7, 129.8, 132.2, 133.0, 133.8, 138.0, 143.4, 190.3 ppm. Anal. Calcd for $C_{15}H_{11}BrO$ Elemental Analysis: C, 62.74; H, 3.86. Found: C, 62.98; H, 3.73.

(*E*)-3-[(1,1′-Biphenyl)-4-yl]-1-phenylprop-2-en-1-one (39):[16m] By following the general procedure, the product was isolated as a yellow solid, 92.3 mg (65%), flash chromatography (petroleum ether/ethyl acetate, 20/1), mp = 108−110 °C (lit.[16m] mp = 110−112 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38 (t, J = 8.0 Hz, 1 H), 7.45−7.56 (m, 4 H), 7.58−7.67 (m, 6 H), 7.73 (d, J = 8.0 Hz, 2 H), 7.86 (d, J = 16.0 Hz, 1 H), 8.03−8.05 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 121.9, 127.1, 127.6, 127.9, 128.5, 128.7, 128.9, 129.0, 132.8, 133.9, 138.3, 140.2, 143.4, 144.4, 190.6 ppm. Anal. Calcd for $C_{21}H_{16}O$ Elemental Analysis: C, 88.70; H, 5.67. Found: C, 88.46; H, 5.78.

(*E*)-4-(3-Oxo-3-phenylprop-1-en-1-yl)benzaldehyde (40):[8b] By following the general procedure, the product was isolated as a pale yellow solid, 74.3 mg (63%), flash chromatography (petroleum ether/ethyl acetate, 7/1), mp = 122−124 °C (lit.[8b] mp = 125 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 (t, J = 8.0 Hz, 2 H), 7.60−7.67 (m, 2 H), 7.78−7.85 (m, 3 H), 7.93 (d, J = 8.0 Hz, 2 H), 8.03−8.05 (m, 2 H), 10.5 (s, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 124.8, 128.6, 128.8, 128.9, 130.2, 133.2, 137.3, 137.8, 140.6, 142.8, 190.0, 191.5 ppm. Anal. Calcd for $C_{16}H_{12}O_2$ Elemental Analysis: C, 81.34; H, 5.12. Found: C, 81.48; H, 5.04.

(*E*)-1-Phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (41):[8b] By following the general procedure, the product was isolated as a colorless solid, 102.1 mg (74%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 126−128 °C (lit.[8b] mp = 128−129 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 (t, J = 8.0 Hz, 2 H), 7.58−7.63 (m, 2 H), 7.68 (d, J = 8.0 Hz, 2 H), 7.75 (d, J = 8.0 Hz, 2 H), 7.81 (d, J = 16.0 Hz, 1 H), 7.82−7.84 (m, 2H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 123.8 (d, J = 271.0 Hz), 124.3, 125.9 (d, J = 3.0 Hz), 128.5, 128.6, 128.8, 132.0 (d, J = 33.0 Hz), 133.2, 137.8, 138.3, 142.8, 190.1 ppm. Anal. Calcd for $C_{16}H_{11}F_3O$ Elemental Analysis: C, 69.56; H, 4.01. Found: C, 69.42; H, 4.08.

(*E*)-3-(4-((*E*)-3-Oxo-3-phenylprop-1-en-1-yl)phenyl)acrylic Acid (42). To a 20 mL Schlenk tube were added benzoylformic acid (75 mg, 0.5 mmol), 1,4-phenylenediacrylic acid (436 mg, 2.0 mmol), $K_2S_2O_8$ (337.5 mg, 1.25 mmol), $HCOONa{\cdot}2H_2O$ (104 mg, 1.0 mmol), and $FeCl_2$ (6.3 mg, 0.05 mmol). The tube was evacuated and backfilled with N_2 three times. DMSO (4.0 mL) was added. The reaction mixture was stirred at 120 °C for 15 h. Upon completion, the resulting mixture was diluted by EtOAc and washed with H_2O. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The resulting residue was purified by column chromatography on silica gel to give the desired product **42** in 45% yield (62.6 mg). Flash chromatography (hexane/acetone, 3/2), pale yellow solid, mp = 252−254 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 6.66 (d, J = 16.0 Hz, 1 H), 7.57−7.69 (m, 4 H), 7.75−7.81 (m, 3 H), 7.96 (d, J = 8.0 Hz, 2 H), 8.03 (d, J = 16.0 Hz, 1 H), 8.18 (d, J = 8.0 Hz, 2 H), 12.47 (brs, 1 H); ^{13}C {^{1}H} NMR (DMSO-d_6, 101 MHz) δ 120.9, 123.4, 129.1, 129.2, 129.3, 129.9, 133.7, 136.7, 136.8, 138.0,

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143.5, 143.6, 168.0, 189.6 ppm. Anal. Calcd for $C_{18}H_{14}O_3$ Elemental Analysis: C, 77.68; H, 5.07. Found: C, 77.61; H, 5.12.

(*E*)-1-Phenyl-3-(pyridin-3-yl)prop-2-en-1-one (43):[16n] By following the general procedure, the product was isolated as a pale yellow solid, 69.0 mg (66%), flash chromatography (petroleum ether/ethyl acetate, 3/1), mp = 102−104 °C (lit.[16n] mp = 104−105 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28−7.31 (m, 1 H), 7.50−7.55 (m, 2 H), 7.59−7.64 (m, 2 H), 7.80 (d, J = 16.0 Hz, 1 H), 7.98 (d, J = 8.0 Hz, 1 H), 8.02−8.04 (m, 2 H), 8.67 (s, 1 H), 8.91 (s, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 124.0, 128.3, 128.6, 128.8, 129.9, 133.2, 135.0, 137.7, 140.8, 149.6, 150.7, 189.8 ppm. Anal. Calcd for $C_{14}H_{11}NO$ Elemental Analysis: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.60; H, 5.34; N, 6.54.

(*E*)-1-Phenyl-3-(pyridin-2-yl)prop-2-en-1-one (44):[16o] By following the general procedure, the product was isolated as a pale yellow solid, 62.7 mg (60%), flash chromatography (petroleum ether/ethyl acetate, 5/1), mp = 50−52 °C (lit.[17n] mp = 59−61 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30−7.33 (m, 1 H), 7.48−7.53 (m, 3 H), 7.60 (d, J = 8.0 Hz, 1 H), 7.74−7.80 (m, 2 H), 8.10−8.16 (m, 3 H), 8.69 (d, J = 4.0 Hz, 1 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 124.5, 125.5, 125.7, 128.7 128.8, 133.1, 137.0, 137.8, 142.7, 150.1, 153.2, 190.5 ppm. Anal. Calcd for $C_{14}H_{11}NO$ Elemental Analysis: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.52; H, 5.36; N, 6.57.

(*E*)-1-Phenyl-3-(thiophen-2-yl)prop-2-en-1-one (45):[16p] By following the general procedure, the product was isolated as yellow solid, 77.0 mg (72%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 42−44 °C (lit.[16p] mp = 42−44 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.00−7.02 (m, 1 H), 7.18−7.29 (m, 2 H), 7.34 (d, J = 4.0 Hz, 1 H), 7.41−7.44 (m, 2 H), 7.48−7.52 (m, 1 H), 7.87 (d, J = 16.0 Hz, 1 H), 7.92−7.94 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 120.8, 128.3, 128.4, 128.6, 128.8, 132.1, 132.8, 137.2, 138.1, 140.4, 189.9 ppm. Anal. Calcd for $C_{13}H_{10}OS$ Elemental Analysis: C, 72.87; H, 4.70. Found: C, 72.98; H, 4.64.

(*E*)-3-(Furan-2-yl)-1-phenylprop-2-en-1-one (46):[16n] By following the general procedure, the product was isolated as a pale yellow oil, 41.6 mg (42%), flash chromatography (petroleum ether/ethyl acetate, 30/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.52 (dd, J = 4.0 Hz, 4.0 Hz, 1 H), 6.73 (d, J = 4.0 Hz, 1 H), 7.45−7.68 (m, 6 H), 8.02−8.04 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 112.7, 116.3, 119.3, 128.4, 128.6, 130.7, 132.8, 138.2, 144.9, 151.7, 189.9 ppm; LRMS: m/z calcd for $C_{13}H_{10}O_2$ (M + H), 199; found, 199.

(2*E*,4*E*)-1-Phenylhexa-2,4-dien-1-one (47):[16n] By following the general procedure, the product was isolated as a pale yellow solid, 27.5 mg (32%), flash chromatography (petroleum ether/ethyl acetate, 30/1), mp = 45−47 °C (lit.[16n] mp = 45−46 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.90 (d, J = 4.0 Hz, 3 H), 6.24−6.38 (m, 2 H), 6.87 (d, J = 4.0 Hz, 1 H), 7.37−7.47 (m, 3 H), 7.49−7.55 (m, 1 H), 7.94 (d, J = 8.0 Hz, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 18.9, 123.4, 128.4, 128.5, 130.6, 132.6, 138.3, 141.2, 145.3, 191.0 ppm. Anal. Calcd for $C_{12}H_{12}O$ Elemental Analysis: C, 83.69; H, 7.02. Found: C, 83.85; H, 6.92.

Dypnone (48):[16q] By following the general procedure, the product was isolated as a pale yellow oil, 62.2 mg (56%), flash chromatography (petroleum ether/ethyl acetate, 30/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.60 (s, 3 H), 7.17 (s, 1 H), 7.39−7.44 (m, 3 H), 7.45−7.49 (m, 2 H), 7.53−7.58 (m, 3 H), 7.98−8.00 (m, 2 H); ^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz) δ 18.9, 122.1, 126.5, 128.3, 128.6, 128.7, 129.2, 132.6, 139.4, 142.8, 155.2, 191.9 ppm; LRMS: m/z calcd for $C_{16}H_{14}O$ (M + H), 223; found, 223.

General Procedure for the Gram-Scale Reaction of Benzoylformic Acid with Cinnamic Acid (Scheme 3). To a 100 mL Schlenk tube were added benzoylformic acid (1.5 g, 10 mmol, 1.0 equiv), cinnamic acid (2.96 g, 20 mmol), $K_2S_2O_8$ (2.5 equiv), $HCOONa{\cdot}2H_2O$ (2.0 equiv), and $FeCl_2$ (10 mol %). The tube was evacuated and backfilled with N_2 three times. H_2O (17 mL), and DMSO (3 mL) was added. The reaction mixture was stirred at 120 °C for 24 h. Upon completion, the resulting mixture was diluted by EtOAc and washed with H_2O. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The resulting residue was purified by column chromatography on silica gel to give the desired product **1** in 62% yield (1.3 g).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The screening of the reaction conditions, control experimental details, radical trapping experimental details, and copies of ^{1}H and ^{13}C {^{1}H} NMR spectra for the products. This material is available free of charge via the Internet athttp://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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