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Organic Dye-Catalyzed Intermolecular Radical Coupling of α-Bromocarbonyls with Olefins: Photocatalytic Synthesis of 1,4-Ketocarbonyls Using Air as an Oxidant

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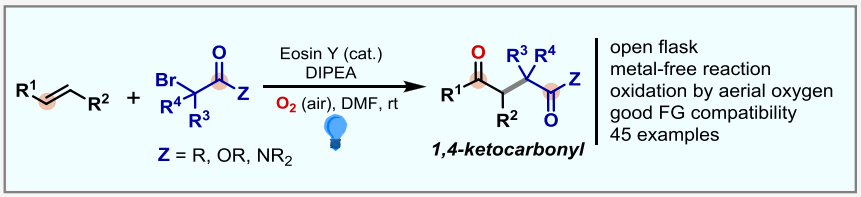

ABSTRACT: An organic dye-catalyzed visible light-promoted ketocarbonylation protocol of vinyl arenes has been disclosed with the help of α-bromocarbonyls where aerial oxygen played a role of an oxidant to install the keto-oxygen functionality. This unique process is compatible with both internal and terminal olefins and tolerates a diverse array of functional groups (ketone, ester, amide, diketones, ketoester, and malonate). This process is mild and environmentally friendly and deals with greener oxidants like oxygen, affording 1,4-ketocarbonyls as a value-added end product.

INTRODUCTION

1,4-Ketocarbonyl compounds have proven themselves a very interesting and versatile building block to access some of the extremely biologically important carbocyclic as well as heterocyclic compounds[1] since 1,4-ketocarbonyls can easily be converted to five-membered heterocycles by Paal−Knorr synthesis.[2] Consequently, numerous attempts have been made to figure out the synthetic route to access 1,4-ketocarbonyl compounds. Traditional approaches to synthesize this class of compounds involve Michael addition of an acyl anion equivalent with unsaturated carbonyl derivatives[3] and nucleophilic substitution of α-haloketones with enolates[4] (Scheme 1A). The conditions and substrates employed in these reactions to generate the reactive intermediates often result in limited scope and functional group compatibility. Recently, numerous methods,[5] including oxidative coupling of enolates,[6] addition of the homoenolate equivalent to acid derivatives,[7] and transition-metal-catalyzed couplings,[8] have been established to produce 1,4-ketocarbonyl compounds.[9] But, these processes frequently suffered by use of metal catalysts with multi-equivalent of toxic oxidants and/or harsh reaction conditions. Despite all significant attempts, a mild environmentally benign general synthetic route to 1,4-ketocarbonyls is still desirable and would be of significant utility.

Owing to their inherent greener reaction parameters,[10] recent years have witnessed the exploration of photoredox-catalyzed organic transformations *via* a free-radical process,[11] of particular attentiveness in the difunctionalization of alkenes by the radical-polar crossover (RPC)[12] mechanism promoted by visible light. Due to their easy access and structural benefits (contains two electrophilic groups: carbonyl and halide), α-halocarbonyls have been widely used as a flexible substrate in organic synthesis.[13] Moreover, recent exploitation of these substrates as a carbonylalkyl radical precursor under photoredox conditions further expands the scope of these substrates in radical reactions under mild conditions.,[13a14] Strategically, oxidative coupling of the carbonyl alkyl radicals with a 2-C-carbonyl synthon unit would render the title compound under radical conditions. Indeed, this strategy has been commonly adopted in the synthesis of γ-ketoesters, where α-haloesters have been oxidatively coupled with functionalized alkenes: enol ethers,[15] enol ester,[16] and enamines[17] (serving as masked keto-oxygen functionality) under radical conditions (Scheme 1B). A similar strategy to access 1,4-ketocarbonyls from simple unfunctionalized alkenes under photocatalytic conditions is rarer and has typically been combined with Kornblum-type oxidation[18] sequence, whereby the cationic intermediate (**II**) of the RPC process was trapped with an oxo-nucleophile, usually DMSO, to introduce the keto-oxygen functionality.[19,20] However, these methods are suffering by using highly expensive heavy-metal photocatalysts under essentially de-

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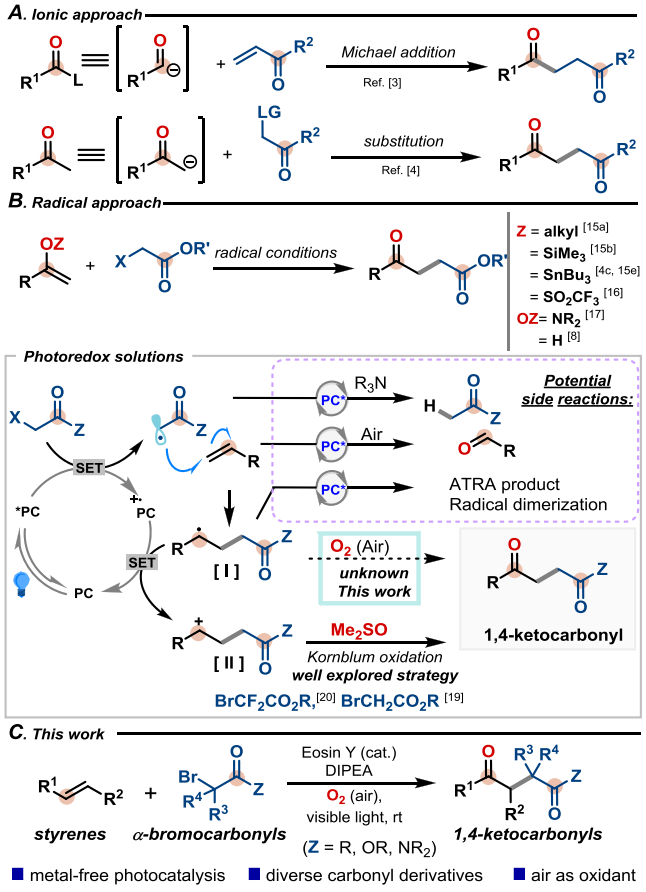
Scheme 1. Strategies of 1,4-Ketocarbonyl Synthesis and Present Work



gassed reaction conditions and the substrate scopes were mainly limited to haloesters[19] and halodifluoro acetamides.[20]

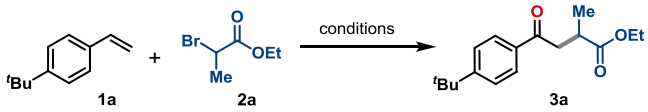
On the other hand, oxygen is the simplest and environmentally benign green oxidant and use of aerobic oxygen in reaction medium is an attractive but very challenging goal in developing new methods.[21] We envision that radical trapping of **I** with oxygen under oxidative conditions would render the formidable mild technique to overcome previously mentioned drawbacks. But, several obstacles need to be overcome to achieve this goal. One is how to trap the radical intermediate **I** with oxygen in a chemo-selective fashion without the influence of competitive ATRA[22] and radical dimerization reactions.[23] The other potential side reaction is the photoredox-catalyzed oxidative cleavage of alkenes to carbonyl compounds in the presence of oxygen.[24] To supress the damage of olefins through this cleavage and promote the oxygenation of **I**, the key challenge is finding an optimal oxygen stream. Additionally, reductive dehalogenation of halocarbonyls[25] by hydrogen atom transfer (HAT) from an amine radical cation (usually used to as a sacrificial electron donor in photocatalytic cycle) further makes this strategy challenging.

As part of our ongoing work on radical difunctionalization of olefin,[26] we report herein that by utilizing an organic dye Eosin Y, oxidative radical coupling of styrenes and diverse bromocarbonyls delivers 1,4-ketocarbonyls under mild aerobic irradiation conditions (Scheme 1C). The reaction proceeds in open air without the use of pure oxygen and exhibits broad functional group compatibility.

RESULTS AND DISCUSSION

Our initial study showed that the 1,4-ketoester **3a** can be formed with a promising 30% yield from 4-*tert*-butyl styrene (**1a**) and ethyl 2-bromopropionate (**2a**) with 2 mol % Eosin Y in the presence of triethyl amine in acetonitrile under air by irradiation with blue LED light (Table 1, entry 1). Improvement in yield was not observed upon screening with other organic photocatalysts such as Rose Bengal, 4-CzIPN, methylene blue, and rhodamin B (entries 2−5). Different common solvents like DCM, THF, and toluene did not enhance the yield (entries 6−8) until changed to highly polar solvent DMF with a satisfactory 56% yield (entry 9). This reaction was very sensitive to base: although organic bases (entries 10−12) could promote this transformation, inorganic bases were just ineffective to start the reaction (see details in Table S1). Among the organic bases screened, DIPEA was proven to be the best fit with a yield of 62%. Further optimization showed that when **2a** (3 equiv) and base (3 equiv) were added into the solution in two portions, the yield was improved to 75% (entry 13). Notably, conducting the reaction with pure oxygen diminished the yield of **3a**, possibly due to the damage of styrene by oxidative cleavage under high oxygen concentration (*vide supra*).[24] Control experiments revealed the importance of all these catalyst, light, air, and bases (entries 15−18). No desired product was observed by dropping any of these aforementioned components.

Table 1. Optimization of the Reaction Condition[a]



entry	photocatalyst	base	solvent	yield (%)[b]
1.	Eosin Y	TEA	CH_3CN	30
2.	Rose Bengal	TEA	CH_3CN	25
3.	4-CzIPN	TEA	CH_3CN	22
4.	methylene blue	TEA	CH_3CN	20
5.	rhodamin B	TEA	CH_3CN	18
6.	Eosin Y	TEA	DCM	24
7.	Eosin Y	TEA	THF	15
8.	Eosin Y	TEA	toluene	12
9.	Eosin Y	TEA	DMF	56
10.	Eosin Y	TMEDA	DMF	44
11.	Eosin Y	DBU	DMF	36
12.	Eosin Y	DIPEA	DMF	62
13.[c]	Eosin Y	DIPEA	DMF	75
14.[d]	Eosin Y	DIPEA	DMF	42
15.		DIPEA	DMF	0
16.[e]	Eosin Y	DIPEA	DMF	0
17.[f]	Eosin Y	DIPEA	DMF	0
18.	Eosin Y		DMF	0

[a]Reaction was carried out with **1a** (0.2 mmol), **2a** (0.4 mmol), base (0.4 mmol), photocatalyst (2 mol %), and solvent (2 mL) in a culture tube at rt. irradiated with a 12 W blue LED for 6 h. [b]Isolated yield. [c]Extra 1 equiv each of **2a** and base were added after 3 h. [d]Using pure oxygen. [e]In the dark. [f]Under degassed conditions.

With suitable conditions identified, the scope and generality of the visible light-mediated metal-free coupling reaction were investigated by employing a variety of styrenes. To explore the scope of terminal olefins, vinyl arenes bearing electron-donating and electron-withdrawing groups were examined

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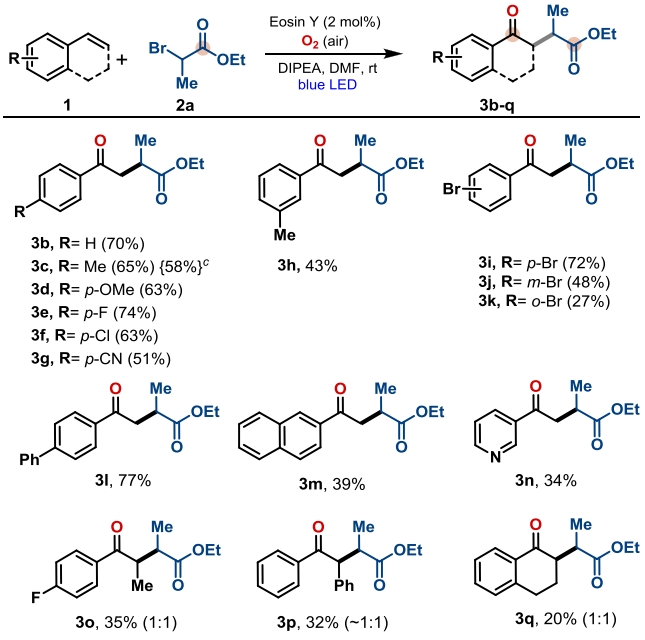
thoroughly (Scheme 2). It was found that that electronic effect had a little influence on the reaction output as both *para*-

Scheme 2. Scope of Olefins[a,b]

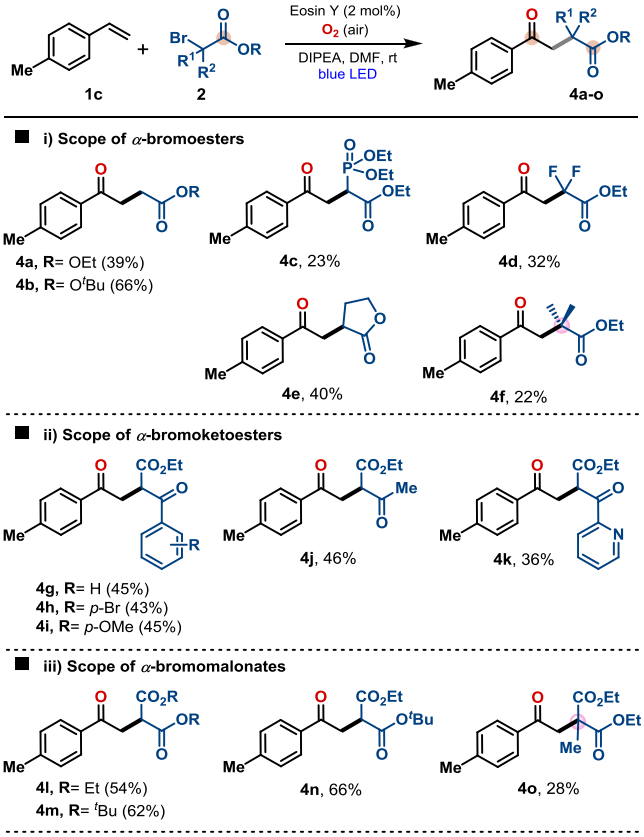


[a]Unless otherwise noted, all reactions were carried out with **1** (0.2 mmol), **2a** (0.6 mmol), DIPEA (0.6 mmol), Eosin Y (2 mol %), and DMF (2 mL) under air at rt. irradiated with a 12 W blue LED for 6 h. **2a** and base were added in two portions at an interval of 3 h. [b]Yields of isolated products. [c]Gram-scale reaction.

substituted electron-donating groups like -alkyl (**3a** and **3c**) and -methoxy (**3d**) and electron-withdrawing groups like -halogen (**3e**, **3f**, and **3i**), -nitrile (**3g**), -phenyl (**3l**) reacted in more or less similar ways with moderate to good conversion of products. Moreover, *meta*-substituted vinyl arenes (**3h** and **3j**) fairly took part in this reaction. Singly occupied *ortho*-substituted styrene (**3k**) finds no problem with taking part in this protocol albeit lower yield. But, vinyl mesitylene and pentafluoro styrene bearing *ortho*-disubstitution around a reacting double bond unfortunately failed to participate in this process. Although the poor reactivity of *ortho*-substituted styrenes could be correlated to their steric crowdedness around the reaction center, the same for *meta*-substrates is unclear. Pleasingly, styrenes bearing a fused aromatic ring (**3m**) or heteroatom (**3n**) reacted smoothly under this condition. With internal vinyl arenes (**3o**−**3q**), the reaction also proceeds under standard conditions but with low yield and no diastreoselectivity. Unfortunately, similar oxidative coupling of aliphatic olefins with **2a**, as proven with dodecene or cyclohexene, failed to afford the desired product. Moreover, a reaction attempt of α-substituted olefins, like α-methylstyrene or α,β,β-trimethyl styrene, with **2a** was proven to fail in this condition.

Next, we examined the substrate scope of various esters by reacting with 4-methyl styrene (**1c**) under the optimized conditions (Scheme 3). α-Bromoesters with varied substitution at the alcohol part of ester have been found effective in this process, giving moderate to good yields of corresponding products (**4a** and **4b**). Additionally, α-bromoesters bearing different substituents, like biologically active α-diethoxyphos-

Scheme 3. Scope of α-Bromoesters[a,b]



[a]Unless otherwise noted, all reactions were carried out with **1c** (0.2 mmol), **2** (0.6 mmol), DIPEA (0.6 mmol), Eosin Y (2 mol %), and DMF (2 mL) under air at rt. irradiated with a 12 W blue LED for 6 h. **2** and base were added in two portions at an interval of 3 h. [b]Yield of isolated products.

phoryl (**4c**) and α-difluoro (**4d**), could also be accommodated smoothly into the protocol to afford moderate yields. Interestingly, the retention of a difluoro handle in product **4d** provides an opportunity for further chemoselective transformations.[27] A biologically important γ-butyrolactone unit could also be integrated as a coupling partner with its corresponding α-bromo derivative. Moreover, highly congested α-dialkyl bromoester (**4f**) containing a β-quaternary carbonyl system also equally participated in this reaction but with a lower yield. On the other hand, α-bromoketoesters containing different benzoyl and ketomethyl groups all reacted smoothly under the standard condition, generating the desired product in moderate yields (**4g**−**4k**).

Halomalonates are prone to undergo reductive dehalogenation under photoredox conditions, and thus, engagement of them under intermolecular oxidative radical conditions is not easy.[28] Fortunately, a number of α-bromomalonates with a diverse structural pattern have successfully participated in this coupling process to deliver the desired products in moderate to good yields (**4l**−**4o**). Interestingly, the product **4n**, generated from the reaction of mixed malonate, is useful for further chemoselective functionalization of the ester groups.[29]

To further evaluate the potential of this strategy, we surveyed with other α-bromo carbonyl derivatives: ketones and amides, which have not been considered before and/or reported to fail in a similar type of coupling reaction with styrenes under photoredox conditions (Scheme 4).[30a] It was

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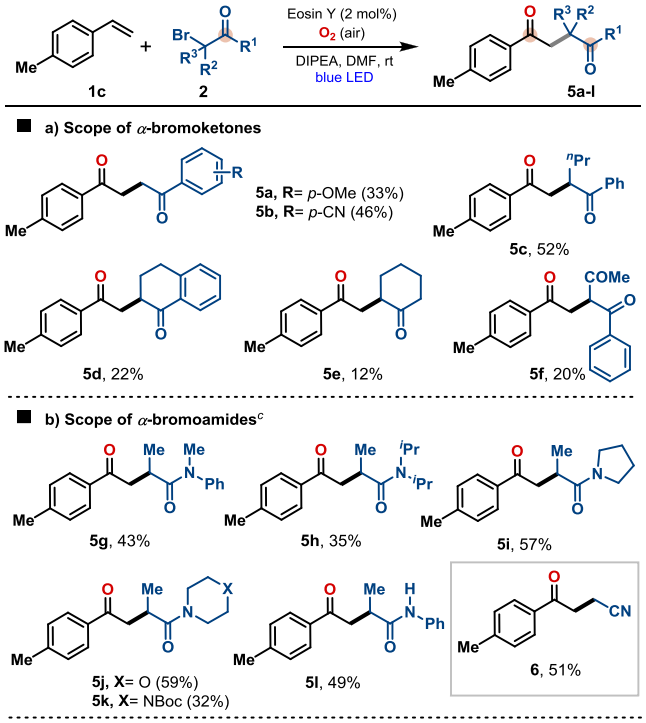
Scheme 4. Scope of α-Bromoketones and Amides[a,b]

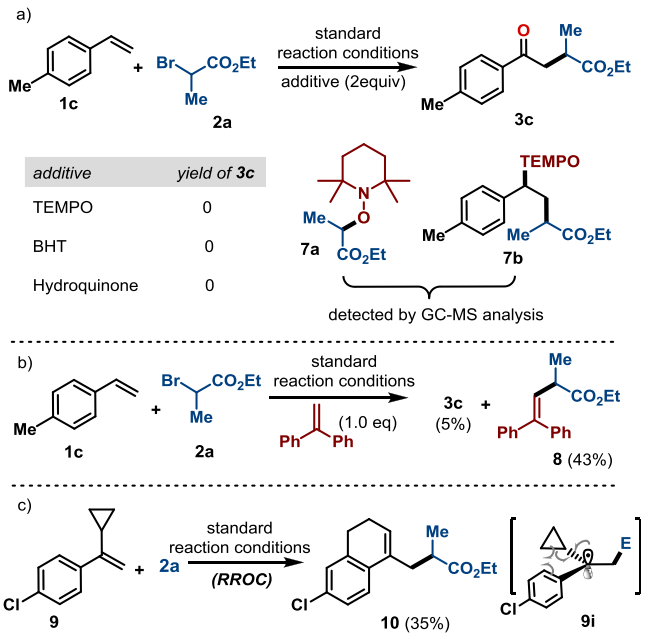


[a]Unless otherwise noted, all reactions were carried out with **1c** (0.2 mmol), **2** (0.6 mmol), DIPEA (0.6 mmol), Eosin Y (2 mol %), and DMF (2 mL) under air at rt. irradiated with a 12 W blue LED for 6 h. **2** and base were added in two portions at an interval of 3 h. [b]Yield of isolated products. [c]*fac*-Ir(ppy)$_3$ (1 mol %) was used as a photocatalyst and acetonitrile as a solvent.

noticeable that primary (**5a** and **5b**) and secondary (**5c** and **5d**) substituted bromoacetopenone produced the desired 1,4-diketone products in moderate yield.[30b] Bromomethyl aliphatic ketone, α-bromocyclohexanone, and α-bromo-1,3-diketone also participated in this process but with low productivity (**5e** and **5f**). Due to their potential applications in medicinal chemistry, next we investigated the possibilities of α-bromoamides as the coupling partner in this process. But unfortunately, they did not react under the standard conditions. Further screwing the catalytic system with *fac*-Ir(ppy)$_3$ enables access to desired products, which were not accessible by the previously reported Kornblum-type oxidation strategy.[19] With the revised catalytic system, the reactions of olefin **1c** with biologically important acetamide derivatives were tested (Scheme 4b). α-Bromoamides with varied functional groups at amide nitrogen including ether (**5j**), amide(**5k**), and even amide with free N−H (**5l**) worked well under this revised photocatalysis conditions, resulting in corresponding keto-amide products in moderate to good yields (**5g**−**5l**). Excitingly, non-carbonyl bromide, like α-bromonitrile could also be directly coupled with olefin under the normal conditions furnishing γ-keto nitrile **6** with moderate yield, but unactivated alkyl bromide like 1-bromobutane was found to be ineffective and cannot be accommodated into this protocol.

To further explore and gain insight into the mechanism, few controlled experiments were performed. When TEMPO (radical scavenger) was introduced to the standard reaction medium, production of **3c** was completely shut down with the formation of alkyl-TEMPO (**7a**) and benzyl-TEMPO (**7b**) adducts, as were detected in GC−MS analysis (Scheme 5a). A similar trend of reaction inhibitions was also observed with

Scheme 5. Mechanistic Investigation



other radical quenchers: BHT and hydroquinone. This result indicates that the reaction might follow a radical pathway, and an α-carbonyl radical could be a reactive species in this process. Moreover, this radical species could be easily trapped by 1,1-diphenylethylene to obtain the product **8** in 43% yield (Scheme 5b). Additionally, a radical-clock experiment further confirmed the participation of an alkyl radical by the formation of dihydronaphthalene derivative **10** resulting from radical ring-opening cyclization of the cyclopropropylmethyl radical (**9i**). In the presence of water or in a nitrogen atmosphere, the formation of the keto-carbonyl **3c** was retarded or completely stopped, indicating that oxygen was essential and acted as the sole oxidant in this transformation. To get a better perspective on the photoreaction, we have analyzed the absorption profile of all reaction components as well as a combination of them. This UV−Vis study ruled out the formation of any photoactive intermediates (EDA complexes) (see Figure S2 in the Supporting Information). Eosin Y is the only constituent among the reaction components with a significant absorbance in the visible range. Furthermore, a Stern−Volmer fluorescence quenching study[31] was conducted to screen the kinetic behavior of the exited Eosin Y in the presence of different reacting components (see Figure S1 in the Supporting Information). Moreover, light on/off experiments (Figure S5 in the Supporting Information) indicated that continuous photoirradiation is essential for this reaction.[34b]

On the basis of the abovementioned results and related literature,[32] a possible reaction mechanism was proposed, as illustrated in Scheme 6. Initially, exposure of Eosin Y to visible light results in the photoexcited Eosin Y*, which then reduces ($E_{EY^{\cdot+}/EY^*}$ = −1.11 V *vs* SCE in CH_3CN)[32d] bromocarbonyl **11** (E^{red} = −0.80 V *vs* SCE in CH_3CN)[32e] to α-carbonylmethyl radical **12** by single-electron transfer (SET) and oxidizes itself to Eosin Y$^{\cdot+}$. This process is supported by the Stern−Volmer fluorescence quenching studies. The reduction of Eosin Y$^{\cdot+}$

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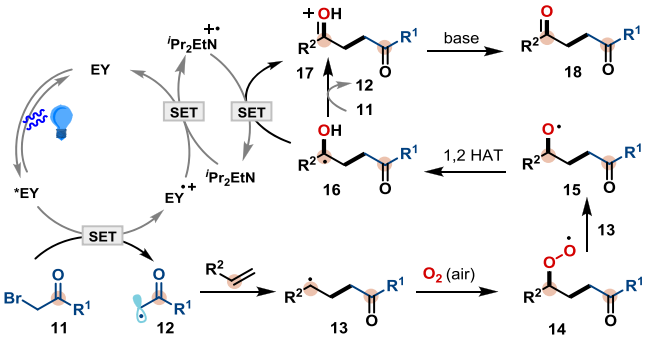
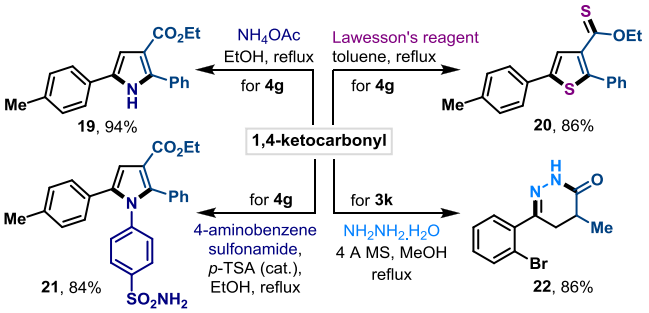
Scheme 6. Plausible Reaction Mechanism



($E_{EY^{\bullet+}/EY}$ = 0.78 V *vs* SCE in CH_3CN)[32d] by sacrificial electron donor diisopropylethylamine (0.72 V *vs* SCE in CH_3CN)[11b] regenerates the catalyst in its neutral form and oxidizes itself to the diisopropylethylamine radical cation. The electron-deficient radical **12** then undergoes intermolecular addition on the double bond of alkene, affording benzyl radical **13**. The latter then reacts with oxygen and generates the peroxy radical **14**, which upon combination with **13** followed by fragmentation converted to an alkoxy radical **15**.[33] This alkoxy radical upon 1,2-hydrogen atom transfer (HAT) rearranges to a carbon-centered radical **16**,[32a] which undergoes oxidation either by chain-terminating photogenerated amine radical cation or by chain-propagating electron transfer to another equivalent of substrate. Finally, deprotonation of **17** affords desired keto-carbonyl product **18**. A reductive quenching cycle initiated by excess amine could not be ruled out at this stage, as the Stern–Volmer experiment has also shown adequate quenching of the exited catalyst by amine.[34]

To demonstrate the synthetic utility of the present oxidative coupling reaction, a versatile set of synthetic transformations was showcased with the end 1,4-ketocarbonyl products (Scheme 7). Treatments of ammonium acetate and Lawesson's

Scheme 7. Derivatization of the Products



reagent separately on **4g** at elevated temperature give rise to pyrrole (**19**) and thiophene (**20**) derivatives, respectively, through Paal–Knorr synthesis.[2] Furthermore, a reaction of **4g** with 4-aminobenzenesulfonamide provides functionalized pyrrole **21**, which is an important structural unit for pharmacological evaluation. Biologically active dihydropyridazinone derivative **22** can also be obtained easily from1,4-ketocarbonyl **3k** by treatment with hydrazine.

CONCLUSIONS

In summary, a visible light-mediated organic dye-catalyzed reaction of α-bromocarbonyls and styrenes has been developed, which provides a facile general strategy toward the synthesis of 1,4-ketocarboyls. Various substitutions on terminal as well as internal vinyl arenes can be well tolerated. Various α-bromoesters and α-bromoketones also serve as suitable substrates for this photocatalytic system. Moreover, less reactive bromoacetamides have also been successfully coupled with styrenes in this current protocol to get γ-ketoamides of biological interest. A preliminary mechanistic study indicated that a visible light-promoted radical pathway was involved in this transformation with aerial oxygen as the sole oxidant, which features this strategy as mild open flask chemistry. Further studies relating expansion of this aerobic coupling strategy to incorporate other functional groups are underway in our group.

EXPERIMENTAL SECTION

General Information. All commercially available chemicals and reagents were used without any further purification unless otherwise stated. All reactions were carried out in oven-dried glassware under an argon or nitrogen atmosphere with freshly distilled anhydrous solvents.[35] Photoreactions were carried out in a borosilicate-made culture tube using a blue-light source (PAR38 12 W blue LED bulb). The progress of the reaction was monitored by thin-layer chromatography (TLC) using a silica gel aluminum sheet (Merck, TLC Silica gel 60 F254). All compounds were purified through column chromatography using a silica gel (230–400 mesh). Nuclear magnetic resonance spectra were recorded on a Bruker Avance III HD 400 instrument. Chemical shifts (δ) are quoted in ppm relative to residual solvent signals, $CDCl_3$, referenced at δ 7.26 ppm for ^1H and 77.16 ppm for $^{13}C\{^1H\}$. TMS are used as the internal standard, and coupling constants (*J*) are quoted in hertz (Hz). Multiplicity is reported with the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, dt = doublet of triplets, td = triplet of doublets, tt = triplet of triplets. HRMS were recorded using a QTOF micro MS system by an ESI technique. GC–MS analysis was done by a Thermo Scientific ISQ QD single quadrupole GC–MS system using a TG-5MS column (30 m × 0.25 mm × 0.25 μm). UV–vis absorption spectroscopy was conducted using a Shimadzu UV-1800 Spectrophotometer. Fluorescence quenching experiments were performed using a PerkinElmer LS 55 Fluorescence Spectrometer. Melting points (°C) are uncorrected.

A. General Procedure for the Ketocarbonylation Reaction. An oven-dried culture tube was charged with a magnetic stir bar, Eosin Y (0.004 mmol), freshly prepared styrene (0.2 mmol), corresponding α-bromocarbonyl (0.4 mmol), and 1 mL of dry DMF. After mixing the reaction components by shaking, 0.4 mmol of DIPEA and another 1 mL of DMF were added to them. The culture tube was sealed with rubber septum. After that, the reaction mixture was stirred and irradiated between two 12 W blue LED lights at a distance of 8 cm from each for 3 h. Then, additional 0.2 mmol of corresponding α-bromocarbonyl and DIPEA was added to the reaction. The completion of the reaction was monitored by TLC. After that, the crude reaction mixture was diluted with water (5 mL) and extracted with ethyl acetate (3 × 6 mL). The combined organic layer was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Then, the mixture was concentrated in a rotary evaporator and the residue was purified by silica gel column chromatography to afford the desired 1,4-ketocarbonyl derivatives.

B. General Procedure for the Ketoamidation Reaction. An oven-dried culture tube was charged with a magnetic stir bar, *fac*-Ir(ppy)$_3$ (0.002 mmol), freshly prepared styrene (0.2 mmol), corresponding α-bromoamide (0.4 mmol), and 1 mL of dry acetonitrile. After mixing the reaction components by shaking, 0.4 mmol of DIPEA and another 1 mL of acetonitrile were added to them. The culture tube was sealed with a rubber septum. After that, the reaction mixture was stirred and irradiated between two 12 W blue LED lights at a distance of 8 cm from each for 3 h. Then, additional 0.2 mmol of corresponding α-bromoamide and DIPEA were added to the reaction mixture. The

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completion of the reaction was monitored by TLC. After that, the crude reaction mixture was diluted with water (5 mL) and extracted with ethyl acetate (3 × 6 mL). The combined organic layer was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Then, the mixture was concentrated in a rotary evaporator and the residue was purified by silica gel column chromatography to afford the desired γ-ketoamides.

Characterization Data of Products. *Ethyl 4-(4-(tert-Butyl)-phenyl)-2-methyl-4-oxobutanoate (**3a**).*[8a] Pale yellow viscous liquid; 75% yield (41 mg); R_f value = 0.6 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1732, 1689, 1606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.89 (d, J = 8.7 Hz, 2H), 7.45 (d, J = 8.7 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 3.43 (dd, J = 17.4, 7.7 Hz, 1H), 3.13−3.07 (m, 1H), 2.98 (dd, J = 17.4, 5.7 Hz, 1H), 1.31 (s, 9H), 1.26−1.20 (m, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 197.8, 176.0, 156.9, 134.2, 128.0, 125.5, 60.6, 41.9, 35.1, 31.1, 17.3, 14.2.

*Ethyl 2-Methyl-4-oxo-4-phenylbutanoate (**3b**).*[17] Pale yellow viscous liquid; 70% yield (31 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1731, 1689, 1598 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.94−7.92 (m, 2H), 7.53−7.49 (m, 1H), 7.43−7.39 (m, 2H), 4.11 (q, J = 7.1 Hz, 2H), 3.44 (dd, J = 17.5, 7.9 Hz, 1H), 3.10−3.05 (m, 1H), 2.97 (dd, J = 17.5, 5.5 Hz, 1H), 1.24 (d, J = 7.2 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 198.1, 175.9, 136.7, 133.1, 128.6, 128.0, 60.5, 41.9, 35.0, 17.3, 14.1.

*Ethyl 2-Methyl-4-oxo-4-(p-tolyl)butanoate (**3c**).*[8a] Pale yellow viscous liquid; 65% yield (30 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1732, 1685, 1607 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.85−7.82 (m, 2H), 7.23−7.21 (m, 2H), 4.12 (q, J = 7.1 Hz, 2H), 3.41 (dd, J = 17.4, 7.8 Hz, 1H), 3.10−3.05 (m, 1H), 2.96 (dd, J = 17.4, 5.6 Hz, 1H), 2.37 (s, 3H), 1.25−1.20 (m, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 197.7, 176.0, 143.9, 134.3, 129.3, 128.2, 60.5, 41.8, 35.1, 21.6, 17.3, 14.2.

*Ethyl 4-(4-Methoxyphenyl)-2-methyl-4-oxobutanoate (**3d**).*[17] Pale yellow viscous liquid; 63% yield (32 mg); R_f value = 0.3 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1732, 1678, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.92 (d, J = 8.9 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 4.14−4.08 (m, 2H), 3.83 (s, 3H), 3.39 (dd, J = 17.3, 7.9 Hz, 1H), 3.09−3.04 (m, 1H), 2.94 (dd, J = 17.3, 5.6 Hz, 1H), 1.25−1.20 (m, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.7, 176.2, 163.6, 130.4, 129.9, 113.8, 60.6, 55.5, 41.6, 35.2, 17.4, 14.2.

*Ethyl 4-(4-Fluorophenyl)-2-methyl-4-oxobutanoate (**3e**).*[17] Pale yellow viscous liquid; 74% yield (35 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1732, 1689, 1598 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.98 (dd, J = 9.0, 5.4 Hz, 2H), 7.13−7.09 (m, 2H), 4.13 (q, J = 7.1 Hz, 2H), 3.44 (dd, J = 17.6, 8.1 Hz, 1H), 3.09 (ddd, J = 8.0, 7.2, 5.4 Hz, 1H), 2.95 (dd, J = 17.6, 5.4 Hz, 1H), 1.26 (d, J = 7.2 Hz, 3H), 1.22 (d, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.6, 175.9, 165.9 ($^1J_{C\text{-}F}$ = 256.0), 133.2 ($^4J_{C\text{-}F}$ = 3.0 Hz), 130.7 ($^3J_{C\text{-}F}$ = 10.1 Hz), 115.8 ($^2J_{C\text{-}F}$ = 22.2), 60.7, 41.9, 35.1, 17.4, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −104.7 (s, 1F).

*Ethyl 4-(4-Chlorophenyl)-2-methyl-4-oxobutanoate (**3f**).*[17] Pale yellow viscous liquid; 63% yield (32 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1735, 1689, 1588 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.88 (d, J = 8.7 Hz, 2H), 7.40 (d, J = 8.7 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 3.42 (dd, J = 17.6, 8.1 Hz, 1H), 3.08 (ddd, J = 8.0, 7.2, 5.3 Hz, 1H), 2.93 (dd, J = 17.6, 5.3 Hz, 1H), 1.26−1.20 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.9, 175.8, 139.6, 135.0, 129.4, 128.9, 60.6, 41.8, 35.0, 17.3, 14.1.

*Ethyl 4-(4-Cyanophenyl)-2-methyl-4-oxobutanoate (**3g**).*[8a] Pale yellow viscous liquid; 51% yield (25 mg); R_f value = 0.4 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 2231, 1730, 1694, 1606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.03 (d, J = 8.6 Hz, 2H), 7.75 (d, J = 8.7 Hz, 2H), 4.12 (q, J = 7.1 Hz, 2H), 3.47 (dd, J = 17.8, 8.4 Hz, 1H), 3.10 (ddd, J = 8.2, 7.2, 5.1 Hz, 1H), 2.96 (dd, J = 17.8, 5.1 Hz, 1H), 1.27 (d, J = 7.2 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 197.0, 175.7, 139.7, 132.6, 128.5, 118.0, 116.5, 60.8, 42.2, 35.0, 17.3, 14.2.

*Ethyl 2-Methyl-4-oxo-4-(m-tolyl)butanoate (**3h**).* Pale yellow viscous liquid; 43% yield (20 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat):1736, 1689, 1608 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.76−7.74 (m, 2H), 7.37−7.31 (m, 2H), 4.14 (q, J = 7.1 Hz, 2H), 3.45 (dd, J = 17.5, 7.8 Hz, 1H), 3.12−3.05 (m, 1H), 2.99 (dd, J = 17.5, 5.6 Hz, 1H), 2.39 (s, 3H), 1.26 (d, J = 5.5 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 198.4, 176.1, 138.4, 136.8, 134.0, 128.6, 128.5, 125.3, 60.7, 42.1, 35.1, 21.4, 17.4, 14.2; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{18}NaO_3$ 257.1154; Found 257.1136.

*Ethyl 4-(4-Bromophenyl)-2-methyl-4-oxobutanoate (**3i**).*[8a] Pale yellow viscous liquid; 72% yield (44 mg); R_f value = 0.6 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1732, 1686, 1586 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.77 (d, J = 8.6 Hz, 2H), 7.53 (d, J = 8.7 Hz, 2H), 4.09 (q, J = 7.1 Hz, 2H), 3.39 (dd, J = 17.6, 8.1 Hz, 1H), 3.04 (ddd, J = 8.0, 7.2, 5.3 Hz, 1H), 2.90 (dd, J = 17.6, 5.3 Hz, 1H), 1.22 (d, J = 7.2 Hz, 3H), 1.19 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 197.0, 175.7, 135.4, 131.8, 129.5, 128.2, 60.6, 41.7, 34.9, 17.3, 14.1.

*Ethyl 4-(3-Bromophenyl)-2-methyl-4-oxobutanoate (**3j**).*[8a] Viscous liquid; 48% yield (29 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1736, 1696, 1564 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.06 (t, J = 1.8 Hz, 1H), 7.88−7.85 (m, 1H), 7.66 (ddd, J = 8.0, 2.0, 1.0 Hz, 1H), 7.32 (t, J = 7.9 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 3.43 (dd, J = 17.7, 8.1 Hz, 1H), 3.08 (ddd, J = 8.0, 7.2, 5.3 Hz, 1H), 2.94 (dd, J = 17.7, 5.3 Hz, 1H), 1.26 (d, J = 7.2 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.9, 175.8, 138.5, 136.1, 131.2, 130.3, 126.6, 123.0, 60.7, 42.0, 35.1, 17.4, 14.2.

*Ethyl 4-(2-Bromophenyl)-2-methyl-4-oxobutanoate (**3k**).* Pale yellow liquid; 27% yield (16 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1740, 1695, 1565 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.60 (dd, J = 7.9, 1.1 Hz, 1H), 7.45 (dd, J = 7.6, 1.7 Hz, 1H), 7.37 (td, J = 7.5, 1.2 Hz, 1H), 7.31−7.27 (m, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.37 (dd, J = 17.8, 8.0 Hz, 1H), 3.15−3.07 (m, 1H), 2.99 (dd, J = 17.8, 5.5 Hz, 1H), 1.28 (d, J = 3.1 Hz, 3H), 1.26 (t, J = 5.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 202.1, 175.7, 141.4, 133.8, 131.8, 128.8, 127.7, 118.7, 60.9, 46.0, 35.4, 17.3, 14.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{16}BrO_3$ 299.0283; Found 299.0275.

*Ethyl 4-([1,1′-Biphenyl]-4-yl)-2-methyl-4-oxobutanoate (**3l**).*[19] White solid; mp: 80−82 °C; 77% yield (46 mg); R_f value = 0.6 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (KBr plate): 1726, 1682, 1560 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.04 (d, J = 8.5 Hz, 2H), 7.68 (d, J = 8.5 Hz, 2H), 7.64−7.62 (m, 2H), 7.49−7.45 (m, 2H), 7.40 (t, J = 7.3 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.51 (dd, J = 17.4, 7.8 Hz, 1H), 3.17−3.12 (m, 1H), 3.04 (dd, J = 17.4, 5.5 Hz, 1H), 1.30 (d, J = 7.2 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 197.8, 176.1, 145.9, 139.9, 135.5, 129.0, 128.7, 128.3, 127.4, 127.3, 60.7, 42.1, 35.2, 17.4, 14.3.

*Ethyl 2-Methyl-4-(naphthalen-2-yl)-4-oxobutanoate (**3m**).*[19] White solid; mp: 56−58 °C; 39% yield (21 mg); R_f value = 0.6 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (KBr plate): 1730, 1676, 1585 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.48 (s, 1H), 8.02 (dd, J = 8.6, 1.7 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.89−7.85 (m, 2H), 7.56 (dddd, J = 19.1, 8.1, 6.9, 1.3 Hz, 2H), 4.17 (q, J = 7.1 Hz, 2H), 3.65−3.58 (m, 1H), 3.20−3.11 (m, 2H), 1.32 (d, J = 7.1 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 198.1, 176.1, 135.7, 134.1, 132.6, 129.8, 129.6, 128.6, 128.5, 127.9, 126.9, 123.8, 60.7, 42.1, 35.2, 17.5, 14.3.

*Ethyl 2-Methyl-4-oxo-4-(pyridin-3-yl)butanoate (**3n**).* Pale brown viscous liquid; 34% yield (15 mg); R_f value = 0.3 [EtOAc/petroleum ether = 2:8 (v/v)]; FTIR ν_{max} (neat): 1730, 1699, 1557 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.13 (dd, J = 2.2, 0.6 Hz, 1H), 8.73 (dd, J = 4.8, 1.7 Hz, 1H), 8.20−8.17 (m, 1H), 7.37 (ddd, J = 8.0, 4.8, 0.8 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.45 (dd, J = 17.7, 8.3 Hz, 1H), 3.08 (ddd, J = 8.2, 7.2, 5.1 Hz, 1H), 2.95 (dd, J = 17.7, 5.1 Hz,

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1H), 1.25 (d, J = 7.2 Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 197.1, 175.7, 153.6, 149.6, 135.4, 131.9, 123.7, 60.7, 42.1, 34.9, 17.3, 14.2; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{16}NO_3$ 222.1130; Found 222.1128.

*Ethyl 4-(4-Fluorophenyl)-2,3-dimethyl-4-oxobutanoate (**3o**).* Pale yellow liquid; 35% yield (18 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1748, 1689, 1562 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) (for mixture): 8.02−7.98 (m, 2H), 7.13 (td, J = 8.5, 6.0 Hz, 2H), 4.18−4.02 (m, 2H), 3.69 (dqd, J = 9.3, 7.1, 5.0 Hz, 1H), 2.98−2.88 (m, 1H), 1.28−1.23 (m, 3H), 1.18−1.16 (m, 3H), 1.13 (dd, J = 9.7, 4.7 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 202.1, 201.1, 175.9, 175.6, 167.2, 167.1, 164.7, 164.5, 133.2, 133.1, 132.6, 132.5, 131.2, 131.1, 131.0, 131.0, 116.1, 115.9, 115.8, 115.7, 60.7, 60.6, 43.6, 43.1, 42.9, 41.9, 16.7, 16.2, 14.8, 14.4, 14.3, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −107.0 (s, 1F); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}FO_3$ 253.1240; Found 253.1237.

*Ethyl 2-Methyl-4-oxo-3,4-diphenylbutanoate (**3p**).* Yellow viscous liquid; 32% yield (19 mg); R_f value = 0.6 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1726, 1645, 1540 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.00−7.95 (m, 2H), 7.50−7.18 (m, 8H), 4.80 (dd, J = 15.3, 10.8 Hz, 1H), 4.15−3.82 (m, 2H), 3.41 (ddd, J = 18.2, 10.7, 7.0 Hz, 1H), 1.27−0.90 (m, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 199.6, 198.1, 176.2, 175.2, 136.9, 136.8, 136.6, 136.5, 133.3, 132.9, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.5, 127.7, 127.6, 60.8, 60.3, 56.7, 56.6, 44.2, 43.1, 16.7, 15.7, 14.2, 13.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}O_3$ 297.1491; Found 297.1483.

*Ethyl 2-(1-Oxo-1,2,3,4-tetrahydronaphthalen-2-yl)propanoate (**3q**).*[15e] Pale yellow viscous liquid; 20% yield (10 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1736, 1675, 1564 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): (for mixture) 8.02 (dd, J = 7.8, 1.3 Hz, 1H), 7.48−7.44 (m, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.23 (d, J = 7.7 Hz, 1H), 4.22−4.09 (m, 2H), 3.21−2.84 (m, 4H), 2.21−2.06 (m, 1H), 1.93 (ddd, J = 26.4, 12.8, 4.6 Hz, 1H), 1.30−1.15 (m, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): (for mixture) 198.2, 198.0, 176.2, 174.8, 144.1, 143.8, 133.5, 133.4, 132.7, 132.5, 128.8, 128.7, 127.6, 126.8, 126.7, 60.6, 60.5, 50.7, 50.3, 39.3, 38.9, 29.5, 29.2, 26.0, 25.4, 14.3, 14.2, 13.6, 13.3.

*Ethyl 4-Oxo-4-phenylbutanoate (**4a**).*[36] Pale yellow oil; 39% yield (17 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1741, 1745, 1685, 1603 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.88 (d, J = 8.2 Hz, 2H), 7.26 (dd, J = 6.0, 2.4 Hz, 2H), 4.16 (q, J = 7.1 Hz, 2H), 3.29 (t, J = 6.7 Hz, 2H), 2.74 (t, J = 6.7 Hz, 2H), 2.41 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 197.9, 173.1, 144.1, 134.3, 129.4, 128.3, 60.8, 33.4, 28.5, 21.8, 14.3.

*tert-Butyl 4-Oxo-4-(p-tolyl)butanoate (**4b**).*[37] White solid; mp: 44−46 °C; 66% yield (33 mg); R_f value = 0.6 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (KBr plate): 1718, 1681, 1606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.88−7.86 (m, 2H), 7.25 (dd, J = 5.9, 4.1 Hz, 2H), 3.23 (t, J = 6.7 Hz, 2H), 2.66 (t, J = 6.7 Hz, 2H), 2.40 (s, 3H), 1.44 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 198.1, 172.4, 144.0, 134.3, 129.4, 128.3, 80.7, 33.5, 29.6, 28.2, 21.8.

*Ethyl 2-(Diethoxyphosphoryl)-4-oxo-4-(p-tolyl)butanoate (**4c**).* Colorless viscous liquid; 23% yield (16 mg); R_f value = 0.5 [EtOAc/petroleum ether = 4:6 (v/v)]; FTIR ν_{max} (neat): 1687, 1457, 1432, 1325, 1248 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.88 (d, J = 8.2 Hz, 2H), 7.26 (q, J = 4.0 Hz, 2H), 4.25−4.16 (m, 6H), 3.84−3.61 (m, 2H), 3.42 (ddd, J = 17.7, 9.4, 2.6 Hz, 1H), 2.41 (s, 3H), 1.35 (q, J = 7.2 Hz, 6H), 1.28 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.20 (d, J_{C-P} = 15.5 Hz), 168.6 (d, J_{C-P} = 5.6 Hz), 144.5, 133.7, 129.4, 128.4, 63.1 (d, J_{C-P} = 7.1 Hz), 61.8, 40.4 (d, J_{C-P} = 131.3 Hz), 35.9 (d, J_{C-P} = 1.7 Hz), 21.8, 16.5−16.3 (m), 14.2; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{25}NaO_6P$ 379.1286; Found 379.1292.

*Ethyl 2,2-Difluoro-4-oxo-4-(p-tolyl)butanoate (**4d**).*[20b] Colorless viscous liquid; 32% yield (16 mg); R_f value = 0.3 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1778, 1687, 1607 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.81 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 7.9 Hz, 2H), 4.37 (q, J = 7.1 Hz, 2H), 3.88 (t, J = 13.4 Hz, 2H), 2.42 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 192.66 ($^3J_{C-F}$ = 5.9 Hz), 163.44 ($^2J_{C-F}$ = 31.3), 145.4, 133.2, 129.7, 128.4, 114.6 ($^1J_{C-F}$ = 250.5), 63.1, 43.8 ($^2J_{C-F}$ = 24.2), 21.8, 13.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −104.4 (s, 2F).

*3-(2-Oxo-2-(p-tolyl)ethyl)dihydrofuran-2(3H)-one (**4e**).* White solid; mp: 112−114 °C; 40% yield (17 mg); R_f value = 0.5 [EtOAc/petroleum ether = 3:7 (v/v)]; FTIR ν_{max} (KBr plate): 1770, 1683, 1605 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.85 (d, J = 8.3 Hz, 2H), 7.26−7.24 (m, 2H), 4.44−4.39 (m, 1H), 4.26 (ddd, J = 10.3, 9.1, 6.7 Hz, 1H), 3.60 (t, J = 11.1 Hz, 1H), 3.17−3.10 (m, 2H), 2.64−2.60 (m, 1H), 2.39 (s, 3H), 1.98−1.93 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.7, 179.3, 144.5, 133.8, 129.5, 128.2, 66.9, 39.3, 35.3, 29.2, 21.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{15}O_3$ 219.1021; Found 219.1019.

*Ethyl 2,2-Dimethyl-4-oxo-4-(p-tolyl)butanoate (**4f**).* Colorless viscous liquid; 22% yield (11 mg); R_f value = 0.7 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1732, 1695, 1632 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.81 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 7.9 Hz, 2H), 4.10 (q, J = 7.1 Hz, 2H), 3.24 (s, 2H), 2.37 (s, 3H), 1.29 (s, 6H), 1.17 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 197.4, 177.5, 143.9, 134.8, 129.3, 128.1, 60.6, 48.4, 40.1, 25.9, 21.7, 14.2; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}NaO_3$ 271.1310; Found 271.1306.

*Ethyl 2-Benzoyl-4-oxo-4-(p-tolyl)butanoate (**4g**).*[38] Yellow liquid; 45% yield (29 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1746, 1685, 1630 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.10−8.08 (m, 2H), 7.89 (d, J = 8.2 Hz, 2H), 7.61−7.57 (m, 1H), 7.51−7.48 (m, 2H), 7.26−7.24 (m, 2H), 5.11 (dd, J = 7.5, 6.2 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.82−3.67 (m, 2H), 2.40 (s, 3H), 1.16 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.6, 195.0, 169.4, 144.5, 136.3, 133.8, 133.6, 129.4, 129.1, 128.8, 128.4, 61.8, 48.9, 38.2, 21.8, 14.0.

*Ethyl 2-(4-Bromobenzoyl)-4-oxo-4-(p-tolyl)butanoate (**4h**).* White solid; mp: 60−62 °C; 43% yield (35 mg); R_f value = 0.4 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (KBr plate): 1732, 1695, 1632 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.95 (d, J = 8.7 Hz, 2H), 7.87 (d, J = 8.2 Hz, 2H), 7.62 (d, J = 8.6 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 5.03 (dd, J = 8.2, 5.5 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.83 (dd, J = 18.2, 8.2 Hz, 1H), 3.67 (dd, J = 18.2, 5.5 Hz, 1H), 2.38 (s, 3H), 1.16 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.5, 194.0, 169.0, 144.5, 135.1, 133.6, 132.0, 130.5, 129.4, 128.8, 128.4, 61.9, 48.8, 38.2, 21.7, 14.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{20}BrO_4$ 403.0545; Found 403.0546.

*Ethyl 2-(4-Methoxybenzoyl)-4-oxo-4-(p-tolyl)butanoate (**4i**).* Pale yellow oil; 45% yield (32 mg); R_f value = 0.3 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1740, 1682, 1645 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.07 (d, J = 8.8 Hz, 2H), 7.88 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 5.07 (t, J = 6.8 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.85 (s, 3H), 3.71 (dd, J = 6.8, 3.2 Hz, 2H), 2.38 (s, 3H), 1.17 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.7, 193.3, 169.6, 164.0, 144.3, 133.8, 131.4, 129.3, 129.1, 128.4, 113.9, 61.7, 55.6, 48.7, 38.1, 21.7, 14.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{23}O_5$ 355.1545; Found 355.1542.

*Ethyl 2-Acetyl-4-oxo-4-(p-tolyl)butanoate (**4j**).*[39] Colorless dense liquid; 46% yield (24 mg); R_f value = 0.6 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1725, 1675, 1624 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.83 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 4.17 (dt, J = 7.0, 4.0 Hz, 3H), 3.64 (dd, J = 18.3, 8.2 Hz, 1H), 3.46 (dd, J = 18.3, 5.7 Hz, 1H), 2.39 (s, 3H), 2.36 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 202.5, 196.7, 169.0, 144.3, 133.6, 129.3, 128.2, 61.7, 53.9, 37.3, 30.2, 21.6, 14.0.

*Ethyl 4-Oxo-2-picolinoyl-4-(p-tolyl)butanoate (**4k**).* Brown viscous liquid; 36% yield (23 mg); R_f value = 0.3 [EtOAc/petroleum ether = 2:8 (v/v)]; FTIR ν_{max} (neat): 1740, 1686, 1641 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.69 (ddd, J = 4.7, 1.7, 0.9 Hz,

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1H), 8.06 (dt, J = 7.8, 1.0 Hz, 1H), 7.88−7.86 (m, 2H), 7.85−7.81 (m, 1H), 7.48−7.41 (m, 1H), 7.23 (d, J = 7.9 Hz, 2H), 5.56 (dd, J = 8.8, 5.2 Hz, 1H), 4.13 (t, J = 7.1 Hz, 2H), 3.85 (dd, J = 17.9, 8.8 Hz, 1H), 3.63 (dd, J = 17.9, 5.2 Hz, 1H), 2.38 (s, 3H), 1.13 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.4, 196.3, 170.4, 152.4, 149.1, 144.2, 137.0, 133.8, 129.3, 128.4, 127.4, 122.5, 61.4, 47.7, 37.8, 21.7, 13.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{20}NO_4$ 326.1392; Found 326.1386.

*Diethyl 2-(2-Oxo-2-(p-tolyl)ethyl)malonate (**4l**).*[26b] Pale yellow viscous liquid; 54% yield (32 mg); R_f value = 0.6 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1747, 1730, 1684 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.88−7.86 (m, 2H), 7.25 (dd, J = 7.3, 1.2 Hz, 2H), 4.22 (ddt, J = 10.7, 7.1, 3.6 Hz, 4H), 4.04 (t, J = 7.1 Hz, 1H), 3.59 (d, J = 7.1 Hz, 2H), 2.40 (s, 3H), 1.28 (t, J = 7.1 Hz, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.3, 169.2, 144.5, 133.8, 129.4, 128.4, 61.8, 47.4, 37.8, 21.8, 14.1.

*Di-tert-butyl 2-(2-Oxo-2-(p-tolyl)ethyl)malonate (**4m**).*[26b] Pale yellow viscous liquid; 62% yield (43 mg); R_f value = 0.7 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1723, 1683, 1422 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm):) 7.88 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.6 Hz, 2H), 3.87 (t, J = 7.1 Hz, 1H), 3.48 (d, J = 7.1 Hz, 2H), 2.40 (s, 3H), 1.47 (s, 18H); $^{13}C\{^1H\}$ NMR (101 MHz, CDCl3) δ (ppm): 196.6, 168.6, 144.2, 134.1, 129.4, 128.4, 81.9, 49.4, 37.8, 28.1, 21.8.

*1-(tert-Butyl) 3-Ethyl 2-(2-oxo-2-(p-tolyl)ethyl)malonate (**4n**).*[26b] Pale yellow viscous liquid; 66% yield (42 mg); R_f value = 0.6 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1741, 1726, 1384 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.85 (d, J = 8.3 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 4.24−4.15 (m, 2H), 3.93 (t, J = 7.1 Hz, 1H), 3.52 (d, J = 6.8 Hz, 2H), 2.37 (s, 3H), 1.44 (s, 9H), 1.26 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.3, 169.5, 168.1, 144.2, 133.9, 129.3, 128.3, 82.1, 61.5, 48.3, 37.7, 27.9, 21.7, 14.1.

*Diethyl 2-Methyl-2-(2-oxo-2-(p-tolyl)ethyl)malonate (**4o**).*[26b] Pale yellow viscous liquid; 28% yield (17 mg); R_f value = 0.6 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1736, 1686, 1607 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.85 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 7.9 Hz, 2H), 4.19 (q, J = 7.1 Hz, 4H), 3.63 (s, 2H), 2.39 (s, 3H), 1.58 (s, 3H), 1.23 (t, J = 7.1 Hz, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 196.2, 171.8, 144.2, 134.3, 129.4, 128.2, 61.6, 51.6, 44.2, 21.7, 20.6, 14.0.

*1-(4-Methoxyphenyl)-4-(p-tolyl)butane-1,4-dione (**5a**).*[40] Colorless gummy syrup; 33% yield (19 mg); R_f value = 0.3 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1672, 1615, 1551, 1401 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.02 (d, J = 9.0 Hz, 2H), 7.94 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 7.7 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 3.87 (s, 3H), 3.41 (dd, J = 3.9, 3.0 Hz, 4H), 2.42 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 198.7, 197.5, 163.7, 144.0, 134.5, 130.5, 130.1, 129.4, 128.4, 113.9, 55.6, 32.7, 32.4, 21.8.

*4-(4-Oxo-4-(p-tolyl)butanoyl)benzonitrile (**5b**).*[41] Colorless solid; mp: 134−136 °C; 46% yield (25 mg); R_f value = 0.4 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (KBr plate): 2235, 1695, 1621, 1405 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.12 (d, J = 8.6 Hz, 2H), 7.92 (d, J = 8.2 Hz, 2H), 7.79 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 7.9 Hz, 2H), 3.47 (ddd, J = 6.1, 5.0, 1.4 Hz, 2H), 3.43−3.40 (m, 2H), 2.42 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 197.9, 197.8, 144.4, 140.0, 134.2, 132.7, 129.5, 128.7, 128.4, 118.1, 116.5, 32.9, 32.7, 21.8.

*1-Phenyl-2-propyl-4-(p-tolyl)butane-1,4-dione (**5c**).* Pale yellow oil; 52% yield (31 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1681, 1608, 1416 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.07 (d, J = 7.1 Hz, 2H), 7.87 (d, J = 8.2 Hz, 2H), 7.55 (d, J = 7.4 Hz, 1H), 7.48 (dd, J = 8.1, 6.8 Hz, 2H), 7.25 (t, J = 6.3 Hz, 2H), 4.15 (dddd, J = 10.3, 7.2, 6.3, 4.2 Hz, 1H), 3.69 (dd, J = 17.9, 9.1 Hz, 1H), 3.15 (dd, J = 17.9, 4.2 Hz, 1H), 2.39 (s, 3H), 1.73 (dt, J = 6.6, 4.2 Hz, 1H), 1.58−1.49 (m, 1H), 1.42−1.31 (m, 2H), 0.90 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm) 203.7, 198.4, 144.0, 137.1, 134.3, 132.9, 129.3, 128.7, 128.6, 128.3, 41.2, 40.8, 34.8, 21.7, 20.7, 14.2; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{23}O_2$ 295.1698; Found 295.1692.

*2-(2-Oxo-2-(p-tolyl)ethyl)-3,4-dihydronaphthalen-1(2H)-one (**5d**).* Pale yellow viscous liquid; 22% yield (12 mg); R_f value = 0.4 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1681, 1608, 1405 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.04 (dd, J = 7.8, 1.2 Hz, 1H), 7.94 (d, J = 8.2 Hz, 2H), 7.48 (td, J = 7.5, 1.4 Hz, 1H), 7.33−7.25 (m, 4H), 3.84 (dd, J = 17.5, 4.6 Hz, 1H), 3.32 (ddt, J = 13.3, 7.3, 4.5 Hz, 1H), 3.18 (ddd, J = 17.0, 12.7, 4.5 Hz, 1H), 3.01−2.93 (m, 2H), 2.42 (s, 3H), 2.32−2.26 (m, 1H), 1.97 (qd, J = 13.0, 4.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 199.3, 198.3, 144.3, 144.0, 134.6, 133.5, 132.4, 129.4, 128.9, 128.4, 127.6, 126.7, 44.3, 38.9, 29.7, 29.5, 21.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{19}O_2$ 279.1385; Found 279.1391.

*2-(2-Oxo-2-(p-tolyl)ethyl)cyclohexan-1-one (**5e**).*[42] White solid; mp: 67−69 °C; 12% yield (6 mg); R_f value = 0.4 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (KBr plate): 1711, 1685, 1605 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.88 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 3.56 (dd, J = 17.6, 6.5 Hz, 1H), 3.14 (dq, J = 12.2, 6.0 Hz, 1H), 2.66 (dd, J = 17.6, 5.8 Hz, 1H), 2.44−2.39 (m, 2H), 2.39 (s, 3H), 2.15 (dddd, J = 15.9, 11.7, 6.6, 3.4 Hz, 2H), 1.90−1.85 (m, 1H), 1.78 (ddd, J = 12.8, 9.2, 3.7 Hz, 1H), 1.73−1.60 (m, 1H), 1.48−1.38 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 211.8, 198.4, 143.9, 134.7, 129.3, 128.3, 46.5, 42.1, 38.3, 34.4, 28.1, 25.5, 21.7.

*3-Benzoyl-1-(p-tolyl)pentane-1,4-dione (**5f**).*[43] Pale yellow syrup; 20% yield (12 mg); R_f value = 0.5 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1720, 1680, 1611 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.07 (dd, J = 8.4, 1.3 Hz, 1H), 7.97 (ddd, J = 6.9, 4.3, 1.5 Hz, 2H), 7.87−7.85 (m, 1H), 7.60−7.58 (m, 1H), 7.50 (dd, J = 8.2, 7.0 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.30 (d, J = 7.9 Hz, 1H), 7.23 (d, J = 7.9 Hz, 1H), 5.28 (dd, J = 9.0, 4.1 Hz, 1H), 3.77 (ddd, J = 18.0, 11.0, 6.9 Hz, 1H), 3.57 (dt, J = 18.2, 6.5 Hz, 1H), 2.40 (d, J = 12.4 Hz, 3H), 2.22 (d, J = 1.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 202.5, 197.0, 196.5, 196.4, 195.9, 144.9, 144.5, 136.2, 136.1, 133.9, 133.7, 133.6, 133.5, 129.7, 129.4, 129.1, 129.0, 128.9, 128.7, 128.4, 128.2, 56.9, 56.7, 38.1, 38.0, 29.6, 29.5, 21.8, 21.7.

*N,2-Dimethyl-4-oxo-N-phenyl-4-(p-tolyl)butanamide (**5g**).* Brown gummy liquid; 43% yield (25 mg); R_f value = 0.3 [EtOAc/petroleum ether = 3:7 (v/v)]; FTIR ν_{max} (neat): 1685, 1657, 1599 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.84 (d, J = 8.2 Hz, 2H), 7.45 (q, J = 8.5 Hz, 4H), 7.36−7.34 (m, 1H), 7.21 (d, J = 8.0 Hz, 2H), 3.62 (dd, J = 17.8, 9.7 Hz, 1H), 3.26 (s, 3H), 3.05 (ddd, J = 9.9, 7.0, 4.0 Hz, 1H), 2.77 (dd, J = 17.8, 4.0 Hz, 1H), 2.37 (s, 3H), 1.05 (d, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 198.6, 175.9, 144.2, 143.8, 134.3, 129.7, 129.2, 128.2, 127.9, 127.8, 43.1, 37.7, 32.4, 21.7, 18.0; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{21}NNaO_2$ 318.1470; Found 318.1487.

*N,N-Diisopropyl-2-methyl-4-oxo-4-(p-tolyl)butanamide (**5h**).* Brown gummy liquid; 35% yield (20 mg); R_f value = 0.3 [EtOAc/petroleum ether = 3:7 (v/v)]; FTIR ν_{max} (neat): 1875, 1683, 1645 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.86 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 4.20−4.17 (m, 1H), 3.56 (dd, J = 17.6, 8.0 Hz, 1H), 3.43 (s, 1H), 3.37−3.28 (m, 1H), 2.87 (dd, J = 17.6, 5.0 Hz, 1H), 2.37 (s, 3H), 1.34 (d, J = 6.8 Hz, 3H), 1.31 (d, J = 6.8 Hz, 3H), 1.29 (d, J = 6.7 Hz, 3H), 1.23 (d, J = 6.7 Hz, 3H), 1.15 (d, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 198.9, 174.7, 143.7, 134.7, 129.2, 128.3, 48.4, 45.7, 42.8, 32.7, 21.7, 21.2, 21.1, 20.8, 20.6, 18.2; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{27}NNaO_2$ 312.1939; Found 312.1918.

*2-Methyl-1-(pyrrolidin-1-yl)-4-(p-tolyl)butane-1,4-dione (**5i**).* Gummy liquid; 57% yield (30 mg); R_f value = 0.3 [EtOAc/petroleum ether = 3:7 (v/v)]; FTIR ν_{max} (neat): 1681, 1624, 1445 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.84 (d, J = 8.1 Hz, 2H), 7.21 (d, J = 8.2 Hz, 2H), 3.77 (dt, J = 9.9, 7.0 Hz, 1H), 3.59 (dd, J = 17.8, 8.8 Hz, 1H), 3.52−3.36 (m, 3H), 3.20 (ddd, J = 8.6, 6.9, 4.6 Hz, 1H), 2.90 (dd, J = 17.8, 4.5 Hz, 1H), 2.37 (s, 3H), 2.00−1.94 (m, 2H), 1.87−1.82 (m, 2H), 1.18 (d, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 198.9, 174.5, 143.9, 134.4, 129.2, 128.3, 46.5,

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45.8, 42.8, 33.5, 26.2, 24.4, 21.7, 17.6; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{21}NNaO_2$ 282.1470; Found 282.1462.

*2-Methyl-1-morpholino-4-(p-tolyl)butane-1,4-dione (**5j**).* Brown gummy liquid; 59% yield (32 mg); R_f value = 0.3 [EtOAc/petroleum ether = 3:7 (v/v)]; FTIR ν_{max} (neat): 2968, 2868, 1681, 1607, 1433, 1268, 1223 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.87−7.85 (m, 2H), 7.23 (d, J = 7.9 Hz, 2H), 3.83−3.89 (m, 1H), 3.71−3.59 (m, 8H), 3.43−3.36 (m, 1H), 2.92 (dd, J = 17.8, 4.5 Hz, 1H), 2.39 (s, 3H), 1.19 (d, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 198.7, 174.7, 144.1, 134.3, 129.3, 128.3, 67.01, 66.9, 46.3, 42.8, 42.4, 30.9, 21.7, 17.9; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{21}NNaO_3$ 298.1419; Found 298.1405.

*tert-Butyl 4-(2-Methyl-4-oxo-4-(p-tolyl)butanoyl)piperazine-1-carboxylate (**5k**).* Pale yellow gummy liquid; 32% yield (24 mg); R_f value = 0.3 [EtOAc/petroleum ether = 3:7 (v/v)]; FTIR ν_{max} (neat): 1685, 1642, 1439 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.85 (d, J = 8.1 Hz, 2H), 7.24 (t, J = 8.8 Hz, 2H), 3.71−3.36 (m, 10H), 2.91 (dd, J = 17.8, 4.3 Hz, 1H), 2.38 (s, 3H), 1.46 (s, 9H), 1.19 (d, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 198.7, 174.7, 154.7, 144.1, 134.3, 129.3, 128.3, 80.3, 45.7, 42.9, 41.8, 31.1, 28.5, 21.7, 17.9; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{21}H_{31}N_2O_4$ 375.2284; Found 375.2281.

*2-Methyl-4-oxo-N-phenyl-4-(p-tolyl)butanamide (**5l**).* White solid: mp: 147−149 °C; 49% yield (28 mg); R_f value = 0.3 [EtOAc/petroleum ether = 3:7 (v/v)]; FTIR ν_{max} (KBr plate): 1680, 1605, 1545 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.19 (s, 1H), 7.86 (d, J = 8.2 Hz, 2H), 7.55−7.53 (m, 2H), 7.25 (td, J = 7.9, 6.8 Hz, 4H), 7.05 (t, J = 7.4 Hz, 1H), 3.57 (dd, J = 18.2, 9.0 Hz, 1H), 3.16 (ddd, J = 8.9, 6.9, 4.0 Hz, 1H), 3.03 (dd, J = 18.2, 4.0 Hz, 1H), 2.40 (s, 3H), 1.33 (d, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 199.1, 174.3, 144.4, 138.3, 134.1, 129.4, 128.9, 128.3, 124.0, 119.8, 42.9, 36.9, 21.8, 18.1; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{19}NNaO_2$ 304.1313; Found 304.1302.

*4-Oxo-4-(p-tolyl)butanenitrile (**6**).*[44] Yellowish solid; mp: 74−75 °C; 51% yield (18 mg); R_f value = 0.3 [EtOAc/petroleum ether = 3:7 (v/v)]; FTIR ν_{max} (KBr plate): 2242, 1683, 1685, 1605 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.85 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 7.9 Hz, 2H), 3.37−3.34 (m, 2H), 2.78−2.75 (m, 2H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 195.1, 145.0, 133.3, 129.7, 128.2, 119.4, 34.2, 21.8, 11.9.

Procedure of Radical Trapping Experiments. An oven-dried culture tube was charged with a magnetic stir bar, Eosin Y (3 mg, 2 mol %), 4-methyl styrene **1c** (26 μL, 0.2 mmol), ethyl 2-bromopropanoate **2a** (52 μL, 0.4 mmol), and 1 mL of dry DMF. After mixing the reaction components by stirring, DIPEA (72 μL, 0.4 mmol), TEMPO (2 equiv), and additional 1 mL of dried DMF were added to them. The resulting solution was allowed to be irradiated for 3 h in blue LED light. The reaction mixture was analyzed by GC−MS.

Procedure of the Competitive Reaction. An oven-dried culture tube was charged with a magnetic stir bar, Eosin Y (3 mg, 2 mol %), 4-methyl styrene **1c** (26 μL, 0.2 mmol), diphenyl ethylene (35 μL, 0.2 mmol), ethyl 2-bromopropanoate **2a** (52 μL, 0.4 mmol), and 1 mL of dry DMF. After mixing the reaction components by stirring, DIPEA (72 μL, 0.4 mmol) and additional 1 mL of dry DMF were added to them. The resulting solution was allowed to be irradiated for 3 h, and after that, another 0.2 mmol of both ethyl 2-bromopropanoate and DIPEA was added to it. Finally, the completion of the reaction was confirmed by TLC and the product was purified as process A described previously.

*Ethyl 2-Methyl-4,4-diphenylbut-3-enoate (**8**).*[14e] Colorless viscous liquid; 43% yield (24 mg); R_f value = 0.8 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1676, 1645, 1607 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.39−7.34 (m, 4H), 7.27−7.20 (m, 6H), 6.12 (d, J = 10.3 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.27 (dq, J = 10.3, 7.0 Hz, 1H), 1.26 (m, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 175.1, 143.1, 142.0, 139.5, 129.9, 128.5, 128.3, 128.0, 127.5, 127.4, 60.7, 40.5, 18.6, 14.3.

Procedure of Radical Clock Experiments. An oven-dried culture tube was charged with a magnetic stir bar, Eosin Y (3 mg, 2 mol %), 1-chloro-4-(1-cyclopropylvinyl) benzene **9** (36 mg, 0.2 mmol), ethyl 2-bromopropanoate **2a** (52 μL, 0.4 mmol), and 1 mL of dry DMF. After mixing the reaction components by stirring, DIPEA (72 μL, 0.4 mmol) and additional 1 mL of dry DMF was added to them. The resulting solution was allowed to be irradiated for 3 h, and after that, another 0.2 mmol of both ethyl 2-bromopropanoate and DIPEA was added to it. Finally, the completion of the reaction was confirmed by TLC and the product was purified as process A described previously.

*Ethyl 3-(6-Chloro-3,4-dihydronaphthalen-1-yl)-2-methylpropanoate (**10**).* Colorless viscous oil; 35% yield (19 mg); R_f value = 0.8[EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (neat): 1688, 1637, 1607 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.16 (d, J = 2.1 Hz, 2H), 7.12−7.12 (m, 1H), 5.88 (t, J = 4.6 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 2.89 (ddd, J = 14.2, 6.9, 1.2 Hz, 1H), 2.71−2.61 (m, 3H), 2.40 (ddd, J = 14.2, 7.8, 0.8 Hz, 1H), 2.25−2.20 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H), 1.14 (d, J = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 176.5, 138.8, 133.4, 132.9, 132.1, 127.8, 127.5, 126.4, 123.9, 60.4, 38.3, 37.0, 28.3, 22.9, 16.9, 14.4; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{20}ClO_2$ 279.1152; Found 279.1149.

Procedure of Gram-Scale Synthesis of Compound 3c. An oven-dried RB was charged with a magnetic stir bar, Eosin Y (104 mg, 0.16 mmol), freshly prepared 4-methyl styrene **1c** (1.05 mL, 8 mmol), ethyl 2-bromopropionate **2a** (2.08 mL, 16 mmol), and 60 mL of dry DMF. After mixing the reaction components by stirring, 16 mmol of DIPEA (2.79 mL) and another 20 mL of DMF were added to them. The RB was sealed with a rubber septum. After that, the reaction mixture was stirred and irradiated between two 12 W blue LED lights at a distance of 8 cm from each for 4 h. Then, additional 8 mmol of ethyl 2-bromopropionate **2a** (1.04 mL) and DIPEA (1.39 mL) were added to the reaction. The completion of the reaction was monitored by TLC. After that, the crude reaction mixture was diluted with water (100 mL) and extracted with ethyl acetate (3 × 150 mL). The combined organic layer was washed with brine (100 mL) and dried over anhydrous Na_2SO_4. Then, the mixture was concentrated in a rotary evaporator and the residue was purified by silica gel column chromatography to afford the compound **3c** (1.09 g) in 58% yield.

Synthesis of Pyrrole 19. In a 10 mL round-bottom flask equipped with a magnetic stir bar, a mixture of 1,4-ketocarbonyl compound **4g** (32 mg, 0.1 mmol) and ammonium acetate (77 mg, 1 mmol) was added to absolute ethanol (2 mL) and the mixture was refluxed for 24 h. The reaction mixture was allowed to cool to room temperature and then diluted with $CHCl_3$ (5 mL) and water (5 mL). The organic and aqueous layers were separated. Then, the aqueous part was further extracted with $CHCl_3$ (2 × 5 mL). Now, the combined organic layer was washed with 5 ml of brine solution and dried over anhydrous Na_2SO_4. The dried organic layer was concentrated under reduced pressure and purified by column chromatography. The desired product **19** appeared as a yellow solid with 94% yield.

*Ethyl 2-Phenyl-5-(p-tolyl)-1H-pyrrole-3-carboxylate (**19**).* White solid; mp: 173−175 °C; 94% yield (29 mg); R_f value = 0.4 [EtOAc/petroleum ether = 1:9 (v/v)]; FTIR ν_{max} (KBr plate): 3310, 2925, 1680, 1462 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.82 (brs, 1H), 7.63−7.61 (m, 2H), 7.44−7.35 (m, 5H), 7.20 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 2.9 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 2.37 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 165.1, 137.6, 136.9, 132.1, 132.0, 129.7, 129.1, 128.9, 128.3, 128.1, 124.1, 113.6, 108.7, 59.9, 21.3, 14.4; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{20}H_{19}NO_2Na$ 328.1313; Found 328.1305.

Synthesis of Thiophene 20. In a 10 mL round-bottom flask equipped with a magnetic stir bar, a mixture of 1,4-ketocarbonyl compound **4g** (32 mg, 0.1 mmol) and Lawesson's reagent (101 mg, 0.25 mmol) was added to anhydrous toluene (1 mL) and the mixture was refluxed for 24 h. The reaction mixture was allowed to cool down to room temperature, and the solvent was removed under reduced pressure. The residue was purified by column chromatography to furnish product **20** as a yellow oil with 86% yield.

*O-Ethyl 2-phenyl-5-(p-tolyl)thiophene-3-carbothioate (**20**).* Yellow oil; 86% yield (29 mg); R_f value = 0.5 [EtOAc/petroleum ether =

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1:19 (v/v)]; FTIR ν_{max} (neat): 1516, 1356, 1313, 1248 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.87 (s, 1H), 7.53−7.51 (m, 2H), 7.44 (dd, J = 6.6, 3.2 Hz, 2H), 7.39−7.38 (m, 3H), 7.21 (d, J = 7.9 Hz, 2H), 4.42 (q, J = 7.0 Hz, 2H), 2.39 (s, 3H), 1.01 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 207.2, 143.8, 142.1, 139.0, 138.1, 134.6, 130.6, 129.7, 129.5, 128.2, 128.1, 127.6, 125.7, 68.1, 21.3, 13.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{19}OS_2$ 339.0877; Found 339.0876.

Synthesis of *N*-Aryl Pyrrole 21. In a 10 mL round-bottom flask equipped with a magnetic stir bar, a mixture of 1,4-ketocarbonyl compound **4g** (32 mg, 0.1 mmol), 4-aminobenzenesulfonamide (17 mg, 0.1 mmol), and 4-toluenesulfonic acid (2 mg, 0.01 mmol) was added to absolute EtOH (1 mL) and the mixture was refluxed for 24 h. After cooling the reaction mixture to room temperature, it was concentrated under reduced pressure and the crude mixture was purified by chromatography. The desired product **21** was obtained as a white solid with 84% yield.

*Ethyl 2-Phenyl-1-(4-sulfamoylphenyl)-5-(p-tolyl)-1H-pyrrole-3-carboxylate (**21**).* White solid; mp: 185−187 °C; 84% yield (39 mg); R_f value = 0.5 [EtOAc/petroleum ether = 4:6 (v/v)]; FTIR ν_{max} (KBr plate): 1660, 1345, 1235, 1174 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.66 (d, J = 8.5 Hz, 2H), 7.46 (s, 2H), 7.28 (ddd, J = 13.7, 8.5, 1.7 Hz, 7H), 7.09 (d, J = 8.1 Hz, 2H), 7.03 (d, J = 8.2 Hz, 2H), 6.83 (s, 1H), 4.08 (q, J = 7.1 Hz, 2H), 2.27 (s, 3H), 1.09 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ (ppm): 164.5, 144.4, 141.2, 140.4, 137.6, 135.6, 132.1, 132.0, 130.6, 129.8, 129.5, 129.3, 128.9, 128.2, 126.9, 115.1, 111.2, 60.0, 21.6, 14.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{25}N_2O_4S$ 461.1535; Found 461.1525.

Synthesis of Dihydropyridazinone 22. In a 10 mL round-bottom flask equipped with a magnetic stir bar, a mixture of 1,4-ketocarbonyl compound **3k** (45 mg, 0.15 mmol), hydrazine hydrate (19 μL, 0.3 mmol), and 10 mg 4A MS was added to methanol (1 mL) and the mixture was refluxed overnight. After that, the reaction mixture was cooled and concentrated under reduced pressure. The crude residue was purified by column chromatography. The desired product **22** appeared as a white solid with 86% yield.

*6-(2-Bromophenyl)-4-methyl-4,5-dihydropyridazin-3(2H)-one (**22**).* White solid; mp: 142−144 °C; 86% yield (34 mg); R_f value = 0.3 [EtOAc/petroleum ether = 3:7 (v/v)]; FTIR ν_{max} (KBr plate): 3225, 1687, 1624, 1467 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.80 (s, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 4.2 Hz, 2H), 7.28−7.24 (m, 1H), 3.02−3.00 (m, 1H), 2.73−2.63 (m, 2H), 1.32 (d, J = 6.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 171.2, 154.1, 138.5, 133.3, 130.6, 130.2, 127.7, 121.4, 33.9, 31.1, 14.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_{12}BrN_2O$ 267.0133; Found 267.0126.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c01985.

Additional screening data; mechanistic experimental details; and copies of ^1H, $^{13}C\{^1H\}$, and ^{19}F NMR spectra of all new products (PDF)

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Notes

The authors declare no competing financial interest.

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