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Palladium-Catalyzed Oxidative Coupling of Aromatic Primary Amines and Alkenes under Molecular Oxygen: Stereoselective Assembly of (*Z*)-Enamines

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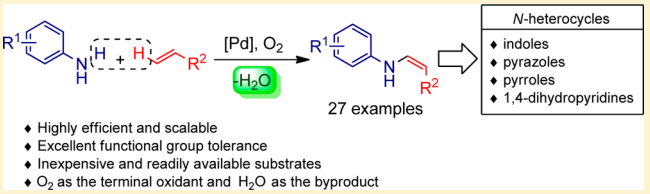
Supporting Information

ABSTRACT: An efficient Pd-catalyzed oxidative coupling of aromatic primary amines and alkenes under molecular oxygen is disclosed. Under mild reaction conditions, it provides a rapid access to (*Z*)-enamine compounds with exceptional functional group tolerance and excellent regio- and stereoselectivity. This attractive route is of great significance due to its applicability to a wide range of aromatic primary amines, most of which could not be efficiently converted into enamines previously. Moreover, this protocol is scalable, and the resultant enamines could be conveniently transformed into a series of N-containing heterocyclics, thus illustrating its potential applications in synthetic and medicinal chemistry.



INTRODUCTION

Oxidative coupling reaction has become a powerful tool in synthetic chemistry over the years, due to its high efficiency in construction of carbon−carbon and carbon-heteroatom bonds.[1−5] Alongside the atom economy advantage, it is a fundamentally fascinating approach to provide complex products from simple starting materials, especially for the dehydrogenative coupling reactions, without the need for prefunctionalized reagents. Under oxidative conditions, two C−H or heteroatom−H bonds could be coupled directly to construct a new bond via mono- or cross-coupling reactions. Transition metal catalysts have been widely used in varieties of oxidative coupling reactions. Notably, palladium-catalyzed processes have attracted considerable attention over the past decades and continue to be an active research topic in chemical synthesis, because of the outstanding superiorities such as the diversity of chemical bond-forming processes available, excellent chemo-, regio-, and stereoselectivity, as well as the great functional-group tolerance generally achieved.[6,7] Among the oxidants commonly used in these reactions, molecular oxygen is undoubtedly an environmentally friendly and inexpensive oxidant, generally producing water as the by-product only, which is in line with the principle of "green chemistry".[8,9]

Enamine derivatives, employed as valuable and highly versatile intermediates in synthetic and medicinal chemistry, have been widely utilized in the formation of numerous heterocycles[10−20] and in the asymmetric synthesis of secondary or tertiary chiral amines.[21−25] Therefore, a variety of methods have been developed to construct the enamine scaffold.[26−39] The transition-metal-catalyzed oxidative coupling between amines and alkenes would be an attractive strategy to give direct access to enamines, which features cost-effective and high stereoselectivity usually observed.[40] In recent years, some successful precedents have been developed by employment of nonbasic nitrogen nucleophiles such as carboxamides, carbamates, sulfoneamides, or diaryl amines.[41−46] Despite these advances, oxidative coupling reactions utilizing simple amines have been relatively less explored so far, and there are few reported examples dedicated to oxidative coupling of alkenes with aromatic primary amines to the best of our knowledge.[47,48] Very recently, Obora and co-workers reported a palladium-catalyzed oxidative amination reaction of alkenes with *ortho*-substituted primary anilines.[47] However, the indispensable *ortho* substituents of anilines and the use of excess amine partner (3 equiv) limited the practical application of this synthetic method. Clearly, such a transformation will only be widely accepted and further used in organic synthesis when a broad spectrum of aromatic primary amines can be utilized as coupling partners with high efficiency.

An inherent challenge in transition-metal-catalyzed reactions involving aromatic primary amines arises from the strong coordination of nitrogen nucleophiles to the metal catalyst center, thus leading to catalyst's inhibition or deactivation. Until now, the only method was to increase the steric hindrance of amines to hamper this coordination, taking introduction of substituents in the *ortho* position of anilines for example.[47] We hypothesized that it would be preferable to develop an efficient catalytic system to completely eliminate this coordination problem. In this article, we disclose the first general catalytic system capable of the oxidative coupling of a wide range of aromatic primary amines and alkenes, in which the appropriate additive played an important role on the efficiency.

We recently reported a novel and efficient palladium-catalyzed dehydrogenative aminohalogenation of alkenes with

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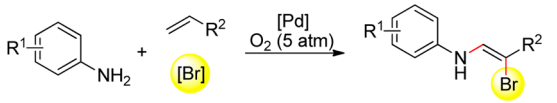
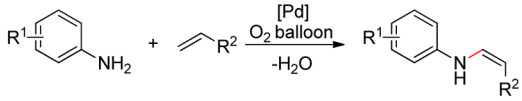
molecular oxygen as the sole oxidant, with unprecedented stereoselectivity and great functional group tolerance (Scheme 1a).[49] The protocol directly employs simple aromatic amines as the nitrogen sources, and provides highly convenient access to a wide range of brominated enamines under mild conditions, which were difficult to prepare by traditional methodologies. The reactions were performed under 5 atm O_2 to give the desired products in good to excellent yields and great stereoselectivity. However, trace of the product was detected by GC−MS with an O_2 balloon; instead, the oxidative coupling of aniline and methyl acrylate was achieved to afford exclusive (*Z*)-enamine compound. Herein, we disclose a highly regio- and stereoselective Pd-catalyzed oxidative coupling of aromatic primary amines and alkenes under molecular oxygen,[49−52] in which varieties of aromatic primary amines could be successfully transformed into the corresponding enamines in excellent *Z*-selectivity (Scheme 1b).

Scheme 1. Palladium-Catalyzed Transformations under Molecular Oxygen

a) Dehydrogenative aminohalogenation of alkenes (our previous work):



b) Oxidative coupling of simple amines with alkenes (this work):

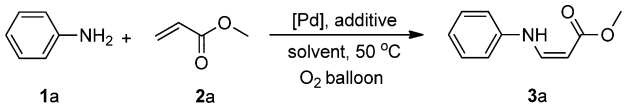


R^1 = H, Me, OMe, F, Cl, Br, I, CF_3, NO_2, CO_2Me, SO_2Me, CN, $HC{=}CH_2$, C≡CH

RESULTS AND DISCUSSION

We commenced our study by investigating the Pd-catalyzed oxidative cross-coupling of aniline (**1a**) and methyl acrylate (**2a**) under 1 atm of molecular oxygen (Table 1). Several additives were screened, such as LiBr, TBAB, NaBr, KBr, NaI, LiCl, and LiBr was found to be the best one (entries 1−6). To our delight, the desired enamine (*Z*)-**3a** was obtained in 91% isolated yield with LiBr (4 equiv) as additive and $Pd(OAc)_2$ as catalyst in THF (entry 1). Further optimization study indicated that the use of 4 equiv of LiBr as additive was important to maintain the efficiency, since only 21% GC yield was acquired when 2 equiv of LiBr was employed (entries 1 and 7). Compared with the red-brown reaction solution obtained with 4 equiv of LiBr (Figure 1b), a heavy yellow precipitate, presumably the metal complex formed from the strong coordination of aniline to palladium catalyst, was observed with 2 equiv of LiBr, thus leading to the deactivation of the catalyst, which was confirmed to contain Pd on the basis of atomic absorption spectroscopy (AAS) analysis (Figure 1a).[53] This was probably due to the competitive coordination of more excess bromide anion to palladium catalyst with that of aniline in the solvent when 4 equiv of LiBr was employed, thus decreasing the chance for the binding of a heterocycle or basic amine, therefore preventing deactivation of the catalyst. The investigation of other palladium catalysts and other solvents resulted in no further improvement of the yield (entries 8−16). The reaction hardly proceeded to yield product **3a** under N_2 atmosphere, with only 9% yield of **3a** obtained and 87% yield of aniline **1a** recovered, probably because of the failure of catalyst regeneration without O_2 (entry 17).[54] Moreover, the reaction using a stroichiometric amount of $Pd(OAc)_2$ under N_2 atmosphere was conducted to probe the mechanism, and good result was obtained, thus suggesting a Pd(0)/Pd(II) process in the reaction (entry 18).

Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3a

entry	catalyst	additive	solvent	yield (%)[b]
1	$Pd(OAc)_2$	LiBr	THF	97 (91)
2	$Pd(OAc)_2$	TBAB	THF	38
3	$Pd(OAc)_2$	NaBr	THF	8
4	$Pd(OAc)_2$	KBr	THF	10
5	$Pd(OAc)_2$	NaI	THF	7
6	$Pd(OAc)_2$	LiCl	THF	6
7[c]	$Pd(OAc)_2$	LiBr	THF	21[d]
8	$PdCl_2$	LiBr	THF	86
9	$Pd(TFA)_2$	LiBr	THF	84
10	$Pd(CH_3CN)_2Cl_2$	LiBr	THF	89
11	$Pd(PPh_3)_2Cl_2$	LiBr	THF	35
12	$Pd(PPh_3)_4$	LiBr	THF	trace
13	$Pd(OAc)_2$	LiBr	DMF	91
14	$Pd(OAc)_2$	LiBr	DMSO	13
15	$Pd(OAc)_2$	LiBr	toluene	0
16	$Pd(OAc)_2$	LiBr	CH_3CN	56
17[e]	$Pd(OAc)_2$	LiBr	THF	9[f]
18[g]	$Pd(OAc)_2$	LiBr	THF	85

[a]Reaction conditions: aniline **1a** (0.5 mmol), methyl acrylate **2a** (0.6 mmol), additive (4 equiv), catalyst (5 mol %), solvent (2 mL), with an O_2 balloon, 50 °C for 8 h. [b]GC yield based on **1a** with tridecane as an internal standard, and isolated yield is given in parentheses. Reaction mixtures analyzed by GC−MS and/or ^{1}H NMR to determine *Z*/*E* ratio. *Z*/*E* > 99:1 unless otherwise noted. [c]2 equiv of LiBr were used. [d]A heavy yellow precipitate was observed. [e]Under N_2 atmosphere. [f]With 87% of aniline recovered. [g]With $Pd(OAc)_2$ (1 equiv), under N_2 atmosphere.

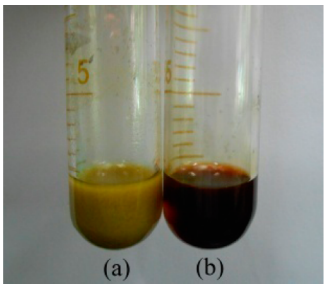


Figure 1. The comparation of solutions after the reactions performed with different amount of LiBr. (a) The same conditions with that in Table 1, entry 7. (b) The same conditions with that in Table 1, entry 1.

A plausible reaction mechanism for this transformation is shown in Scheme 2. The reaction is initiated by the coordination of a Pd(II) catalyst to the olefin **2a** to give complex **I**, which undergoes nucleophilic attack by aniline **1a** to generate the σ-alkylpalladium complex **II**. Subsequent β-H elimination from the complex **II** results in (*Z*)-enamine **3a** exclusively and releases Pd(0), which could be oxidized by O_2 to recover the Pd(II) catalyst. The excellent stereoselectivity

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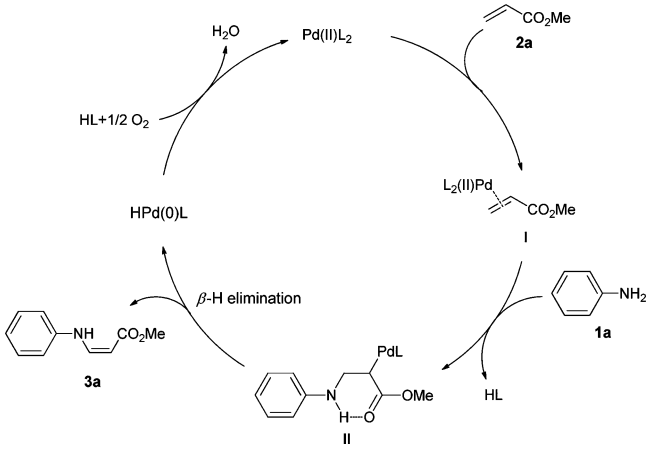
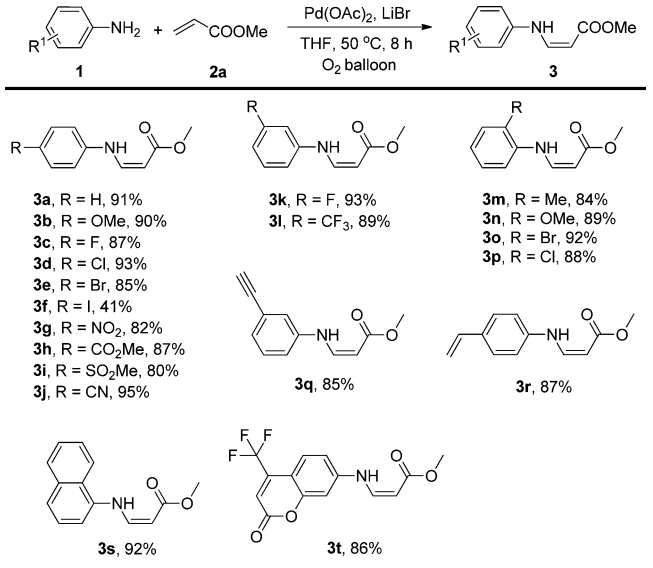
Scheme 2. Plausible Mechanism for Pd-Catalyzed Oxidative Coupling Reaction of Aromatic Primary Amines and Alkenes



observed in this transformation is mainly attributed to the favorable formation of the σ-alkylpalladium intermediate **II**, which bears an intramolecular hydrogen bond. In addition, the role of excess bromide anion in the reaction system is to prevent Pd(II) catalyst from deactivation by strong coordination to aromatic primary amines, thus facilitating the catalytic cycle.

We next investigated the substrate scope of this transformation (Scheme 3). The present catalytic systems were

Scheme 3. Pd-Catalyzed Oxidative Coupling of Various Aromatic Primary Amines with Methyl Acrylate for the Synthesis of *Z*-Enamines[a]

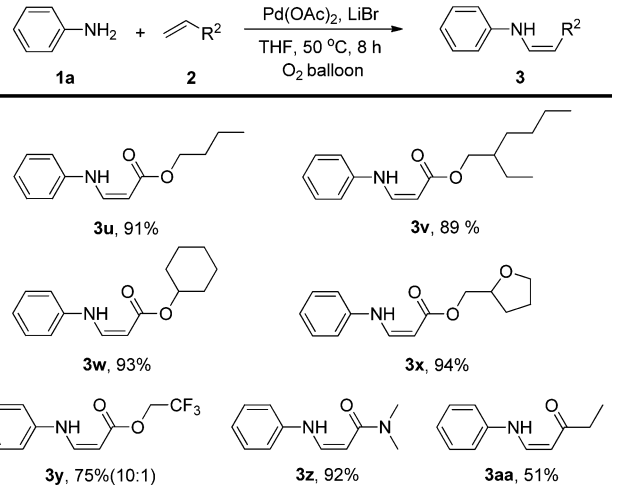


[a]Reaction conditions: amine **1** (0.5 mmol), methyl acrylate **2a** (0.6 mmol), $Pd(OAc)_2$ (5 mol %), LiBr (4 equiv), in THF (2 mL), with an O_2 balloon, 50 °C for 8 h.

applicable to the oxidative coupling of methyl acrylate with a variety of aromatic primary amines. A series of functional groups, such as methyl, methoxyl, fluoro, chloro, bromo, ester, mesyl, cyanide, trifluoromethyl, and even nitro, were well tolerated at the *ortho*, *meta*, and *para* positon on the phenyl ring of amines, and the desired products were isolated in excellent yields. 4-Iodoaniline was also an effective substrate, albeit affording **3f** in a relatively low yield (41%). Notably, most of these substrates were not reactive enough or even unreactive in previous reports concerning the oxidative coupling of aromatic primary amines with alkenes, releasing the corresponding enamines in low yields generally (<38%).[47,48] Intriguingly, 3-ethynylaniline and 4-vinylaniline could also successfully undergo oxidative coupling reactions with methyl acrylate, providing **3q** and **3r** in 85 and 87% yield, respectively, thus providing ample opportunity for further derivatization of the products. In addition, α-naphthylamine proceeded smoothly to give the product **3s** in excellent yield (92%). It is noteworthy that coumarin 151 was also productive, leading to product **3t** in 86% yield, hence illustrating the potential applications of this protocol in the synthesis of biologically active substances.

As for the alkene partner, other acrylates with various functional groups, such as tetrahydrofuran, cyclohexyl and trifluoromethyl, showed good reactivities in the oxidative coupling reactions with aniline to give the desired products (**3u**−**3y**) in good to excellent yields as illustrated in Scheme 4.

Scheme 4. Pd-Catalyzed Oxidative Coupling of Aniline with Various Alkenes for the Synthesis of *Z*-Enamines[a]



[a]Reaction conditions: aniline **1a** (0.5 mmol), alkene **2** (0.6 mmol), $Pd(OAc)_2$ (5 mol %), LiBr (4 equiv), in THF (2 mL), with an O_2 balloon, 50 °C for 8 h.

N,*N*-Dimethylacrylamide was also smoothly transformed into the enamine product **3z** in 92% yield. Gratifyingly, pent-1-en-3-one, a more electron-deficient alkene, could be converted to the desired product **3aa** in 51% yield, accompanied by some aza-Michael addition product generated. Unfortunately, the disubstituted olefin, such as methyl methacrylate and methyl but-2-enoate, could not undergo this transformation in the current reaction system, with no desired corresponding products obtained and aniline almost completely recovered.

Moreover, this oxidative cross-coupling reaction could be scaled up to 20 mmol without significant decrease in the yield and stereoselectivity of the product even with 3 mol % $Pd(OAc)_2$ and 2 equiv of LiBr under oxygen atmosphere (Scheme 5), illustrating its potential industrial applications in the future.

As mentioned above, enamines are versatile intermediates and building blocks in organic synthesis. Enaminoesters, especially with both the nucleophilicity of an enamine and the electrophilicity of an enone in one molecule, are an

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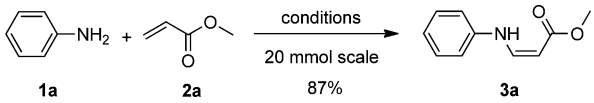
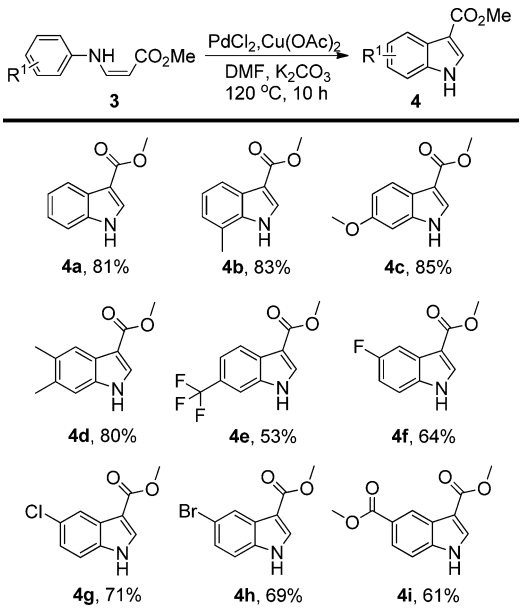
Scheme 5. Large Scale Experiment[a]



[a]Reaction conditions: amine **1** (20 mmol), alkene **2** (24 mmol), $Pd(OAc)_2$ (3 mol %), LiBr (2 equiv), in THF (40 mL), with an O_2 balloon, 50 °C for 8 h.

important class of them. Thus, to further demonstrate the synthetic utility of this protocol, we investigated transformations of enamines **3** to prepare a series of functionalized molecules. The intramolecular oxidative cyclization of the enamines could be successfully accomplished to deliver 3-substituted indoles (Scheme 6).[55] It was found that enamines

Scheme 6. Indole Synthesis from Enamines via Pd-Catalyzed Intramolecular Oxidative Cyclizaiton[a]

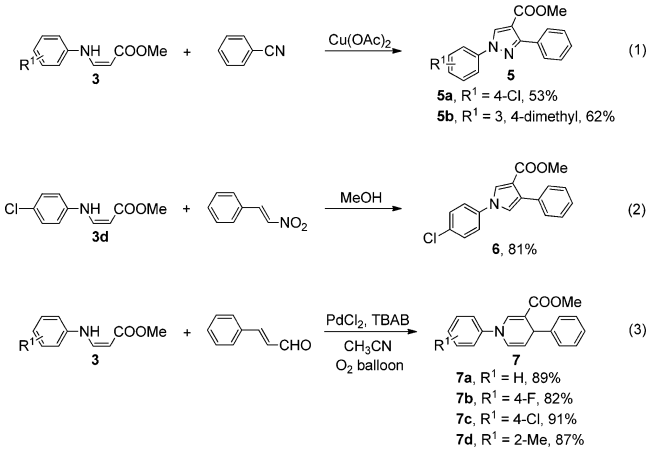


[a]Reaction conditions: enamine **3** (0.3 mmol), $PdCl_2$ (10 mol %), $Cu(OAc)_2$ (3 equiv), K_2CO_3 (2 equiv), in DMF (3 mL), 120 °C for 10 h.

with electron-donating groups on the phenyl ring showed better reactivity than those with electron-withdrawing groups. In the case of *meta*-substituted enamines, excellent selectivity to the C−H bond with less steric hindrance was observed, regardless of the electronic character of the substituents in the *meta* position (**4c**−**4e**).

In addition, the enamine products could also be utilized to construct various N-containing heterocyclic compounds. When treated with benzonitrile, enamines could be converted into pyrazoles in moderate yields (Scheme 7, eq 1).[16] The pyrrole **6** could be easily obtained from the cyclization of enamine product and *β*-nitrostyrene in 81% yield (Scheme 7, eq 2).[19] Notably, 1,4-conjugated addition of **3** and cinnamaldehyde, followed by intramolecular cyclization and dehydration, afforded unsymmetric 1,4-dihydropyridines **7** in excellent yields (Scheme 7, eq 3). The structure of **7b** was further characterized by X-ray crystal diffraction measurement.[56]

Scheme 7. Synthesis of Various *N*-Heterocycles from Enamines[a]



[a]Reagents and conditions: (1) enamine **3** (0.3 mmol), $Cu(OAc)_2$ (0.9 mmol), PhCN (1 mL), 120 °C for 20 h; (2) enamine **3** (0.3 mmol), *β*-nitrostyrene (0.2 mmol), in CH_3OH (1.5 mL), 120 °C for 12 h; (3) enamine **3** (0.3 mmol), cinnamaldehyde (0.3 mmol), $PdCl_2$ (0.03 mmol), TBAB (0.15 mmol), in MeCN (1.5 mL), with an O_2 balloon, 70 °C for 10 h.

CONCLUSION

In conclusion, we have developed an efficient Pd-catalyzed oxidative cross-coupling of aromatic primary amines and alkenes under molecular oxygen, providing highly regio- and stereoselective approach to (*Z*)-enamines. The resultant enamines were demonstrated to be versatile building blocks for the synthesis of N-containing heterocyclics such as indoles, pyrazoles, pyrroles, and 1,4-dihydropyridines. The addition of LiBr was crucial to the success of the transformation, because of its important role in avoiding the deactivation of palladium catalyst arising from the strong coordination of aromatic primary amines to it. This catalytic system is applicable to a variety of aromatic primary amines, most of which are not efficiently converted into enamines in previous reports. The process is scalable and environmentally benign, with O_2 employed as the terminal oxidant and H_2O formed as the only byproduct. Moreover, the use of inexpensive and readily available starting materials as well as the exceptional functional group tolerance makes this atom-economical approach particularly attractive.

EXPERIMENTAL SECTION

Typical Procedure for Pd-Catalyzed Oxidative Cross-Coupling Reactions. A 25 mL Schlenk tube was charged with a solution of $Pd(OAc)_2$ (0.025 mmol), LiBr (2 mmol), amine **1** (0.5 mmol), and alkene **2** (0.6 mmol) in THF (2 mL) with an O_2 balloon, and the mixture was heated at 50 °C under magnetic stirring for 8 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc/Et_3N) to afford the corresponding products **3**.

Procedure for Large Scale Reaction. A 100 mL round-bottom flask was charged with a solution of $Pd(OAc)_2$ (0.6 mmol), LiBr (40 mmol), aniline **1a** (20 mmol), and methyl acylate **2a** (24 mmol) in THF (40 mL) with a O_2 balloon, and the mixture was heated at 50 °C under magnetic stirring for 8 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (petroleum ether/EtOAc/Et_3N) to afford 3.08 g (87%) of product **3a**.

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(*Z*)-Methyl 3-(phenylamino)acrylate (3a).[57] Light yellow solid (80.5 mg, 91%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.87 (d, J = 10.4 Hz, 1H), 7.30−7.21 (m, 3H), 7.00−6.94 (m, 3H), 4.84 (d, J = 8.4 Hz, 1H), 3.70 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 143.1, 140.6, 129.6, 122.5, 115.3, 86.9, 50.6 ppm; MS (EI) m/z 77, 91, 117, 145, 177.

(*Z*)-Methyl 3-((4-methoxyphenyl)amino)acrylate (3b). Light yellow oil (93.1 mg, 90%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.78 (d, J = 12.0 Hz, 1H), 7.15 (dd, J = 12.8, 8.4 Hz, 1H), 6.91 (d, J = 9.2 Hz, 2H), 6.85 (d, J = 9.2 Hz, 2H), 4.78 (d, J = 8.4 Hz, 1H), 3.78 (s, 3H), 3.71 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.8, 155.6, 144.3, 134.4, 117.0, 114.9, 85.6, 55.6, 50.5 ppm; HRMS-ESI (m/z) calcd for $C_{11}H_{13}NO_3$, $[M + H]^+$ 208.0968, found 208.0960.

(*Z*)-Methyl 3-((4-fluorophenyl)amino)acrylate (3c). Light yellow solid (84.8 mg, 87%): mp 61−63 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.84 (d, J = 10.0 Hz, 1H), 7.15 (dd, J = 12.8, 8.4 Hz, 1H), 7.00 (t, J = 8.6 Hz, 2H), 6.92−6.89 (m, 2H), 4.84 (d, J = 8.0 Hz, 1H), 3.71 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 158.6, 143.6, 137.0, 116.8, 116.3, 86.9, 50.6 ppm; HRMS-ESI (m/z) calcd for $C_{10}H_{10}FNO_2$, $[M + H]^+$ 196.0768, found 196.0764.

(*Z*)-Methyl 3-((4-chlorophenyl)amino)acrylate (3d). Light yellow solid (98.3 mg, 93%): mp 57−58 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.87 (d, J = 11.2 Hz, 1H), 7.25 (d, J = 8.8 Hz, 2H), 7.17 (dd, J = 12.4, 8.4 Hz, 1H), 6.88 (d, J = 8.8 Hz, 2H), 4.87 (d, J = 8.4 Hz, 1H), 3.72 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 142.7, 139.3, 129.6, 127.5, 116.5, 87.7, 50.7 ppm; HRMS-ESI (m/z) calcd for $C_{10}H_{10}ClNO_2$, $[M + H]^+$ 212.0473, found 212.0478.

(*Z*)-Methyl 3-((4-bromophenyl)amino)acrylate (3e). Light yellow solid (108.8 mg, 85%): mp 130−132 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.88 (d, J = 11.6 Hz, 1H), 7.39 (d, J = 8.8 Hz, 2H), 7.18 (dd, J = 12.6, 8.4 Hz, 1H), 6.84 (d, J = 8.8 Hz, 2H), 4.88 (d, J = 8.0 Hz, 1H), 3.72 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 142.6, 139.8, 132.6, 116.9, 114.8, 87.9, 50.7 ppm; HRMS-ESI (m/z) calcd for $C_{10}H_{10}BrNO_2$, $[M + H]^+$ 255.9968, found 255.9966.

(*Z*)-Methyl 3-((4-iodophenyl)amino)acrylate (3f). Light yellow oil (62.1 mg, 41%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.87 (d, J = 11.6 Hz, 1H), 7.57 (d, J = 8.8 Hz, 2H), 7.18 (dd, J = 12.8, 8.4 Hz, 1H), 6.73 (d, J = 8.8 Hz, 2H), 4.88 (d, J = 8.0 Hz, 1H), 3.72 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 142.4, 140.4, 138.4, 117.2, 88.0, 84.7, 50.7 ppm; HRMS-ESI (m/z) calcd for $C_{10}H_{10}INO_2$, $[M + H]^+$ 303.9829, found 303.9830.

(*Z*)-Methyl 3-((4-nitrophenyl)amino)acrylate (3g). Light yellow oil (91.0 mg, 82%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.26 (d, J = 10.8 Hz, 1H), 8.20 (d, J = 8.0 Hz, 2H), 7.29−7.24 (m, 1H), 7.00 (d, J = 8.0 Hz, 2H), 5.07 (d, J = 8.8 Hz, 1H), 3.75 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 146.0, 142.2, 140.7, 126.1, 114.3, 91.8, 51.1 ppm; HRMS-ESI (m/z) calcd for $C_{10}H_{10}N_2O_4$, $[M - H]^-$ 221.0568, found 221.0566.

(*Z*)-Methyl 4-((3-methoxy-3-oxoprop-1-en-1-yl)amino)-benzoate (3h).[58] Light yellow solid (102.2 mg, 87%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.05 (d, J = 12.0 Hz, 1H), 7.97 (d, J = 8.8 Hz, 2H), 7.27 (dd, J = 12.6, 8.6 Hz, 1H), 6.96 (d, J = 8.8 Hz, 2H), 4.95 (d, J = 8.4 Hz, 1H), 3.88 (s, 3H), 3.72 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 166.5, 144.4, 141.6, 131.6, 123.8, 114.3, 89.5, 51.9, 50.8 ppm; MS (EI) m/z 59, 89, 144, 172, 203, 235.

(*Z*)-Methyl 3-((4-(methylsulfonyl)phenyl)amino)acrylate (3i). Light yellow oil (102.0 mg, 80%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.16 (d, J = 12.0 Hz, 1H), 7.86 (d, J = 8.4 Hz, 2H), 7.29 (dd, J = 11.8, 9.0 Hz, 1H), 7.08 (d, J = 8.4 Hz, 2H), 5.03 (d, J = 8.8 Hz, 1H), 3.75 (s, 3H), 3.05 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 145.1, 141.0, 133.2, 129.5, 114.8, 90.8, 51.0, 44.7 ppm; HRMS-ESI (m/z) calcd for $C_{11}H_{13}NO_4S$, $[M + H]^+$ 256.0638, found 256.0636.

(*Z*)-Methyl 3-((4-cyanophenyl)amino)acrylate (3j). Light yellow solid (95.9 mg, 95%): mp 156−158 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.10 (d, J = 11.6 Hz, 1H), 7.56 (d, J = 8.8 Hz, 2H), 7.22 (d, J = 12.4, 8.4 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 5.00 (d, J = 8.4 Hz, 1H), 3.73 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 144.1, 140.9, 133.9, 119.0, 115.0, 104.8, 90.7, 51.0 ppm; HRMS-ESI (m/z) calcd for $C_{11}H_{10}N_2O_2$, $[M - H]^-$ 201.0670, found 201.0666.

(*Z*)-Methyl 3-((3-fluorophenyl)amino)acrylate (3k). Light yellow solid (90.6 mg, 93%): mp 54−56 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.91 (d, J = 10.8 Hz, 1H), 7.26−7.15 (m, 2H), 6.73−6.65 (m, 3H), 4.89 (d, J = 8.4 Hz, 1H), 3.72 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 163.7, 142.4, 142.3, 130.9, 111.1, 109.1, 102.3, 88.2, 50.7 ppm; HRMS-ESI (m/z) calcd for $C_{10}H_{10}FNO_2$, $[M + H]^+$ 196.0768, found 196.0771.

(*Z*)-Methyl 3-((3-(trifluoromethyl)phenyl)amino)acrylate (3l). Light yellow solid (109.0 mg, 89%): mp 41−43 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.02 (d, J = 11.2 Hz, 1H), 7.41 (t, J = 7.8 Hz, 1H), 7.28−7.23 (m, 2H), 7.20 (s, 1H), 7.12 (d, J = 8.0 Hz, 1H), 4.94 (d, J = 8.4 Hz, 1H), 3.74 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 142.2, 141.2, 132.2, 130.2, 123.8, 118.9, 118.5, 111.7, 88.8, 50.8 ppm; HRMS-ESI (m/z) calcd for $C_{11}H_{10}F_3NO_2$, $[M - H]^-$ 244.0591, found 244.0585.

(*Z*)-Methyl 3-(*o*-tolylamino)acrylate (3m).[47] Light yellow oil (80.2 mg, 84%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.00 (d, J = 10.4 Hz, 1H), 7.32 (dd, J = 12.6, 8.2 Hz, 1H), 7.19 (t, J = 8.6 Hz, 2H), 7.04 (d, J = 7.6 Hz, 1H), 6.94 (t, J = 7.4 Hz, 1H), 4.90 (d, J = 8.0 Hz, 1H), 3.74 (s, 3H), 2.34 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 143.4, 139.1, 131.0, 127.1, 125.3, 122.4, 112.9, 87.1, 50.7, 17.4 ppm; MS (EI) m/z 77, 91, 118, 130, 159, 191.

(*Z*)-Methyl 3-((2-methoxyphenyl)amino)acrylate (3n). Light yellow oil (92.1 mg, 89%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.14 (d, J = 12.4 Hz, 1H), 7.26 (dd, J = 13.2, 8.4 Hz, 1H), 7.02 (dd, J = 7.4, 1.8 Hz, 1H), 6.94−6.86 (m, 3H), 4.87 (d, J = 8.4 Hz, 1H), 3.90 (s, 3H), 3.72 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 147.7, 141.9, 130.2, 122.1, 120.9, 112.0, 110.8, 87.2, 55.7, 50.5 ppm; HRMS-ESI (m/z) calcd for $C_{11}H_{13}NO_3$, $[M + H]^+$ 208.0968, found 208.0973.

(*Z*)-Methyl 3-((2-bromophenyl)amino)acrylate (3o).[48] Light yellow oil (117.7 mg, 92%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.32 (d, J = 11.6 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.28−7.21 (m, 2H), 7.06 (d, J = 8.0 Hz, 1H), 6.85 (t, J = 7.6 Hz, 1H), 4.97 (d, J = 8.4 Hz, 1H), 3.76 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 141.4, 137.5, 130.1, 127.8, 122.5, 121.9, 113.3, 89.3, 50.9 ppm; MS (EI) m/z 77, 89, 116, 145, 195, 223, 255.

(*Z*)-Methyl 3-((2-chlorophenyl)amino)acrylate (3p). Light yellow oil (93.1 mg, 88%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.36 (d, J = 10.8 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 7.22 (d, J = 8.0 Hz, 1H), 7.09 (d, J = 8.4 Hz, 1H), 6.92 (t, J = 8.4 Hz, 1H), 4.97 (d, J = 8.4 Hz, 1H), 3.76 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 141.4, 137.5, 130.1, 127.8, 122.5, 121.9, 113.3, 89.3, 50.9 ppm; HRMS-ESI (m/z) calcd for $C_{10}H_{10}ClNO_2$, $[M + H]^+$ 212.0473, found 212.0475.

(*Z*)-Methyl 3-((3-ethynylphenyl)amino)acrylate (3q). Light yellow oil (85.4 mg, 85%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.87 (d, J = 11.6 Hz, 1H), 7.21 (dd, J = 13.2, 8.0 Hz, 2H), 7.13−7.09 (m, 2H), 6.93 (dd, J = 8.0, 1.6 Hz, 1H), 4.88 (d, J = 8.4 Hz, 1H), 3.72 (s, 3H), 3.08 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 142.6, 140.7, 129.6, 126.2, 123.5, 118.4, 116.1, 87.9, 83.1, 77.6, 50.7 ppm; HRMS-ESI (m/z) calcd for $C_{12}H_{11}NO_2$, $[M + H]^+$ 202.0863, found 202.0856.

(*Z*)-Methyl 3-((4-vinylphenyl)amino)acrylate (3r). Light yellow solid (88.3 mg, 87%): mp 176−177 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.91 (d, J = 12.4 Hz, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.25 (dd, J = 12.6, 8.2 Hz, 1H), 6.92 (d, J = 8.4 Hz, 2H), 6.65 (dd, J = 17.6, 10.8 Hz, 1H), 5.64 (d, J = 17.6 Hz, 1H), 5.16 (d, J = 10.8 Hz, 1H), 4.86 (d, J = 8.4 Hz, 1H), 3.72 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 142.8, 140.1, 135.9, 132.2, 127.5, 115.3, 112.3, 87.2, 50.6 ppm; HRMS-ESI (m/z) calcd for $C_{12}H_{13}NO_2$, $[M + H]^+$ 204.1019, found 204.1009.

(*Z*)-Methyl 3-(naphthalen-1-ylamino)acrylate (3s). Light yellow oil (104.4 mg, 92%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.73 (d, J = 11.6 Hz, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 8.8 Hz, 1H), 7.54−7.46 (m, 3H), 7.37 (t, J = 8.0 Hz, 2H), 7.07 (d, J = 7.6 Hz, 1H), 4.97 (d, J = 8.4 Hz, 1H), 3.77 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 144.2, 136.5, 134.3, 128.4, 126.4, 126.2, 125.8, 124.5, 122.9, 120.5, 109.6, 87.9, 50.7 ppm; HRMS-ESI (m/z) calcd for $C_{14}H_{13}NO_2$, $[M + H]^+$ 228.1019, found 228.1010.

(*Z*)-Methyl 3-((2-oxo-4-(trifluoromethyl)-2*H*-chromen-7-yl)-amino)acrylate (3t). Light yellow solid (134.6 mg, 86%): mp 177−178 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.22 (d, J = 12.0 Hz,

1H), 7.62 (dd, J = 8.6, 1.4 Hz, 1H), 7.26−7.21 (m, 1H), 6.92−6.89 (m, 2H), 6.61 (s, 1H), 5.07 (d, J = 8.4 Hz, 1H), 3.75 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 159.2, 156.3, 144.8, 141.3, 140.6, 126.9, 115.0, 112.8, 112.4, 108.0, 101.7, 91.7, 51.1 ppm; HRMS-ESI (m/z) calcd for $C_{14}H_{10}F_3NO_4$, $[M + H]^+$ 314.0635, found 314.0627.

(*Z*)-Butyl 3-(phenylamino)acrylate (3u).[47] Light yellow oil (99.6 mg, 91%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.89 (d, J = 12.0 Hz, 1H), 7.28 (t, J = 8.0 Hz, 2H), 7.25−7.21 (m, 1H), 6.99 (d, J = 7.2 Hz, 1H), 6.95 (d, J = 8.0 Hz, 2H), 4.83 (d, J = 8.4 Hz, 1H), 4.12 (t, J = 6.8 Hz, 2H), 1.69−1.61 (m, 2H), 1.46−1.37 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 142.9, 140.7, 129.6, 122.4, 115.3, 87.4, 63.2, 30.9, 19.2, 13.7 ppm; MS (EI) m/z 77, 91, 117, 145, 163, 201, 219.

(*Z*)-2-Ethylhexyl 3-(phenylamino)acrylate (3v). Light yellow oil (122.4 mg, 89%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.89 (d, J = 12.4 Hz, 1H), 7.31−7.22 (m, 3H), 7.00 (d, J = 7.2 Hz, 1H), 6.96 (d, J = 7.6 Hz, 2H), 4.85 (d, J = 8.4 Hz, 1H), 4.04 (dd, J = 5.8, 3.4 Hz, 2H), 1.64−1.59 (m, 1H), 1.39−1.31 (m, 8H), 0.94−0.90 (m, 6H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 142.8, 140.7, 129.6, 122.4, 115.3, 87.5, 65.8, 38.9, 30.4, 29.0, 23.8, 23.0, 14.0, 11.0 ppm; HRMS-ESI (m/z) calcd for $C_{17}H_{25}NO_2$, $[M + H]^+$ 276.1958, found 276.1949.

(*Z*)-Cyclohexyl 3-(phenylamino)acrylate (3w). Light yellow oil (113.9 mg, 93%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.95 (d, J = 12.0 Hz, 1H), 7.33−7.24 (m, 3H), 7.03−6.97 (m, 3H), 4.86−4.79 (m, 2H), 1.95−1.77 (m, 4H), 1.61−1.58 (m, 1H), 1.50−1.40 (m, 4H), 1.34−1.27 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 142.7, 140.7, 129.6, 122.4, 115.2, 88.0, 71.6, 31.9, 25.4, 23.9 ppm; HRMS-ESI (m/z) calcd for $C_{15}H_{19}NO_2$, $[M + H]^+$ 246.1489, found 246.1482.

(*Z*)-(Tetrahydrofuran-2-yl)methyl 3-(phenylamino)acrylate (3x). Light yellow oil (116.1 mg, 94%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.84 (d, J = 12.0 Hz, 1H), 7.31−7.23 (m, 3H), 7.01−6.95 (m, 3H), 4.89 (d, J = 8.4 Hz, 1H), 4.24−4.08 (m, 2H), 3.90 (t, J = 7.4 Hz, 1H), 3.82 (t, J = 6.8 Hz, 1H), 2.05−1.86 (m, 4H), 1.67−1.60 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 143.3, 140.6, 129.6, 122.6, 115.3, 87.1, 76.8, 68.4, 65.3, 28.0, 25.6 ppm; HRMS-ESI (m/z) calcd for $C_{14}H_{17}NO_3$, $[M + H]^+$ 248.1281, found 248.1271.

(*Z*)-2,2,2-Trifluoroethyl 3-(phenylamino)acrylate (3y). Light yellow oil (91.9 mg, 75%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.77 (d, J = 11.6 Hz, 1H), 7.38−7.31 (m, 3H), 7.06 (t, J = 7.4 Hz, 1H), 7.00 (d, J = 8.0 Hz, 2H), 4.92 (d, J = 8.0 Hz, 1H), 4.52 (q, J = 8.4 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1, 145.0, 140.1, 129.7, 123.3, 123.3, 115.8, 85.1, 59.3 ppm; HRMS-ESI (m/z) calcd for $C_{11}H_{10}F_3NO_2$, $[M + H]^+$ 246.0736, found 246.0729.

(*Z*)-*N*,*N*-Dimethyl-3-(phenylamino)acrylamide (3z). Light yellow oil (87.4 mg, 92%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.86 (d, J = 11.2 Hz, 1H), 7.26 (t, J = 8.0 Hz, 2H), 7.17 (dd, J = 12.0, 8.4 Hz, 1H), 6.95−6.91 (m, 3H), 5.00 (d, J = 8.4 Hz, 1H), 3.00 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 141.2, 140.7, 129.5, 121.6, 115.0, 86.3, 37.3, 34.9 ppm; HRMS-ESI (m/z) calcd for $C_{11}H_{14}N_2O$, $[M + H]^+$ 191.1179, found 191.1175.

(*Z*)-1-(Phenylamino)pent-1-en-3-one (3aa). Light yellow solid (44.6 mg, 51%): mp 109−111 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.27 (t, J = 7.6 Hz, 2H), 7.19−7.15 (m, 3H), 6.82 (d, J = 6.4 Hz, 1H), 4.91 (d, J = 6.4 Hz, 1H), 1.82 (q, J = 7.6 Hz, 2H), 0.49 (t, J = 7.6 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.6, 155.5, 150.7, 128.0, 125.4, 125.0, 93.3, 31.6, 10.5 ppm; HRMS-ESI (m/z) calcd for $C_{11}H_{13}NO$, $[M + H]^+$ 176.1070, found 176.1064.

Typical Procedure for the Enamine Products' Transformation into Indoles.[18] The enamine product **3** (0.3 mmol) was stirred with $PdCl_2$ (0.03 mmol), $Cu(OAc)_2$ (0.9 mmol) and K_2CO_3 (0.6 mmol) in DMF (3 mL) at 120 °C for 10 h. Then the mixture is cooled to room temperature and diluted with ethyl acetate, washed with brine and dried with $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding products **4**.

Methyl 1*H*-indole-3-carboxylate (4a).[59] Off-white solid (42.5 mg, 81%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.94 (s, 1H), 8.19−8.17 (m, 1H), 7.89 (d, J = 2.8 Hz, 1H), 7.42−7.38 (m, 1H), 7.29−7.23 (m, 2H), 3.92 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9, 136.1, 131.2, 125.7, 123.2, 122.0, 121.4, 111.6, 108.6, 51.1 ppm; MS (EI) m/z 63, 89, 116, 144, 175.

Methyl 7-methyl-1*H*-indole-3-carboxylate (4b). Off-white solid (47.1 mg, 83%): mp 163−165 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.94 (s, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 2.8 Hz, 1H), 7.20 (t, J = 7.6 Hz, 1H), 7.07 (d, J = 7.2 Hz, 1H), 3.94 (s, 3H), 2.50 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.0, 135.7, 130.9, 125.4, 123.7, 122.2, 120.8, 119.0, 108.9, 51.1, 16.5 ppm; HRMS-ESI (m/z) calcd for $C_{11}H_{11}NO_2$, $[M + H]^+$ 190.0863, found 190.0856.

Methyl 6-methoxy-1*H*-indole-3-carboxylate (4c).[60] Off-white solid (52.3 mg, 85%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.95 (d, J = 12.8 Hz, 1H), 8.04 (d, J = 8.8 Hz, 1H), 7.79 (d, J = 2.4 Hz, 1H), 6.92 (dd, J = 8.8, 1.6 Hz, 1H), 6.85 (s, 1H), 3.91 (s, 3H), 3.80 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.0, 157.0, 137.0, 130.2, 122.0, 119.9, 111.8, 108.4, 95.0, 55.5, 51.1 ppm; MS (EI) m/z 76, 103, 146, 162, 174, 190, 205.

Methyl 5,6-dimethyl-1*H*-indole-3-carboxylate (4d). Off-white solid (48.7 mg, 80%): mp 202−205 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.60 (s, 1H), 7.93 (s, 1H), 7.79 (d, J = 2.8 Hz, 1H), 7.17 (s, 1H), 3.92 (s, 3H), 2.38 (s, 3H), 2.36 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9, 135.0, 132.3, 130.9, 130.3, 124.1, 121.4, 111.8, 108.1, 51.0, 20.4, 20.1 ppm; HRMS-ESI (m/z) calcd for $C_{12}H_{13}NO_2$, $[M + H]^+$ 204.1019, found 204.1011.

Methyl 6-(trifluoromethyl)-1*H*-indole-3-carboxylate (4e). Off-white oil (38.6 mg, 53%): ^{1}H NMR (DMSO-d_6, 400 MHz) δ 12.30 (s, 1H), 8.31 (s, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.83 (s, 1H), 7.49 (d, J = 8.4 Hz, 1H), 3.83 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ 164.5, 135.4, 135.4, 128.4, 125.2, 123.0, 121.4, 117.7, 110.0, 106.9, 51.0 ppm; HRMS-ESI (m/z) calcd for $C_{11}H_8F_3NO_2$, $[M - H]^-$ 242.0434, found 242.0439.

Methyl 5-fluoro-1*H*-indole-3-carboxylate (4f).[61] Off-white solid (37.0 mg, 64%): ^{1}H NMR (DMSO-d_6, 400 MHz) δ 12.04 (s, 1H), 8.14 (d, J = 3.2 Hz, 1H), 7.65 (dd, J = 9.6, 2.4 Hz, 1H), 7.49 (dd, J = 8.8, 4.4 Hz, 1H), 7.06 (td, J = 9.2, 2.4 Hz, 1H), 3.80 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ 164.5, 158.3, 134.0, 133.0, 126.2, 113.7 110.7, 106.6, 105.2, 50.7 ppm; MS (EI) m/z 81, 107, 134, 162, 193.

Methyl 5-chloro-1*H*-indole-3-carboxylate (4g).[62] Off-white solid (44.6 mg, 71%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.80 (s, 1H), 8.16 (s, 1H), 7.92 (d, J = 2.8 Hz, 1H), 7.33 (d, J = 8.4 Hz, 1H), 7.22 (dd, J = 8.6, 1.8 Hz, 1H), 3.93 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.2, 134.4, 132.0, 128.0, 126.8, 123.7, 121.2, 112.5, 108.7, 51.2 ppm; MS (EI) m/z 75, 89, 114, 150, 178, 209.

Methyl 5-bromo-1*H*-indole-3-carboxylate (4h).[63] Off-white solid (52.6 mg, 69%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.79 (s, 1H), 8.32 (s, 1H), 7.91 (d, J = 2.0 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.29 (d, J = 8.8 Hz, 1H), 3.93 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.1, 134.7, 131.8, 127.4, 126.3, 124.2, 115.7, 112.9, 108.6, 51.2 ppm; MS (EI) m/z 71, 115, 143, 194, 222, 253.

Dimethyl 1*H*-indole-3,5-dicarboxylate (4i).[64] Off-white solid (42.6 mg, 61%): ^{1}H NMR (DMSO-d_6, 400 MHz) δ 12.26 (s, 1H), 8.69 (s, 1H), 8.22 (d, J = 2.8 Hz, 1H), 7.83 (d, J = 8.8 Hz, 1H), 7.57 (d, J = 8.4 Hz, 1H), 3.87 (s, 3H), 3.84 (s, 3H) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ 167.0, 164.4, 139.0, 134.3, 125.2, 123.3, 122.7, 112.5, 107.4, 51.9, 50.9 ppm; MS (EI) m/z 71, 114, 142, 174, 202, 233.

Typical Procedure for the Enamine Products' Transformation into Pyrazoles.[16] To a mixture of enamine (0.3 mmol) and $Cu(OAc)_2$ (0.9 mmol) was added 1 mL of PhCN. The reaction mixture was stirred vigorously at room temperature to suspend the solids well and then stirred at 120 °C for 20 h. After cooling to room temperature, EtOAc (5 mL) was added, and the mixture was shortly stirred at room temperature to suspend the metallic precipitates, followed by filtration and subsequent concentration in vacuo. The residue was purified by column chromatography on silica gel to afford the corresponding products **5**.

Methyl 1-(4-chlorophenyl)-3-phenyl-1*H*-pyrazole-4-carboxylate (5a). Light yellow solid (49.6 mg, 53%): mp 142−143 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.48 (s, 1H), 7.86 (dd, J = 7.8, 1.4 Hz, 2H), 7.73 (d, J = 8.8 Hz, 2H), 7.48−7.42 (m, 5H), 3.82 (s, 3H) ppm;

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^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.2, 154.3, 137.7, 133.1, 132.2, 131.8, 129.7, 129.3, 128.9, 128.0, 120.6, 113.7, 51.5 ppm; HRMS-ESI (m/z) calcd for $C_{17}H_{13}ClN_2O_2$, $[M + H]^+$ 313.0738, found 313.0730.

Methyl 1-(3,4-dimethylphenyl)-3-phenyl-1*H*-pyrazole-4-carboxylate (5b). Light yellow solid (56.9 mg, 62%): mp 149−150 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.45 (s, 1H), 7.87 (d, J = 8.0 Hz, 2H), 7.58 (s, 1H), 7.47−7.40 (m, 4H), 7.23 (d, J = 8.0 Hz, 1H), 3.82 (s, 3H), 2.34 (s, 3H), 2.31 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.4, 153.8, 138.1, 137.2, 136.1, 132.2, 130.5, 129.3, 128.6, 127.9, 123.5, 120.8, 116.8, 112.9, 51.4, 19.9, 19.3 ppm; HRMS-ESI (m/z) calcd for $C_{19}H_{18}N_2O_2$, $[M + H]^+$ 307.1441, found 307.1436.

Typical Procedure for the Enamine Products' Transformation into Pyrrole.[19] A pressure tube (15 mL) was charged with β-nitrostyrene (0.2 mmol), enamine (0.3 mmol), and CH_3OH (1.5 mL). The mixture was stirred at 120 °C for 12 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel to afford the corresponding product **6**.

Methyl 1-(4-chlorophenyl)-4-phenyl-1*H*-pyrrole-3-carboxylate (6). Light yellow solid (50.4 mg, 81%): mp 94−96 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.72 (d, J = 2.4 Hz, 1H), 7.52 (d, J = 7.2 Hz, 2H), 7.46−7.43 (m, 2H), 7.40−7.37 (m, 4H), 7.31 (t, J = 7.4 Hz, 1H), 7.03 (d, J = 2.4 Hz, 1H), 3.77 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.7, 138.1, 134.0, 132.6, 129.9, 129.2, 128.8, 127.9, 126.9, 125.9, 122.0, 119.6, 115.5, 51.1 ppm; HRMS-ESI (m/z) calcd for $C_{18}H_{14}ClNO_2$, $[M + H]^+$ 312.0786, found 312.0776.

Typical Procedure for the Enamine Products' Transformation into 1,4-Dihydropyridines. A 25 mL Schlenk tube was charged with $PdCl_2$ (0.03 mmol), TBAB (0.15 mmol), cinnamaldehyde (0.3 mmol), and enamine (0.3 mmol) in MeCN (1.5 mL) with an O_2 balloon, and the mixture was heated at 70 °C under magnetic stirring for 10 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel to afford the corresponding products **7**.

Methyl 1,4-diphenyl-1,4-dihydropyridine-3-carboxylate (7a). Light yellow oil (77.7 mg, 89%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75 (d, J = 1.2 Hz, 1H), 7.42−7.30 (m, 6H), 7.23−7.18 (m, 4H), 6.48 (d, J = 8.0 Hz, 1H), 5.12 (dd, J = 8.0, 4.8 Hz, 1H), 4.60 (d, J = 4.8 Hz, 1H), 3.62 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1, 147.2, 143.7, 137.3, 129.7, 128.4, 127.8, 126.4, 125.2, 124.9, 119.6, 110.4, 105.3, 51.1, 38.6 ppm; HRMS-ESI (m/z) calcd for $C_{19}H_{17}NO_2$, $[M + Na]^+$ 314.1152, found 314.1162.

Methyl 1-(4-fluorophenyl)-4-phenyl-1,4-dihydropyridine-3-carboxylate (7b). Light yellow oil (76.0 mg, 82%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64 (s, 1H), 7.36−7.30 (m, 4H), 7.22−7.16 (m, 3H), 7.09 (t, J = 8.6 Hz, 2H), 6.37 (d, J = 8.0 Hz, 1H), 5.10 (dd, J = 8.0, 4.8 Hz, 1H), 4.59 (d, J = 4.8 Hz, 1H), 3.61 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1, 160.1, 147.2, 140.2, 137.5, 128.4, 127.8, 126.5, 125.4, 121.7, 116.4, 110.3, 105.2, 51.1, 38.5 ppm; HRMS-ESI (m/z) calcd for $C_{19}H_{16}FNO_2$, $[M + Na]^+$ 332.1057, found 332.1058.

Methyl 1-(4-chlorophenyl)-4-phenyl-1,4-dihydropyridine-3-carboxylate (7c). Light yellow oil (88.8 mg, 91%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.60 (d, J = 2.0 Hz, 1H), 7.29−7.21 (m, 6H), 7.14−7.10 (m, 1H), 7.06 (d, J = 8.8 Hz, 2H), 6.34 (d, J = 7.2 Hz, 1H), 5.05 (dd, J = 7.6, 4.8 Hz, 1H), 4.50 (d, J = 4.4 Hz, 1H) 3.54 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.9, 146.9, 142.2, 136.8, 130.2, 129.7, 128.4, 127.8, 126.5, 124.8, 120.7, 110.8, 106.0, 51.1, 38.5 ppm; HRMS-ESI (m/z) calcd for $C_{19}H_{16}ClNO_2$, $[M + Na]^+$ 348.0762, found 348.0752.

Methyl 4-phenyl-1-(*o*-tolyl)-1,4-dihydropyridine-3-carboxylate (7d). Light yellow oil (79.6 mg, 87%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42−7.39 (m, 3H), 7.34 (t, J = 7.6 Hz, 2H), 7.28−7.18 (m, 5H), 6.07 (dd, J = 7.6, 0.8 Hz, 1H), 5.02 (dd, J = 8.0, 4.8 Hz, 1H), 4.61 (d, J = 4.8 Hz, 1H), 3.59 (s, 3H), 2.36 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.3, 147.8, 143.3, 139.8, 134.0, 131.6, 128.4, 127.8, 127.5, 127.3, 127.2, 126.3, 125.9, 108.4, 102.9, 50.9, 38.3, 18.0 ppm; HRMS-ESI (m/z) calcd for $C_{20}H_{19}NO_2$, $[M + Na]^+$ 328.1308, found 328.1304.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all compounds and crystallographic information (CIF) for compound **7b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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