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Iodine/Copper Iodide-Mediated C−H Functionalization: Synthesis of Imidazo[1,2-*a*]pyridines and Indoles from *N*-Aryl Enamines

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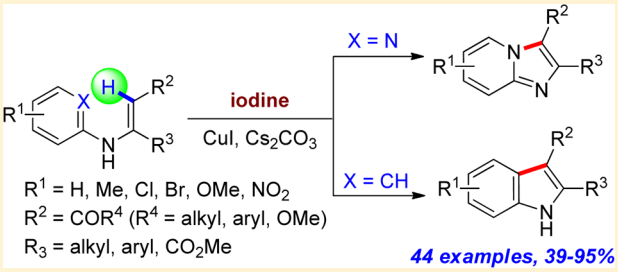
Supporting Information

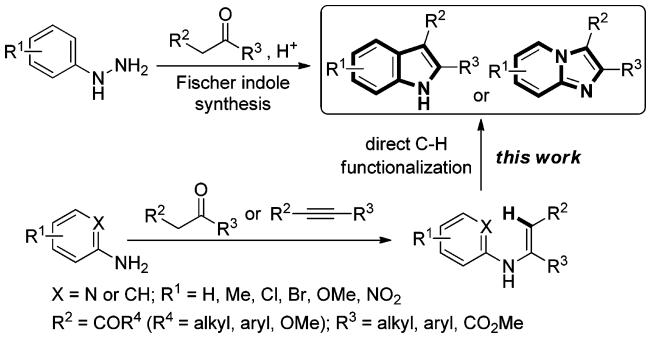
ABSTRACT: A practical intramolecular C−H functionalization reaction of *N*-aryl enamines has been carried out with molecular iodine (I_2) as the sole oxidant in the presence of copper iodide (CuI). The efficient and versatile synthetic method described here is compatible with both *N*-heteroaryl and *N*-aryl substituted enamines and produces diverse imidazo[1,2-*a*]pyridine and indole derivatives via I_2-mediated oxidative C−N and C−C bond formation, respectively. This ligand-free C−H functionalization methodology also works well with crude enamines, which allows for the sequential synthesis of the products directly from arylamines and ketones (or alkynes) without purification of the enamine intermediates.



INTRODUCTION

Indole[1] and imidazo[1,2-*a*]pyridine[2] structures are widely distributed in a broad variety of natural products and synthetic molecules with diverse pharmaceutical properties, and considerable efforts have been made to synthesize these 5,6-fused bicyclic frameworks.[1a−c,2a−d] In addition to Fischer indole synthesis, one of most straightforward strategies is oxidative cyclization of *N*-aryl enamines which are readily accessible via direct C−H functionalization[3] (Scheme 1). Such transformations have been previously accomplished using oxidants such as $Cu(OAc)_2$,[3a] hypervalent iodine(III) reagents,[3b] and NBS,[3c] or by Pd(II) or Cu(I) catalyzed aerobic oxidation.[3d−f] These are elegant methods, but it remains important to develop simpler and more efficient approaches, especially those that could lead to both these heterocyclic skeletons.

Scheme 1. Two Important Strategies To Construct Indole and Imidazo[1,2-*a*]pyridine Skeletons: Fischer Indole Synthesis and Direct C−H Functionalization of *N*-Aryl Enamines



The C−H functionalization reaction has emerged as a valuable tool for the transformation of unreactive C−H bonds in an atom- and step-economic fashion.[4] The benefits of this synthetic strategy include no preliminary activation of the reaction centers, facilitative preparation of the required substrates, and formation of fewer wasteful byproducts. In recent years, impressive achievements have been made in heterocycle synthesis by such convenient methods from simple and readily available precursors.[4a,c] These cross-dehydrogenative coupling reactions have been successfully achieved via metal-catalyzed aerobic oxidation,[4a] iodine(III)-mediated oxidative cyclization,[4b] or radical pathways.[4c] Alternatively, we developed several C−H functionalization reactions using molecular iodine (I_2) as the sole oxidant to synthesize 1,3,4-oxadiazoles,[5] pyrazoles,[6] and quinazolin-4(3*H*)-ones.[7] As a continuation of this research, we describe in this paper a versatile and efficient method for the synthesis of imidazo[1,2-*a*]pyridines and indoles[8] by I_2/CuI-mediated oxidative C−N and C−C bond formation, respectively, from C−H bond.

RESULTS AND DISCUSSION

We began this study by investigating the oxidative cyclization of the enamine **1c**, obtained through the *p*-TsOH-catalyzed condensation of 5-methylpyridin-2-amine and 1,3-cyclohexanedione (see the Supporting Information). Treatment of **1c** with molecular iodine under basic conditions gave only the vinyl iodide (**2c′**) in 60% yield (Scheme 2). The CuI-catalyzed coupling cyclization of **2c′** afforded the imidazo[1,2-*a*]pyridine (**2c**) in excellent yield. These two steps were carried out in the same solvent, so we examined the feasibility of the direct conversion of substrate **1c** to the desired product (**2c**) in a one-

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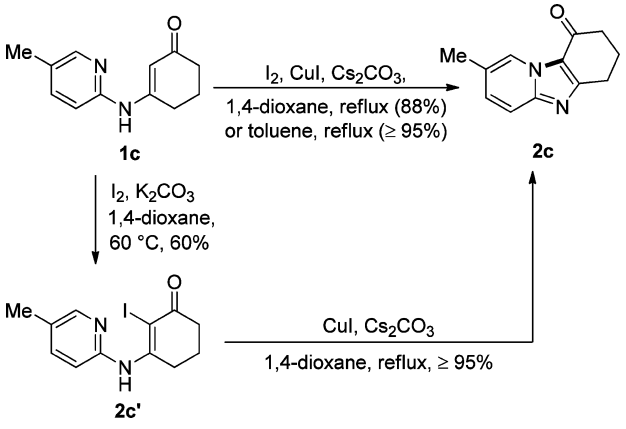
Scheme 2. Synthesis of Fused Imidazo[1,2-*a*]pyridine 2c from Enamine 1c[a]

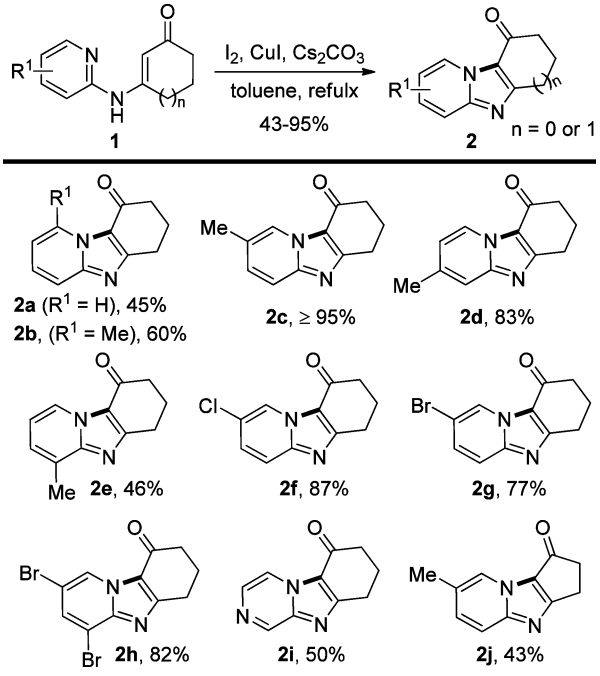


[a]Optimal reaction conditions: **1c** (0.5 mmol), CuI (0.1 mmol), I_2 (0.6 mmol), Cs_2CO_3 (1.5 mmol), toluene, reflux (isolated yields are given).

pot reaction. Indeed, I_2/CuI-mediated oxidative C−H functionalization of **1c** in the presence of Cs_2CO_3 in 1,4-dioxane at reflux temperature resulted in **2c** in a higher overall yield (88%). Further optimization indicated that toluene is the most effective solvent for this transformation.

A range of *N*-pyridylcyclohexenamines (**1**) (Scheme 3) were subjected to the optimal reaction conditions above, to examine

Scheme 3. Substrate Scope for Synthesis of Fused Imidazo[1,2-*a*]pyridines 2[a]

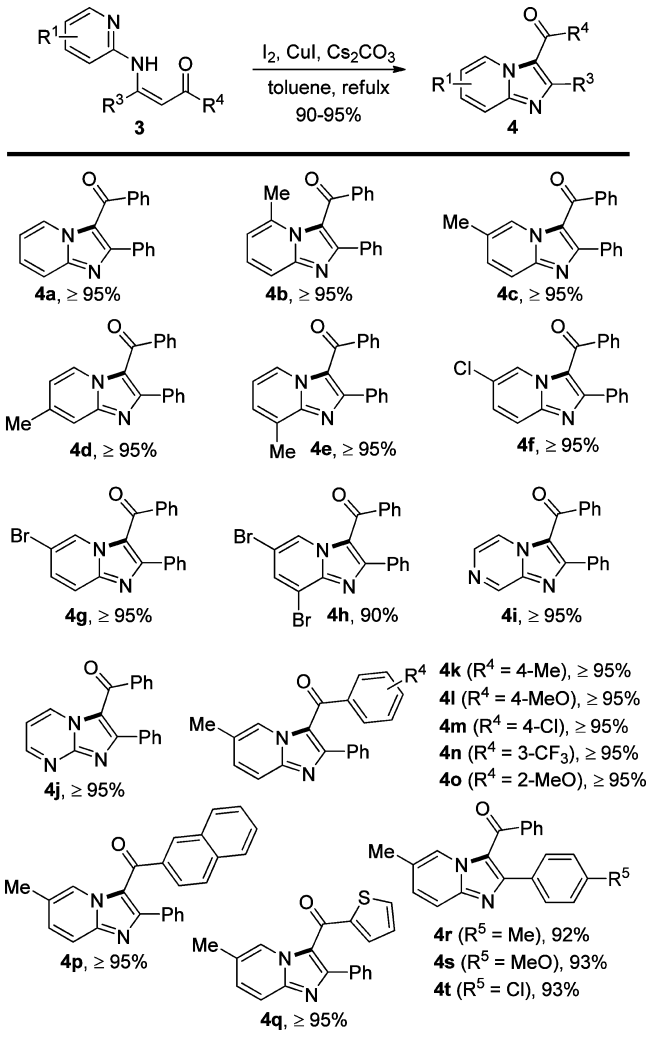


[a]Optimal reaction conditions: **1** (0.5 mmol), CuI (0.1 mmol), I_2 (0.6 mmol), Cs_2CO_3 (1.5 mmol), toluene, reflux (isolated yields are given).

the scope and generality of this method. All the substrates bearing methyl groups and halogens at the different positions of the pyridyl moiety were smoothly cyclized to the corresponding fused imidazo[1,2-*a*]pyridines (**2a**−**h**) in moderate to excellent yields. In addition, both *N*-pyrazyl and cyclopentenamino substrates were also transformed into the desired products (**2i**−**j**).

N-Pyridylenaminone substrates (**3**) were easily prepared by conjugated addition of 2-aminopyridines to *α*,*β*-ynones (see the Supporting Information). Under the optimum C−H functionalization conditions, all these enamine substrates were converted into the expected products in excellent yield (Scheme 4). This methodology can tolerate both electron-

Scheme 4. Substrate Scope for Synthesis of Imidazo[1,2-*a*]pyridines 4[a]



[a]Optimal reaction conditions: **3** (0.5 mmol), CuI (0.1 mmol), I_2 (0.6 mmol), Cs_2CO_3 (1.5 mmol), toluene, reflux (isolated yields are given).

donating groups (EDGs) (**4b**−**e**) and electron-withdrawing groups (EWGs) (**4f**−**h**) on the pyridine ring. Pyrazidoimidazoles (**4i**) and pyrimidoimidazoles (**4j**) were also produced by this synthetic process. Substituents on the phenyl ring at the R^4 position (**4k**−**o**) and replacement of this phenyl with *β*-naphthyl or 2-thienyl groups (**4p**−**q**) did not affect the conversion. The yields were slightly reduced due to the presence of substituents at the R^3 position of the phenyl ring (**4r**−**t**). To simplify the synthetic procedure operationally, we probed the feasibility of direct synthesis from 2-aminopyridines and ynones, omitting purification of the enamine intermediates. Taking the preparation of **4c** and **4r** as examples, after the first-step addition was complete, the reaction mixture was filtered

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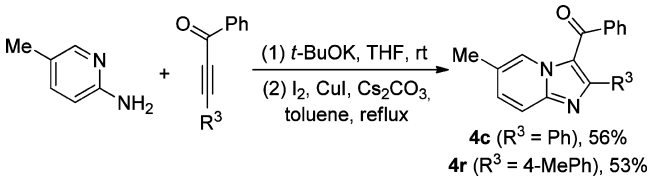
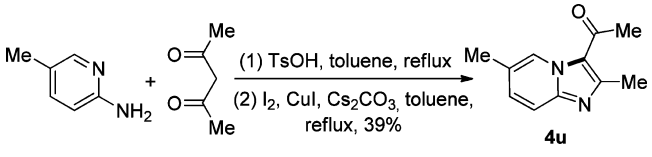
and concentrated, and the resulting crude enamines were subjected directly to the I_2/CuI-mediated oxidative cyclization conditions. The desired products were produced in yields (Scheme 5) that were equally good to those obtained in the

Scheme 5. Sequential Synthesis of Imidazo[1,2-*a*]pyridines 4c and 4r from 2-Aminopyridines and Ynones



reactions via purified enanimes. The 2-methyl-3-acetyl derivative (**4u**) was successfully prepared directly from 5-methylpyridin-2-amine and acetylacetone, without isolation of the unstable condensation intermediate (Scheme 6).

Scheme 6. Sequential Synthesis of Imidazo[1,2-*a*]pyridine 4u from Acetylacetone



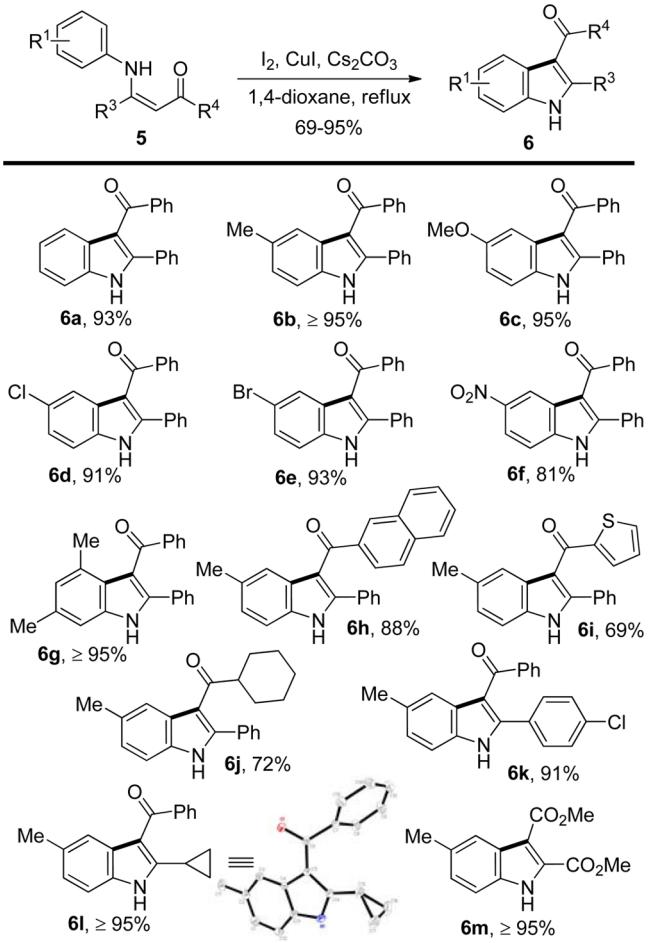
In the light of these encouraging results, we further extended the substrate scope of this C−H functionalization reaction using *N*-phenylenamines (**5**) for indole synthesis (Scheme 7). Further optimization of the reaction conditions showed 1,4-dioxane to be the optimal solvent for the transformation of **5** to the indoles (**6**). The reaction is compatible with both EDGs (**6b−c**, **6g**) and EWGs (**6d−f**) on the phenyl ring, and either aryl (**6h−i**, **6k**) or alkyl substituents (**6j**, **6l**) at the R^2 and R^3 positions. In particular, oxidative cyclization of the enamine **5l** produced the 2-cyclopropyl substituted indole (**6l**) in excellent yield, and the reaction conditions had no effect on the sensitive cyclopropane ring. The structure of **6l** was confirmed by X-ray crystallography[9] (see the Supporting Information). In addition, a 2,3-dimethyl ester derivative (**6m**) was also obtained by addition of aniline to dimethyl 2-butynedioate, followed by I_2/CuI-mediated oxidative C−C bond formation.

Based on the experimental results, a plausible mechanism for this I_2/CuI-mediated C−H functionalization reaction is proposed (Scheme 8). Using the formation of imidazo[1,2-*a*]pyridine **2c** as an example, the reaction of enamine **1c** with molecular iodine under basic conditions produces the *β*-iodo enamide **2c′**. Then oxidative addition of Cu(I) to the iodide **2c′** followed by a base-promoted cyclization results in intermediate **B**. Finally, the subsequent reductive elimination affords the imidazo[1,2-*a*]pyridine framework **2c** and restores the copper(I) catalyst.

CONCLUSIONS

A practical and efficient I_2/CuI-mediated direct C−H functionalization reaction has been established. The versatile synthetic method described here is compatible with both *N*-heteroaryl and *N*-aryl substituted enamines and produces diverse imidazo[1,2-*a*]pyridine and indole derivatives. Under the optimum reaction conditions, imidazo[1,2-*a*]pyridines and

Scheme 7. Substrate Scope for Synthesis of Indoles 6[a]



[a]Optimal reaction conditions: **5** (0.5 mmol), CuI (0.1 mmol), I_2 (0.6 mmol), Cs_2CO_3 (1.5 mmol), 1,4-dioxane, reflux (isolated yields are given).

indoles were obtained in good yield from the corresponding precursors by I_2-mediated oxidative C−N and C−C bond formation, respectively. This ligand-free C−H functionalization reaction works well with crude enamines, and this allows for the sequential synthesis of the expected products directly from arylamines and ketones (or alkynes) without purification of the enamine intermediates.

EXPERIMENTAL SECTION

General Information. ^1H and ^{13}C NMR spectra were recorded on a 400 MHz (100 MHz for ^{13}C NMR) spectrometer. Chemical shift values are given in parts per million (ppm) with tetramethylsilane (TMS) as the internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; hept, heptet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets. The coupling constants (*J*) are reported in Hertz (Hz). Melting points were determined on a micromelting point apparatus and are uncorrected. High-resolution mass spectra (HRMS) were obtained on a TOF-Q mass spectrometer equipped with an electrospray ion source (ESI), operated in the positive mode. Flash column chromatography was performed over silica gel 200−300 mesh, and the eluents were distilled prior to use. Toluene, used in the synthesis of **1**, **2**, and **4**, was analytical reagent grade and used without any pretreatment; 1,4-dioxane, in the synthesis of **2c′** and **6**, was dried over 4 Å molecular sieves prior to use; THF, in the preparation of **3**, was distilled from sodium/benzophenone ketyl under nitrogen; and

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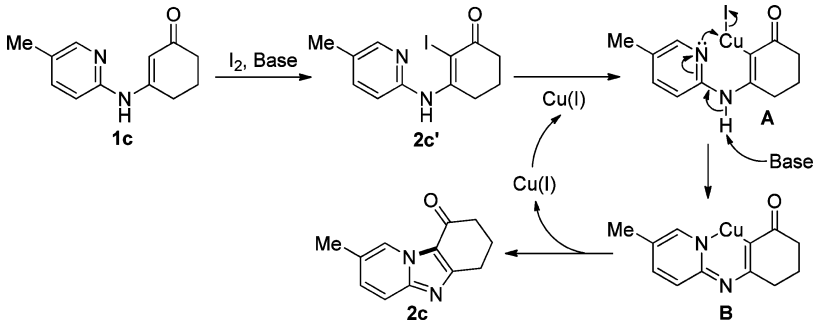
Scheme 8. Proposed Mechanism for the Formation of Imidazo[1,2-*a*]pyridine 2c



MeOH, in the preparation of **5**, was dried over 4 Å molecular sieves prior to use.

General Procedure A for the Preparation of Enamines 1. To a solution of substituted 2-aminopyridine (5 mmol, 2-aminopyrazine for **1i**) in toluene (20 mL) at room temperature were added 1,3-cyclohexanedione (6.25 mmol, 1,3-cyclopentanedione for **1j**) and *p*-toluenesulfonic acid monohydrate (190 mg, 1 mmol) in sequence. The reaction was heated to reflux under a nitrogen atmosphere until the consumption of the 2-aminopyrimidine as monitored by TLC was complete. After cooling to room temperature, the reaction mixture was treated with cold 5% $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (20 mL × 5). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and then purified through silica gel column chromatography, giving the enamine (**1**) in 26−90% yield.

*3-(Pyridin-2-ylamino)cyclohex-2-enone (**1a**).*[10] Eluent: EtOAc/petroleum ether (PE) 67:33; 4 h; yield: 292 mg, 31%; brown solid, mp 176−177 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, J = 4.8 Hz, 1H), 7.65−7.58 (m, 2H), 7.11 (d, J = 8.0 Hz, 1H), 6.98−6.95 (m, 1H), 6.39 (s, 1H), 2.59 (t, J = 6.0 Hz, 2H), 2.41 (t, J = 6.0 Hz, 2H), 2.09−2.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.4, 158.7, 152.7, 148.4, 138.0, 118.6, 114.1, 104.1, 36.6, 30.0, 21.7; HRMS (m/z) [M + Na]$^+$ calcd for $C_{11}H_{12}N_2NaO$ 211.0842, found 211.0847.

*3-((6-Methylpyridin-2-yl)amino)cyclohex-2-enone (**1b**).* Eluent: EtOAc/PE 67:33; 4 h; yield: 627 mg, 62%; pale yellow solid, mp 180−181 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (t, J = 7.6 Hz, 1H), 7.27 (br, s, 1H, overlapped with the peak of chloroform), 6.90 (d, J = 8.0 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H), 6.38 (s, 1H), 2.56 (t, J = 6.0 Hz, 2H), 2.46 (s, 3H), 2.40 (t, J = 6.0 Hz, 2H), 2.08−2.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.3, 158.7, 157.7, 151.9, 138.2, 118.1, 111.0, 103.9, 36.6, 30.2, 24.2, 21.8; HRMS (m/z) [M + Na]$^+$ calcd for $C_{12}H_{14}N_2NaO$ 225.0998, found 225.0997.

*3-((5-Methylpyridin-2-yl)amino)cyclohex-2-enone (**1c**).*[10] Eluent: EtOAc/PE 67:33; 4 h; yield: 678 mg, 67%; off-white solid, mp 162−164 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (s, 1H), 7.51−7.44 (m, 2H), 7.06 (d, J = 8.4 Hz, 1H), 6.23 (s, 1H), 2.56 (t, J = 6.4 Hz, 2H), 2.40 (t, J = 6.4 Hz, 2H), 2.29 (s, 3H), 2.08−2.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.3, 159.4, 150.5, 148.1, 138.7, 128.2, 114.2, 103.1, 36.6, 29.8, 21.8, 17.8; HRMS (m/z) [M + Na]$^+$ calcd for $C_{12}H_{14}N_2ONa$ 225.0998, found 225.0998.

*3-((4-Methylpyridin-2-yl)amino)cyclohex-2-enone (**1d**).* Eluent: EtOAc/PE 67:33; 4 h; yield: 617 mg, 61%; pale yellow solid, mp 188−190 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 5.2 Hz, 1H), 7.71 (br, s, 1H), 6.98 (s, 1H), 6.80 (d, J = 5.2 Hz, 1H), 6.28 (s,1H), 2.57 (t, J = 6.4 Hz, 2H), 2.40 (t, J = 6.0 Hz, 2H), 2.32 (s, 3H), 2.08−2.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.3, 158.9, 152.7, 149.7, 147.9, 120.1, 114.8, 103.6, 36.6, 30.1, 21.7, 21.2; HRMS (m/z) [M + Na]$^+$ calcd for $C_{12}H_{14}N_2NaO$ 225.0998, found 225.0996.

*3-((3-Methylpyridin-2-yl)amino)cyclohex-2-enone (**1e**).* Eluent: EtOAc/PE 67:33; 4 h; yield: 496 mg, 49%; yellow solid, mp 100−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22−8.21 (m, 1H), 7.47 (d, J = 7.6 Hz, 1H), 6.98−6.94 (m, 1H), 6.80 (br, s, 1H), 6.34−6.30 (m, 1H), 2.60 (t, J = 6.0 Hz, 2H), 2.37 (t, J = 6.0 Hz, 2H), 2.26 (s, 3H), 2.10−2.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.2, 159.2, 151.2, 145.9, 139.1, 123.5, 119.6, 104.8, 36.6, 29.8, 21.9, 17.3; HRMS (m/z) [M + Na]$^+$ calcd for $C_{12}H_{14}N_2NaO$ 225.0998, found 225.0997.

*3-((5-Chloropyridin-2-yl)amino)cyclohex-2-enone (**1f**).* Eluent: EtOAc/PE 67:33; 4 h; yield: 991 mg, 89%; white solid, mp 173−175 °C; ^{1}H NMR (400 MHz, CD_3OD): δ 8.28 (s, 1H), 7.70 (d, J = 8.8 Hz, 1H), 7.01 (d, J = 8.8 Hz, 1H), 6.93 (s, 1H), 2.64 (t, J = 5.6 Hz, 2H), 2.37 (t, J = 6.0 Hz, 2H), 2.06−2.03 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ 201.7, 161.2, 152.4, 145.7, 137.4, 125.1, 114.9, 104.2, 35.7, 28.8, 21.6; HRMS (m/z) [M + Na]$^+$ calcd for $C_{11}H_{11}ClN_2NaO$ 245.0452, found 245.0446.

*3-((5-Bromopyridin-2-yl)amino)cyclohex-2-enone (**1g**).* Eluent: EtOAc/PE 67:33; 14 h; yield: 868 mg, 65%; yellow solid, mp 191−193 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, J = 2.4 Hz, 1H), 7.69 (dd, J = 8.8, 2.8 Hz, 1H), 7.48 (br, s, 1H), 6.97 (d, J = 8.4 Hz, 1H), 6.45 (s, 1H), 2.58 (t, J = 6.0 Hz, 2H), 2.40 (t, J = 6.4 Hz, 2H), 2.09−2.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.5, 158.3, 151.5, 149.1, 140.4, 115.1, 113.5, 105.1, 36.6, 30.0, 21.7; HRMS (m/z) [M + Na]$^+$ calcd for $C_{11}H_{11}BrN_2NaO$ 290.9927, found 290.9926.

*3-((3,5-Dibromopyridin-2-yl)amino)cyclohex-2-enone (**1h**).* Eluent: EtOAc/PE 50:50; 21 h; yield: 779 mg, 45%; white solid, mp 137−138 °C (lit.[10] mp 132−134 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, J = 2.0 Hz, 1H), 7.93 (d, J = 2.4 Hz, 1H), 7.05 (s, 1H), 6.86 (br, s, 1H), 2.61 (t, J = 6.0 Hz, 2H), 2.42 (t, J = 6.4 Hz, 2H), 2.13−2.07 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.6, 155.5, 148.8, 147.3, 142.3, 111.9, 108.7, 108.5, 36.6, 30.2, 21.8; HRMS (m/z) [M + Na]$^+$ calcd for $C_{11}H_{10}Br_2N_2NaO$ 368.9032, found 368.9019.

*3-(Pyrazin-2-ylamino)cyclohex-2-enone (**1i**).* Eluent: EtOAc/PE 67:33; 4 h; yield: 246 mg, 26%; brown solid, mp 179−181 °C; ^{1}H NMR (400 MHz, CD_3OD): δ 8.32−8.31 (m, 2H), 8.13 (d, J = 2.4 Hz, 1H), 7.08 (s, 1H), 2.68 (t, J = 6.0 Hz, 2H), 2.40 (t, J = 6.4 Hz, 2H), 2.11−2.04 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ 201.9, 160.5, 151.3, 141.7, 136.6, 136.2, 105.7, 35.8, 28.7, 21.5; HRMS (m/z) [M + Na]$^+$ calcd for $C_{10}H_{11}N_3NaO$ 212.0794, found 212.0796.

*3-((5-Methylpyridin-2-yl)amino)cyclopent-2-enone (**1j**).* Eluent: EtOAc/PE 67:33; 4 h; yield: 847 mg, 90%; yellow solid, mp 233−234 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.01 (s, 1H), 8.14 (s, 1H), 7.55 (dd, J = 8.4, 2.0 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 6.30 (s, 1H), 2.75 (t, J = 4.8 Hz, 2H), 2.22−2.19 (m, 5H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 205.9, 169.8, 152.0, 147.9, 139.1, 127.0, 112.7, 107.0, 32.8, 29.2, 17.6; HRMS (m/z) [M + Na]$^+$ calcd for $C_{11}H_{12}N_2NaO$ 211.0842, found 211.0850.

General Procedure B for the Preparation of Enamines 3. A stirred mixture of [Pd(PPh$_3$)$_2$Cl$_2$] (70 mg, 0.1 mmol) and CuI (38 mg, 0.2 mmol) in THF (20 mL) was stirred and degassed with nitrogen before Et_3N (0.7 mL, 5 mmol), acyl chloride (5 mmol), and aryl acetylene (5 mmol) were added successively. The reaction mixture was then stirred for 1 h at room temperature (TLC indicated that the reaction was complete). The solvents were evaporated, and the residue was purified through silica gel column chromatography (eluent: EtOAc/PE 0:100 to 5:95) as a light-yellow oil or solid in 75−95% yields. A solution of the above ynone (3 mmol) in THF (10 mL) was treated with substituted 2-aminopyridine (3.6 mmol) and *t*-BuOK (673 mg, 6 mmol) in sequence and then stirred at room temperature for 1 h (TLC indicated that the reaction was complete). The reaction mixture was filtered through a neutral Al_2O_3 pad. The filtrate was concentrated and then purified through silica gel column chromatography to give the enamine (**3**) in 38−71% yield.

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J. Org. Chem. 2016, 81, 9326−9336

(Z)-1,3-Diphenyl-3-(pyridin-2-ylamino)prop-2-en-1-one (**3a**). Eluent: EtOAc/PE 10:90; yield: 496 mg, 55%; yellow solid, mp 103−104 °C (lit.[3f] mp 107−109 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.69 (s, 1H), 8.21 (dd, J = 4.8, 1.2 Hz, 1H), 7.99−7.97 (m, 2H), 7.52−7.32 (m, 9H), 6.84 (dd, J = 6.8, 5.2 Hz, 1H), 6.41 (d, J = 8.4 Hz, 1H), 6.17 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2, 158.9, 153.0, 148.6, 139.7, 137.0, 136.4, 131.6, 129.8, 128.6, 128.4, 128.0, 127.5, 118.5, 115.4, 99.5; HRMS (m/z) [M + Na]$^+$ calcd for $C_{20}H_{16}N_2NaO$ 323.1155, found 323.1161.

(Z)-3-((6-Methylpyridin-2-yl)amino)-1,3-diphenylprop-2-en-1-one (**3b**).[3f] Eluent: EtOAc/PE 10:90; yield: 547 mg, 58%; yellow solid, mp 95−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.71 (s, 1H), 7.98−7.95 (m, 2H), 7.46−7.30 (m, 8H), 7.15 (t, J = 8.0 Hz, 1H), 6.65 (d, J = 7.6 Hz, 1H), 6.12−6.10 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.9, 159.1, 157.6, 152.2, 139.7, 137.3, 136.5, 131.6, 129.7, 128.6, 128.4, 128.0, 127.5, 118.0, 112.3, 99.1, 24.1; HRMS (m/z) [M + H]$^+$ calcd for $C_{21}H_{19}N_2O$ 315.1492, found 315.1482.

(Z)-3-((5-Methylpyridin-2-yl)amino)-1,3-diphenylprop-2-en-1-one (**3c**). Eluent: EtOAc/PE 10:90; yield: 556 mg, 59%; yellow solid, mp 116−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.70 (s, 1H), 8.04 (d, J = 2.0 Hz, 1H), 7.98−7.96 (m, 2H), 7.51−7.33 (m, 8H), 7.16 (dd, J = 8.4, 2.4 Hz, 1H), 6.33 (d, J = 8.4 Hz, 1H), 6.13 (s, 1H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.0, 159.3, 150.7, 148.6, 139.8, 137.8, 136.5, 131.5, 129.6, 128.6, 128.4, 128.0, 127.4, 115.4, 98.8, 17.7; HRMS (m/z) [M + H]$^+$ calcd for $C_{21}H_{19}N_2O$ 315.1492, found 315.1492.

(Z)-3-((4-Methylpyridin-2-yl)amino)-1,3-diphenylprop-2-en-1-one (**3d**). Eluent: EtOAc/PE 10:90; yield: 566 mg, 60%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.68 (s, 1H), 8.03 (d, J = 5.2 Hz, 1H), 7.99−7.96 (m, 2H), 7.52−7.34 (m, 8H), 6.68 (d, J = 4.8 Hz, 1H), 6.29 (s, 1H), 6.16 (s, 1H), 2.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2, 159.3, 153.0, 148.4, 148.1, 139.7, 136.6, 131.6, 129.6, 128.5, 128.4, 128.0, 127.5, 119.9, 116.2, 99.3, 21.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{21}H_{19}N_2O$ 315.1492, found 315.1482.

(Z)-3-((3-Methylpyridin-2-yl)amino)-1,3-diphenylprop-2-en-1-one (**3e**). Eluent: EtOAc/PE 10:90; yield: 594 mg, 63%; yellow solid, mp 82−83 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.85 (s, 1H), 8.00−7.97 (m, 2H), 7.81 (dd, J = 4.8, 1.6 Hz, 1H), 7.52−7.28 (m, 9H), 6.79 (dd, J = 7.6, 4.8 Hz, 1H), 6.27 (s, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.7, 160.9, 151.6, 145.5, 139.7, 138.6, 137.5, 131.6, 129.2, 128.5, 128.1, 127.7, 127.5, 124.0, 119.1, 100.0, 17.7; HRMS (m/z) [M + H]$^+$ calcd for $C_{21}H_{19}N_2O$ 315.1492, found 315.1487.

(Z)-3-((5-Chloropyridin-2-yl)amino)-1,3-diphenylprop-2-en-1-one (**3f**).[11] Eluent: EtOAc/PE 5:95; yield: 653 mg, 65%; pale yellow solid, mp 122−123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.70 (s, 1H), 8.14 (d, J = 2.0 Hz, 1H), 7.98−7.96 (m, 2H), 7.52−7.36 (m, 8H), 7.30 (dd, J = 8.8, 2.8 Hz, 1H), 6.33 (d, J = 8.8 Hz, 1H), 6.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.5, 158.5, 151.4, 147.2, 139.5, 136.8, 136.1, 131.9, 130.0, 128.8, 128.5, 127.9, 127.5, 125.9, 115.9, 100.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{20}H_{16}ClN_2O$ 335.0946, found 335.0932.

(Z)-3-((5-Bromopyridin-2-yl)amino)-1,3-diphenylprop-2-en-1-one (**3g**). Eluent: EtOAc/PE 5:95; yield: 694 mg, 61%; pale yellow solid, mp 137−139 °C (lit.[3f] mp 140−142 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.67 (s, 1H), 8.24 (d, J = 2.0 Hz, 1H), 7.98−7.96 (m, 2H), 7.53−7.37 (m, 9H), 6.28 (d, J = 8.8 Hz, 1H), 6.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.5, 158.3, 151.7, 149.4, 139.5, 139.4, 136.0, 131.8, 130.0, 128.8, 128.5, 127.9, 127.5, 116.3, 113.8, 100.1; HRMS (m/z) [M + Na]$^+$ calcd for $C_{20}H_{15}BrN_2NaO$ 401.0260, found 401.0255.

(Z)-3-((3,5-Dibromopyridin-2-yl)amino)-1,3-diphenylprop-2-en-1-one (**3h**). Eluent: EtOAc/PE 5:95; yield: 935 mg, 68%; yellow solid, mp 148−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.86 (s, 1H), 8.02−7.99 (m, 2H), 7.95 (d, J = 2.0 Hz, 1H), 7.85 (d, J = 2.0 Hz, 1H), 7.55−7.50 (m, 1H), 7.48−7.44 (m, 2H), 7.41−7.32 (m, 5H), 6.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.0, 158.4, 149.4, 146.9, 142.7, 139.1, 137.0, 132.1, 129.3, 128.5, 128.3, 127.7, 127.4, 112.8, 110.8, 102.4; HRMS (m/z) [M + Na]$^+$ calcd for $C_{20}H_{14}Br_2N_2NaO$ 480.9346, found 480.9340.

(Z)-1,3-Diphenyl-3-(pyrazin-2-ylamino)prop-2-en-1-one (**3i**). Eluent: EtOAc/PE 10:90; yield: 551 mg, 61%; yellow solid, mp 114−115 °C (lit.[3f] mp 114−116 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.71 (s, 1H), 8.14−8.08 (m, 2H), 8.00−7.98 (m, 2H), 7.82 (s, 1H), 7.55−7.38 (m, 8H), 6.28 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.8, 158.0, 149.9, 142.5, 139.2, 138.3, 137.5, 135.8 132.1, 130.2, 129.0, 128.5, 127.8, 127.6, 100.9; HRMS (m/z) [M + Na]$^+$ calcd for $C_{19}H_{15}N_3NaO$ 324.1107, found 324.1100.

(Z)-1,3-Diphenyl-3-(pyrimidin-2-ylamino)prop-2-en-1-one (**3j**).[3f] Eluent: EtOAc/PE 10:90; yield: 353 mg, 39%; off-white solid, mp 103−104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.55 (s, 1H), 8.30 (d, J = 4.8 Hz, 2H), 8.01−7.98 (m, 2H), 7.54−7.34 (m, 8H), 6.76 (t, J = 4.8 Hz, 1H), 6.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.7, 159.1, 157.7, 157.6, 139.4, 137.4, 132.0, 129.3 128.5, 128.1, 127.7, 127.5, 115.0, 102.4; HRMS (m/z) [M + Na]$^+$ calcd for $C_{19}H_{15}N_3NaO$ 324.1107, found 324.1101.

(Z)-3-((5-Methylpyridin-2-yl)amino)-3-phenyl-1-(p-tolyl)prop-2-en-1-one (**3k**). Eluent: EtOAc/PE 10:90; yield: 581 mg, 59%; yellow solid, mp 114−115 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.68 (s, 1H), 8.03 (d, J = 2.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 2H), 7.44−7.33 (m, 5H), 7.26−7.23 (m, 2H, overlapped with the peak of chloroform), 7.15 (dd, J = 8.0, 2.0 Hz, 1H), 6.32 (d, J = 8.4 Hz, 1H), 6.12 (s, 1H), 2.40 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.8, 158.9, 150.8, 148.5, 142.1, 137.7, 137.1, 136.6, 129.6, 129.1, 128.5, 128.0, 127.9, 127.5, 115.2, 98.8, 21.5, 17.7; HRMS (m/z) [M + H]$^+$ calcd for $C_{22}H_{21}N_2O$ 329.1648, found 329.1642.

(Z)-1-(4-Methoxyphenyl)-3-((5-methylpyridin-2-yl)amino)-3-phenylprop-2-en-1-one (**3l**). Eluent: EtOAc/PE 10:90; yield: 651 mg, 63%; yellow solid, mp 118−119 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.65 (s, 1H), 8.02 (d, J = 2.4 Hz, 1H), 7.98−7.96 (m, 2H), 7.45−7.33 (m, 5H), 7.15 (dd, J = 8.4, 2.0 Hz, 1H), 6.95−6.92 (m, 2H), 6.31 (d, J = 8.4 Hz, 1H), 6.10 (s, 1H), 3.86 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.0, 162.4, 158.6, 150.8, 148.5, 137.7, 136.7, 132.5, 129.53, 129.48, 128.5, 128.0, 127.7, 115.1, 113.6, 98.7, 55.4, 17.7; HRMS (m/z) [M + H]$^+$ calcd for $C_{22}H_{21}N_2O_2$ 345.1598, found 345.1591.

(Z)-1-(4-Chlorophenyl)-3-((5-methylpyridin-2-yl)amino)-3-phenylprop-2-en-1-one (**3m**). Eluent: EtOAc/PE 10:90; yield: 544 mg, 52%; yellow solid, mp 138−139 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.70 (s, 1H), 8.05 (d, J = 1.6 Hz, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.43−7.34 (m, 7H), 7.17 (dd, J = 8.4, 2.4 Hz, 1H), 6.33 (d, J = 8.4 Hz, 1H), 6.06 (s, 1H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.5, 159.8, 150.5, 148.6, 138.1, 137.8, 137.7, 136.3, 129.8, 128.8, 128.62, 128.61, 128.3, 128.0, 115.4, 98.2, 17.7; HRMS (m/z) [M + H]$^+$ calcd for $C_{21}H_{18}ClN_2O$ 349.1102, found 349.1089.

(Z)-3-((5-Methylpyridin-2-yl)amino)-3-phenyl-1-(3-(trifluoromethyl)phenyl)prop-2-en-1-one (**3n**). Eluent: EtOAc/PE 10:90; yield: 608 mg, 53%; yellow solid, mp 155−156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.76 (s, 1H), 8.21 (s, 1H), 8.15 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 2.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.45−7.36 (m, 5H), 7.18 (dd, J = 8.0, 2.0 Hz, 1H), 6.35 (d, J = 8.4 Hz, 1H), 6.09 (s, 1H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.0, 160.5, 150.3, 148.7, 140.4, 137.9, 136.1, 130.9 (q, J_{C-F} = 32.5 Hz), 130.6, 129.9, 129.0, 128.7, 128.6, 128.0, 127.9 (q, J_{C-F} = 3.6 Hz), 124.3 (q, J_{C-F} = 3.8 Hz), 124.0 (d, J_{C-F} = 270.8 Hz), 115.6, 98.0, 17.7; HRMS (m/z) [M + H]$^+$ calcd for $C_{22}H_{18}F_3N_2O$ 383.1366, found 383.1366.

(Z)-1-(2-Methoxyphenyl)-3-((5-methylpyridin-2-yl)amino)-3-phenylprop-2-en-1-one (**3o**). Eluent: EtOAc/PE 10:90; yield: 393 mg, 38%; yellow solid, mp 143−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.51 (s, 1H), 8.03 (d, J = 2.4 Hz, 1H), 7.70 (dd, J = 7.6, 1.6 Hz, 1H), 7.43−7.30 (m, 6H), 7.15 (dd, J = 8.4, 2.0 Hz, 1H), 7.03−6.99 (m, 1H), 6.95 (d, J = 8.4 Hz, 1H), 6.32 (d, J = 8.0 Hz, 1H), 6.14 (s, 1H), 3.88 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.2, 157.8, 157.4, 150.9, 148.5, 137.7, 136.6, 131.8, 130.8, 130.1, 129.4, 128.4, 128.1, 127.7, 120.6, 115.4, 111.6, 104.1, 55.8, 17.7; HRMS (m/z) [M + H]$^+$ calcd for $C_{22}H_{21}N_2O_2$ 345.1598, found 345.1581.

(Z)-3-((5-Methylpyridin-2-yl)amino)-1-(naphthalen-2-yl)-3-phenylprop-2-en-1-one (**3p**). Eluent: EtOAc/PE 10:90; yield: 776 mg, 71%; yellow solid, mp 150−151 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.80 (s, 1H), 8.49 (s, 1H), 8.10−8.06 (m, 2H), 7.95 (d, J = 7.6 Hz, 1H), 7.91−7.86 (m, 2H), 7.57−7.37 (m, 7H), 7.17 (d, J = 8.0 Hz,

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J. Org. Chem. 2016, 81, 9326−9336

1H), 6.36 (d, J = 8.0 Hz, 1H), 6.30 (s, 1H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.8, 159.4, 150.7, 148.6, 137.8, 137.1, 136.6, 135.0, 132.8, 129.7, 129.4, 128.6, 128.2, 128.1, 127.7, 127.6, 126.5, 124.2, 115.4, 99.0, 17.7; HRMS (m/z) $[M + H]^+$ calcd for $C_{25}H_{21}N_2O$ 365.1648, found 365.1646.

*(Z)-3-((5-Methylpyridin-2-yl)amino)-3-phenyl-1-(thiophen-2-yl)-prop-2-en-1-one (**3q**).* Eluent: EtOAc/PE 10:90; yield: 519 mg, 54%; yellow solid, mp 126−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.38 (s, 1H), 8.01 (d, J = 1.6 Hz, 1H), 7.68−7.67 (m, 1H), 7.54−7.53 (m, 1H), 7.43−7.33 (m, 5H), 7.16 (dd, J = 8.4, 2.0 Hz, 1H), 7.11−7.09 (m, 1H), 6.32 (d, J = 8.4 Hz, 1H), 6.00 (s, 1H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.7, 159.0, 150.6, 148.5, 146.7, 137.8, 136.3, 131.5, 129.7, 129.0, 128.6, 128.0, 127.9, 115.2, 98.7, 17.7; HRMS (m/z) $[M + H]^+$ calcd for $C_{19}H_{17}N_2OS$ 321.1056, found 321.1056.

*(Z)-3-((5-Methylpyridin-2-yl)amino)-1-phenyl-3-(p-tolyl)prop-2-en-1-one (**3r**).* Eluent: EtOAc/PE 10:90; yield: 483 mg, 49%; yellow solid, mp 96−98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.68 (s, 1H), 8.06 (d, J = 2.4 Hz, 1H), 7.98−7.95 (m, 2H), 7.50−7.41 (m, 3H), 7.34−7.32 (m, 2H), 7.17−7.15 (m, 3H), 6.33 (d, J = 8.4 Hz, 1H), 6.12 (s, 1H), 2.38 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.9, 159.4, 150.8, 148.5, 140.0, 139.9, 137.7, 133.5 131.4, 129.3, 128.3, 128.0, 127.9, 127.4, 115.4, 98.6, 21.4, 17.7; HRMS (m/z) $[M + H]^+$ calcd for $C_{22}H_{21}N_2O$ 329.1648, found 329.1642.

*(Z)-3-(4-Methoxyphenyl)-3-((5-methylpyridin-2-yl)amino)-1-phenylprop-2-en-1-one (**3s**).* Eluent: EtOAc/PE 10:90; yield: 548 mg, 53%; yellow solid, mp 126−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.66 (s, 1H), 8.07 (d, J = 2.0 Hz, 1H), 7.98−7.96 (m, 2H), 7.50−7.41 (m, 3H), 7.39−7.36 (m, 2H), 7.18 (dd, J = 8.4, 2.0 Hz, 1H), 6.87 (d, J = 8.8 Hz, 2H), 6.36 (d, J = 8.0 Hz, 1H), 6.11 (s, 1H), 3.83 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.8, 160.9, 159.1, 151.0, 148.6, 140.0, 137.8, 131.4, 129.6, 128.5, 128.4, 128.0, 127.4, 115.6, 114.0, 98.4, 55.4, 17.7; HRMS (m/z) $[M + H]^+$ calcd for $C_{22}H_{21}N_2O_2$ 345.1598, found 345.1594.

*(Z)-3-(4-Chlorophenyl)-3-((5-methylpyridin-2-yl)amino)-1-phenylprop-2-en-1-one (**3t**).* Eluent: EtOAc/PE 10:90; yield: 733 mg, 70%; yellow solid, mp 107−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.66 (s, 1H), 8.01 (d, J = 1.6 Hz, 1H), 7.97−7.95 (m, 2H), 7.52−7.42 (m, 3H), 7.38−7.31 (m, 4H), 7.25−7.23 (m, 1H), 6.45 (d, J = 8.4 Hz, 1H), 6.11 (s, 1H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2, 158.1, 150.4, 148.6, 139.6, 138.1, 135.6, 135.2, 131.7, 129.4, 128.8, 128.5, 128.3, 127.5, 115.4, 99.0, 17.7; HRMS (m/z) $[M + Na]^+$ calcd for $C_{21}H_{17}ClN_2NaO$ 371.0922, found 371.0912.

General Procedure C for the Preparation of Enamines 5. A mixture of the corresponding ynone (2.5 mmol, obtained according to General Procedure B, dimethyl 2-butynedioate for **5m**) and substituted aniline (2.5 mmol) in MeOH (5 mL) was stirred in an oven-dried sealed tube at 80 °C for 6 h (TLC indicated that the reaction was complete). After cooling to room temperature, the reaction was concentrated and then purified through silica gel column chromatography to afford the enamine (**5**) in 22−95% yield.

*(Z)-1,3-Diphenyl-3-(phenylamino)prop-2-en-1-one (**5a**).*[3e] Eluent: EtOAc/PE 5:95; yield: 718 mg, ≥95%; yellow solid, mp 95−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.90 (s, 1H), 7.98−7.96 (m, 2H), 7.50−7.31 (m, 8H), 7.12 (t, J = 8.0 Hz, 2H), 6.98 (t, J = 7.6 Hz, 1H), 6.79 (d, J = 8.0 Hz, 2H), 6.09 (br, s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.7, 161.5, 139.9, 139.4, 135.8, 131.3, 129.7, 128.7, 128.6, 128.4, 127.3, 124.1, 123.2, 97.0; HRMS (m/z) $[M + Na]^+$ calcd for $C_{21}H_{17}NNaO$ 322.1202, found 322.1202.

*(Z)-1,3-Diphenyl-3-(p-tolylamino)prop-2-en-1-one (**5b**).* Eluent: EtOAc/PE 5:95; yield: 736 mg, 94%; yellow solid, mp 127−129 °C (lit.[3e] mp 127−128 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.90 (s, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.50−7.31 (m, 8H), 6.92 (d, J = 8.0 Hz, 2H), 6.69 (d, J = 8.0 Hz, 2H), 6.06 (br, s, 1H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.5, 161.8, 140.0, 136.8, 135.9, 133.9, 131.2, 129.6, 129.4, 128.5, 128.43, 128.39, 127.3, 123.3, 96.6, 20.8; HRMS (m/z) $[M + Na]^+$ calcd for $C_{22}H_{19}NNaO$ 336.1359, found 336.1347.

*(Z)-3-((4-Methoxyphenyl)amino)-1,3-diphenylprop-2-en-1-one (**5c**).* Eluent: EtOAc/PE 5:95; yield: 815 mg, ≥95%; yellow solid, mp 122−123 °C (lit.[3e] mp 122−123 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.91 (s, 1H), 7.98−7.95 (m, 2H), 7.49−7.30 (m, 8H), 6.77−6.73 (m, 2H), 6.69−6.65 (m, 2H), 6.05 (s, 1H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.3, 162.2, 156.5, 140.0, 135.9, 132.5, 131.2, 129.6, 128.51, 128.49, 128.4, 127.2, 124.9, 114.0, 96.1, 55.4; HRMS (m/z) $[M + Na]^+$ calcd for $C_{22}H_{19}NNaO_2$ 352.1308, found 352.1293.

*(Z)-3-((4-Chlorophenyl)amino)-1,3-diphenylprop-2-en-1-one (**5d**).* Eluent: EtOAc/PE 5:95; yield: 751 mg, 90%; yellow solid, mp 146−147 °C (lit.[3e] mp 142−143 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.85 (s, 1H), 7.96 (d, J = 6.8 Hz, 2H), 7.52−7.34 (m, 8H), 7.09 (d, J = 8.8 Hz, 2H), 6.71 (d, J = 8.4 Hz, 2H), 6.11 (br, s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.0, 161.1, 139.7, 138.2, 135.5, 131.5, 129.9, 129.4, 128.9, 128.8, 128.5, 128.4, 127.3, 124.3, 97.5; HRMS (m/z) $[M + Na]^+$ calcd for $C_{21}H_{16}ClNNaO$ 356.0813, found 356.0796.

*(Z)-3-((4-Bromophenyl)amino)-1,3-diphenylprop-2-en-1-one (**5e**).* Eluent: EtOAc/PE 5:95; yield: 851 mg, 90%; yellow solid, mp 151−152 °C (lit.[3e] mp 155−156 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.84 (s, 1H), 7.97−7.95 (m, 2H), 7.52−7.33 (m, 8H), 7.24−7.22 (m, 2H), 6.66−6.63 (m, 2H), 6.11 (br, s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.9, 160.9, 139.6, 138.6, 135.4, 131.8, 131.5, 129.9, 128.7, 128.4, 128.3, 127.3, 124.5, 117.0, 97.6; HRMS (m/z) $[M + Na]^+$ calcd for $C_{21}H_{16}BrNNaO$ 400.0307, found 400.0295.

*(Z)-3-((4-Nitrophenyl)amino)-1,3-diphenylprop-2-en-1-one (**5f**).* Eluent: EtOAc/PE 5:95; yield: 189 mg, 22%; yellow solid, mp 166−167 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.89 (s, 1H), 8.00−7.97 (m, 4H), 7.56−7.40 (m, 8H), 6.80−6.76 (m, 2H), 6.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.8, 159.1, 145.9, 142.8, 139.1, 135.0, 132.1, 130.5, 129.2, 128.6, 128.1, 127.5, 124.8, 121.3, 100.3; HRMS (m/z) $[M + Na]^+$ calcd for $C_{21}H_{16}N_2NaO_3$ 367.1053, found 367.1044.

*(Z)-3-((3,5-Dimethylphenyl)amino)-1,3-diphenylprop-2-en-1-one (**5g**).*[3e] Eluent: EtOAc/PE 5:95; yield: 778 mg, 95%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.88 (s, 1H), 7.97−7.95 (m, 2H), 7.49−7.31 (m, 8H), 6.62 (s, 1H), 6.40 (s, 2H), 6.05 (br, s, 1H), 2.12(s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.4, 161.6, 140.0, 139.2, 138.3, 136.1, 131.2, 129.6, 128.5, 128.4, 128.3, 127.3, 125.9, 120.9, 96.7, 21.2; HRMS (m/z) $[M + Na]^+$ calcd for $C_{23}H_{21}NNaO$ 350.1515, found 350.1514.

*(Z)-1-(Naphthalen-2-yl)-3-phenyl-3-(p-tolylamino)prop-2-en-1-one (**5h**).* Eluent: EtOAc/PE 5:95; yield: 881 mg, ≥95%; yellow solid, mp 178−179 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.00 (s, 1H), 8.47 (s, 1H), 8.07 (dd, J = 8.8, 1.6 Hz, 1H), 7.95−7.85 (m, 3H), 7.56−7.49 (m, 2H), 7.45−7.33 (m, 5H), 6.94 (d, J = 8.4 Hz, 2H), 6.71 (d, J = 8.4 Hz, 2H), 6.21 (br, s, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.2, 161.8, 137.2, 136.8, 135.9, 134.8, 133.9, 132.8, 129.6, 129.34, 129.28, 128.5, 128.4, 128.1, 127.8, 127.7, 127.4, 126.4, 124.1, 123.2, 96.8, 20.8; HRMS (m/z) $[M + Na]^+$ calcd for $C_{26}H_{21}NNaO$ 386.1515, found 386.1504.

*(Z)-3-Phenyl-1-(thiophen-2-yl)-3-(p-tolylamino)prop-2-en-1-one (**5i**).*[12] Eluent: EtOAc/PE 5:95; yield: 783 mg, ≥95%; yellow solid, mp 106−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.57 (s, 1H), 7.64 (dd, J = 3.6, 0.8 Hz, 1H), 7.51 (dd, J = 5.2, 1.2 Hz, 1H), 7.41−7.31 (m, 5H), 7.09 (dd, J = 4.8, 3.6 Hz, 1H), 6.91 (d, J = 8.0 Hz, 2H), 6.65 (d, J = 8.4 Hz, 2H), 5.92 (br, s, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.3, 161.4, 146.9, 136.8, 135.7, 133.9, 131.0, 129.7, 129.4, 128.6, 128.42, 128.39, 128.0, 123.1, 96.4, 20.8; HRMS (m/z) $[M + Na]^+$ calcd for $C_{20}H_{17}NNaOS$ 342.0923, found 342.0916.

*(Z)-1-Cyclohexyl-3-phenyl-3-(p-tolylamino)prop-2-en-1-one (**5j**).* Eluent: EtOAc/PE 5:95; yield: 751 mg, 94%; yellow solid, mp 99−101 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.38 (s, 1H), 7.37−7.26 (m, 5H), 6.88 (d, J = 8.4 Hz, 2H), 6.60 (d, J = 8.4 Hz, 2H), 5.37 (s, 1H), 2.37−2.29 (m, 1H), 2.21 (s, 3H), 1.92−1.79 (m, 4H), 1.70−1.67 (m, 1H), 1.50−1.40 (m, 2H), 1.35−1.20 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.4, 160.2, 137.1, 135.9, 133.3, 129.4, 129.2, 128.4, 128.3, 122.9, 98.5, 50.7, 29.8, 26.1, 26.0, 20.7; HRMS (m/z) $[M + Na]^+$ calcd for $C_{22}H_{25}NNaO$ 342.1828, found 342.1829.

*(Z)-3-(4-Chlorophenyl)-1-phenyl-3-(p-tolylamino)prop-2-en-1-one (**5k**).*[12] Eluent: EtOAc/PE 5:95; yield: 852 mg, ≥95%; yellow solid, mp 117−119 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.82 (s, 1H), 7.96−7.94 (m, 2H), 7.49−7.44 (m, 3H), 7.34−7.29 (m, 4H), 6.95 (d, J = 8.0 Hz, 2H), 6.69 (d, J = 8.4 Hz, 2H), 6.02 (s, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.6, 160.4, 139.8, 136.6, 135.7, 134.4,

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J. Org. Chem. 2016, 81, 9326−9336

134.2, 131.4, 129.8, 129.5, 128.9, 128.4, 127.3, 123.4, 96.6, 20.9; HRMS (m/z) $[M + Na]^+$ calcd for $C_{22}H_{18}ClNNaO$ 370.0969, found 370.0952.

*(Z)-3-Cyclopropyl-1-phenyl-3-(p-tolylamino)prop-2-en-1-one (**5l**).* Eluent: EtOAc/PE 5:95; yield: 631 mg, 91%; off-white solid, mp 93−95 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 13.31 (s, 1H), 7.87−7.85 (m, 2H), 7.46−7.39 (m, 3H), 7.22−7.16 (m, 4H), 5.51 (s, 1H), 2.36 (s, 3H), 1.78−1.72 (m, 1H), 0.99−0.97 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.6, 168.3, 140.6, 135.9, 135.5, 130.6, 129.7, 128.2, 126.9, 125.1, 86.3, 21.0, 12.8, 10.0; HRMS (m/z) $[M + Na]^+$ calcd for $C_{19}H_{19}NNaO$ 300.1359, found 300.1345.

*Dimethyl 2-(p-Tolylamino)fumarate (**5m**).*[13] Eluent: EtOAc/PE 5:95; yield: 455 mg, 73%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.63 (s, 1H), 7.07 (d, J = 8.0 Hz, 2H), 6.80 (d, J = 8.4 Hz, 2H), 5.33 (s, 1H), 3.72 (s, 3H), 3.68 (s, 3H), 2.30(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 164.9, 148.4, 137.7, 134.1, 129.8, 120.9, 92.6, 52.8, 51.2, 20.8; HRMS (m/z) $[M + Na]^+$ calcd for $C_{13}H_{15}NNaO_4$ 272.0893, found 272.0885.

Synthesis of Vinyl Iodide 2c′. A stirred mixture of substrate **1c** in 1,4-dioxane (10 mL) was treated sequentially with K_2CO_3 (207 mg, 1.5 mmol) and iodine (152 mg, 0.6 mmol) and then heated to reflux under a nitrogen atmosphere until the consumption of **1c**, as monitored by TLC, was complete (1.5 h). After cooling to room temperature, the reaction was quenched with 5% $Na_2S_2O_3$ (5 mL), followed by addition of brine (10 mL), and then extracted with EtOAc (15 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and then purified through silica gel column chromatography (eluent: EtOAc/PE 25:75), affording the product (**2c′**). Yield: 98 mg, 60%; off-white solid, mp 121−123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.68 (s, 1H), 7.52 (d, J = 7.6 Hz, 1H), 6.92 (d, J = 8.0 Hz, 1H), 3.09 (t, J = 6.0 Hz, 2H), 2.64 (t, J = 6.4 Hz, 2H), 2.33 (s, 3H), 2.02−1.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.0, 162.1, 149.6, 148.6, 139.0, 129.5, 115.5, 82.2, 36.5, 29.2, 22.1, 17.8; HRMS (m/z) $[M + Na]^+$ calcd for $C_{12}H_{13}IN_2NaO$ 350.9965, found 350.9958.

General Procedure D for the Synthesis of Imidazo[1,2-*a*]pyridines 2 and 4. A stirred mixture of enamine (**1** or **3**, 0.5 mmol) in toluene (10 mL) was treated with Cs_2CO_3 (489 mg, 1.5 mmol), CuI (19 mg, 0.1 mmol), and iodine (152 mg, 0.6 mmol) in sequence and then heated to reflux under a nitrogen atmosphere until consumption of the substrate was complete (as monitored by TLC). After cooling to room temperature, the reaction was quenched with 5% $Na_2S_2O_3$ (5 mL), followed by addition of brine (10 mL), and then extracted with CH_2Cl_2 (15 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and then purified through silica gel column chromatography to afford the product (**2** or **4**) in 43−95% yield.

*7,8-Dihydrobenzo[4,5]imidazo[1,2-a]pyridin-9(6H)-one (**2a**).* Eluent: EtOAc/PE 75:25; 4 h; yield: 42 mg, 45%; white solid, mp 139−141 °C, (lit.[14] mp 142−144 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.29 (d, J = 6.8 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.51−7.47 (m, 1H), 7.07−7.03 (m, 1H) 3.08 (t, J = 6.0 Hz, 2H), 2.67 (t, J = 6.4 Hz, 2H), 2.29−2.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.3, 160.3, 147.9, 129.5, 128.4, 119.6, 116.8, 114.4, 38.4, 25.5, 23.8; HRMS (m/z) $[M + H]^+$ calcd for $C_{11}H_{11}N_2O$ 187.0866, found 187.0869.

*1-Methyl-7,8-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-9(6H)-one (**2b**).* Eluent: EtOAc/PE 75:25; 3.5 h; yield: 60 mg, 60%; white solid, mp 169−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J = 8.8 Hz, 1H), 7.43−7.39 (m, 1H), 6.79 (d, J = 7.2 Hz, 1H), 3.07 (t, J = 6.0 Hz, 2H), 2.98 (s, 3H), 2.68 (t, J = 6.0 Hz, 2H), 2.25−2.18 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.6, 162.6, 150.5, 141.1, 130.3, 122.1, 115.6, 114.3, 39.8, 26.7, 23.1, 23.0; HRMS (m/z) $[M + H]^+$ calcd for $C_{12}H_{13}N_2O$ 201.1022, found 201.1025.

*2-Methyl-7,8-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-9(6H)-one (**2c**).*[15] Eluent: EtOAc/PE 75:25; 2.5 h; yield: 99 mg, ≥95%; white solid, mp 105−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.11 (s, 1H), 7.57 (d, J = 8.8 Hz, 1H), 7.34 (dd, J = 9.2, 1.6 Hz, 1H), 3.05 (t, J = 6.0 Hz, 2H), 2.65 (t, J = 6.0 Hz, 2H), 2.41 (s, 3H), 2.27−2.21 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.2, 160.2, 146.9, 132.3, 126.5, 124.5, 119.4, 116.1, 38.4, 25.5, 23.8, 18.1; HRMS (m/z) $[M + H]^+$ calcd for $C_{12}H_{13}N_2O$ 201.1022, found 201.1032.

*3-Methyl-7,8-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-9(6H)-one (**2d**).* Eluent: EtOAc/PE 75:25; 3.5 h; yield: 83 mg, 83%; off-white solid, mp 104−106 °C (lit.[16] mp 108−109 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.13 (d, J = 6.8 Hz, 1H), 7.43 (s, 1H), 6.87 (dd, J = 6.8, 1.2 Hz 1H), 3.04 (t, J = 6.4 Hz, 2H), 2.64 (t, J = 6.0 Hz, 2H), 2.48 (s, 3H), 2.27−2.21 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.9, 160.6, 148.4, 141.2, 127.5, 119.4, 116.8, 115.6, 38.3, 25.5, 23.8, 21.7; HRMS (m/z) $[M + H]^+$ calcd for $C_{12}H_{13}N_2O$, 201.1022, found 201.1024.

*4-Methyl-7,8-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-9(6H)-one (**2e**).* Eluent: EtOAc/PE 75:25; 6.5 h; yield: 46 mg, 46%; off-white solid, mp 95−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.16 (d, J = 6.8 Hz, 1H), 7.28 (d, J = 6.0 Hz, 1H, overlapped with the peak of chloroform), 6.95 (t, J = 6.8 Hz, 1H), 3.09 (t, J = 6.4 Hz, 2H), 2.68−2.65 (m, 5H), 2.29−2.22 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.3, 159.7, 148.0, 128.6, 126.7, 126.1, 120.0, 114.4, 38.4, 25.6, 23.9, 17.0. HRMS (m/z) $[M + H]^+$ calcd for $C_{12}H_{13}N_2O$, 201.1022, found 201.1031.

*2-Chloro-7,8-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-9(6H)-one (**2f**).*[16] Eluent: EtOAc/PE 60:40; 3.5 h; yield: 96 mg, 87%; off-white solid, mp 105−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.35−9.34 (m, 1H), 7.63−7.60 (m, 1H), 7.47−7.44 (m, 1H), 3.07 (t, J = 6.4 Hz, 2H), 2.69−2.66 (m, 2H), 2.28−2.25 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.4, 160.6, 146.1, 130.5, 126.3, 122.6, 119.8, 117.1, 38.3, 25.4, 23.7. HRMS (m/z) $[M + H]^+$ calcd for $C_{11}H_{10}ClN_2O$, 221.0476, found 221.0483.

*2-Bromo-7,8-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-9(6H)-one (**2g**).* Eluent: EtOAc/PE 60:40; 6 h; yield: 102 mg, 77%; off-white solid, mp 126−128 °C (lit.[16] mp 121−123 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.44 (s, 1H), 7.59−7.53 (m, 2H), 3.08−3.05 (m, 2H), 2.69−2.66 (m, 2H), 2.29−2.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.5, 160.4, 146.3, 132.7, 128.4, 119.7, 117.4, 109.1, 38.3, 25.4, 23.7; HRMS (m/z) $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2O$ 264.9971, found 264.9979.

*2,4-Dibromo-7,8-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-9(6H)-one (**2h**).* Eluent: EtOAc/PE 30:70; 7 h; yield: 141 mg, 82%; white solid, mp 186−188 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.43 (d, J = 1.6 Hz, 1H), 7.83 (d, J = 1.6 Hz, 1H), 3.12 (t, J = 6.0 Hz, 2H), 2.68 (t, J = 6.0 Hz, 2H), 2.30−2.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.9, 160.4, 144.5, 134.4, 127.5, 120.9, 111.3, 108.2, 38.3, 25.5, 23.6; HRMS (m/z) $[M + H]^+$ calcd for $C_{11}H_9Br_2N_2O$ 344.9056, found 344.9056.

*8,9-Dihydrobenzo[4,5]imidazo[1,2-a]pyrazin-6(7H)-one (**2i**).* Eluent: EtOAc/PE 60:40; 5.5 h; yield: 47 mg, 50%; white solid, mp 168−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.20 (d, J = 1.6 Hz, 1H), 9.10 (dd, J = 4.4, 1.2 Hz, 1H), 8.18 (d, J = 4.4 Hz, 1H), 3.14 (t, J = 6.4 Hz, 2H), 2.72 (t, J = 6.0 Hz, 2H), 2.34−2.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.4, 160.3, 143.0, 141.7, 132.3, 120.5, 119.9, 38.6, 25.4, 23.6; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{10}N_3O$ 188.0818, found 188.0817.

*7-Methyl-2,3-dihydro-1H-cyclopenta[4,5]imidazo[1,2-a]pyridin-1-one (**2j**).* Eluent: EtOAc/PE 75:25; 3.5 h; yield: 40 mg, 43%; white solid, mp 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44−8.43 (m, 1H), 7.60 (d, J = 9.2 Hz, 1H), 7.37−7.34 (m, 1H), 3.12−3.09 (m, 2H), 3.06−3.03 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.3, 175.3, 153.4, 132.5, 125.7, 125.2, 124.3, 117.0, 41.4, 22.2, 17.9; HRMS (m/z) $[M + H]^+$ calcd for $C_{11}H_{11}N_2O$ 187.0866, found 187.0868.

*Phenyl(2-phenylimidazo[1,2-a]pyridin-3-yl)methanone (**4a**).* Eluent: EtOAc/PE 20:80; 3.5 h; yield: 148 mg, ≥95%; white solid, mp 130−132 °C (lit.[3f] mp 130−132 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.55 (dt, J = 7.2, 1.2 Hz, 1H), 7.81 (dt, J = 8.8, 1.2 Hz, 1H), 7.55−7.50 (m, 3H), 7.34−7.31 (m, 2H), 7.27−7.23 (m, 1H, overlapped with the peak of chloroform), 7.15−7.06 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.4, 155.0, 147.4, 138.7, 134.0, 131.8, 130.2, 129.6, 129.2, 128.3, 127.8, 120.0, 117.5, 114.6; HRMS (m/z) $[M + H]^+$ calcd for $C_{20}H_{15}N_2O$ 299.1179, found 299.1178.

*(5-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl) (Phenyl)-methanone (**4b**).*[3f] Eluent: EtOAc/PE 20:80; 3.5 h; yield: 155 mg,

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≥95%; yellow solid, mp 88−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82−7.80 (m, 2H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.49−7.46 (m, 2H), 7.43−7.37 (m, 2H), 7.28−7.24 (m, 2H, overlapped with the peak of chloroform), 7.18−7.14 (m, 3H), 6.78 (d, *J* = 6.8 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.0, 150.1, 147.8, 138.3, 137.9, 133.6, 133.3, 130.4, 129.4, 128.4, 128.1, 128.0, 127.6, 120.5, 115.3, 115.0, 22.3; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{21}H_{17}N_2O$ 313.1335, found 313.1337.

*(6-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl) (Phenyl)-methanone (**4c**).*[17] Eluent: EtOAc/PE 20:80; 3.5 h; yield: 151 mg, ≥95%; white solid, mp 163−164 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.37 (m, 1H), 7.70 (d, *J* = 9.2 Hz, 1H), 7.52−7.49 (m, 2H), 7.38 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.32−7.30 (m, 2H), 7.27−7.22 (m, 1H), 7.14−7.05 (m, 5H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.3, 154.8, 146.4, 138.8, 134.1, 132.1, 131.7, 130.1, 129.6, 128.1, 127.7, 126.1, 124.6, 119.8, 116.7, 18.5; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{21}H_{17}N_2O$ 313.1335, found 313.1335.

*(7-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl) (Phenyl)-methanone (**4d**).* Eluent: EtOAc/PE 20:80; 3.5 h; yield: 153 mg, ≥95%; white solid, mp 142−144 °C (lit.[18] mp 140−142 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.45 (d, *J* = 7.2 Hz, 1H), 7.56 (m, 1H), 7.50−7.48 (m, 2H), 7.32−7.29 (m, 2H), 7.26−7.22 (m, 1H), 7.14−7.04 (m, 5H), 6.93 (dd, *J* = 6.8, 1.6 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.1, 155.3, 147.9, 140.9, 138.8, 134.1, 131.6, 130.2, 129.5, 128.2, 127.7, 127.5, 119.8, 117.1, 116.1, 21.6; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{21}H_{17}N_2O$ 313.1335, found 313.1339.

*(8-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl) (Phenyl)-methanone (**4e**).* Eluent: EtOAc/PE 10:90; 3.5 h; yield: 155 mg, ≥95%; off-white solid, mp 139−141 °C (lit.[18] mp 139−141 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.41 (d, *J* = 6.8 Hz, 1H), 7.51−7.48 (m, 2H), 7.35−7.31 (m, 3H), 7.26−7.22 (m, 1H), 7.14−7.05 (m, 5H), 7.00 (t, *J* = 7.2 Hz, 1H), 2.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.4, 154.5, 147.6, 138.8, 134.3, 131.6, 130.3, 129.5, 128.1, 127.72, 127.67, 127.5, 126.0, 120.5, 114.6, 17.1; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{21}H_{17}N_2O$ 313.1335, found 313.1344.

*(6-Chloro-2-phenylimidazo[1,2-a]pyridin-3-yl) (Phenyl)-methanone (**4f**).*[19] Eluent: EtOAc/PE 20:80; 3.5 h; yield: 165 mg, ≥95%; white solid, mp 122−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (dd, *J* = 2.0, 0.8 Hz, 1H), 7.76−7.73 (m, 1H), 7.52−7.48 (m, 3H), 7.33−7.26 (m, 3H, overlapped with the peak of chloroform), 7.17−7.07 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.3, 155.0, 145.6, 138.2, 133.5, 132.1, 130.4, 130.1, 129.6, 128.5, 127.84, 127.83, 126.2, 122,9, 120.2, 117.7; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{20}H_{14}ClN_2O$ 333.0789, found 333.0787.

*(6-Bromo-2-phenylimidazo[1,2-a]pyridin-3-yl) (Phenyl)-methanone (**4g**).* Eluent: EtOAc/PE 20:80; 3.5 h; yield: 187 mg, ≥95%; white solid, mp 135−137 °C (lit.[3f] mp 135−137 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.71 (d, *J* = 1.6 Hz, 1H), 7.70−7.68 (m, 1H), 7.60−7.57 (m, 1H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.32−7.30 (m, 2H), 7.28−7.26 (m, 1H, overlapped with the peak of chloroform), 7.16−7.07 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.3, 154.9, 145.7, 138.2, 133.5, 132.5, 132.1, 130.1, 129.6, 128.5, 128.4, 127.83, 127.82, 120.1, 118.0, 109.4; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{20}H_{14}BrN_2O$ 377.0284, found 377.0277.

*(6,8-Dibromo-2-phenylimidazo[1,2-a]pyridin-3-yl) (Phenyl)-methanone (**4h**).*[20] Eluent: EtOAc/PE 10:90; 3.5 h; yield: 205 mg, 90%; white solid, mp 258−259 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.63 (d, *J* = 1.6 Hz, 1H), 7.87 (d, *J* = 1.6 Hz, 1H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.35−7.33 (m, 2H), 7.31−7.27 (m, 1H), 7.17−7.07 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.5, 154.8, 143.9, 137.8, 134.1, 133.1, 132.4, 130.4, 129.6, 128.7, 127.92, 127.89, 127.4, 121,3, 111.9, 108.3; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{20}H_{12}Br_2N_2NaO$ 478.9189, found 478.9174.

*Phenyl(2-phenylimidazo[1,2-a]pyrazin-3-yl)methanone (**4i**).*[3f] Eluent: EtOAc/PE 25:75; 3.5 h; yield: 148 mg, ≥95%; white solid, mp 146−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.31 (s, 1H), 9.24 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.19 (d, *J* = 4.8 Hz, 1H), 7.56−7.53 (m, 2H), 7.38−7.31 (m, 3H), 7.21−7.11 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.6, 154.4, 143.8, 141.4, 137.5, 133.0, 132.6, 132.1, 130.2, 129.6, 128.9, 128.0, 120.3, 120.2; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{19}H_{13}N_3NaO$ 322.0951, found 322.0946.

*Phenyl(2-phenylimidazo[1,2-a]pyrimidin-3-yl)methanone (**4j**).* Eluent: EtOAc/PE 50:50; 3.5 h; yield: 148 mg, ≥95%; off-white solid, mp 169−171 °C (lit.[14] mp 168−170 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.77 (dd, *J* = 6.8, 2.0 Hz, 1H), 8.81(q, *J* = 2.0 Hz, 1H), 7.53−7.51 (m, 2H), 7.41−7.38 (m, 2H), 7.32−7.28 (m, 1H), 7.19−7.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.5, 155.9, 153.6, 150.0, 137.9, 136.0, 133.1, 132.2, 130.5, 129.5, 128.8, 127.9, 127.8, 118.1, 110.8; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{19}H_{14}N_3O$ 300.1131, found 300.1132.

*(6-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)(p-tolyl)-methanone (**4k**).* Eluent: EtOAc/PE 25:75; 3.5 h; yield: 162 mg, ≥95%; off-white solid, mp 180−182 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.29 (s, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.37−7.32 (m, 3H), 7.15−7.06 (m, 3H), 6.88 (d, *J* = 8.0 Hz, 2H), 2.43 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.1, 154.2, 146.3, 142.4, 136.0, 134.2, 131.9, 130.1, 129.8, 128.4, 128.0, 127.7, 126.0, 124.4, 119.9, 116.6, 21.5, 18.5; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{22}H_{19}N_2O$ 327.1492, found 327.1496.

*(4-Methoxyphenyl)(6-methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)methanone (**4l**).* Eluent: EtOAc/PE 25:75; 3.5 h; yield: 169 mg, ≥95%; off-white solid, mp 185−187 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.21 (t, *J* = 0.8 Hz, 1H), 7.69 (d, *J* = 9.2 Hz, 1H), 7.56−7.52 (m, 2H), 7.38−7.32 (m, 3H), 7.17−7.10 (m, 3H), 6.61−6.58 (m, 2H), 3.73 (s, 3H), 2.42 (d, *J* = 0.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.1, 162.7, 153.5, 146.2, 134.2, 132.0, 131.7, 131.2, 130.2, 128.1, 127.8, 125.9, 124.2, 119.8, 116.6, 113.1, 55.3, 18.5; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{22}H_{19}N_2O_2$ 343.1441, found 343.1438.

*(4-Chlorophenyl)(6-methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)-methanone (**4m**).*[21] Eluent: EtOAc/PE 25:75; 3.5 h; yield: 172 mg, ≥95%; white solid, mp 147−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.35 (d, *J* = 0.8 Hz, 1H), 7.71 (d, *J* = 9.2 Hz, 1H), 7.44−7.38 (m, 3H), 7.31−7.28 (m, 2H), 7.21−7.17 (m, 1H), 7.14−7.10 (m, 2H), 7.06−7.03 (m, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.8, 155.0, 146.5, 137.9, 137.2, 133.9, 132.4, 130.9, 130.2, 128.4, 128.0, 127.9, 126.2, 124.8, 119.7, 116.7, 18.5; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{21}H_{16}ClN_2O$ 347.0946, found 347.0945.

*(6-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)(4-(trifluoromethyl)phenyl)methanone (**4n**).* Eluent: EtOAc/PE 25:75; 3.5 h; yield: 188 mg, ≥95%; white solid, mp 136−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.43 (s, 1H), 7.75−7.71 (m, 2H), 7.66 (br, s, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.45−7.42 (m, 1H), 7.29−7.25 (m, 3H, overlapped with the peak of chloroform), 7.15−7.05 (m, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.4, 155.7, 146.7, 139.5, 133.7, 132.7, 132.4, 130.18 (q, J_{C-F} = 32.7 Hz), 130.17, 128.51, 128.45, 127.92, 127.88, 126.5 (q, J_{C-F} = 3.9 Hz), 126.3, 125.1, 123.4 (q, J_{C-F} = 271.0 Hz), 119.6, 116.8, 18.5; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{22}H_{16}F_3N_2O$ 381.1209, found 381.1209.

*(2-Methoxyphenyl)(6-methyl-2-phenylimidazo[1,2-a]pyridin-3-yl)methanone (**4o**).* Eluent: EtOAc/PE 25:75; 3.5 h; yield: 169 mg, ≥95%; yellow solid, mp 119−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.80 (br, s, 1H), 7.73 (br, s, 1H), 7.42 (s, 1H), 7.27−7.23 (m, 3H, overlapped with the peak of chloroform), 7.13−7.03 (m, 4H), 6.76 (t, *J* = 7.6 Hz, 1H), 6.39 (d, *J* = 8.4 Hz, 1H), 3.49 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.1, 156.6, 132.2, 131.8, 129.9, 129.7, 129.5, 127.9, 127.0, 125.0, 120.1, 116.9, 110.2, 106.8, 100.0, 55.1, 18.6; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{22}H_{19}N_2O_2$ 343.1441, found 343.1442.

*(6-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl) (naphthalen-2-yl)-methanone (**4p**).* Eluent: EtOAc/PE 25:75; 3.5 h; yield: 179 mg, ≥95%; yellow solid, mp 186−188 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.39 (d, *J* = 0.8 Hz, 1H), 7.98 (s, 1H), 7.75−7.67 (m, 3H), 7.63−7.61 (m, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.48−7.44 (m, 1H), 7.40−7.32 (m, 4H), 6.94−6.85 (m, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.1, 154.7, 146.4, 135.7, 134.7, 134.1, 132.1, 132.0, 131.7, 130.0, 129.0, 128.0, 127.8, 127.70, 127.66, 127.5, 126.18, 126.15, 125.3, 124.6, 120.1, 116.7, 18.5; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{25}H_{19}N_2O$ 363.1492, found 363.1481.

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J. Org. Chem. 2016, 81, 9326−9336

*(6-Methyl-2-phenylimidazo[1,2-a]pyridin-3-yl) (thiophen-2-yl)-methanone (**4q**).* Eluent: EtOAc/PE 25:75; 3.5 h; yield: 158 mg, ≥95%; off-white solid, mp 177−179 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.06 (s, 1H), 7.68 (d, *J* = 9.2 Hz, 1H), 7.54−7.51 (m, 2H), 7.45 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.33 (dd, *J* = 9.2, 1.2 Hz, 1H), 7.23−7.21 (m, 3H), 7.09 (dd, *J* = 3.6, 0.8 Hz, 1H), 6.68−6.66 (m, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.8, 153.0, 146.2, 143.7, 134.4, 134.3, 133.0, 131.8, 130.0, 128.4, 128.1, 127.3, 125.6, 124.3, 119.6, 116.7, 18.4; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{19}H_{15}N_2OS$ 319.0900, found 319.0900.

*(6-Methyl-2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl) (Phenyl)-methanone (**4r**).* Eluent: EtOAc/PE 20:80; 3.5 h; yield: 150 mg, 92%; off-white solid, mp 156−158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.35 (t, *J* = 0.8 Hz, 1H), 7.69 (d, *J* = 9.2 Hz, 1H), 7.52−7.50 (m, 2H), 7.36 (dd, *J* = 9.2, 1.6 Hz, 1H), 7.28−7.24 (m, 1H, overlapped with the peak of chloroform), 7.20 (d, *J* = 8.0 Hz, 2H), 7.11−7.07 (m, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 2.44 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.4, 154.9, 146.4, 138.8, 138.0, 132.0, 131.5, 131.1, 130.1, 129.6, 128.4, 127.7, 126.1, 124.4, 119.7, 116.6, 21.2, 18.5; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{22}H_{19}N_2O$ 327.1492, found 327.1495.

*(2-(4-Methoxyphenyl)-6-methylimidazo[1,2-a]pyridin-3-yl) (Phenyl)methanone (**4s**).* Eluent: EtOAc/PE 30:70; 3.5 h; yield: 159 mg, 93%; yellow solid, mp 111−113 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.36 (s, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.53−7.51 (m, 2H), 7.37 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.30−7.23 (m, 3H, overlapped with the peak of chloroform), 7.12 (t, *J* = 8.0 Hz, 2H), 6.63−6.60 (m, 2H), 3.72 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.3, 159.6, 154.5, 146.3, 138.8, 132.1, 131.7, 131.5, 129.6, 127.8, 126.5, 126.2, 124.4, 119.5, 116.5, 113.3, 55.2, 18.5; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{22}H_{19}N_2O_2$ 343.1441, found 343.1441.

*(2-(4-Chlorophenyl)-6-methylimidazo[1,2-a]pyridin-3-yl) (Phenyl)methanone (**4t**).* Eluent: EtOAc/PE 20:80; 4 h; yield: 161 mg, 93%; white solid, mp 149−151 °C (lit.[17] mp 148−150 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.35 (d, *J* = 0.8 Hz, 1H), 7.70 (d, *J* = 9.2 Hz, 1H), 7.51−7.48 (m, 2H), 7.39 (dd, *J* = 9.2, 1.6 Hz, 1H), 7.34−7.30 (m, 1H), 7.26−7.23 (m, 2H), 7.15−7.11 (m, 2H), 7.07−7.03 (m, 2H), 2.45 (d, *J* = 0.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.1, 153.3, 146.4, 138.6, 134.3, 132.7, 132.3, 131.9, 131.3, 129.5, 127.9, 126.1, 124.8, 119.9, 116.7, 18.5; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{21}H_{16}ClN_2O$ 347.0946, found 347.0943.

Sequential Synthesis of Imidazo[1,2-*a*]pyridine 4u. The reaction was performed on a 1 mmol scale. To a solution of 5-methylpyridin-2-amine (108 mg, 1 mmol) in toluene (5 mL) at room temperature were added acetylacetone (125 mg, 1.25 mmol) and *p*-toluenesulfonic acid monohydrate (38 mg, 0.2 mmol) in sequence. The reaction was heated to reflux for 4.5 h under a nitrogen atmosphere until consumption of the 2-aminopyrimidine, as monitored by TLC, was complete. After cooling to room temperature, the reaction mixture was treated with cold 5% $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (10 mL × 5). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated to give the crude enamine intermediate, which was then directly subjected to the above reaction conditions for 3 h to afford the product (**4u**). Eluent: EtOAc/PE 75:25; yield: 73 mg, 39% (from 5-methylpyridin-2-amine); pale yellow solid, mp 102−104 °C (lit.[22] mp 101−103 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.56 (s, 1H), 7.53 (d, *J* = 8.8 Hz, 1H), 7.32−7.29 (m, 1H), 2.77 (s, 3H), 2.61 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.5, 152.6, 145.8, 131.9, 127.1, 124.4, 121.7, 115.6, 30.2, 18.4; HRMS (*m*/*z*) [M + H]$^+$ calcd for $C_{11}H_{13}N_2O$, 189.1022, found 189.1027.

General Procedure E for the Synthesis of Indoles 6. A stirred solution of the enamine (**5**, 0.5 mmol) in 1,4-dioxane (10 mL) was treated with Cs_2CO_3 (489 mg, 1.5 mmol), CuI (19 mg, 0.1 mmol) and iodine (152 mg, 0.6 mmol) in sequence and then heated to reflux under a nitrogen atmosphere until the complete consumption, as monitored by TLC, of the substrate. After cooling slightly, the reaction was diluted with CH_2Cl_2 (10 mL). The reaction mixture was treated at room temperature with 5% $Na_2S_2O_3$ (5 mL), followed by addition of brine (10 mL). Then, the organic layer was separated, and the aqueous layer was further extracted with CH_2Cl_2 (15 mL × 2). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and then purified through silica gel column chromatography to afford the product (**6**) in 69−95% yield.

*Phenyl(2-phenyl-1H-indol-3-yl)methanone (**6a**).* Eluent: EtOAc/PE 20:80; 5 h; yield: 138 mg, 93%; white solid, mp 223−224 °C (lit.[3e] mp 223−224 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.23 (s, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.54−7.52 (m, 3H), 7.40−7.35 (m, 3H), 7.27−7.15 (m, 7H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.6, 144.6, 140.3, 136.3, 132.0, 131.8, 130.0, 129.5, 128.9, 128.7, 128.5, 128.2, 123.4, 121.9, 121.1, 112.6, 112.3; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{21}H_{15}NNaO$ 320.1046, found 320.1032.

*(5-Methyl-2-phenyl-1H-indol-3-yl) (Phenyl)methanone (**6b**).*[3e] Eluent: EtOAc/PE 10:90; 5 h; yield: 153 mg, ≥95%; white solid, mp 208−209 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.09 (s, 1H), 7.60 (s, 1H), 7.50 (d, *J* = 7.6 Hz, 2H), 7.41−7.32 (m, 4H), 7.23−7.17 (m, 5H), 7.08 (d, *J* = 8.0 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.6, 144.6, 140.4, 134.7, 132.2, 131.7, 130.6, 130.0, 129.5, 129.0, 128.8, 128.5, 128.2, 124.9, 120.7, 112.3, 112.0, 21.9; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{22}H_{17}NNaO$ 334.1202, found 334.1194.

*(5-Methoxy-2-phenyl-1H-indol-3-yl) (Phenyl)methanone (**6c**).* Eluent: EtOAc/PE 20:80; 6 h; yield: 156 mg, 95%; white solid, mp 186−187 °C (lit.[3e] mp 186−187 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.10 (s, 1H), 7.49 (d, *J* = 7.2 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 1H), 7.35−7.32 (m, 4H), 7.23−7.16 (m, 5H), 6.89 (dd, *J* = 8.8, 2.4 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.5, 155.6, 145.1, 140.4, 132.2, 131.6, 131.3, 130.0, 129.5, 128.8, 128.4, 128.2, 113.3, 113.1, 112.4, 102.8, 55.7; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{22}H_{17}NNaO_2$ 350.1152, found 350.1144.

*(5-Chloro-2-phenyl-1H-indol-3-yl) (Phenyl)methanone (**6d**).*[3e] Eluent: EtOAc/PE 20:80; 6 h; yield: 151 mg, 91%; white solid, mp 274−276 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.43 (s, 1H), 7.80 (s, 1H), 7.55−7.49 (m, 3H), 7.38−7.34 (m, 3H), 7.29−7.17 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.3, 146.2, 139.9, 134.8, 131.9, 131.6, 130.1, 129.8, 129.5, 129.2, 128.5, 128.2, 126.6, 123.4, 120.2, 114.0, 112.2; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{21}H_{14}ClNNaO$ 354.0656, found 354.0644.

*(5-Bromo-2-phenyl-1H-indol-3-yl) (Phenyl)methanone (**6e**).* Eluent: EtOAc/PE 20:80; 4 h; yield: 175 mg, 93%; white solid, mp 262−264 °C (lit.[3e] mp 263−264 °C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.43 (s, 1H), 7.94 (d, *J* = 1.6 Hz, 1H), 7.50−7.48 (m, 3H), 7.40−7.33 (m, 4H), 7.29−7.17 (m, 5H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.3, 146.0, 139.9, 135.1, 131.9, 131.5, 130.4, 130.1, 129.5, 129.3, 128.5, 128.2, 126.0, 123.2, 114.6, 114.4, 112.0; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{21}H_{14}BrNNaO$ 398.0151, found 398.0146.

*(5-Nitro-2-phenyl-1H-indol-3-yl) (Phenyl)methanone (**6f**).* Eluent: EtOAc/PE 20:80; 6 h; yield: 139 mg, 81%; white solid, mp 260−261 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.89 (s, 1H), 8.73 (d, *J* = 2.4 Hz, 1H), 8.17 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.70 (d, *J* = 8.8 Hz, 1H), 7.55−7.53 (m, 2H), 7.42−7.37 (m, 3H), 7.33−7.19 (m, 5H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.2, 147.9, 142.9, 139.6, 139.4, 132.3, 131.0, 130.2, 129.7, 129.6, 128.6, 128.3, 128.0, 118.8, 117.6, 113.8, 113.0; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{21}H_{14}N_2NaO_3$ 365.0897, found 365.0892.

*(4,6-Dimethyl-2-phenyl-1H-indol-3-yl) (Phenyl)methanone (**6g**).*[3e] Eluent: EtOAc/PE 10:90; 6 h; yield: 159 mg, ≥95%; yellow solid, mp 197−198 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (s, 1H), 7.81−7.79 (m, 2H), 7.40−7.34 (m, 3H), 7.27−7.18 (m, 5H, overlapped with the peak of chloroform), 7.05 (s, 1H), 6.79 (s, 1H), 2.42 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.8, 139.5, 138.5, 136.3, 133.4, 132.7, 131.8, 130.9, 130.1, 128.6, 128.3, 128.24, 128.16, 125.1, 124.9, 114.6, 108.7, 21.6, 20.9; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{23}H_{19}NNaO$ 348.1359, found 348.1345.

*(5-Methyl-2-phenyl-1H-indol-3-yl) (Naphthalen-2-yl)methanone (**6h**).* Eluent: EtOAc/PE 20:80; 6 h; yield: 159 mg, 88%; white solid, mp 96−98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.82 (br, s, 1H), 8.09 (s, 1H), 7.80−7.78 (m, 2H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 8.8 Hz, 2H), 7.49−7.45 (m, 1H), 7.40−7.30 (m, 4H), 7.11 (d, *J* = 8.4 Hz, 1H), 7.04−6.96 (m, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$):

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J. Org. Chem. 2016, 81, 9326−9336

δ 193.2, 143.8, 136.8, 134.8, 133.9, 132.2, 131.83, 131.77, 131.5, 129.09, 129.05, 129.0, 128.5, 128.2, 127.6, 127.5, 126.1, 125.7, 125.2, 121.3, 113.5, 110.8, 21.6; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{26}H_{19}NNaO$ 384.1359, found 384.1336.

(5-Methyl-2-phenyl-1H-indol-3-yl) (Thiophen-2-yl)methanone ***(6i)***. Eluent: EtOAc/PE 20:80; 6 h; yield: 110 mg, 69%; yellow solid, mp 211−213 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.08 (s, 1H), 7.79 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.54 (s, 1H), 7.49−7.47 (m, 2H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.37−7.31 (m, 3H), 7.19−7.18 (m, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.87−6.85 (m, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 184.4, 145.6, 142.7, 134.6, 134.3, 133.9, 132.3, 130.4, 129.6, 129.0, 128.9, 128.7, 128.2, 125.0, 120.2, 112.5, 112.1, 21.8; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{20}H_{15}NNaOS$ 340.0767, found 340.0763.

Cyclohexyl(5-methyl-2-phenyl-1H-indol-3-yl)methanone ***(6j)***. Eluent: EtOAc/PE 10:90; 8 h; yield: 114 mg, 72%; white solid, mp 174−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 (br, s, 1H), 8.13 (s, 1H), 7.53−7.43 (m, 5H), 7.28−7.25 (m, 1H, overlapped with the peak of chloroform), 7.08 (dd, *J* = 8.0, 1.2 Hz, 1H), 2.60−2.53 (m, 1H), 2.47 (s, 3H), 1.68−1.58 (m, 4H), 1.51−1.33 (m, 3H), 1.15−1.03 (m, 1H), 0.90−0.74 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.6, 143.5, 133.5, 133.1, 132.0, 129.41, 129.38, 128.5, 127.9, 125.0, 122.0, 114.1, 110.5, 48.3, 29.4, 25.8, 21.7; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{22}H_{23}NNaO$ 340.1672, found 340.1655.

(2-(4-Chlorophenyl)-5-methyl-1H-indol-3-yl) (Phenyl)methanone ***(6k)***. Eluent: EtOAc/PE 20:80; 4 h; yield: 157 mg, 91%; white solid, mp 270−271 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.17 (s, 1H), 7.56 (s, 1H), 7.52−7.50 (m, 2H), 7.42−7.35 (m, 4H), 7.30−7.28 (m, 2H), 7.23 (t, *J* = 8.0 Hz, 2H), 7.09 (dd, *J* = 8.4, 1.6 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 197.2, 147.9, 145.0, 139.4, 138.4, 136.6, 136.4, 135.8, 135.5, 134.3, 133.6, 133.2, 133.1, 129.9, 125.5, 117.3, 116.8, 26.6; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{22}H_{16}ClNNaO$ 368.0813, found 368.0806.

(2-Cyclopropyl-5-methyl-1H-indol-3-yl) (Phenyl)methanone ***(6l)***. Eluent: EtOAc/PE 20:80; 4 h; yield: 135 mg, ≥95%; white solid, mp 197−198 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.27 (s, 1H), 7.66 (d, *J* = 7.2 Hz, 2H), 7.60−7.49 (m, 3H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.15 (s, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 2.26 (s, 3H), 2.21−2.16 (m, 1H), 1.01−0.94 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.2, 150.3, 142.2, 133.7, 131.5, 130.0, 128.8, 128.7, 128.3, 123.7, 120.2, 113.4, 111.4, 21.8, 10.3; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{19}H_{17}NNaO$ 298.1202, found 298.1189.

Dimethyl 5-Methyl-1H-indole-2,3-dicarboxylate ***(6m)***.[3d] Eluent: EtOAc/PE 20:80; 4 h; yield: 121 mg, ≥95%; white solid, mp 128−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.49 (br, s, 1H), 7.83 (s, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 1H), 3.99 (s, 3H), 3.96 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.8, 161.5, 133.3, 132.2, 127.94, 127.89, 127.1, 121.9, 111.6, 111.3, 52.7, 51.8, 21.6; HRMS (*m*/*z*) [M + Na]$^+$ calcd for $C_{13}H_{13}NNaO_4$ 270.0737, found 270.0739.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01960.

Copies of ^{1}H and ^{13}C NMR spectra of compounds **1**−**6** (PDF)

X-ray structures and data of compound **6l** (CIF)

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Notes

The authors declare no competing financial interest.

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