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FULL PAPER

Three Step Synthesis of Fully and Differently Arylated Pyridines

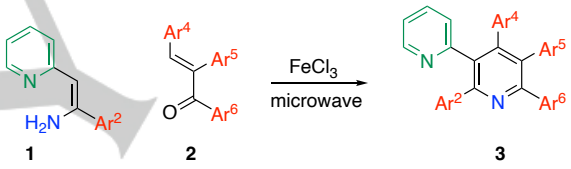
Mao Arita,[a] Soichi Yokoyama,[a,b] Haruyasu Asahara,*[a,b,c] and Nagatoshi Nishiwaki*[a,b]

Abstract: Condensation of β-(2-pyridyl)enamine and α,β-unsaturated ketone in the presence of $FeCl_3$ under air afforded highly substituted pyridines. In this transformation, $FeCl_3$ acted as not only an acid catalyst but also an oxidant for the intermediate dihydropyridine. The substituents could be easily modified by altering the substrates to obtain tri- and tetraarylpyridines including bipyridines and terpyridine. Synthesis of differently substituted pentaarylpyridines was consequently achieved *via* only three steps from commercially available reagents with simple experimental manipulations.

Introduction

Polyarylpyridines are widely used in various applications, such as synthetic intermediates for medicines,[1] ligands for organometals,[2] and fluorophorescent chemosensors.[3] In recent years, they have also been found to play an important role in materials science because of their specific electronic properties.[4] While the utility of polyarylpyridines has increased, introduction of the desired aryl/alkyl group at the desired position remains difficult, and considerable efforts have been undertaken in this regard.[5–10] Although Suzuki-Miyaura coupling is usually employed for arylation of the pyridine framework,[6] different leaving groups should be introduced in advance for site-selective arylation *via* multistep reactions, which increases the difficulty of synthesis and decreases the total yields. Indeed, there are only three papers reporting fully and differently arylated pyridines.[7–10] In 2014, Schmitt *et al*. synthesized pyridines possessing five different aryl groups for the first time *via* 13 steps, which included regiocontrolled modification of the pyridine ring and subsequent Suzuki-Miyaura coupling reactions.[7] Later, Yamaguchi *et al*. succeeded in reducing the number of reaction steps by adopting Diels-Alder-type ring transformation as the key step.[8,9] Despite the successful synthesis of fully and differently arylated pyridines, the substituents could not be readily altered to other aryl or alkyl groups readily because of the tedious experimental manipulations, poor availability of the corresponding substrates, and need for separation of spontaneously formed regioisomers. Hence, there is great demand for a simple method to synthesize diverse arylated pyridines.

In our previous work,[11] we demonstrated an efficient synthetic method for polysubstituted nicotinates *via* the condensation of an enamino ester with an α,β-unsaturated carbonyl compound in the presence of $FeCl_3$. This protocol facilitates the introduction of different alkyl/aryl groups at the desired positions of the pyridine framework by simply altering the starting materials. This advantage prompted us to employ β-pyridylenamine **1** as a push-pull alkene instead of the enamino ester, which afforded fully arylated pyridines *via* only three steps including the synthesis of substrates **1** and **2** (Scheme 1).



1 2 3

Scheme 1. Synthesis of fully and differently arylated pyridines **3**.

Results and Discussion

β-(2-Pyridyl)enamines **1A–D** were efficiently prepared as a single isomer by the condensation of benzonitriles with 2-methylpyridine[12] (Table 1, Entries 1–4). On the other hand, condensation using 4-methylpyridine afforded only the hydrolysis product of **1E** (Entry 5). In the case of *p*-nitrotoluene, a complex mixture was obtained without any detectable formation of **1F** (Entry 6). Hence, the 2-pyridyl group is considered to stabilize enamine **1** by intramolecular hydrogen bonding. Indeed, the ^1H NMR spectrum showed a signal due to one of the NH hydrogens at δ ~6 ppm, but a signal due to the other hydrogen was not observed because of exchange with water present in the solvent. Enones **2a–l** were easily prepared by simply mixing the corresponding aldehydes and ketones under alkaline conditions, respectively. For the preparation of α,β-disubstituted enones **2m–t**, it was more effective to heat a solution of an aldehyde and a ketone in toluene using Dean-Stark apparatus in the presence of piperidinium acetate.

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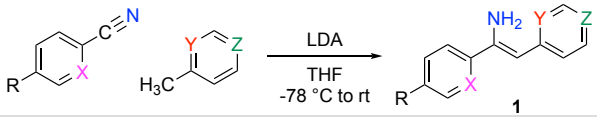
Table 1. Preparation of enamines **1**.



Entry	R	X	Y	Z	Enamine **1**	Yield/%
1	H	CH	N	CH	**1A**	98
2	Me	CH	N	CH	**1B**	91
3	Cl	CH	N	CH	**1C**	94
4	CF_3	CH	N	CH	**1D**	86
5	Me	CH	CH	N	**1E**	0[a]
6	Me	CH	CH	C-NO_2	**1F**	0
7	H	N	N	CH	**1G**	78

[a] 1-(4-Methylphenyl)-2-(4-pyridyl)ethanone was obtained in 75% yield.

When benzylideneacetone **2a** was reacted with β-(2-pyridyl)enamine **1A** in the presence of $FeCl_3$ in a sealed tube at 180 °C under microwave irradiation, 6-methyl-2,4-diphenyl-3-(2-pyridyl)pyridine (**3Aa**) was isolated in 84% yield (Table 2, Entry 1). This reaction was not suppressed by the presence of the bulky naphthyl group at the reaction site (Entry 2). While an electron-donating methyl group on the α-phenyl group (R^2) of **1** facilitated the condensation, electron-withdrawing groups slightly decreased the yields of pyridines **3**, presumably due to the decreased nucleophilicity of enamines **1C** and **1D** (Entries 3–5).

Chalcone derivatives **2c–l** were more easily treatable than methyl ketones **2a** and **2b**, and underwent the condensation to afford 2,3,4,6-tetraarylpyridines, which facilitated the modification of the substituents at the 4-, 5- and 6-positions of the pyridine framework (Entries 6–20). The reaction using enones **2c–f** readily proceeded without any notable effect of the electronic nature of R^4 to give the corresponding products **3Bc–f** and **3Ce** respectively (Entries 6–10). On the contrary, this reaction was considerably affected by the substituent on the phenyl group (R^6) (Entries 11–13). Since both electron-donating and electron-withdrawing groups decreased the yields of products **3Bh** and **3Bi**, the low reactivity was considered to be due to the poor solubility of enones **2h** and **2i**. Indeed, 2-methoxyphenyl ketone **2j** showed higher reactivity than **2i** because of its increased solubility (Entries 13 and 14). Furthermore, 2,3,5,6-tetraarylpyridines **3Bm** and **3Bn** could be prepared by using α-arylated enones **2m** and **2n** were used (Entries 17 and 18).

Next, we attempted the synthesis of fully substituted pyridines using α,β-disubstituted enones **2o–r**. In the case of α-methylated enone **2o**, pyridine **3Bo** was obtained in a similar yield as **3Bg** (Entries 11 and 19). When α-arylated enone **2p** was used, fully and differently substituted pentaarylpyridine **3Bp** was obtained, although the yield was considerably decreased (Entry 20). The low reaction efficiency of **2p** was considered to be due to the instability caused by the disturbed conjugation. Structural optimization by DFT calculations [B3LYP/6-31g(d,p)] indicated that both chlorophenyl and benzoyl groups were distorted by around 40° angles as a result of steric repulsion with the α-aryl group, and the α-aryl group itself was distorted by around 85° angle from the enone plane (Figures 1 and S1). Indeed, when enone **2p** was subjected to the reaction conditions in the absence of **1B**, 82% of **2p** was decomposed to afford a complex mixture. This problem was overcome by increasing the molar ratio (**2p**:**1B**) from 1:5 to 1:2 (Entries 20 and 21). Consequently, pentaarylpyridines **3Bp–r** were synthesized in only three steps, among which the structure of **3Br** was confirmed by X-ray crystallography (Entries 20–23 and Figure 2). With this method, the aryl groups could be easily modified by altering benzonitriles, benzaldehyde, and benzyl phenyl ketones.

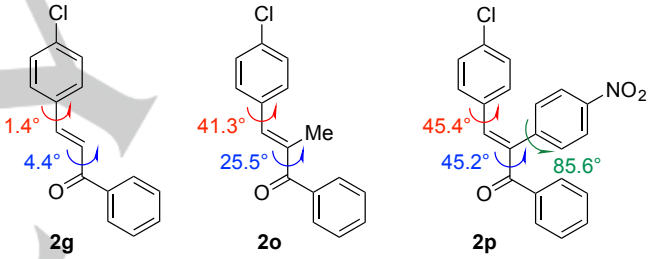


Figure 1. optimized structures of **2g**, **2o** and **2p**.

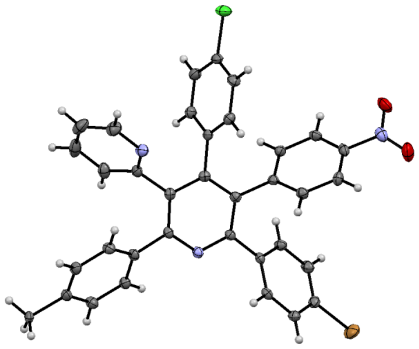
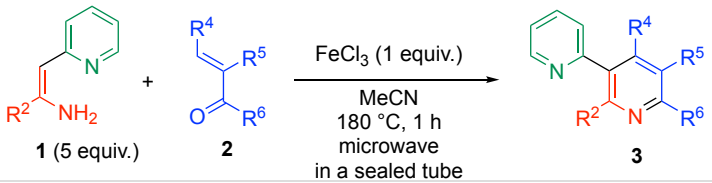


Figure 2. ORTEP of the single crystal structure of **3Br**. Ellipsoids are shown at the 50% probability level.

Table 2. Synthesis of polyarylated pyridines **3**.



Entry	Enamine **1**		Enone **2**				Product	
	R^2		R^4	R^5	R^6			Yield/%
1	Ph	**1A**	Ph	H	Me	**2a**	**3Aa**	84
2	4-MeC_6H_4	**1B**	2-Naphthyl	H	Me	**2b**	**3Bb**	66
3	4-MeC_6H_4	**1B**	Ph	H	Me	**2a**	**3Ba**	86
4	4-ClC_6H_4	**1C**	Ph	H	Me	**2a**	**3Ca**	71
5	4-$F_3CC_6H_4$	**1D**	Ph	H	Me	**2a**	**3Da**	69
6	4-MeC_6H_4	**1B**	4-$MeOC_6H_4$	H	4-MeC_6H_4	**2c**	**3Bc**	56
7	4-MeC_6H_4	**1B**	Ph	H	4-MeC_6H_4	**2d**	**3Bd**	67
8	4-MeC_6H_4	**1B**	4-FC_6H_4	H	4-MeC_6H_4	**2e**	**3Be**	64
9	4-ClC_6H_4	**1C**	4-FC_6H_4	H	4-MeC_6H_4	**2e**	**3Ce**	76
10	4-MeC_6H_4	**1B**	4-NCC_6H_4	H	4-MeC_6H_4	**2f**	**3Bf**	76
11	4-MeC_6H_4	**1B**	4-ClC_6H_4	H	Ph	**2g**	**3Bg**	72
12	4-MeC_6H_4	**1B**	4-ClC_6H_4	H	4-$O_2NC_6H_4$	**2h**	**3Bh**	35
13	4-MeC_6H_4	**1B**	4-ClC_6H_4	H	4-$MeOC_6H_4$	**2i**	**3Bi**	39
14	4-MeC_6H_4	**1B**	4-ClC_6H_4	H	2-$MeOC_6H_4$	**2j**	**3Bj**	61
15	4-MeC_6H_4	**1B**	4-*tert*-BuC_6H_4	H	4-ClC_6H_4	**2k**	**3Bk**	57
16	4-MeC_6H_4	**1B**	4-$MeOC_6H_4$	H	4-$O_2NC_6H_4$	**2l**	**3Bl**	29
17	4-MeC_6H_4	**1B**	H	4-$O_2NC_6H_4$	Ph	**2m**	**3Bm**	51
18	4-MeC_6H_4	**1B**	H	4-$O_2NC_6H_4$	4-$MeOC_6H_4$	**2n**	**3Bn**	38
19	4-MeC_6H_4	**1B**	4-ClC_6H_4	Me	Ph	**2o**	**3Bo**	62
20	4-MeC_6H_4	**1B**	4-ClC_6H_4	4-$O_2NC_6H_4$	Ph	**2p**	**3Bp**	13
21[a]	4-MeC_6H_4	**1B**	4-ClC_6H_4	4-$O_2NC_6H_4$	Ph	**2p**	**3Bp**	26
22[a]	4-MeC_6H_4	**1B**	Ph	4-$O_2NC_6H_4$	Ph	**2q**	**3Bq**	21
23[a]	4-MeC_6H_4	**1B**	4-ClC_6H_4	4-$O_2NC_6H_4$	4-BrC_6H_4	**2r**	**3Br**	10

[a] 2 Equiv. of enamine **1B** were used.

When the reaction atmosphere was changed from air to argon, the yield of **3Ba** decreased to 64%, which indicated that oxygen is necessary for the efficient reaction (Table 3, Entries 1 and 2). However, a complicated mixture of compounds was obtained when the reaction was conducted under oxygen (Entry 3), and decomposition of the substrates was observed. When a catalytic amount of $FeCl_3$ was used under argon atmosphere, the reaction was considerably suppressed; however, the same reaction under air afforded **3Ba** in 72% yield (Entries 4 and 5).

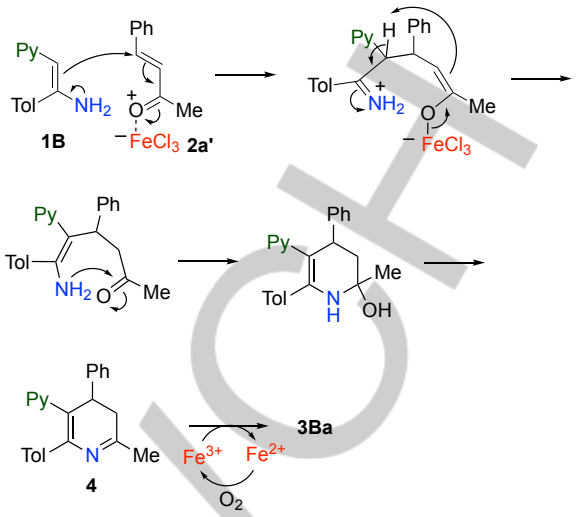
Table 3. Study on reaction atmosphere and catalyst loading in the reaction of **1B** and **2a**.

Entry	$FeCl_3$/equiv.	Atmosphere	Yield of **3Ba**/%
1	1	Air	86
2	1	Argon	64
3	1	Oxygen	69
4	0.2	Argon	39
5	0.2	Air	72
6	0.2[a]	Air	69
7	0.2[b]	Air	78

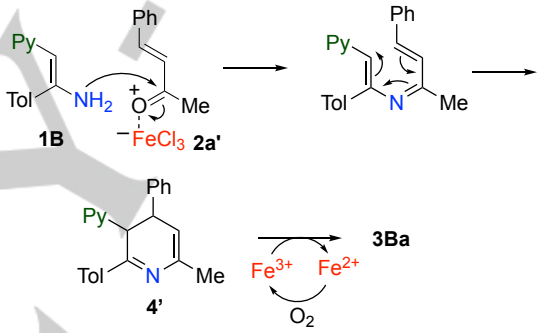
[a] Molecular sieves 3A (100 mg) was added. [b] *p*-Benzoquinone (1 equiv.) was added.

A plausible mechanism for the reaction is shown in Scheme 2. The reaction is initiated by the attack of **1B** onto enone **2a'** activated by $FeCl_3$. After cyclization and dehydration, the resulting dihydropyridine **4** was oxidized by $FeCl_3$ to afford **3Ba**, and oxygen in the air reoxidized the reduced iron species, and the reaction proceeded with a catalytic amount of $FeCl_3$. Another reaction mechanism initiated by imine formation is also acceptable (Scheme 3). We consider the former mechanism is more plausible based on our insights obtained from the study using push-pull alkenes, β-nitroenamines.[13]

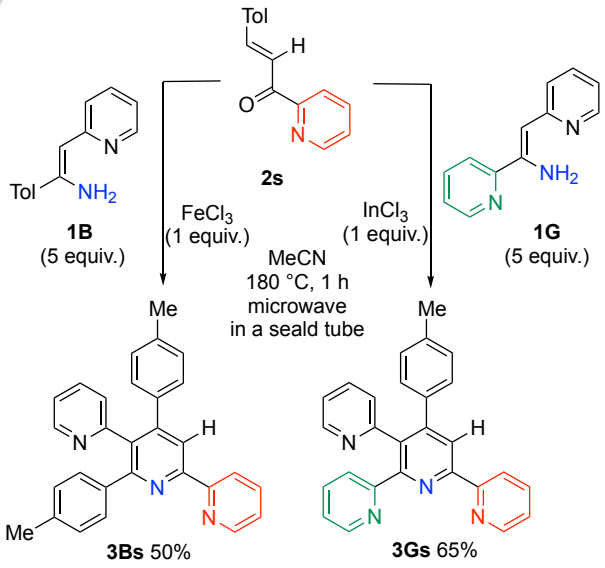
In both reaction mechanisms, a water is eliminated during the condensation between an amino and a carbonyl group, which might cause the competitive hydrolysis of the substrates. However, no effect was observed even when the reaction was conducted in the presence of molecular sieves (Table 3, Entry 6). This is presumably due to the reversible releasing of water under the employed conditions. Furthermore, *p*-benzoquinone was added to facilitate the oxidation of intermediately formed dihydropyridine **4** or **4'**, which increased the yield of **3Ba** to 78% (Entry 7), which indicates a possibility to establish an efficient catalytic system for synthesis of polysubstituted pyridines.



Scheme 2. A plausible mechanism.

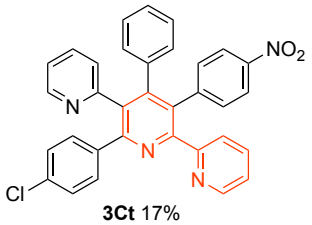


Scheme 3. Another acceptable reaction mechanism.



Scheme 4. Synthesis of oligopyridines **3Bs** and **3Gs**.

Our protocol facilitated the synthesis and molecular design of multiply substituted pyridines **3** by simple alteration of substrates **1** and **2**. This advantage prompted us to synthesize substituted bipyridine **3Bs** and terpyridine **3Gs** (Scheme 4). Enamine **1B** reacted with enone **2s** to furnish bipyridine **3Bs**. However, α-(2-pyridyl)enamine **1G** did not undergo the reaction at all; this is thought to be due to the formation of a complex of **1G** with $FeCl_3$ because the reaction mixture became purple immediately after the addition of $FeCl_3$. This abovementioned problem was overcome by replacing the Lewis acid from $FeCl_3$ to the non-coordinating $InCl_3$, and terpyridine **3Gs** was successfully produced although 1 equiv. $InCl_3$ was necessary for the efficient reaction. Furthermore, fully arylated bipyridine **3Ct** could be synthesized in 17% yield by the condensation of enamine **1C** with (α,β-diaryl)ethenyl pyridyl ketone **2t** in the presence of $FeCl_3$ (Figure 3).



3Ct 17%

Figure 3. Fully arylated bipyridine **3Ct**.

Conclusions

We have demonstrated the synthesis of polyarylpyridines by the condensation of β-(2-pyridyl)enamine **1** and α,β-unsaturated ketone **2** in the presence of $FeCl_3$ under air. In this reaction, $FeCl_3$ plays the role of not only an acid catalyst but also an oxidant for the intermediate dihydropyridine. The substituents can be easily modified by altering the substrates to obtain tri-, tetra- and pentaarylpyridines **3** from commercially available reagents *via* only three steps. Moreover, this protocol is applicable to the synthesis of polyarylated bipyridines and terpyridine.

Experimental Section

General. All reagents were purchased from commercial sources and used without further purification. Dry acetonitrile was also purchased from commercial source and used as received. ^1H and ^{13}C NMR spectra were recorded on Bruker DPX-400 spectrometer (400 MHz and 100 MHz, respectively) in $CDCl_3$ using TMS as an internal standard. When stereoisomers were obtained as a mixture, integral value for the *E* isomer was indicated as H_E, and that for the *Z* isomer was indicated as H_Z in the ^1H NMR. The assignments of the ^{13}C NMR were performed by DEPT experiments. IR spectra were recorded on a JASCO FT/IR-4200 spectrometer equipped with an ATM detector. High-resolution mass spectra were obtained on an AB SCEIX Triplet TOF 4600 mass spectrometer. Melting points were recorded on an SRS-Optimelt automated melting point system and were uncorrected. Microwave heating was performed by Anton-Paar Microwave 300 (850 W, 2455 MHz) using 10 mL glass vessel. Data collection for X-ray crystal analysis was performed on Rigaku/R-AXIS RAPID (CuKα λ = 1.54187 Å) and Rigaku/XtaLAB Synergy-S/Cu (CuKα λ = 1.54187 Å) diffractometers. The single crystal of **3Br** was obtained by recrystallization from $CHCl_3$–Hexane. The X-ray measurement was performed at −150 °C. The structures were solved by direct methods (SHELXT) and refined through full-matrix least-squares techniques on F2 using SHELXL and OLEX2 crystallographic software packages.[14–16] All non-hydrogen atoms were refined with anisotropic displacement parameters and hydrogen atoms were placed at calculated positions and refined "riding" on their corresponding carbon atoms. The geometrical optimization was carried out for at the B3LYP/6-31g(d,p) level of theory implemented on Gaussian 09 package.[17]

Synthesis of enamines 1. Enamines **1** were prepared according to the method described in literature.[12] To a solution of diisopropylamine (1.0 g, 10 mmol) in tetrahydrofuran (10 mL), a solution of butyllithium (11 mmol) was added at -70 °C. After stirring for 0.5 h at the same temperature, 2-methylpyridine (0.73 g, 10 mmol) was added dropwise, and the resultant mixture was stirred for further 1 h. Benzonitrile (1.0 g, 10 mmol) was gradually added to the solution, and stirred at -70 °C for 1 h. After elevating the reaction temperature, the solution was stirred at room temperature for further 1 h. After quenching the reaction with water, the mixture was extracted with ethyl acetate (30 mL × 3). The organic layer was dried over magnesium sulfate, and concentrated under reduced pressure. The residue was washed with hexane (30 mL) to afford 1-amino-1-phenyl-2-(2-pyridyl)ethene (**1A**)[12] as a yellow solid (1.92 g, 9.8 mmol, 98%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.44 (1H, ddd, *J* = 4.8, 2.0, 1.2 Hz), 7.63–7.61 (2H, m), 7.48 (1H, ddd, *J* = 8.0, 8.0, 2.0 Hz), 7.39–7.36 (3H, m), 7.00 (1H, ddd, *J* = 8.0, 1.2, 1.2 Hz), 6.84 (1H, ddd, *J* = 8.0, 4.8, 2.0 Hz), 6.90–6.63 (1H, br), 5.48 (1H, s). Other enamines **1B–D** and **1G** were prepared by condensation of the corresponding benzonitrile derivatives and methylarenes in the same way.

1-Amino-1-(4-methylphenyl)-2-(2-pyridyl)ethene (1B).[18] Yellow solid (1.91 g, 9.1 mmol, 91%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.44 (1H, ddd, *J* = 4.8, 1.2, 0.8 Hz), 7.52 (2H, d, *J* = 8.0 Hz), 7.49 (1H, ddd, *J* = 8.4, 8.4, 1.6 Hz), 7.21 (2H, d, *J* = 8.0 Hz), 7.00 (1H, ddd, *J* = 8.4, 0.8, 0.8 Hz), 6.84 (1H ddd, *J* = 8.4, 4.8, 1.2 Hz), 6.93–6.67 (1H, br), 5.47 (1H, s), 2.38 (3H, s).

1-Amino-1-(4-chlorophenyl)-2-(2-pyridyl)ethene (1C).[18] Yellow solid (2.17 g, 9.4 mmol, 94%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.45 (1H, ddd, *J* = 6.0, 1.6, 1.2 Hz), 7.55 (2H, d, *J* = 8.4 Hz), 7.49 (1H, ddd, *J* = 8.0, 1.6, 1.6 Hz), 7.36 (2H, d, *J* = 8.4 Hz), 7.00 (1H, ddd, *J* = 8.0, 1.2, 1.2 Hz), 6.84 (1H ddd, *J* = 8.0, 6.0, 1.6 Hz), 6.83–6.65 (1H, br), 5.45 (1H, s).

1-Amino-2-(2-pyridyl)-1-[4-(trifluoromethyl)phenyl]ethene (1D). Yellow solid (2.28 g, 8.6 mmol, 86%). Mp 120.3–120.7 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (1H, ddd, *J* = 4.8, 1.2, 0.8 Hz), 7.75 (2H, d, *J* = 8.0 Hz), 7.65 (2H, d, *J* = 8.0 Hz), 7.53 (1H, ddd, *J* = 8.0, 8.0, 1.6 Hz), 7.05 (1H, ddd, *J* = 8.0, 0.8, 0.8 Hz), 6.91 (1H ddd, *J* = 8.0, 4.8, 1.2 Hz), 6.99–6.67 (1H, br), 5.52 (1H, s), 2.38 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3 (C), 148.6 (C), 147.6 (CH), 143.5 (C), 135.8 (CH), 130.5 (C, q, *J* = 136.0 Hz), 126.4 (CH), 125.6 (CH, q, *J* = 3.8 Hz), 125.5 (C, q, *J* =271.0 Hz), 122.6 (CH), 118.0 (CH), 97.19 (CH); IR (KBr/cm^{-1}) 3466, 1733, 1618, 1473, 1335, 1168, 1112, 1077, 845, 800, 749; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{14}H_{12}F_3N_2$: 265.0947, found: 265.0945.

1-Amino-1,2-bis(2-pyridyl)ethene (1G).[19] Yellow solid (1.53 g, 7.8 mmol, 78%). ^1H NMR (400 MHz, CD_3CN) δ 8.59 (1H, ddd, *J* = 4.8, 2.0, 1.2 Hz), 8.46 (1H, ddd, *J* = 4.8, 2.0, 0.8 Hz), 7.88 (1H, ddd, *J* =8.4, 0.8, 0.8), 7.76 (1H, ddd, *J* = 8.4, 8.4, 2.0 Hz), 7.56 (1H, ddd, *J* = 8.0, 8.0, 2.0 Hz), 7.30 (1H, ddd, *J* = 8.4, 4.8, 0.8 Hz), 7.13 (1H, ddd, *J* = 8.0, 0.8, 0.8 Hz), 6.91 (1H, ddd *J* = 8.0, 4.8, 2.0 Hz), 6.83–6.65 (1H, br), 5.99 (1H, s).

Synthesis of enones 2. Enones **2** were prepared by aldol condensation by **Method a** or **Method b** except for commercially available **2a**.

Method a: To a methanol solution (30 mL) of 2-napthaldehyde (1.56 g, 10 mmol) and acetone (0.74 mL, 10 mmol), 0.5 M aqueous solution of potassium hydroxide (20 mL, 10 mmol) was added. The resultant mixture was stirred at room temperature for 0.5 h. Precipitated solid was collected by filtration to afford 4-(2-naphthyl)-3-buten-2-one (**2b**)[20] as a colorless solid (1.96 g, 10 mmol, quant.). The product was used for the subsequent condensation with enamine **1** without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (1H, s), 7.86–7.81 (3H, m), 7.68–7.64 (1H, m), 7.65 (1H, d, *J* = 16.4 Hz), 7.52–7.50 (2H, m), 2.41 (3H, s). Other enones **2c–l** were prepared in the same way. When product was formed as an oil, the mixture was extracted with dichloromethane (30 mL × 3), and the organic layer was dried over magnesium sulfate, and concentrated. The residual oil was used for the subsequent condensation with enamine **1** without further purification. For the preparation of α,β-disubstituted enones, **Method b** was effective rather than **Method a**.

3-(4-Methoxyphenyl)-1-(4-methylphenyl)-2-propen-1-one (2c).[21] Colorless solid (1.01 g, 4.0 mmol, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (2H, d, *J* = 8.4 Hz), 7.77 (1H, d, *J* = 15.6 Hz), 7.60 (2H, d, *J* = 8.8 Hz), 7.34 (1H, d, *J* = 15.6 Hz), 7.29 (2H, d, *J* = 8.4 Hz), 6.93 (2H, *J* = 8.8 Hz), 3.85 (3H, s), 2.43 (3H, s).

1-(4-Methylphenyl)-3-phenyl-2-propen-1-one (2d).[21] Yellow oil (2.00 g, 9.0 mmol, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (2H, d, *J*= 8.4 Hz), 7.79 (1H, d, *J* = 15.6 Hz), 7.64–7.62 (2H, m), 7.52 (1H, d, *J* = 15.6 Hz), 7.41–7.39 (3H, m), 7.29 (2H, d, *J* = 8.4 Hz), 2.42 (3H, s).

3-(4-Fluorophenyl)-1-(4-methylphenyl)-2-propen-1-one (2e).[22] Colorless solid (2.11 g, 8.8 mmol, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (2H, d, *J* = 8.0 Hz), 7.76 (1H, d, *J* = 16.0 Hz), 7.65–7.61 (2H, m), 7.45 (1H, d, *J* = 16.0 Hz), 7.30 (2H, d, *J* = 8.0 Hz), 7.13–7.08 (2H, m), 2.44 (3H, s).

3-(4-Cyanophenyl)-1-(4-methylphenyl)-2-propen-1-one (2f).[23] Colorless solid (1.21 g, 4.9 mmol, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (2H, d, *J* = 8.0 Hz), 7.76 (1H, d, *J* = 18.0 Hz), 7.41–7.69 (4H, m), 7.60 (1H, d, *J* = 18.0 Hz), 7.32 (2H, d, *J* = 8.0Hz), 2.45 (3H, s).

3-(4-Chlorophenyl)-1-phenyl-2-propen-1-one (2g).[24] Yellow solid (1.65 g, 6.8 mmol, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03–8.00 (2H, m), 7.75 (1H, d, *J* = 16.0 Hz), 7.56–7.57 (3H, m), 7.52–7.48 (2H, m), 7.39 (2H, d, *J* = 8.4 Hz).

3-(4-Chlorophenyl)-1-(4-nitrophenyl)-2-propen-1-one (2h).[25] Yellow solid (2.88 g, 10 mmol, quant.) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (2H, d, *J* = 8.8 Hz), 8.12 (2H, d, *J* = 8.8 Hz), 7.80 (1H, d, *J* =16.4 Hz), 7.59 (2H, d, *J* = 8.4 Hz), 7.45 (1H, d, *J* = 16.4 Hz), 7.42 (2H, d, *J* = 8.4 Hz).

3-(4-Chlorophenyl)-1-(4-methoxyphenyl)-2-propen-1-one (2i).[25] Yellow solid (1.80 g, 6.6 mmol, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (2H, d, *J* = 8.8 Hz), 7.74 (1H, d, *J* = 16.0 Hz), 7.56 (2H, d, *J* = 8.4 Hz), 7.50 (1H, d, *J* = 16.0 Hz), 7.38 (2H, *J* = 8.4 Hz), 6.98 (2H, d, *J* = 8.6 Hz), 3.89 (3H, s).

3-(4-Chlorophenyl)-1-(2-methoxyphenyl)-2-propen-1-one (2j).[26] Yellow oil (2.62 g, 9.6 mmol. 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (1H, dd, *J* = 7.6, 1.6 Hz), 7.57 (1H, d, *J* = 16.0 Hz), 7.50–7.46 (3H, m), 7.38–7.35 (2H, m), 7.35 (1H, d, *J* = 16.0 Hz), 7.05 (1H, ddd, *J* = 7.6, 7.6, 1.2 Hz), 7.00 (1H, d, *J* = 8.4 Hz), 3.91 (3H, s).

1-(4-Chlorophenyl)-3-[4-(1,1-dimethylethyl)phenyl]-2-propen-1-one (2k).[27] Colorless solid (1.97 g, 6.6 mmol, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (2H, d, *J* = 8.8 Hz), 7.80 (1H, d, *J* = 15.6 Hz), 7.58 (2H, d, *J* = 8.4 Hz), 7.48 (2H, d, *J* = 8.4 Hz), 7.45 (1H, d, *J* = 15.6 Hz), 7.44 (2H, d, *J* = 8.8 Hz), 1.35 (9H, s).

3-(4-Methoxyphenyl)-1-(4-nitrophenyl)-2-propen-1-one (2l).[28] Yellow solid (2.07 g, 7.3 mmol, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (2H, d, *J* = 9.2 Hz), 8.13 (2H, d, *J* = 9.2 Hz), 7.82 (1H, d, *J* = 15.6 Hz), 7.62 (2H, d, *J* = 8.4 Hz), 7.35 (1H, d, *J* = 15.6 Hz), 6.96 (2H, d, *J* = 8.4 Hz), 3.87 (3H, s).

Method b: To a toluene solution (50 mL) of 4-chlorobenzaldehyde (1.40 g, 10 mmol) and propanoylbenzene (1.34 g, 10 mmol), piperidine (0.20 mL, 2.0 mmol) and acetic acid (0.11 mL, 2.0 mmol) were added. The resultant mixture was heated under reflux using Dean-Stark apparatus for 1 d. After concentration, the residue was treated with column chromatography on silica gel to afford 3-(4-chlorophenyl)-2-methyl-1-phenyl-2-propen-1-one (**2o**)[29] as colorless needles (1.05 g, 4.1 mmol, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.72 (2H, m), 7.55 (1H, ddd, *J* = 7.6, 0.6, 0.6 Hz), 7.47–7.44 (2H, m), 7.38–7.32 (4H, m), 7.10 (1H, d, *J* = 1.2 Hz), 2.23 (3H, d, *J* = 1.2 Hz). Other enones **2m–t** were prepared in the same way.

2-(4-Nitrophenyl)-1-phenyl-2-propen-1-one (2m).[30] Yellow oil (1.24 g, 4.9 mmol, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (2H, d, *J* = 8.8 Hz), 7.90–7.87 (2H, m), 7.62 (2H, d, *J* = 8.8 Hz), 7.49–7.45 (3H, m), 6.26 (1H,s), 5.88 (1H, s).

1-(4-Methoxyphenyl)-2-(4-nitrophenyl)-2-propen-1-one (2n). Yellow oil (2.21 g, 7.8 mmol, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (2H, d, *J* = 9.2 Hz), 7.90 (2H, d, *J* = 9.2 Hz), 7.61 (2H, d, *J* = 8.8 Hz), 6.94 (2H, d, *J* = 8.8 Hz), 6.18 (1H, s), 5.79 (1H, s), 3.88 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.8 (C), 164.1 (C), 147.6 (C), 146.5 (C), 143.5 (C), 132.4 (CH), 129.3 (C), 127.9 (CH), 123.9 (CH), 123.0 (CH_2), 113.9 (CH), 55.57 (CH_3); IR (ATR/cm^{-1}) 1654, 1593, 1512, 1342, 1257, 1165, 848, 705; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{16}H_{14}NO_4$: 284.0917, found: 284.0909.

3-(4-Chlorophenyl)-2-(4-nitrophenyl)-1-phenyl-2-propen-1-one (2p). Colorless needles (1.49 g, 4.1 mmol, 41%). Mp 133.9–134.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (2H, d, *J* = 8.8 Hz), 7.85–7.83 (2H, m), 7.61–7.57 (1H, m), 7.51–7.45 (4H, m), 7.32 (1H, s), 7.19 (2H, d, *J* = 8.4 Hz), 6.98 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2 (C), 147.6 (C), 143.2 (C), 140.9 (CH), 139.1 (C), 137.4 (C), 135.7 (C), 132.7 (CH), 132.3 (C), 131.4 (CH), 130.9 (CH), 129.7, (CH), 128.9 (CH), 128.6 (CH), 124.1 (CH); IR (KBr/cm^{-1}) 1725, 1650, 159, 1518, 1254, 1091, 854, 752, 700; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{21}H_{15}ClNO_3$: 364.0735, found: 364.0723.

2-(4-Nitrophenyl)-1,3-diphenyl-2-propen-1-one (2q). White powder (2.37 g, 7.2 mmol, 72%, *E*/*Z* = 61/39). Mp 157.2−158.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22–8.19 ($2H_E$, m), 8.22–8.19 ($2H_Z$, m), 7.96–7.94 ($2H_Z$, m), 7.86–7.84 ($2H_E$, m), 7.62 ($2H_Z$, d, *J* = 6.8 Hz), 7.61–7.57 ($1H_E$, m), 7.51–7.46 ($2H_E$, m), 7.51–7.46 ($2H_Z$, m), 7.39–7.19 ($6H_E$, m), 7.39–7.19 ($7H_Z$, m), 7.04 ($2H_E$, d, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3 (C), 196.6 (C), 147.4 (C), 147.3 (C), 144.3 (C), 143.7 (C), 142.7 (CH), 138.64 (C), 138.62 (C), 137.7 (C), 135.8 (C), 134.5 (C), 134.2 (CH), 133.8 (C), 133.6 (CH), 132.6 (CH), 131.0 (CH), 130.3 (CH), 129.8 (CH), 129.7 (CH), 129.6 (CH), 129.2 (CH), 128.9 (CH), 128.6 (CH), 128.5 (CH), 127.1 (CH), 124.2 (CH), 123.9 (CH) Signals for these isomers could not be distinguished, and a CH signal is lacked presumably due to overlapping; IR (KBr/cm^{-1}) 1594, 1647, 1517, 1344, 1253, 848, 695; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{21}H_{16}NO_3$: 330.1124, found: 330.1113.

1-(Bromophenyl)-3-(4-chlorophenyl)-2-(4-nitrophenyl)-2-propen-1-one (2r). Yellow powder (2.86 g, 6.5 mmol, 65%, *E*/*Z* = 70/30). Mp 168.7−169.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24–8.20 (2H$_E$, m), 8.24–8.20 (2H$_Z$, m), 7.79 (2H$_Z$, d, *J* = 8.8 Hz), 7.69 (2H$_E$, d, *J* = 8.8 Hz), 7.62 (2H$_E$, d, *J* = 8.8 Hz), 7.59 (2H$_Z$, d, *J* = 9.2 Hz), 7.53 (2H$_Z$, d, *J* = 9.2 Hz), 7.44 (2H$_E$, d, *J* = 8.8 Hz), 7.31 (1H$_E$, s), 7.29 (1H$_Z$, s), 7.22–7.19 (2H$_E$, m), 7.22–7.19 (2H$_E$+2H$_Z$, m), 6.97 (2H$_Z$, d, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0 (C), 195.1 (C), 147.6 (C), 143.6 (C), 142.9 (C), 141.2 (CH), 138.8 (C), 138.7 (C) 136.2 (C), 136.0 (C), 134.4 (C), 132.8 (C), 132.5 (CH), 132.3 (CH), 132.0 (C), 131.9 (CH), 131.5 (CH), 131.2 (CH), 130.9 (CH), 130.8 (CH), 130.3 (CH), 129.1 (CH), 129.0 (CH), 127.9 (C), 127.1 (CH), 124.3 (CH), 124.1 (CH) three quaternary carbon signals could not be observed; IR (KBr/cm^{-1})1657, 1585, 1515, 1346, 1251, 1017, 1010, 852, 819; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{21}H_{14}BrClNO_3$: 441.9840, found: 441.9834.

3-(4-Methylphenyl)-1-(2-pyridyl)-2-propen-1-one (2s).[31] Dark brown solid (0.71 g, 3.2 mmol, 32%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (1H, ddd, *J* = 4.8, 1.2, 0.8 Hz), 8.25 (1H, d, *J* = 16.0 Hz), 8.18 (1H, ddd, *J* = 8.0, 1.2, 1.2 Hz), 7.93 (1H, d, *J* = 16.0 Hz), 7.88 (1H, ddd, *J* = 8.0, 8.0, 1.2 Hz), 7.64 (2H, d, *J* = 8.0 Hz), 7.48 (1H, ddd, *J* = 8.0, 4.8, 1.2 Hz), 7.22 (2H, d, *J* = 8.0 Hz), 2.39 (3H, s).

2-(4-Nitrophenyl)-3-phenyl-1-(2-pyridyl)-2-propen-1-one (2t). Brown oil (1.55 g, 4.7 mmol, 47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 8.20 (2H, d, *J* = 8.8 Hz), 7.96–7.94 (2H, m), 7.71 (2H, d, *J* = 8.8 Hz), 7.62 (1H, ddd, *J* = 8.0, 8.0, 1.2 Hz), 7.48 (1H, tt, *J* = 7.2, 1.2 Hz), 7.39–7.33 (3H, m), 7.27 (1H, s), 7.04 (1H, ddd, *J* = 8.0, 4.8, 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1 (C), 152.4 (C), 148.9 (CH), 147.6 (C), 143.3 (C), 141.9 (C), 137.1 (C), 136.6 (CH) 133.0 (CH), 130.7 (CH), 128.7 (CH), 128.6 (C), 127.3 (CH), 124.5 (CH), 124.2 (CH), 122.7 (CH); IR (KBr/cm^{-1}) 1668, 1595, 1516, 1343, 1222, 1109, 854, 719; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{20}H_{15}N_2O_3$: 331.077, found: 331.1075.

General method of synthesis of polysubstitued pyridines 3. To a solution of 1-amino-1-phenyl-2-(2-pyridinyl)ethene (**1A**) (98.1 mg, 0.5 mmol) in dry acetonitrile (15 mL), were added 4-phenyl-3-buten-2-one (**2a**) (15.0 mg, 0.1 mmol) and iron(III) chloride (12.7 mg, 0.1 mmol), and the resultant solution was heated at 180 °C for 1 h under microwave irradiation. After evaporation of the solvent, the residue was dissolved in ethyl acetate (10 mL). The solution was filtered through silica gel short column, and was further eluted with ethyl acetate (30 mL). The eluted solution was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate = 8/2) to afford polysubstituted pyridine **3Aa** (27.1 mg, 0.084 mmol, 84%) as a yellow oil. When other enamines **1B**–**D** and enones **2b**–**t** were used, reactions were performed in the same way.

6-Methyl-2,4-diphenyl-3-(2-pyridyl)pyridine (**3Aa**). Yellow oil (27.1 mg, 0.084 mmol, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (1H, ddd, *J* = 4.9, 1.6, 0.9 Hz), 7.34 (1H, ddd, *J* = 7.7, 7.7, 1.8 Hz), 7.27–7.26 (2H, m), 7.23 (1H, s), 7.20–7.16 (6H, m), 7.10–7.07 (2H, m), 6.96 (1H, ddd, *J* = 7.7, 4.9, 0.9 Hz), 6.89 (1H, ddd, *J* = 7.7, 0.9, 0.9 Hz), 2.70 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8 (C), 157.7 (C), 157.6 (C), 151.2 (C), 150.0 (C), 148.9 (CH), 140.7 (C), 139.3 (CH), 135.2 (CH), 131.2 (C), 129.6 (CH), 129.0 (CH), 127.9 (CH), 127.7 (CH), 127.3 (CH), 126.7 (CH), 123.0 (CH), 121.2 (CH), 24.5 (CH_3); IR (ATR/cm^{-1}) 1589, 1539, 1280, 1029, 748, 698; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{23}H_{19}N_2$: 323.1542, found: 323.1540.

6-Methyl-2-(4-methylphenyl)-4-phenyl-3-(2-pyridyl)pyridine (**3Ba**). Yellow solid (29.0 mg, 0.086 mmol, 86%). Mp 58.2–58.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 7.35 (1H, ddd, *J* = 7.6, 7.6, 1.2 Hz), 7.20–7.15 (6H, m), 7.09–7.07 (2H, m), 6.99–6.96 (3H, m) 6.89 (1H, ddd, *J* = 8.0, 1.2, 1.2 Hz), 2.69 (3H, s), 2.26 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9 (C), 157.9 (C), 157.8 (C), 150.0 (C), 148.9 (CH), 139.5 (C), 137.8 (C), 137.1 (C), 135.3 (CH), 131.0 (C), 129.5 (CH), 129.0(CH), 128.4 (CH), 127.9 (CH), 127.3 (CH), 126.8 (CH), 122.8 (CH), 121.2 (CH), 24.6 (CH_3), 21.1 (CH_3); IR (ATR/cm^{-1}) 1587, 1565, 1539, 1444, 1019, 700; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{24}H_{21}N_2$: 337.1699, found: 337.1708.

2-(4-Methylphenyl)-6-methyl-4-(2-naphthyl)-3-(2-pyridyl)pyridine (**3Bb**). Yellow solid (25.5 mg, 0.066 mmol, 66%). Mp 107.3–107.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (1H, dd, *J* = 5.2, 2.0 Hz), 7.75–7.69 (3H, m), 7.60 (1H, d, *J* = 8.4 Hz), 7.45–7.43 (2H, m), 7.34–7.29 (1H, ddd, *J* = 7.6, 7.6, 1.2 Hz), 7.32 (1H, s), 7.20 (2H, d, *J* = 8.0 Hz), 7.10 (1H, dd, *J* = 8.4, 1.6 Hz), 6.98 (2H, d, *J* = 8.4 Hz), 6.95 (1H, d, *J* = 7.6 Hz), 6.93 (1H, d, *J* = 7.6 Hz), 2.72 (3H, s), 2.26 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9 (C), 157.8 (C), 149.9 (C), 148.9 (CH), 137.8 (C), 137.1 (C), 137.3 (CH), 135.4 (CH), 133.0 (C), 133.3 (C), 132.3 (C), 131.2 (C), 129.6 (CH), 128.5 (CH), 128.4 (CH), 127.5 (CH), 127.3 (CH), 126.9 (CH), 126.8 (CH), 126.2 (CH), 126.1 (CH), 123.1 (CH), 121.3 (CH), 24.5 (CH_3), 21.2 (CH_3) One signal (C) was not observed presumably due to overlapping; IR (ATR/cm^{-1}) 1586, 1539, 1508, 1470, 1435, 822, 802, 748; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{28}H_{23}N_2$: 387.1855, found: 387.1841.

4-(4-Methoxylphenyl)-2,6-bis(4-methylphenyl)-3-(2-pyridyl)pyridine (**3Bc**). Yellow solid (24.8 mg, 0.056 mmol, 56%). Mp 72.3–72.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 8.07 (2H, d, *J* = 8.4 Hz), 7.72 (1H, s), 7.41 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.27 (2H, d, *J* = 8.4 Hz), 7.26 (2H, d, *J* = 8.8 Hz), 7.07 (2H, d, *J* = 6.4 Hz), 7.04 (1H, ddd, *J* = 7.6, 4.8, 1.6 Hz), 6.99 (2H, d, *J* = 8.0 Hz), 6.97 (1H, ddd, *J* = 8.6, 4.8, 4.8 Hz), 6.72 (2H, d, *J* = 8.8 Hz), 3.76 (3H, s), 2.41 (3H, s), 2.28 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9 (C), 158.1 (C), 157.8 (C), 156.2 (C), 150.2 (C), 149.0 (CH), 139.0 (C), 138.1 (C), 137.2 (C), 136.4 (C), 135.5 (CH), 131.9 (C), 131.8 (C), 130.3 (CH), 129.8 (CH), 129.4 (CH), 128.4 (CH), 127.0 (CH), 126.8 (CH), 121.4 (CH), 119.6 (CH), 113.4 (CH), 55.2 (CH_3), 21.3 (CH_3), 21.2 (CH_3); IR (KBr/cm^{-1}) 1510, 1462, 1442, 1370, 1112, 1021, 736, 622; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{31}H_{27}N_2O$: 443.2117, found: 443.2106.

2,6-Bis(4-methylphenyl)-4-phenyl-3-(2-pyridyl)pyridine (**3Bd**). Yellow solid (27.7 mg, 0.067 mmol, 67%). Mp 69.1–70.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 8.07 (2H, d, *J* = 8.4 Hz), 7.74 (1H, s), 7.40 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.29–7.26 (4H, m), 7.23–7.21 (3H, m), 7.15–7.14 (2H, m), 7.03–7.00 (3H, m), 6.96 (1H, ddd, *J* = 7.6, 0.8, 0.8 Hz), 2.41 (3H, s), 2.28 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9 (C), 157.8 (C), 156.3 (C), 150.6 (C), 148.9 (CH), 142.0 (C), 139.7 (C), 139.1 (C), 137.9 (C), 137.3 (C), 136.3 (C), 135.4 (CH), 129.8 (CH), 129.4 (CH), 129.1 (CH), 128.4 (CH), 127.9 (CH), 127.3 (CH), 127.0 (CH), 126.8 (CH), 121.4 (CH), 119.6 (CH), 21.3 (CH_3), 21.2 (CH_3); IR (KBr/cm^{-1}) 1587, 1531, 1508, 1292, 1248, 1180, 826, 803; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{30}H_{25}N_2$: 413.2012, found: 413.2012.

4-(4-Fluorophenyl)-2,6-bis(4-methylphenyl)-3-(2-pyridyl)pyridine (**3Be**). Yellow plates (30.6 mg, 0.071 mmol, 71%). Mp 163.6–164.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 8.07 (2H, d, *J* = 8.0 Hz), 7.71 (1H, s), 7.41 (1H, ddd, *J* = 7.6, 7.6, 2.0 Hz), 7.27–7.26 (4H, m), 7.13 (2H, m), 7.05–6.99 (3H, m), 6.94 (1H, ddd, *J* = 7.6, 2.0, 2.0 Hz), 6.92–6.88 (2H, m), 2.41 (3H, s), 2.29 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1 (C, d, *J* = 245.0 Hz), 157.9 (C), 157.8 (C), 156.4 (C), 149.6 (C), 149.1 (CH), 139.2 (C), 137.9 (C), 137.4 (C), 136.2 (C), 135.7 (C, d, *J* = 3.1 Hz), 135.5 (CH), 131.8 (C), 130.8 (CH, d, *J* = 8.1 Hz), 129.8 (CH), 129.4 (CH), 128.4 (CH), 127.0 (CH), 126.7 (CH), 121.5 (CH), 119.5 (CH), 115.1 (CH, d, *J* = 21.2 Hz), 21.3 (CH_3), 21.2 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.58 (tt, *J* = 5.6, 2.6 Hz); IR (ATR/cm^{-1}) 1724, 1585, 1504, 1275, 1118, 1018, 821, 802, 756; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{30}H_{24}FN_2$: 431.1918, found: 431.1928.

4-(4-Cyanophenyl)-2,6-bis(4-methylphenyl)-3-(2-pyridyl)pyridine (**3Bf**). Yellow solid (33.3 mg, 0.076 mmol, 76%). Mp 118.3–119.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (1H, ddd, *J* = 4.0, 1.8, 0.8 Hz), 8.07 (2H, d, *J* = 8.0 Hz), 7.69 (1H, s), 7.51 (2H, d, *J* = 8.4 Hz), 7.42 (1H, ddd, *J* = 7.6, 7.6, 1.8 Hz), 7.29 (2H, d, *J* = 8.0 Hz), 7.28–7.24 (4H, m), 7.05 (1H, ddd, *J* = 7.6, 4.8, 1.2 Hz), 7.02 (2H, d, *J* = 7.9 Hz), 6.95 (1H, ddd, *J* = 7.6, 0.8, 0.8 Hz), 2.42 (3H, s), 2.29 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0 (C), 157.1 (C), 156.6 (C), 149.2 (CH), 148.9 (C), 144.7 (C), 139.5 (C), 137.7 (C), 137.4 (C), 135.8 (C), 135.7 (CH), 131.7 (CH), 131.5 (C), 129.8 (CH), 129.8 (CH), 129.5 (CH), 128.5 (CH), 127.0 (CH), 126.7 (CH), 121.7 (CH), 118.8 (CH), 118.6 (C), 111.3 (C), 21.3 (CH_3), 21.2 (CH_3); IR (ATR/cm^{-1}) 2228, 1724, 1586, 1503, 1421, 1370, 1184, 1115, 1021, 826, 803, 624 ; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{31}H_{24}N_3$: 438.1964, found: 438.1944.

4-(4-Chlorophenyl)-2-(4-methylphenyl)-6-phenyl-3-(2-pyridyl)pyridine (**3Bg**). Yellow solid (31.2 mg, 0.072 mmol, 72%). Mp 154.8–155.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 8.18 (2H, d, *J* = 8.4 Hz), 7.72 (1H, s), 7.50–7.41 (4H, m), 7.26 (2H, d, *J* = 8.0 Hz), 7.20 (2H, d, *J* = 8.4 Hz), 7.09 (2H, d, *J* = 8.4 Hz), 7.04 (1H, ddd, *J* = 4.8, 1.2, 1.2 Hz), 7.01 (2H, d, *J* = 8.0 Hz), 6.94 (1H, ddd, *J* = 7.6, 4.8, 0.8 Hz), 2.28 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0 (C), 157.5 (C), 156.4 (C), 149.5 (C), 149.2 (CH), 138.9 (C), 138.1 (C), 137.7 (C), 137.5 (C), 135.6 (CH), 133.6 (C), 132.0 (C), 130.4 (CH), 129.8 (CH), 129.2 (CH), 128.7 (CH), 128.5 (CH), 128.2 (CH), 127.2 (CH), 126.7 (CH), 121.6 (CH), 119.7 (CH), 21.2 (CH_3); IR (ATR/cm^{-1}) 1586, 1531, 1491, 1419, 1371, 1018, 826, 749; HRMS (ESI/TOF) calcd. for [M+H]+ $C_{29}H_{22}ClN_2$: 433.1466, found: 433.1466.

4-(4-Chlorophenyl)-2-(4-methylphenyl)-6-(4-nitrophenyl)-3-(2-pyridyl)pyridine (**3Bh**). Yellow solid (16.7 mg, 0.035 mmol, 35%). Mp 100.9–101.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (1H, ddd, *J* = 4.9, 2.0, 0.8 Hz), 8.27 (4H, br s), 7.73 (1H, s), 7.37 (1H, ddd, *J* = 7.7, 7.7, 1.8 Hz), 7.25 (2H, d, *J* = 7.8 Hz), 7.22 (2H, d, *J* = 8.6 Hz), 7.09 (2H, d, *J* = 8.6 Hz), 7.07–7.06 (1H, m), 7.03 (2H, d, *J* = 7.8 Hz), 6.96 (1H, ddd, *J* = 7.7, 0.8, 0.8 Hz), 2.30 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6 (C), 155.9 (C), 152.7 (C), 149.0 (C), 148.2 (CH), 147.3 (C), 143.7 (C), 136.9 (C), 136.5 (C), 136.1 (C), 134.7 (CH), 132.9 (C), 132.4 (C), 129.2 (CH), 128.6 (CH), 127.5 (CH), 127.3 (CH), 126.8 (CH), 125.5 (CH), 122.9 (CH), 120.8 (CH), 119.3 (CH), 20.1 (CH_3); IR (ATR/cm^{-1}) 1585, 1516, 1342, 1261, 1091, 1018, 802, 729, 698; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{29}H_{21}CN_3O_2$: 478.1316, found: 478.1301.

4-(4-Chlorophenyl)-6-(4-methoxyphenyl)-2-(4-methylphenyl)-3-(2-pyridyl)pyridine (**3Bi**). White solid (13.9 mg, 0.039 mmol, 39%). Mp 79.7–80.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (1H, ddd, *J* = 4.0, 1.6, 0.8 Hz), 8.13 (2H, d, *J* = 9.2 Hz), 7.68 (1H, s), 7.41 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.25 (2H, d, *J* = 8.0 Hz), 7.19 (2H, d, *J* = 8.8 Hz), 7.09 (2H, d, *J* = 8.0 Hz), 7.07–6.99 (5H, m), 6.94 (1H, ddd, *J* = 7.6, 0.8, 0.8 Hz), 3.87 (3H, s), 2.29 (3H, s); ^{13}C (100 MHz, $CDCl_3$) δ 160.7 (C), 157.8 (C), 157.6 (C), 156.0 (C), 149.4 (C), 149.1 (CH), 138.2 (C), 137.8 (C), 137.4 (C), 135.5 (CH), 133.5 (C), 131.5 (C), 131.3 (C), 130.3 (CH), 129.8 (CH), 128.44 (CH), 128.41 (CH), 128.2 (CH), 126.7 (CH), 121.5 (CH), 118.8 (CH), 114.0 (CH), 55.3 (CH_3), 21.1(CH_3); IR (KBr/cm^{-1}) 1500, 1370, 1112, 1021, 736, 622; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{23}H_{17}ClN_2$: 357.1153, found: 357.1147.

4-(4-Chlorophenyl)-6-(2-methoxyphenyl)-2-(4-methylphenyl)-3-(2-pyridyl)pyridine (**3Bj**). Yellow solid (28.2 mg, 0.061 mmol, 61%). Mp 141.3–141.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 8.00 (1H, dd, *J* = 7.6, 2.0 Hz), 7.87 (1H, s), 7.43–7.36 (2H, m), 7.23 (2H, d, *J* = 8.0 Hz), 7.17 (2H, d, *J* = 8.8 Hz), 7.08 (2H, d, *J* = 8.8 Hz), 7.11–6.95 (6H, m), 3.88 (3H, s), 2.27 (3H, s); ^{13}C (100 MHz, $CDCl_3$) δ 157.8 (C), 157.7 (C), 157.3 (C), 155.2 (C), 149.1 (CH), 148.2 (C), 138.3 (C), 137.8 (C), 137.2 (C), 135.6 (CH), 133.4 (C), 131.6 (CH), 130.5 (CH), 130.1 (CH), 129.8 (CH), 128.8 (C), 128.6 (C), 128.4 (CH), 128.1 (CH), 126.7 (CH), 124.4 (CH), 121.5 (CH), 121.2 (CH), 111.5 (CH), 55.7 (CH_3), 21.2 (CH_3); IR (KBr/cm^{-1}) 1500, 1370, 1112, 1021, 736, 622; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{30}H_{23}ClN_2O$: 463.1571, found:463.1571.

2-(4-chlororphenyl)-4-[(1,1-dimethylethyl)-phenyl]-6-(4-methylphenyl)-5-(2-pyridyl)pyridine (**3Bk**). White solid (27.9 mg, 0.057 mmol, 57%). Mp 118.9–119.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (1H, ddd, *J* = 4.9, 1.8, 0.9 Hz), 8.11 (2H, d, *J* = 8.6 Hz), 7.74 (1H, s), 7.43 (2H, d, *J* = 8.6 Hz), 7.39 (1H, ddd, *J* = 7.7, 7.7, 1.8 Hz), 7.26-7.21 (4H, m), 7.06 (2H, d, *J* = 8.5 Hz), 7.04–7.00 (3H, m), 6.96 (1H, ddd, *J* = 7.7, 0.9, 0.9 Hz), 2.28 (3H, s), 1.27 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1 (C), 157.7 (C), 154.8 (C), 150.7 (C), 150.5 (C), 149.0 (CH), 137.8 (C), 137.6 (C), 137.3 (C), 136.3 (C), 135.4 (CH), 135.1 (C), 132.4 (C), 129.7 (CH), 128.8 (CH), 128.7 (CH), 128.41 (CH), 128.40 (CH), 126.7 (CH), 124.9 (CH), 121.4 (CH), 119.8 (CH), 34.5 (CH_3), 31.2 (C), 21.1 (CH_3); IR (ATR/cm^{-1}) 1585, 1531, 1492, 1365, 1091, 1014, 829, 802; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{33}H_{30}ClN_2$: 489.2092, found: 489.2073.

6-(4-Methoxyphenyl)-2-(4-methylphenyl)-4-(4-nitrophenyl)-3-(2-pyridyl)pyridine (**3Bl**). Yellow needles (13.7 mg, 0.029 mmol, 29%). Mp 115.8–116.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 8.36–8.31 (4H, m), 7.82 (1H, s) 7.44 (1H, ddd, *J* = 7.6, 7.6, 2.0 Hz), 7.25 (2H, d, *J* = 8.4 Hz), 7.09–7.04 (5H, m), 6.98 (1H, ddd, *J* = 7.6, 0.8, 0.8 Hz) 6.77 (2H, ddd, *J* = 8.8, 2.8, 2.8 Hz), 3.77 (3H, s), 2.30 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3 (C), 158.6 (C), 157.5 (C), 153.6(C), 150.8 (C), 149.2 (CH), 148.2 (C), 145.1 (C), 137.7 (C), 137.5 (C), 135.6 (CH), 133.5 (C), 131.3 (C), 130.3 (CH), 129.7 (CH), 128.5(CH), 127.9 (CH), 126.6 (CH), 123.9 (CH), 121.7 (CH), 120.7 (CH), 113.7 (CH), 55.2 (CH_3), 21.2 (CH_3); IR (ATR/cm^{-1}) 1512, 1341, 1249, 1179, 1022, 700; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{30}H_{24}N_3O_3$: 474.1812, found: 474.1813.

2-(4-Methylphenyl)-5-(4-nitrophenyl)-6-phenyl-3-(2-pyridyl)pyridine (**3Bm**). White solid (24.4 mg, 0.051 mmol, 51%). Mp 255.5–256.2 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (1H, ddd, *J* = 4.4, 1.6, 0.8 Hz), 8.14 (2H, d, *J* = 8.8 Hz), 8.09 (1H, s), 7.50 (1H, ddd, *J* = 8.0, 8.0, 2.0 Hz), 7.46 (2H, d, *J* = 8.8 Hz), 7.45 (2H, *J* = 8.0 Hz), 7.40 (2H, d, *J* = 8.0 Hz), 7.30–7.29 (3H, m), 7.22 (1H, ddd, *J* = 7.6, 4.8, 1.2 Hz), 7.11–7.08 (3H, m), 2.34 (3H, s); ^{13}C (100 MHz, $CDCl_3$) δ 157.3 (C), 156.7 (C), 156.2 (C), 150.0 (CH), 146.9 (C), 146.7 (C), 140.9 (CH), 139.1 (C), 138.5 (C), 136.5 (C), 135.8 (CH), 133.3 (C), 131.9 (C), 130.4 (CH), 130.1 (CH), 129.9 (CH), 128.9 (CH), 128.5 (CH), 128.2 (CH), 125.3 (CH), 123.6 (CH), 122.2 (CH), 21.3 (CH_3); IR (ATR/cm^{-1}) 1595, 1518, 1427, 750, 701; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{29}H_{21}ClN_3O_2$: 478.1316, found: 478.1301.

6-(4-Methoxyphenyl)-2-(4-methylphenyl)-5-(4-nitrophenyl)-3-(2-pyridyl)pyridine (**3Bn**). White solid (18.0 mg, 0.038 mmol, 38%). Mp 234.4–235.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (1H, ddd, *J* = 4.8, 1.8, 0.9 Hz), 8.16 (2H, d, *J* = 8.9 Hz), 8.06 (1H, s), 7.50 (1H, ddd, *J* = 7.7, 7.7, 1.8 Hz), 7.47 (2H, d, *J* = 8.9 Hz), 7.40 (2H, d, *J* = 8.9 Hz), 7.39 (2H, d, *J* = 8.0 Hz), 7.20 (1H, ddd, *J* = 7.7, 4.8, 0.9 Hz), 7.10 (2H, d, *J* = 8.0 Hz), 7.07 (1H, ddd, *J* = 7.7, 0.9, 0.9 Hz), 6.80 (2H, d, *J* = 8.9 Hz), 3.80 (3H, s), 2.34 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9 (C), 157.4 (C), 156.5 (C), 155.7 (C), 151.6 (C), 149.9 (CH), 147.1 (C), 146.8 (C), 141.0 (CH), 138.4 (C), 136.6 (C), 135.7 (CH), 132.8 (C), 131.6 (CH), 131.5 (C), 130.4 (CH), 129.9 (CH), 128.8 (CH), 125.2 (CH), 123.6 (CH), 122.1 (CH), 113.6 (CH), 55.2 (CH_3), 21.2 (CH_3); IR (ATR/cm^{-1}) 1516, 1504, 1427, 1342, 1249, 1172, 1029, 852, 794, 698; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{30}H_{24}N_3O_3$: 474.1812, found: 474.1797.

4-(4-Chlorophenyl)-5-methyl-2-(methylphenyl)-6-phenyl-3-(2-pyridyl)pyridine (**3Bo**). Yellow solid (27.7 mg, 0.062 mmol, 62%). Mp 86.4–87.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 7.65 (2H, ddd, *J* = 6.8, 1.6, 1.6 Hz), 7.45 (2H, ddd, *J* = 7.2, 1.2, 1.2 Hz), 7.41–7.32 (2H, m), 7.22–7.17 (4H, m), 7.02–7.01 (2H, brd, *J* = 7.6

Hz), 6.96–6.93 (3H, m), 6.89 (1H, ddd, *J* = 7.6, 1.2, 1.2 Hz), 2.24 (3H, s), 2.11 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5 (C), 149.7 (C), 148.8 (CH), 141.1 (C), 137.5 (C), 137.1 (C), 137.0 (C), 135.3 (CH), 132.9 (C), 132.8 (C), 130.65 (CH), 130.62 (C), 129.6 (CH), 129.4 (C), 129.2 (C), 128.4 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.2 (CH), 126.3 (CH), 121.2 (CH), 21.1 (CH_3), 18.2 (CH_3); IR (ATR/cm^{-1}) 1585.4, 1566.2, 1539.2, 1492.9, 1392.6, 1087.8, 1018.4, 8293, 771.5, 744.5, 702.1; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{30}H_{24}ClN_2$: 447.1622, found: 447.1639.

4-(4-Chlorophenyl)-2-(4-methylphenyl)-5-(4-nitrophenyl)-6-phenyl-3-(2-pyridyl)pyridine (**3Bp**). Yellow solid (7.2 mg, 0.013 mmol, 13%). Mp 165.3–166.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 7.90 (2H, d, *J* = 8.8 Hz), 7.38 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.33–7.28 (4H, m), 7.23–7.20 (3H, m), 7.07 (2H, d, *J* = 8.8 Hz), 7.02–6.98 (3H, m), 6.95–6.91 (3H, m), 6.77–6.73 (2H, br), 2.28 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3 (C), 157.2 (C), 157.1 (C), 149.0 (CH), 148.8 (C), 146.3 (C), 145.5 (C), 139.8 (C), 137.9 (C), 137.0 (C), 135.6 (CH), 133.0 (C), 132.1 (CH), 131.2 (C), 130.1 (CH), 129.8 (CH), 128.5 (CH), 128.0 (CH), 127.9 (CH), 127.7 (CH), 126.3 (CH), 122.8 (CH), 121.6 (CH), 21.2 (CH_3), Three signals (CH×1, C×2) were not observed presumably due to overlapping.; IR (ATR/cm^{-1}) 1585, 1519, 1489, 1388, 1346, 1018, 852, 763, 736, 702; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{35}H_{25}ClN_3O_2$: 554.1629, found: 554.1611.

2-(4-Methylphenyl)-5-(4-nitrophenyl)-4,6-diphenyl-3-(2-pyridyl)pyridine (**3Bq**). White solid (10.9 mg, 0.021 mmol, 21%). Mp 263.1–263.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 7.86 (2H, d, *J* = 8.8 Hz), 7.35–7.31 (5H, m), 7.22–7.19 (3H, m), 7.06 (2H, d, *J* = 9.2 Hz), 7.00 (2H, d, *J* = 8.0 Hz), 6.97–6.92 (5H, m), 6.86–6.74 (2H, br), 2.28 (3H, s); ^{13}C (100 MHz, $CDCl_3$) δ 157.5 (C), 157.2 (C), 156.9 (C), 150.0 (C), 148.8 (CH), 146.1 (C), 145.9 (C), 140.1 (C), 137.7 (C), 137.3 (C), 137.1 (C), 135.4 (CH), 133.1 (C), 132.2 (CH), 131.4 (C), 130.1 (CH), 129.8 (CH), 128.5 (CH), 128.4 (CH), 127.9 (CH), 127.8 (CH), 127.4 (CH), 126.8 (CH), 126.3 (CH), 122.6 (CH), 121.4 (CH), 21.2 (CH_3); IR (KBr/cm^{-1}) 1586, 1518, 1396, 1345, 1275, 851, 749, 701; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{35}H_{26}N_3O_2$: 520.2019, found: 520.2018.

6-(4-Bromophenyl)-4-(4-chlorophenyl)-2-(4-methylphenyl)-5-(4-nitrophenyl)-3-(2-pyridyl)pyridine (**3Br**). Colorles needles (6.3 mg, 0.010 mmol, 10%). Mp 264.6–265.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 7.94 (2H, d, *J* = 8.8 Hz), 7.40 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.34 (2H, d, *J* = 8.8 Hz), 7.27 (2H, d, *J* = 7.6 Hz), 7.21 (2H, d, *J* = 8.4 Hz), 7.06 (2H, d, *J* = 8.8 Hz), 7.02–7.00 (3H, m), 6.94 (2H, d, *J* = 8.8 Hz), 6.93 (1H, d, *J* = 7.6 Hz), 6.77–6.73 (2H, br), 2.28 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5 (C), 157.0 (C), 155.7 (C), 149.0 (CH), 146.4 (C), 145.1 (C), 138.7 (C), 138.0 (C), 136.8 (C), 135.6 (CH), 135.4 (C), 133.3 (C), 133.1 (C), 132.1 (CH), 131.7 (CH), 131.1 (CH), 129.7 (CH), 128.6 (CH), 127.7 (CH), 126.2 (CH), 123.1 (CH), 122.7 (C), 121.7 (CH), 21.2 (CH_3), Three signals (CH×1, C×2) were not observed presumably due to overlapping.; IR (ATR/cm^{-1}) 1520, 1485, 1346, 1087, 1010, 748; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{35}H_{24}BrClN_3O_2$: 632.0734, found: 632.0708. CCDC number: 1951931.

2,4-Bis(4-methylphenyl)-3,6-di(2-pyridyl)pyridine (**3Bs**). White solid (20.7 mg, 0.050 mmol, 50%). Mp 89.9–90.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 8.63 (1H, ddd, *J* = 7.2, 0.8, 0.8 Hz), 8.61 (1H, s), 8.44 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 7.81 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.40 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.31 (1H, ddd, *J* = 7.6, 4.8, 1.2 Hz), 7.27 (2H, d, *J* = 6.8 Hz), 7.08–6.97 (8H, m), 2.29 (3H, s), 2.28 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9 (C), 157.6 (C), 156.1 (C), 154.9 (C), 150.9 (C), 149.1 (CH), 149.0 (CH), 137.9 (C), 137.3 (C), 137.1 (C), 136.8 (CH), 136.4 (C), 135.4 (CH), 133.6 (C), 129.8 (CH), 129.1 (CH), 128.6 (CH), 128.4 (CH), 126.8 (CH), 123.7 (CH), 121.6 (CH), 121.4 (CH), 120.6 (CH), 21.2 (CH_3), 21.1 (CH_3); IR (ATR/cm^{-1})1585, 1511, 1260, 793, 749; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{29}H_{23}N_3$: 414.1964, found: 414.1964.

2-(4-Chlorolphenyl)-6-methyl-4-phenyl-3-(2-pyridyl)pyridine (**3Ca**). Yellow solid (25.3 mg, 0.071 mmol, 71%). Mp 108.9–109.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 7.37 (1H, ddd, *J* = 7.6, 7.6, 2.0 Hz), 7.23 (1H, s), 7.22–7.17 (5H, m), 7.14 (2H, d, *J* = 8.6 Hz), 7.08—7.06 (2H, m), 7.00 (1H, ddd, *J* = 7.6, 4.8, 0.8 Hz), 6.88 (1H, ddd, *J* = 7.6, 0.8, 0.8 Hz), 2.69 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9 (C), 157.3 (C), 156.5 (C), 150.2 (C), 149.1 (CH), 139.2 (C), 139.1 (C), 135.5 (CH), 133.5 (C), 131.2 (C), 130.9 (CH), 129.0 (CH), 128.0 (CH), 128.9 (CH), 127.4 (CH), 126.6 (CH), 123.2 (CH), 121.5 (CH), 24.5 (CH_3); IR (ATR/cm^{-1}) 1577, 1543, 1435, 1377, 1284, 1087, 1014, 844; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{23}H_{17}ClN_2$: .357.1153, found: 357.1147.

2-(4-Chlorophenyl)-4-(4-fluorophenyl)-6-(4-methylphenyl)-3-(2-pyridyl)pyridine (**3Ce**). Yellow plates (28.9 mg, 0.064 mmol, 64%). Mp 163.4–164.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (1H, ddd, *J* = 4.8, 1.6, 0.9 Hz), 8.05 (2H, d, *J* = 8.4 Hz), 7.74 (1H, s), 7.41 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.34–7.29 (4H, m), 7.18 (2H, d, *J* = 6.8 Hz), 7.13–7.11 (2H, m), 7.07 (1H, ddd, *J* = 7.6 , 1.6, 1.2 Hz), 6.94–6.89 (3H, m), 2.41 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8 (C, d, *J* = 246.3 Hz), 157.3 (C), 156.8 (C), 156.6 (C), 149.8 (C), 149.3 (CH), 139.4 (C), 139.2 (C), 135.9 (C), 135.7 (CH), 135.3 (C, d, *J* = 3.5 Hz), 133.7 (C), 131.9 (C), 131.2 (CH), 130.8 (CH, d, *J* = 8.1 Hz), 129.5 (CH), 127.9 (CH), 126.9 (CH), 126.6 (CH), 121.7 (CH), 119.9 (CH), 115.1 (CH, d, *J* = 21.3Hz), 21.3 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.2 (tt, *J* = 5.3, 3.0 Hz) IR (ATR/cm^{-1}) 1558, 1508, 1419, 1369, 1157, 1087, 1014, 837, 810; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{29}H_{21}ClFN_2$: 451.1371, found: 451.1362.

2-(4-Chlorophenyl)-5-(4-nitrophenyl)-4-phenyl-3,6-bis(2-pyridyl)pyridine (**3Ct**). Yellow plates (9.2 mg, 0.017 mmol, 17%). Mp 285.0–285.9 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (1H, ddd, *J* = 4.4, 1.6, 0.4 Hz), 8.23 (1H, ddd, *J* = 4.9, 1.5, 1.0 Hz), 8.25 (2H, d, *J* = 8.9 Hz), 7.39 (1H, ddd, *J* = 7.7, 1.8, 1.8 Hz), 7.37–7.32 (4H, m), 7.30 (1H, ddd, *J* = 7.7, 1.6, 1.6 Hz), 7.27–7.22 (3H, m), 7.18 (2H, d, *J* = 8.9 Hz), 7.12 (2H, br d, *J* = 7.9 Hz), 7.03 (1H, d, *J* = 7.8 Hz), 6.98 (1H, ddd, *J* = 4.9, 4.9, 1.0 Hz), 6.91 (1H, ddd, *J* = 4.9, 4.9, 1.0 Hz), 6.87 (1H, d, *J* = 7.8 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 157.4 (C), 156.3 (C), 156.3 (C), 155.9 (C), 149.2 (C), 148.9 (CH), 148.6 (CH), 146.4 (C), 145.2 (C), 139.5 (C), 138.4 (C), 135.6 (CH), 135.3 (CH), 134.3 (C), 132.9 (C), 132.0 (CH), 131.6 (C), 131.3 (CH), 130.0 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 126.5 (CH), 125.7 (CH), 122.7 (CH), 121.8 (CH), 121.7 (CH); IR (KBr/cm^{-1}) 1587, 1518, 1492, 1471, 1396, 1287, 1012, 850, 752, 702 ; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{33}H_{21}ClN_4O_2$: 541.1425, found: 541.1399.

2-[(4-Trifluoroethyl)phenyl]-6-methyl-4-phenyl-3-(2-pyridyl)pyridine (**3Da**). Yellow solid (27.0 mg, 0.069 mmol, 69%). Mp 132.2–133.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 7.43 (2H, d, *J* = 8.0 Hz), 7.39 (2H, d, *J* = 8.0 Hz), 7.35 (1H, ddd, *J* = 7.6, 7.6, 2.0 Hz), 7.28 (1H, s), 7.21–7.19 (3H, m) 7.10–7.08 (2H, m), 7.01 (1H, ddd, *J* = 7.6, 4.8, 1.2 Hz), 6.89 (1H, ddd, *J* = 8.0, 0.8, 0.8 Hz), 2.71 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1 (C), 157.1 (C), 156.4 (C), 150.3 (C), 149.1 (CH), 144.4 (C), 138.9 (C), 135.5 (CH), 131.4 (C), 129.9 (CH), 129.4 (C, q, *J* = 270.3 Hz), 129.0 (CH), 128.0 (CH), 127.5 (CH), 126.7 (CH), 124.7 (CH, q, *J* =3.7 Hz), 124.3 (C, q, *J* =32.2 Hz) 123.6 (CH), 121.6 (CH), 24.5 (CH_3); IR (ATR/cm^{-1}) 1586, 1534, 1491, 1369, 1275, 1242, 1182, 1089, 1020, 827, 805; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{24}H_{18}F_3N_2$: 391.1416, found: 391.1431.

4-(4-Methylphenyl)-2,3,6-tris(2-pyridyl)pyridine (**3Gs**). Brown oil (26.1 mg, 0.065 mmol, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (1H, ddd, *J* = 4.0, 1.6, 0.8 Hz), 8.67 (1H, d, *J* = 5.2 Hz), 8.53 (1H, s), 8.31 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 8.29 (1H, ddd, *J* = 4.8, 1.6, 0.8 Hz), 7.84 (1H, d, *J* = 8.0

Hz), 7.80 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.67 (1H, *J* = 7.6, 7.6, 1.6 Hz), 7.38 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 7.30 (1H, ddd, *J* = 7.2, 3.6, 0.8 Hz), 7.10–7.06 (3H, m), 7.59–6.95 (4H, m), 2.28 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8 (C), 157.7 (C), 156.7 (C), 155.9 (C), 154.9 (C), 151.0 (C), 149.1 (CH), 148.5 (CH), 148.1 (CH), 137.3 (C), 136.8 (CH), 136.1 (C), 136.0 (CH), 135.2 (CH), 134.3 (C), 129.2 (CH), 128.7 (CH), 126.7 (CH), 124.8 (CH), 123.8 (CH), 122.0 (CH), 121.7 (CH), 121.6 (CH), 121.1 (CH), 21.5 (CH_3); IR (ATR/cm^{-1}) 1585.4, 1562.3, 1535.3, 1512.2, 1473.6, 1415.7, 821.6, 790.8, 740.6; HRMS (ESI/TOF) calcd. for $[M+H]^+$ $C_{27}H_{21}N_4$: 401.1760, found: 401.1764.

Keywords: Cyclization• Microwave Chemistry •Enones • Nitrogen heterocycles • Synthetic methods

[1] a) M. Baumann, I. R. Baxendale, *Beilstein J. Org. Chem.* **2013**, *9,* 2265–2319; b) R. Karki, P. Thapa, H. Y. Yoo, T. M. Kadayat, P.-H. Park, Y. Na, E. Lee, K.-H. Jeon, W.-J. Cho, H. Choi, Y. Kwon, E.-S. Lee, *Eur. J. Med. Chem.* **2012**, *49*, 219−228; c) B. Corry, N. M. Smith, *Chem. Commun.* **2012**, *48*, 8958–8960.

[2] a) M. J. Bezdek, P. J. Chirik, *J. Am. Chem. Soc.* **2018**, *140*, 13817–13826; b) K. Nisbett, Y.-J. Tu, C. Turro, J. J. Kodanko, H. B. Schlegel, *Inorg Chem.* **2018**, 57, 231–240.

[3] a) A. G. Fang, J. V. Mello, N. S. Finney, *Tetrahedron.* **2004**, *60*, 11075–11087; b) B. Tang, F. Yu, P. Li, L. Tong, X. Duan, T. Xie, X. A. Wang, *J. Am. Chem. Soc.* **2009**, *131*, 3016–3023.

[4] S. Lachmanová, G. Dupeyre, J. Tarábek, P. Ochsenbein, C. Perruchot, I. Ciofini, M. Hromadová, L. Pospísil, P. P. Lainé, *J. Am. Chem. Soc.* **2015**, *137*, 11349–11364.

[5] a) E. K. J. Lui, D. Hergesell, L. L. Schafer, *Org. Lett.* **2018**, *20*, 6663−6667; b) Z. He, D. Dobrovolsky, P. Trinchera, A. K. Yudin, *Org. Lett.* **2013**, *15*, 334−337; c) N. S. Y. Loy, A. Singh, X. Xu, C.-M. Park, *Angew. Chem. Int. Ed.* **2013**, *52*, 2212−2216; d) P. K. Tapaswi, C. Mukhopadhyay, *ARKIVOC* **2011** (*x*) 287−298*;* e) B. Jiang, W.-J. Hao, X. Wang, F. Shi, S.-J. Tu, *J. Comb. Chem.* **2009**, *11*, 846–850; F. Palacios, C. Alonso, G. Rubiales, J. M. Ezpeleta, *Eur. J. Org. Chem.* **2001**, 2115−2122.

[6] a) R. P. Rivera, P. Ehlers, L. Ohlendorf, E. T. Rodríguez, A. Villinger, P. Langer, *Eur. J. Org. Chem.* **2018**, 990−1003; b) P. Pomaranski, P. Roszkowski, J. K. Maurin, A. Budzianowski, Z. Czarnocki, *Tetrahedron Lett.* **2017**, *58*, 462−465; c) E. Karadeniz, M. Zora, N. Z. Kılıçaslan, *Tetrahedron* **2015**, *71*, 8943−8952; d) S. Reimann, P. Ehlers, A. Petrosyan, S. Kohse, A. Spannenberg, A. E. Surkus, T. V. Ghochikyan, A. S. Saghyan, S. Lochbrunner, O. Kühn, R. Ludwig, P. Langer, *Adv. Synth. Catal.* **2014**, *356*, 1987−2008.

[7] C. Doebelin, P. Wanger, F. Bihel, N. Humbert, C. A. Kenfack, Y. Mely, J.-J. Bourguignon, M. Schmitt, *J. Org. Chem.* **2014**, *79*, 908–918.

[8] S. Suzuki, Y. Segawa, K. Itami, J. Yamaguchi, *Nat. Chem.* **2015**, *7*, 227–233.

[9] T. Asako, W. Hayashi, K. Amaike, S. Suzuki, K. Itami, K. Muto, J. Yamaguchi, *Tetrahedron* **2017**, *73*, 3669–3676.

[10] P. Pomaranski, Z. Czarnocki, *Synthesis* **2019**, *51*, 587–611.

[11] S. Hirai, Y. Horikawa, H. Asahara, N. Nishiwaki, *Chem. Commun.* **2017**, *53*, 2390–2393.

[12] T. Sasada, F. Kobayashi, N. Sakai, T. Konakahara, *Org. Lett.* **2009**, *11*, 2161–2164.

[13] a) Y. Nakaike, H. Asahara, N. Nishiwaki, *Russ. Chem. Bull., Int. Ed.* **2016**, *65*, 2129–2142; b) H. Asahara, M. Hamada, Y. Nakaike, N. Nishiwaki, *RSC Adv.* **2015**, *5*, 90778−90784; c) Y. Nakaike, N. Nishiwaki, M. Ariga, Y. Tobe, *J. Org. Chem.* **2014**, *79*, 2163−2169.

[14] H. Puschmann, *J. Appl. Crystallogr.* **2009**, *42*, 339−341.

[15] G. M. Sheldrick, *Acta Crystallogr.* **2015**, *A71*, 3−8.

[16] G. M. Sheldrick, *Acta Crystallogr.* **2015**, *C71*, 3−8.

[17] Gaussian 09, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian, Inc., Wallingford CT, **2010**.

[18] T. Konakahara, M. Matsuki, S. Sugimoto, K. Sato, *J. Chem. Soc., Perkin. Trans. 1* **1987**, 1489–1493.

[19] M. Westerhausen, A. N. Kneifel, A. Kalisch, *Angew. Chem. Int. Ed.* **2004**, *44*, 96–98.

[20] L. V. R. B. Syamala, T. M. Khopade, P. K. Warghude, R. G. Bhat, *Tetrahedron Lett.* **2019**, *60*, 88–91.

[21] G. F. Ozdemir, I. O. Ihan, S. Akkoc, *Synth. Commun.* **2019**, *49*, 2417–2424.

[22] A. H. Bansode, G. Suryavanshi, *ACS Omega* **2019**, *4*, 9636–9644.

[23] A. Koch, M. Ravikanth, *J. Org. Chem.* **2019**, *84*, 10775–10784.

[24] G. Zhang, Q. Fan, Y. Zhao, C. Ding, *Eur. J. Org. Chem.* **2019**, 5801–5806.

[25] T. Venkatesh, Y. D. Bodke, N. M. Joy, B. M. Vinoda, Y. Shiralgi, B. L. Dhananjaya, *Lett. Org. Chem.* **2016**, *13*, 661–671.

[26] Y. Beniyama, K. Matsuno, H. Miyachi, *Bioorg. Med. Chem. Lett.* **2013**, *23*, 1662–1666.

[27] J. T. Schott, C. E. Mordaunt, A. J. Vargas, M. A. Leon, K. H. Chen, M. Singh, M. Satoh, E. L. Cardenas, S. Maitra, N. V. Patel, H. J. P. de Lijser, *Chem. Pharm. Bull.* **2013**, *61*, 229–236.

[28] S. Gaikwad, A. Goswami, S. De, M. A. Shmittel, *Angew. Chem. Int. Ed.* **2016**, *55*, 10512–10517.

[29] Y. Nomura, M. Kimura, T. Shibata, Y. Takeuchi, S. Tomoda, *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3343–3344.

[30] B. Alcaide, P. Almendros, E. Busto, A. Luna, *Adv. Synth. Catal.* **2016**, *358*, 1526–1533.

[31] V. Sharma, A. Kaur, S. C. Sahoo, S. S. Chimni, *Org. Biomol. Chem.* **2018**, *16*, 6470–6478.

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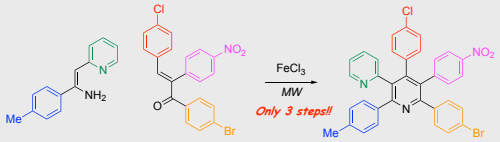

Condensation of β-(2-pyridyl)enamine and α,β-unsaturated ketone in the presence of $FeCl_3$ under air afforded highly substituted pyridines. Synthesis of differently substituted pentaarylpyridines was consequently achieved *via* only three steps from commercially available reagents with simple experimental manipulations.

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Three Step Synthesis of Fully and Differently Arylated Pyridines