

An improved Ullmann–Ukita–Buchwald–Li conditions for CuI-catalyzed coupling reaction of 2-pyridones with aryl halides

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Abstract—An effective CuI-*trans*-*N,N'*-dimethylcyclohexane-1,2-diamine (DMCDA)-K₂CO₃-catalyzed coupling reaction of 2-pyridones with aryl halides is described. Under our conditions, DMCDA was found to be an effective catalyst that facilitates the coupling reactions even in toluene, a common industrial solvent. In addition, 3-bromopyridine could also be coupled effectively under these conditions, indicating that the catalytic reactivity of this system is high. The reaction could be applied for polymer modification and iterative oligo-pyridone synthesis.

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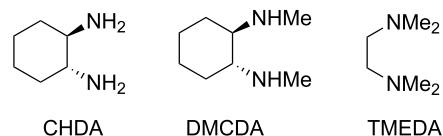
1. Introduction

N-Substituted pyrid-2-ones have attracted synthetic organic chemists because of their chemical reactivity, photochemical behavior, as well as their biological activities.^{1,2} Direct C–N bond formation is one of the most convenient synthetic approaches for *N*-alkylpyridones.³ However, synthetic examples for *N*-arylpyridones are rare.⁴ Traditional copper-catalyzed Ullmann type C–N bond formation often requires the use of high temperatures as well as stoichiometric amounts of copper reagents.⁵ Recently, palladium catalyzed *N*-arylations have been extensively explored.⁶ In addition, Ullmann-type copper-catalyzed processes for C–N bond formation such as *N*-arylation of amines,⁷ anilines,⁸ amides,⁹ imidazole,¹⁰ indoles,⁹ and hydrazines¹¹ have been reported. The reactivity of the copper catalyst strongly relies on the ligand system used in the reaction. *N,N'*-Dimethylethylenediamines and derivatives are known effective ligands to promote the reactions.

Ukita has recently reported the copper-catalyzed Ullmann *N*-arylation of 2-hydroxypyridine.^{4a} Copper halides, oxides, or copper powder facilitates the reaction. However, high temperatures of 120–150 °C in DMF are usually required. The reaction is sensitive to steric hindrance. *Ortho*-substituted aryl halides are ineffective toward the coupling reaction.

Li has recently reported a modification of the Ukita conditions, using CuI–MeNHCH₂CH₂NHMe–K₃PO₄ in dioxane to promote the coupling reaction.^{4b} In his work, detail electronic effects on pyridones as well as on the aryl halides have been evaluated.

In this report, we noted that CuI could facilitate the coupling of aryl halides with 2-hydroxypyridines under milder conditions in the presence of *N,N'*-dimethylcyclohexane-1,2-diamine (DMCDA) as the ligand. The reaction could proceed in toluene instead of dioxane or DMF.¹² Toluene is a common solvent that could be used for industrial applications.



Recently, we have attempted the synthesis of 2-amino-pyridines.¹³ In one experiment, we accidentally observed that 2 equiv of 2-bromopyridine (**1**) would undergo self-condensation in the presence of CuI/DMCDA/K₂CO₃ as the catalyst to give *N*-(pyrid-2-yl)pyrid-2-one (**2**) as the major product. Although we could not conclusively differentiate the *N*-arylated or *O*-arylated structure on the basis of the NMR spectrum, X-ray crystallographic analysis of the self-condensation product (**4**) unambiguously shows that the pyridyl group is attached to the pyridone nitrogen atom (Fig. 1, Scheme 1).

Keywords: 2-Pyridones; Copper reagents; C–N coupling; Toluene.

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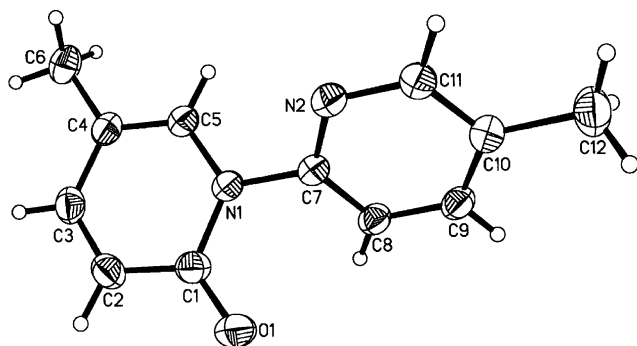
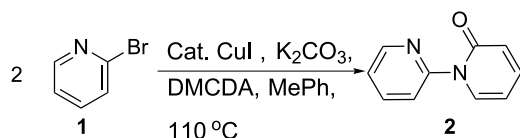


Figure 1. The ORTEP of 4.



Scheme 1.

It is noteworthy that unsubstituted or tetrasubstituted 1,2-diamines such as *trans*-cyclohexane-1,2-diamine (CHDA) or tetramethylethylene-1,2-diamine (TMEDA) do not promote the self-condensation reaction, indicating that DMCDA is essential for the reaction. When CHDA was applied, no reaction occurred. On the other hand, bromo-iodo exchange reaction occurred to give 2-iodopyridine (20%) in the presence of TMEDA. The self-condensation reaction could be applied to other 2-halopyridines (Table 1).

However, 2-chloropyridine was found to be sluggish in the self-condensation reaction. Although no direct evidence was obtained for the reaction mechanism, we suspect that hydrolysis of 2-bromopyridine (**1**) under the reaction conditions would occur to give 2-hydroxypyridine. The newly generated 2-hydroxypyridine would then be further coupled with 2-bromopyridine to give (**2**). Since we could not isolate any 2-hydroxypyridine from the reaction mixture, we proposed that the coupling of 2-hydroxypyridine with 2-bromopyridine is relatively fast in comparison to the 2-hydroxypyridine formation. These observations suggested that cross coupling of 2-hydroxypyridine with other 2-aryl halides might be feasible under similar reaction conditions (Table 2).

In our initial screening experiments, 2-hydroxypyridine and bromobenzene were used as the prototype substrates for searching the reaction conditions. In contrast to Ukita's reaction conditions^{4a} in which no reaction would occur in mesitylene, our reaction proceeds smoothly in toluene at reflux temperature. More surprisingly, the reaction is very specific to 2-hydroxypyridine. Other phenolic derivatives such as 3- and 4-hydroxypyridines, 2-hydroxypyrimidine, and phenol or phthalimide do not couple with bromobenzene under the above conditions. The choice of the ligand strongly affects the reactivity of the cross-coupling reaction. The use of CHDA under similar conditions gave *N*-phenylpyrid-2-one (**5**) in low yield (3%). TMEDA does not promote the reaction.

Both KOAc and K₂CO₃ were found to be effective as bases.

Table 1. Self-condensation of 2-halopyridines

Substrate	CuI, L (equiv)	Product (yield %)
	0.2, 0.2	X=Br (56) X=I (44) ^a
	0.2, 0.2	(57) ^b
	0.2, 0.2	(36) ^b
	0.2, 1	(7) ^c

L: *trans*-*N,N'*-Dimethyl-cyclohexane-1,2-diamine.

^a 16 h.

^b 20 h.

^c 24 h.

Table 2. Cross coupling of 2-hydroxypyridine with various aryl halides

Entry	Aryl halide	Product (%)	Entry	Aryl halide	Product (%)
1		 5	X=Br (91) X=I (84)	11	 15 (59)
2		 6 (89)		12	 16 (79)
3		 7 (70)			
4		 8 (38)		13	 2 (68)
5		 9 (82)		14	 17 (76)
6		 10 (61)		15	 18 (65)
7		 11 (81)		16	 19 (33)
8		 12 (2) ^a		17	 20 (74)
9		 13 (37)		18	 21 (62)
10		 14 (<1)		19	 22 (80)

^a In DMF.

However, KO^tBu will attack 2-bromopyridine to give 2-*tert*-butoxypyridine.¹⁴ The reaction will also proceed in other solvents such as DMF or dioxane.

However, the use of toluene gave the best results. The optimized reaction conditions of 20 mol% CuI, 20 mol% DMCDa, and 2 equiv K₂CO₃ were applied to the *N*-arylation of 2-hydroxypyridine with a number of aryl halides (Table 2). Functional groups that are compatible with this CuI-catalyzed *N*-arylation protocol include ether, thioether, triarylamine, nitrile, nitro group, styrene, and ester. No significant electronic effects on the aryl halides were observed in the reaction. As can be seen, the electron-deficient aryl bromides such as 3-NO₂C₆H₄Br and 4-CNC₆H₄Br, as well as the electron-rich aryl bromides such as 4-MeOC₆H₄Br or Ph₂NC₆H₄Br are effectively coupled in the reaction.

Electronic effects on 2-hydroxypyridine are significant, however. Electron-withdrawing substituents that would reduce the nucleophilicity of 2-hydroxypyridine do retard its reactivity toward the coupling reaction. Thus, the reaction of 2-hydroxy-5-nitropyridine is very sluggish. Similar results were reported in Li's conditions.

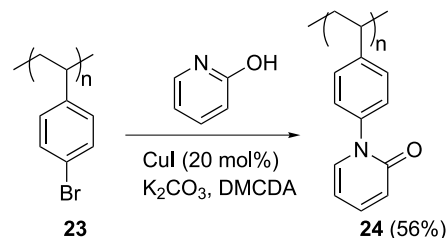
The reaction could also be applied to heterocyclic aryl halides such as pyridine, thiophene, and thiazole. In contrast to the results of Ukita's and Li's conditions, our conditions could also be applied to 3-bromopyridine to give the corresponding pyridone **17** in high yield.

The reaction is very sensitive to the steric environment of the aryl halides. Usually, *o*-substituted aryl bromides do not show enough reactivity in the reaction. Thus, regioselective coupling would occur at the 4-position of 2,4-dibromoanisole to give the *para* substituted product (entry 9, Table 2).

Similarly, although 2-bromonaphthalene could react smoothly to give the desired pyridone, as mentioned in Ukita's paper, 1-bromonaphthalene does not react under these conditions (compare entries 5 and 10, Table 2). We have applied this method for purifying 1-bromonaphthalene. Commercially available 1-bromonaphthalene is usually contaminated by a few percent of 2-bromonaphthalene. Since they have similar polarity and boiling point, they are difficult to separate. When the contaminated 1-bromonaphthalene was treated with 2-hydroxypyridine in the presence of the copper catalyst, the 2-bromo impurity was selectively converted to the more polar pyridone and removed by liquid chromatography. No bromo-iodo exchange was observed under these reaction conditions.

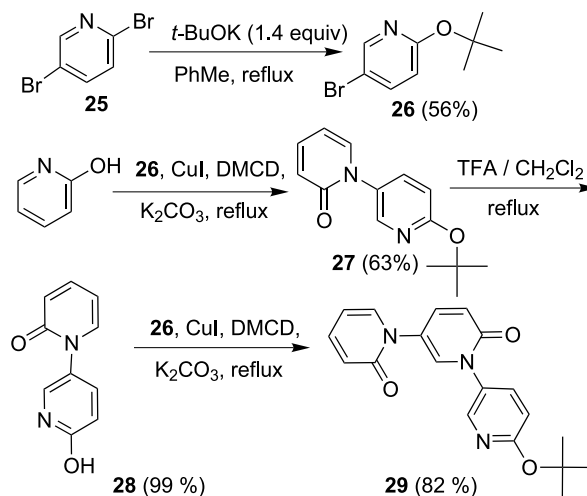
The reactivity of the reaction is so high that it could be successfully applied to polymer modification. Treatment of the commercially available poly(4-bromostyrene) (**23**) with 2-hydroxypyridine under the same conditions affords the target polypyridone (**24**) in reasonable yield. The structural assignment was supported by IR and NMR spectroscopy. The final polymer shows characteristic IR absorption bands of pyridone at 1663 and 1590 cm⁻¹, along with the disappearance of the characteristic IR absorption band of poly(4-bromostyrene) at 1073 cm⁻¹. In addition, five

aromatic ¹H NMR signals at δ 6.14 (1H), 6.42 (1H), 6.81 (2H), 7.23 (2H), and 7.41 (2H), and nine sets of sp² ¹³C NMR signals at δ 105.2, 120.3, 125.9, 127.6, 138.2, 138.7, 140.0, 144.9 and 160.8 suggested the polypyridone formation (Scheme 2).



Scheme 2.

The reaction could be extended to iterative oligo-pyridone synthesis (Scheme 3). As mentioned before, the bromo group of 2-bromopyridine could be replaced by *tert*-butoxide in the presence of KO^tBu. Thus, reaction of **25** with KO^tBu afforded **26**. CuI-catalyzed condensation of 2-hydroxypyridine with **26** gave **27** in moderated yield.



Scheme 3.

Deprotection of **27** by removal of the *tert*-butyl group in TFA afforded **28** in high yield. Compound **28** is slightly hygroscopic and has to be dried under vacuum at 110 °C before use in order to obtain the third generation of oligo-pyridone **29** in high yield. This iterative approach proved to be effective. Further application of this approach to the synthesis of tailored oligo-pyridones is ongoing (Scheme 3).

2. Experimental

2.1. The CuI-catalyzed self-condensation of 2-bromopyridine

trans-*N,N'*-Dimethylcyclohexane-1,2-diamine (DMCDa)

was prepared according to the supporting information in literature.^{9c}

2.2. General procedure

To an oven-dried double-necked flask containing a stir-bar was charged CuI (20 mol%) and K₂CO₃ (2 equiv). The flask was evacuated and backfilled with nitrogen. A solution of 2-bromopyridine in toluene (1 M, 1 equiv) and DMCD (20 mol%) were injected under nitrogen. The reaction mixture was stirred and heated at reflux temperature for the time specified. The resulting mixture was cooled to room temperature, diluted with dichloromethane, and filtered. The filtrate was washed with water. The organic phase was collected, dried over anhydrous MgSO₄, and concentrated. The crude product was purified by flash chromatography on silica gel (ethyl acetate/dichloromethane).

2.2.1. 1-(2-Pyridyl)-1H-pyridin-2-one (2).¹⁵ Reaction time: 16 h, white solid (56%). Mp 53–54 °C (from hexane); ¹H NMR (400 MHz, CDCl₃) δ 8.54 (d, *J*=5.2 Hz, 1H), 7.91 (d, *J*=6.8 Hz, 1H), 7.79–7.84 (m, 2H), 7.36 (ddd, *J*=9.2, 6.8, 2.4 Hz, 1H), 7.29 (ddd, *J*=6.8, 5.2, 1.2 Hz, 1H), 6.61 (d, *J*=9.2 Hz, 1H), 6.27 (td, *J*=6.8, 1.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 161.9, 151.5, 148.6, 140.0, 137.5, 135.8, 123.0, 121.8, 121.2, 106.1; IR (KBr): 3058, 2991, 1673 (C=O), 1612, 1540 cm⁻¹; FAB (NBA) 173.1 (M⁺ + H); HRMS calcd for C₁₀H₉N₂O 173.0715, found 173.0712 (M⁺ + H), calcd for C₁₀H₈N₂O 172.0637, found 172.0639 (M⁺). Anal. calcd for C₁₀H₈N₂O C, 69.76; H, 4.68; N, 16.27. Found C, 69.73; H, 4.70; N, 16.26.

2.2.2. 1-(4-Methylpyridid-2-yl)-4-methyl-1H-pyridin-2-one (3).¹⁵ Reaction time: 20 h, colorless solid (57%). Mp 79–81 °C (from hexane); ¹H NMR (400 MHz, CDCl₃) δ 8.37 (d, *J*=5.2 Hz, 1H), 7.70–7.72 (m, 2H), 7.09 (ddd, *J*=5.2, 1.2, 0.8 Hz, 1H), 6.41 (bs, 1H), 6.10 (dd, *J*=7.2, 2 Hz, 1H), 2.40 (s, 3H), 2.20 (d, *J*=0.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.9, 151.8, 151.7, 149.1, 148.2, 134.9, 124.0, 121.9, 119.9, 108.8, 21.4, 21.3; IR (CH₂Cl₂): 3044, 2922, 1670 (C=O), 1614, 1599, 1537, 1406 cm⁻¹; FAB (NBA) 201.1 (M⁺ + H), 200.1 (M⁺); HRMS calcd for C₁₂H₁₃N₂O 201.1028, found 201.1031 (M⁺ + H), calcd for C₁₂H₁₂N₂O 200.0950, found 200.0951 (M⁺). Anal. calcd for C₁₂H₁₂N₂O C, 71.98; H, 6.04; N, 13.99. Found C, 71.89; H, 6.09; N, 13.98.

2.2.3. 1-(5-Methylpyridid-2-yl)-5-methyl-1H-pyridin-2-one (4).¹⁶ Reaction time: 24 h, colorless solid (36%). Mp 106–107 °C (from hexane); ¹H NMR (400 MHz, CD₂Cl₂) δ 8.36 (bs, 1H), 7.72 (d, *J*=8 Hz, 1H), 7.63 (dd, *J*=8, 2 Hz, 1H), 7.58 (dd, *J*=2.4, 0.8 Hz, 1H), 7.25 (dd, *J*=9.2, 2.4 Hz, 1H), 6.48 (d, *J*=9.6 Hz, 1H), 2.38 (s, 3H), 2.11 (d, *J*=1.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 161.4, 149.7, 148.7, 142.7, 138.1, 133.1, 132.7, 121.4, 120.7, 115.0, 18.1, 17.3; IR (CH₂Cl₂): 3047, 2926, 1681 (C=O), 1614, 1593, 1530, 1498 cm⁻¹; FAB (NBA) 201.1 (M⁺ + H), 200.1 (M⁺); HRMS calcd for C₁₂H₁₃N₂O 201.1028, found 201.1026 (M⁺ + H), calcd for C₁₂H₁₂N₂O 200.0950, found 200.0946 (M⁺). Anal. calcd for C₁₂H₁₂N₂O C, 71.98; H, 6.04; N, 13.99. Found C, 71.97; H, 6.07; N, 13.98.

2.3. General procedure for the CuI-catalyzed *N*-arylation of 2-hydroxypyridine

To an oven-dried double-necked flask containing a stir-bar was charged 2-hydroxypyridine (1 equiv), CuI (20 mol%), and K₂CO₃ (2 equiv). The flask was evacuated and backfilled with nitrogen. A solution of arylbromide in toluene (1 M, 1 equiv) and DMCD (20 mol%) were injected under nitrogen. The reaction mixture was stirred and heated at reflux temperature for the time specified. The resulting mixture was cooled to room temperature, diluted with dichloromethane, and filtered. The filtrate was washed with water. The organic phase was collected, dried over anhydrous MgSO₄, and concentrated. The crude product was purified by flash chromatography on silica gel (ethyl acetate/dichloromethane).

2.3.1. 1-Phenyl-1H-pyridin-2-one (5).¹⁷ Reaction time: 18 h, colourless solid (91%). Mp 153–154 °C (from CH₂Cl₂/hexane = 1:10); ¹H NMR (400 MHz, d₆-DMSO) δ 7.62 (dd, *J*=7.2, 1.6 Hz, 1H), 7.47–7.52 (m, 3H), 7.44 (d, *J*=7.2 Hz, 1H), 7.33–7.41 (m, 2H), 6.47 (d, *J*=8.8 Hz, 1H), 6.30 (td, *J*=6.8, 1.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 162.1, 140.7, 139.6, 137.8, 129.1, 128.3, 126.3, 121.7, 105.8; IR (KBr): 3038, 1671 (C=O), 1611, 1585, 1499, 1447 cm⁻¹; FAB (NBA) 172.1 (M⁺ + H), HRMS calcd for C₁₁H₁₀NO 171.0762, found 172.0759 (M⁺ + H), calcd for C₁₁H₉NO 171.0684, found 171.0686 (M⁺). Anal. calcd for C₁₁H₉NO: C, 77.17; H, 5.30; N, 8.18. Found C, 77.30; H, 5.12; N, 8.11.

2.3.2. 1-(4-Methoxyphenyl)-1H-pyrid-2-one (6). Reaction time: 20 h, white solid (89%). Mp 110–111 °C (from CH₂Cl₂/hexane = 1:10); ¹H NMR (400 MHz, d₆-acetone) δ 7.5 (ddd, *J*=7, 2.2, 0.8 Hz, 1H), 7.43 (ddd, *J*=9.2, 6.7, 2.2 Hz, 1H), 7.32 (dt, *J*=9.2, 2.8 Hz, 2H), 7.02 (dt, *J*=9.2, 2.8 Hz, 2H), 6.42 (ddd, *J*=9.2, 1.2, 0.8 Hz, 1H), 6.24 (td, *J*=6.7, 1.6 Hz, 1H), 3.85 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.4, 159.1, 139.5, 138.1, 133.6, 127.4, 121.6, 114.4, 105.6, 55.5; IR (KBr): 3024, 2363, 2325, 1661 (C=O), 1599, 1499, 1435 cm⁻¹; FAB (NBA) 202.1 (M⁺ + H); HRMS calcd for C₁₂H₁₂NO₂ 202.0868, found 202.0865 (M⁺ + H), calcd for C₁₂H₁₁NO₂ 201.0790, found 201.0797 (M⁺). Anal. calcd for C₁₂H₁₁NO₂: C, 71.63; H, 5.51; N, 6.96. Found C, 71.93; H, 5.29; N, 6.87.

2.3.3. 1-(4-Cyanophenyl)-1H-pyridin-2-one (7).¹⁸ Reaction time: 12 h, white solid (70%). Mp 165–166 °C (from CH₂Cl₂/hexane = 1:10); ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, *J*=8.4 Hz, 2H), 7.51 (d, *J*=8.4 Hz, 2H), 7.39 (ddd, *J*=9.2, 6.8, 2.2 Hz, 1H), 7.28 (dd, *J*=7, 2.2 Hz, 1H), 6.61 (d, *J*=9.2 Hz, 1H), 6.26 (t, *J*=6.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 161.5, 144.1, 140.1, 136.5, 133.0, 127.3, 121.9, 117.7, 112.1, 106.6; IR (KBr): 3100, 3038, 2362, 2325, 1673 (C=O), 1599, 1523, 1499 cm⁻¹; FAB (NBA) 197.0 (M⁺ + H); HRMS calcd for C₁₂H₉N₂O 197.0715, found 197.0711 (M⁺ + H), calcd for C₁₂H₈N₂O 196.0637, found 196.0643 (M⁺). Anal. calcd for C₁₂H₈N₂O: C, 73.46; H, 4.11; N, 14.28. Found C, 73.28; H, 3.98; N, 14.16.

2.3.4. 1-(Biphenyl-4-yl)-1H-pyridin-2-one (8).¹⁹ Reaction time: 14 h, white solid (38%). Mp 226–227 °C (from CH₂Cl₂/hexane = 1:10); ¹H NMR (400 MHz, CDCl₃) δ

7.68 (dd, $J=6.6, 1.8$ Hz, 2H), 7.58 (d, $J=9.2$ Hz, 2H), 7.34–7.46 (m, 7H), 6.68 (d, $J=9.2$ Hz, 1H), 6.29 (td, $J=6.6, 1.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.2, 141.4, 139.9, 139.8, 139.7, 137.7, 128.7, 127.9, 127.6, 127.1, 126.6, 121.7, 106.0; IR (KBr): 3062, 3024, 2363, 2337, 1661 (C=O), 1585, 1535, 1485 cm^{-1} ; FAB (NBA) 248.1 ($\text{M}^+ + \text{H}$); HRMS calcd for $\text{C}_{17}\text{H}_{14}\text{NO}$ 248.1075, found 248.1074 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_{17}\text{H}_{13}\text{NO}$ 247.0997, found 247.0993 (M^+). Anal. calcd for $\text{C}_{17}\text{H}_{13}\text{NO}$: C, 82.57; H, 5.30; N, 5.66. Found C, 82.26; H, 5.17; N, 5.46.

2.3.5. 1-(Naphthalen-2-yl)-1H-pyridin-2-one (9). Reaction time: 18 h, white solid, (82%). Mp 160–161 °C (from $\text{CH}_2\text{Cl}_2/\text{hexane}=1:10$); ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, $J=8.8$ Hz, 1H), 7.81–7.89 (m, 2H), 7.79 (d, $J=2$ Hz, 1H), 7.48–7.54 (m, 3H), 7.37–7.43 (m, 2H), 6.68 (dd, $J=9.8, 1.4$ Hz, 1H), 6.25 (td, $J=6.8, 0.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.3, 139.7, 138.5, 138.0, 133.2, 132.6, 129.0, 127.9, 127.6, 126.7, 126.6, 124.7, 124.4, 121.8, 105.9; IR (KBr): 3024, 2362, 2337, 1661 (C=O), 1585, 1535, 1499, 1461 cm^{-1} ; FAB (NBA) 222.1 ($\text{M}^+ + \text{H}$), 221.1 (M^+); HRMS calcd for $\text{C}_{15}\text{H}_{12}\text{NO}$ 222.0919, found 222.0921 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_{15}\text{H}_{11}\text{NO}$ 221.0841, found 221.0841 (M^+). Anal. calcd for $\text{C}_{15}\text{H}_{11}\text{NO}$: C, 81.43; H, 5.01; N, 6.33. Found C, 81.16; H, 5.11; N, 6.31.

2.3.6. 1-(4-Vinylphenyl)-1H-pyridin-2-one (10). Reaction time: 9 h, white solid (61%). Mp 115–116 °C (from $\text{CH}_2\text{Cl}_2/\text{hexane}=1:10$); ^1H NMR (400 MHz, CDCl_3) δ 7.49 (dt, $J=8.4, 2$ Hz, 2H), 7.36 (ddd, $J=9.2, 6.8, 2.4$ Hz, 1H), 7.28–7.34 (m, 3H), 6.72 (dd, $J=17.6, 10.8$ Hz, 1H), 6.63 (d, $J=9.2$ Hz, 1H), 6.21 (td, $J=6.8, 1.6$ Hz, 1H), 5.77 (dd, $J=17.6, 0.8$ Hz, 1H), 5.30 (dd, $J=10.8, 0.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) only 10 sets of ^{13}C signals was observed δ 162.1, 140.0, 139.6, 137.6, 135.5, 126.9, 126.4, 121.8, 115.2, 105.8; IR (KBr): 3029, 1668 (C=O), 1582, 1530, 1490, 1455 cm^{-1} ; FAB (NBA) 198.1 ($\text{M}^+ + \text{H}$), 197.1 (M^+); HRMS calcd for $\text{C}_{13}\text{H}_{12}\text{NO}$ 198.0919, found 198.0918 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_{13}\text{H}_{11}\text{NO}$ 197.0841, found 197.0839 (M^+). Anal. calcd for $\text{C}_{13}\text{H}_{11}\text{NO}$: C, 79.17; H, 5.62; N, 7.10. Found C, 79.33; H, 5.64; N, 7.28.

2.3.7. 4,4'-Bis(2-oxo-2H-pyridin-1-yl)biphenyl-2,2'-dicarboxylic acid dimethyl ester (11). Reaction time: 16 h, white solid (81%). Mp 218–219 °C (from CH_3CN); ^1H NMR (400 MHz, CDCl_3) δ 8.07 (d, $J=2.4$ Hz, 2H), 7.63 (dd, $J=8, 2$ Hz, 2H), 7.40–7.46 (m, 4H), 7.37 (d, $J=8.4$ Hz, 2H), 6.68 (d, $J=9.2$ Hz, 2H), 6.29 (t, $J=6.8$ Hz, 2H), 3.66 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.7, 162.0, 142.3, 139.9, 139.7, 137.4, 131.0, 130.0, 129.6, 127.8, 121.8, 106.2, 52.1; IR (KBr): 3626, 3450, 3062, 3038, 2951, 2363, 2336, 1737 (C=O), 1661 (C=O), 1585, 1523, 1473 cm^{-1} ; FAB (NBA) 457.1 ($\text{M}^+ + \text{H}$), 456.1 (M^+); HRMS calcd for $\text{C}_{26}\text{H}_{21}\text{N}_2\text{O}_6$ 457.1400, found 457.1408 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_{26}\text{H}_{20}\text{N}_2\text{O}_6$ 456.1321, found 456.1326 (M^+). Anal. calcd for $\text{C}_{26}\text{H}_{20}\text{N}_2\text{O}_6$: C, 68.42; H, 4.42; N, 6.14. Found C, 68.17; H, 4.34; N, 6.17.

2.3.8. 1-(2-Methoxyphenyl)-1H-pyridin-2-one (12).²⁰ Reaction time: 16 h (in DMF), white solid (2%). Mp 86–87 °C (from Et_2O); ^1H NMR (400 MHz, CDCl_3) δ 7.35–7.41 (m, 2H), 7.25 (dd, $J=7.6, 1.6$ Hz, 1H), 7.18 (dd, $J=7.6, 1.6$ Hz, 1H), 7.01–7.05 (m, 2H), 6.64 (d, $J=9.2$ Hz,

1H), 6.18 (td, $J=6.4, 1.2$ Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.2, 154.0, 139.7, 138.8, 130.1, 129.5, 128.4, 121.7, 120.8, 112.3, 105.3, 55.9; IR (neat): 3062, 2989, 1661 (C=O), 1599, 1523, 1485 cm^{-1} ; FAB (NBA) 202.0 ($\text{M}^+ + \text{H}$); HRMS calcd for $\text{C}_{12}\text{H}_{12}\text{NO}_2$ 202.0868, found 202.0868 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_{12}\text{H}_{11}\text{NO}_2$ 201.0790, found 201.0784 (M^+).

2.3.9. 1-(3-Bromo-4-methoxyphenyl)pyridin-2-one (13). Reaction time: 14 h, white solid (37%). Mp 146–147 °C (from THF); ^1H NMR (400 MHz, d_6 -DMSO) δ 7.65 (d, $J=2.8$ Hz, 1H), 7.61 (dd, $J=6.8, 1.8$ Hz, 1H), 7.48 (td, $J=9.2, 6.8, 2.4$ Hz, 1H), 7.38 (dd, $J=8.8, 2.8$ Hz, 1H), 7.21 (d, $J=8.8$ Hz, 1H), 6.45 (d, $J=9.2$ Hz, 1H), 6.28 (td, $J=6.8, 1.2$ Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.1, 155.5, 139.7, 137.6, 133.9, 131.1, 126.5, 121.5, 111.6, 111.5, 105.8, 56.4; IR (KBr): 3100, 3062, 3024, 2988, 2939, 2363, 2337, 1661 (C=O), 1585, 1535, 1485 cm^{-1} ; FAB (NBA) 280.0 ($\text{M}^+ + \text{H}$); HRMS calcd for $\text{C}_{12}\text{H}_{11}\text{BrNO}_2$ 279.9973, found 279.9971 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_{12}\text{H}_{10}\text{BrNO}_2$ 278.9895, found 278.9896 (M^+). Anal. calcd for $\text{C}_{12}\text{H}_{10}\text{BrNO}_2$: C, 51.45; H, 3.60; N, 5.00. Found C, 51.19; H, 3.58; N, 5.03.

2.3.10. 1-(4-(Diphenylamino)phenyl)pyrid-2-one (15). Reaction time: 24 h, white solid (59%). Mp 220–221 °C (from $\text{CH}_2\text{Cl}_2/\text{hexane}=1:10$); ^1H NMR (400 MHz, d_6 -acetone) δ 7.56 (ddd, $J=6.4, 2.4, 0.8$ Hz, 1H), 7.44 (ddd, $J=9.2, 6.7, 2.4$ Hz, 1H), 7.29–7.36 (m, 6H), 7.05–7.13 (m, 8H), 6.44 (dd, $J=9.2, 0.8$ Hz, 1H), 6.26 (td, $J=6.7, 1.2$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.3, 147.7, 147.0, 139.5, 138.0, 134.3, 129.2, 126.9, 124.8, 123.4, 122.7, 121.6, 105.9; IR (KBr): 3076, 3038, 2363, 2337, 1661 (C=O), 1585, 1485, 1473 cm^{-1} ; FAB (NBA) 339.1 ($\text{M}^+ + \text{H}$), 338.1 (M^+); HRMS calcd for $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}$ 339.1497, found 339.1493 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}$ 338.1419, found 338.1417 (M^+). Anal. calcd for $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}$: C, 81.63; H, 5.36; N, 8.28. Found C, 81.48; H, 5.26; N, 8.41.

2.3.11. 1-(4'-(Diphenylamino)biphenyl-4-yl)-1H-pyridin-2-one (16). Reaction time: 20 h, white solid (79%). Mp 232–234 °C (from $\text{CH}_2\text{Cl}_2/\text{hexane}=1:10$); ^1H NMR (400 MHz, d_6 -DMSO) δ 7.74 (dt, $J=8.8, 2.2$ Hz, 2H), 7.68 (dd, $J=7, 1.4$ Hz, 1H), 7.64 (dt, $J=8.8, 2.2$ Hz, 2H), 7.51 (ddd, $J=8.8, 6.7, 2.2$ Hz, 1H), 7.45 (dt, $J=8.8, 2.2$ Hz, 2H), 7.33 (t, $J=9.2$ Hz, 4H), 7.02–7.09 (m, 8H), 6.48 (d, $J=8.8$ Hz, 1H), 6.32 (td, $J=6.7, 0.8$ Hz, 1H), 6.32 (td, $J=6.7, 0.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.3, 147.4, 147.3, 140.8, 139.7, 139.3, 137.8, 133.5, 129.2, 127.7, 127.3, 126.6, 124.5, 123.4, 123.0, 121.8, 105.9; IR (KBr): 3076, 3038, 2363, 2337, 1661 (C=O), 1585, 1485, 1473 cm^{-1} ; FAB (NBA) 415.1 ($\text{M}^+ + \text{H}$); HRMS calcd for $\text{C}_{29}\text{H}_{22}\text{N}_2\text{O}$ 414.1732, found 414.1735 (M^+). Anal. calcd for $\text{C}_{29}\text{H}_{22}\text{N}_2\text{O}$: C, 84.03; H, 5.35; N, 6.76. Found C, 83.74; H, 5.22; N, 7.08.

2.3.12. 1-(Pyridin-3-yl)-1H-pyridin-2-one (17).²¹ Reaction time: 15 h, tint brown solid (76%). Mp 144–145 °C (from $\text{CH}_2\text{Cl}_2/\text{hexane}=1:10$); ^1H NMR (400 MHz, d_6 -DMSO) δ 8.61–8.63 (m, 2H), 7.91 (d, $J=8.8$ Hz, 1H), 7.71 (dt, $J=6.8, 0.8$ Hz, 1H), 7.50–7.57 (m, 2H), 6.51 (d, $J=8.8$ Hz, 1H), 6.35 (t, $J=6.8$ Hz, 1H); ^{13}C NMR (100 MHz, d_6 -DMSO) δ 160.8, 148.7, 147.2, 140.8, 138.5, 137.0,

134.4, 123.6, 120.3, 105.8; IR (KBr): 3063, 3012, 2363, 2337, 1661 (C=O), 1573, 1535 cm^{-1} ; FAB (NBA) 173.1 ($\text{M}^+ + \text{H}$); HRMS calcd for $\text{C}_{10}\text{H}_9\text{N}_2\text{O}$ 173.0715, found 173.0712 ($\text{M}^+ + \text{H}$). Anal. calcd for $\text{C}_{10}\text{H}_8\text{N}_2\text{O}$: C, 69.76; H, 4.68; N, 16.27. Found C, 69.63; H, 4.60; N, 15.97.

2.3.13. 1-(6-(2-Oxopyridin-1(2H)-yl)pyridin-2-yl)pyridin-2(1H)-one (18). Reaction time: 4 h, white solid (65%). Mp 176–177 °C (from $\text{CH}_2\text{Cl}_2/\text{hexane} = 1:10$); ^1H NMR (400 MHz, CDCl_3) δ 7.89–7.97 (m, 3H), 7.79 (dd, $J = 6.8, 2$ Hz, 2H), 7.36 (ddd, $J = 9.2, 6.8, 2$ Hz, 2H), 6.60 (d, $J = 9.2$ Hz, 2H), 6.25 (t, $J = 6.8$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.7, 150.6, 140.1, 139.3, 135.6, 121.9, 120.4, 106.3; IR (KBr): 3100, 3051, 2363, 2337, 1673 (C=O), 1599, 1573, 1535 cm^{-1} ; FAB (NBA) 266.0 ($\text{M}^+ + \text{H}$); HRMS calcd for $\text{C}_{15}\text{H}_{12}\text{N}_3\text{O}_2$ 266.0930, found 266.0922 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}_2$ 265.0851, found 265.0848 (M^+). Anal. calcd for $\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}_2$: C, 67.92; H, 4.18; N, 15.84. Found C, 67.66; H, 4.09; N, 15.68.

2.3.14. 1-(Thiazol-2-yl)-1H-pyridin-2-one (19). Reaction time: 14 h, tint yellow solid (33%). Mp 85.5–86 °C (from $\text{CH}_2\text{Cl}_2/\text{hexane} = 1:15$); ^1H NMR (400 MHz, d_6 -DMSO) δ 8.76 (ddd, $J = 7.6, 2, 0.8$ Hz, 1H), 7.77 (d, $J = 3.2$ Hz, 1H), 7.59–7.64 (m, 2H), 6.73 (dd, $J = 8, 0.8$ Hz, 1H), 6.58 (td, $J = 7.6, 0.8$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.1, 155.7, 139.3, 137.5, 131.6, 121.2, 118.4, 107.2; IR (KBr): 3114, 3068, 2357, 2335, 1670 (C=O), 1599, 1541, 1495 cm^{-1} ; FAB (NBA) 179.0 ($\text{M}^+ + \text{H}$); HRMS calcd for $\text{C}_8\text{H}_7\text{N}_2\text{OS}$ 179.0279, found 179.0282 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_8\text{H}_6\text{N}_2\text{OS}$ 178.0201, found 178.0204 (M^+). Anal. calcd for $\text{C}_8\text{H}_6\text{N}_2\text{OS}$: C, 53.92; H, 3.39; N, 15.72; S, 17.99. Found C, 53.97; H, 3.40; N, 15.59; S, 17.67.

2.3.15. 1-(Thiophen-3-yl)-1H-pyridin-2-one (20).¹⁷ Reaction time: 22 h, brown solid (74%). Mp 116–117 °C (from $\text{CH}_2\text{Cl}_2/\text{hexane} = 1:15$); ^1H NMR (400 MHz, d_6 -DMSO) δ 7.75 (dd, $J = 3.2, 1.4$ Hz, 1H), 7.70 (dd, $J = 6.8, 2.4$ Hz, 1H), 7.62 (dd, $J = 5.2, 3.2$ Hz, 1H), 7.47 (ddd, $J = 9.2, 6.8, 2.4$ Hz, 1H), 7.28 (dd, $J = 5, 1.4$ Hz, 1H), 6.47 (d, $J = 9.2$ Hz, 1H), 6.29 (td, $J = 6.8, 1.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.8, 139.4, 138.6, 137.4, 125.4, 124.8, 121.8, 119.6, 106.0; IR (KBr): 3112, 3066, 2361, 2333, 1661 (C=O), 1583, 1515 cm^{-1} ; FAB (NBA) 178.0 ($\text{M}^+ + \text{H}$); HRMS calcd for $\text{C}_9\text{H}_8\text{NOS}$ 178.0327, found 178.0326 ($\text{M}^+ + \text{H}$). Anal. calcd for $\text{C}_9\text{H}_7\text{NOS}$: C, 60.99; H, 3.98; N, 7.90; S, 18.09. Found C, 61.00; H, 3.95; N, 7.83; S, 18.15.

2.3.16. 1-(3-Nitrophenyl)-1H-pyridin-2-one (21).²² Reaction time: 15 h, tint yellow solid (62%). Mp 185–186 °C (from $\text{CH}_2\text{Cl}_2/\text{hexane} = 1:10$); ^1H NMR (400 MHz, CDCl_3) δ 8.27–8.27 (m, 2H), 7.79 (dt, $J = 8, 1.6$ Hz, 1H), 7.67 (t, $J = 8$ Hz, 1H), 7.43 (ddd, $J = 9.2, 6.6, 2.4$ Hz, 1H), 7.33 (dd, $J = 6.6, 1.6$ Hz, 1H), 6.67 (d, $J = 9.2$ Hz, 1H), 6.30 (t, $J = 6.6$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.7, 148.4, 141.4, 140.3, 136.7, 132.8, 130.0, 123.2, 122.1, 121.9, 106.7; IR (KBr): 3080, 3023, 2361, 2333, 1671 (C=O), 1593, 1525 cm^{-1} ; FAB (NBA) 217.0 ($\text{M}^+ + \text{H}$); HRMS calcd for $\text{C}_{11}\text{H}_9\text{N}_2\text{O}_3$ 217.0613, found 217.0612 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_{11}\text{H}_8\text{N}_2\text{O}_3$ 216.0535, found 216.0534 (M^+). Anal. calcd for $\text{C}_{11}\text{H}_8\text{N}_2\text{O}_3$: C, 61.11; H, 3.73; N, 12.96. Found C, 61.30; H, 3.79; N, 12.88.

2.3.17. 1-(4-(Methylthio)phenyl)-1H-pyridin-2-one (22). Reaction time: 5 h, white solid (80%). Mp 141–142 °C (from $\text{CH}_2\text{Cl}_2/\text{hexane} = 1:10$); ^1H NMR (400 MHz, d_6 -DMSO) δ 7.60 (dd, $J = 6.6, 2$ Hz, 1H), 7.48 (ddd, $J = 9.2, 6.6, 2$ Hz, 1H), 7.30–7.38 (m, 4H), 6.45 (d, $J = 9.2$ Hz, 1H), 6.29 (td, $J = 6.6, 1.2$ Hz, 1H), 2.5 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.0, 139.6, 139.1, 137.6, 137.4, 126.6, 126.5, 121.5, 105.8, 15.7; IR (KBr): 3046, 2980, 2922, 2361, 2342, 1660 (C=O), 1591, 1525, 1487 cm^{-1} ; FAB (NBA) 218.0 ($\text{M}^+ + \text{H}$); HRMS calcd for $\text{C}_{12}\text{H}_{12}\text{NOS}$ 218.0640, found 218.0642 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_{12}\text{H}_{11}\text{NOS}$ 217.0561, found 217.0554 (M^+). Anal. calcd for $\text{C}_{12}\text{H}_{11}\text{NOS}$: C, 66.33; H, 5.10; N, 6.45; S, 14.76. Found C, 66.36; H, 4.96; N, 6.40; S, 14.91.

2.3.18. 5-Nitro-1-phenyl-1H-pyridin-2-one. Reaction time: 16 h, tint yellow solid (3%). Mp 169.5–170 °C (from $\text{CH}_2\text{Cl}_2/\text{hexane} = 1:10$); ^1H NMR (400 MHz, CDCl_3) δ 8.64 (d, $J = 3.2$ Hz, 1H), 8.14 (dd, $J = 10.4, 3.2$ Hz, 1H), 7.47–7.56 (m, 3H), 7.36–7.39 (m, 2H), 6.64 (d, $J = 10.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.9, 139.6, 139.0, 133.3, 130.8, 129.64, 129.61, 126.1, 120.3; IR (KBr): 3085, 2361, 2333, 1667 (C=O), 1621, 1553, 1497, 1450 cm^{-1} ; FAB (NBA) 217.0 ($\text{M}^+ + \text{H}$); HRMS calcd for $\text{C}_{11}\text{H}_9\text{N}_2\text{O}_3$ 217.0613, found 217.0613 ($\text{M}^+ + \text{H}$), calcd for $\text{C}_{11}\text{H}_8\text{N}_2\text{O}_3$ 216.0535, found 216.0530 (M^+). Anal. calcd for $\text{C}_{11}\text{H}_8\text{N}_2\text{O}_3$: C, 61.11; H, 3.73; N, 12.96. Found C, 60.91; H, 3.76; N, 12.62.

2.3.19. 2-tert-Butoxy-5-bromopyridine (26). To an oven-dried 100 mL double-necked flask was charged a solution of 2,5-dibromopyridine (4.90 g, 21 mmol) and sodium *tert*-butoxide (3.25 g, 30 mmol) in toluene (30 ml). The reaction mixture was stirred and heated at reflux temperature for 2.5 h. The resulting suspension was cooled to room temperature and filtered through celite. The collected organic phase was concentrated, and purified by flash chromatography on silica gel (hexane/dichloromethane) to give colorless liquid (2.65 g, 56%). Note that the compound is a slightly hygroscopic liquid and should be distilled before use. Bp 70 °C (0.15 mmHg). ^1H NMR (400 MHz, d_6 -DMSO) δ 8.20 (d, $J = 2.4$ Hz, 1H), 7.80 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.66 (d, $J = 8.8$ Hz, 1H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.4, 146.8, 140.5, 114.9, 111.2, 80.2, 28.6; IR (neat): 2980, 2933, 2353, 2343, 1573, 1545, 1459, 1363 cm^{-1} ; HRMS (EI, 70 eV) calcd for $\text{C}_9\text{H}_{12}\text{BrNO}$ 229.0102, found 229.0097 (M^+). Anal. calcd for $\text{C}_9\text{H}_{12}\text{BrNO}$: C, 46.98; H, 5.26; N, 6.09. Found C, 46.93; H, 5.41; N, 5.93.

2.3.20. 1-(6-tert-Butoxypyridin-3-yl)-1H-pyridin-2-one (27). To an oven-dried 25 mL double-necked flask was charged 2-hydroxypyridine (1.26 g, 13.2 mmol), CuI (20 mol%), and K_2CO_3 (2 equiv). The flask was evacuated and backfilled with nitrogen. A solution of 2-*tert*-butoxy-5-bromopyridine (3.03 g, 13.2 mmol) in toluene (13.2 mL) and DMCA (20 mol%) were injected under nitrogen. The reaction mixture was stirred and heated at reflux temperature for 11 h. The resulting mixture was cooled to room temperature, diluted with dichloromethane, and filtered. The filtrate was washed with water. The collected organic phase was dried over anhydrous MgSO_4 and concentrated. The crude product was purified by flash chromatography on

silica gel (ethyl acetate/dichloromethane) to give white solid (2.03 g, 63%). Mp 188–189 °C (from CH₂Cl₂/hexane = 1:10); ¹H NMR (400 MHz, d₆-acetone) δ 8.14 (d, *J* = 2.8 Hz, 1H), 7.71 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.57 (ddd, *J* = 6.8, 2, 0.8 Hz, 1H), 7.47 (ddd, *J* = 9.2, 6.8, 2 Hz, 1H), 6.75 (d, *J* = 9.2 Hz, 1H), 6.45 (dt, *J* = 9.2, 0.8 Hz, 1H), 6.28 (td, *J* = 6.8, 1.2 Hz, 1H), 1.60 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 163.1, 162.2, 143.1, 139.9, 137.8, 136.5, 130.6, 121.5, 113.1, 106.0, 80.3, 28.6; IR (KBr): 3047, 2971, 2923, 2361, 2333, 1667 (C=O), 1583, 1535, 1477 cm⁻¹; FAB (NBA) 245.1 (M⁺ + H); HRMS calcd for C₁₄H₁₇N₂O₂ 245.1290, found 245.1289 (M⁺ + H). Anal. calcd for C₁₄H₁₆N₂O₂: C, 68.83; H, 6.60; N, 11.47. Found C, 68.77; H, 6.82; N, 11.40.

2.3.21. 1-(6-Hydroxypyridin-3-yl)-1*H*-pyridin-2-one (28). To an oven-dried 25 mL flask was charged 1-(6-*tert*-butoxypyridin-3-yl)pyridin-2(1*H*)-one (0.75 g, 3.06 mmol), CH₂Cl₂ (15 mL), and TFA (5%). The reaction mixture was stirred and heated at reflux temperature for 1 h. The resulting solution was concentrated and washed with hexane to give white solid. Note that this compound is hygroscopic and soluble in water. Normal extraction workup procedure is inappropriate in this case. The white solid was dried under vacuum at 110 °C for overnight to afford 0.57 g, 99% yield of **28**. Mp 284–285 °C (from CH₂Cl₂/hexane = 1:5); ¹H NMR (400 MHz, d₆-DMSO) δ 12.07 (bs, 1H), 7.60–7.63 (m, 2H), 7.44–7.51 (m, 2H), 6.44 (d, *J* = 9.6 Hz, 1H), 6.40 (d, *J* = 10 Hz, 1H), 6.26 (td, *J* = 6.8, 1.2 Hz, 1H); ¹³C NMR (100 MHz, d₆-DMSO) δ 161.3, 161.2, 140.6, 140.5, 139.4, 133.7, 121.7, 121.0, 118.6, 105.5; IR (KBr): 3446, 3140, 3065, 2799, 2353, 1677 (C=O), 1621, 1583, 1525, 1469 cm⁻¹; FAB (NBA) 189.1 (M⁺ + H); HRMS calcd for C₁₀H₉N₂O₂ 189.0664, found 189.0667 (M⁺ + H), calcd for C₁₀H₈N₂O₂ 188.0586, found 188.0587 (M⁺). Anal. calcd for C₁₀H₈N₂O₂: C, 63.82; H, 4.28; N, 14.89. Found C, 63.41; H, 4.57; N, 15.01.

2.3.22. 1-(1-(6-*tert*-Butoxypyridin-3-yl)-1,6-dihydro-6-oxopyridin-3-yl)-1*H*-pyridin-2-one (29). To an oven-dried 10 mL double-necked flask containing a stir-bar was charged with 1-(6-hydroxypyridin-3-yl)-1*H*-pyridin-2-one (0.19 g, 1.01 mmol), CuI (20 mol%), and K₂CO₃ (2 equiv). The flask was evacuated and backfilled with nitrogen. A solution of 2-*tert*-butoxy-5-bromopyridine (0.28 g, 1.21 mmol) in toluene (1 mL) and DMCD (20 mol%) were injected under nitrogen. The reaction mixture was stirred and heated at reflux temperature for 12 h. The resulting mixture was cooled to room temperature, diluted with dichloromethane, and filtered. The filtrate was washed with water. The collected organic phase was dried over anhydrous MgSO₄ and concentrated. The crude product was purified by flash chromatography on silica gel (ethyl acetate/dichloromethane/MeOH) to give white solid (0.28 g, 82%). Mp 216–217 °C (from CH₂Cl₂/hexane = 1:10); ¹H NMR (400 MHz, d₆-DMSO) δ 8.22 (d, *J* = 2.8 Hz, 1H), 8.00 (d, *J* = 2.8 Hz, 1H), 7.78 (dd, *J* = 8.8, 2.8 Hz, 1H), 7.73 (dd, *J* = 7.2, 2 Hz, 1H), 7.62 (dd, *J* = 10, 2.8 Hz, 1H), 7.49 (ddd, *J* = 9.2, 6.8, 2 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.53 (d, *J* = 10 Hz, 1H), 6.46 (d, *J* = 9.2 Hz, 1H), 6.29 (td, *J* = 6.8, 1.2 Hz, 1H), 1.60 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 163.4, 162.1, 161.0, 143.2, 140.3, 139.1, 137.3, 136.4, 135.5, 130.0, 122.0, 121.7, 121.5, 113.3, 106.5, 80.6, 28.6;

IR (KBr): 3055, 2970, 2361, 2333, 1679 (C=O), 1661 (C=O), 1619, 1573, 1525, 1463 cm⁻¹; FAB (NBA) 338.2 (M⁺ + H); HRMS calcd for C₁₉H₂₀N₃O₃ 338.1505, found 338.1503 (M⁺ + H), calcd for C₁₉H₁₉N₃O₃ 337.1426, found 337.1439 (M⁺). Anal. calcd for C₁₉H₁₉N₃O₃ C, 67.64; H, 5.68; N, 12.45. Found C, 67.40; H, 5.63; N, 12.59.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2005.01.063

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