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Iron catalysed regioselective direct arylation at C-3 position of *N*-alkyl-2-pyridone

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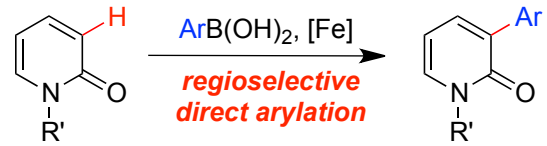


ABSTRACT

A number of pharmaceutical compounds possess arylated-2-pyridone moiety. The existing reports using expensive starting materials and/or superstoichiometric metal salts have prompted us to explore the possible user-friendly method for their synthesis. In this report, we have demonstrated an easy-to-handle reaction condition with iron catalyst for the exclusive generation of C3-arylated pyridone *via* C-H functionalization.

INTRODUCTION

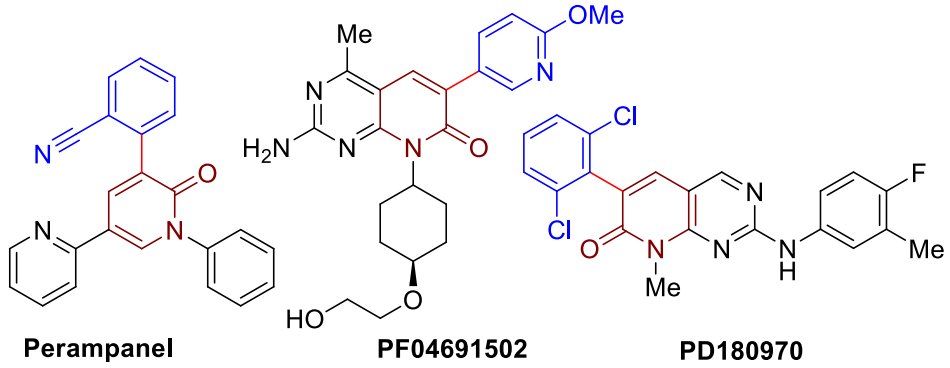
Functionalization of pyridone core has drawn serious attention in recent years primarily due to its presence as building block in a number of pharmaceutical compounds (Figure 1).[1] A

regioselective direct C–H functionalization protocol for the synthesis of pyridine derivatives is preferred over the conventional coupling reaction (*e.g.* Suzuki coupling) as it avoids the use of a pre-functionalized substrate.[2] Recently, direct olefination and arylation at electron rich C-5 position of 2-pyridone were achieved through palladium catalyst.[3, 4] Hiyama group reported direct alkylation and alkenylation at electrophilic C-6 position of 2-pyridone by using nickel catalyst in combination with Lewis acid.[5] Miura and coworkers developed a copper mediated selective C-6 dehydrogenative heteroarylation protocol for 1-(2-pyridyl)-2-pyridone.[6] By blocking C-5 position, C-3 was alkenylated and arylated with structurally biased substrates.[4,7] Very recently Zografos and coworkers reported a palladium catalyzed selective C-3 arylation of *N*-protected pyridone, but scope of the method was limited to only 4-hydoxy-pyridone moiety.[8] Hirano and Miura reported alternative pathways for C-3 alkylation and arylation of 2-pyridone through homolytic radical aromatic substitution (HAS).[9] Although the alkylation at C-3 position was achieved with catalytic amount of nickel,[9a] the C-3 arylation required superstoichiometric amount of manganese salt with boronic acid as the coupling partner.[9b]

Iron catalyzed direct arylation of heterocycles and quinones has recently been reported by Komeyama's group by using arylboronic acids.[10] We have also independently reported similar arylation reactions involving heterocycles and quinones.[11] Unfortunately, when our reaction condition was applied to *N*-methyl-2-pyridone, only 7% arylated pyridone was obtained. Notably, Wunk has recently reported two examples of Pd catalyzed C3-arylated pyridone starting from 3-bromopyridone (Scheme 1).[12] In this work, we demonstrate an easy-to-handle reaction condition for the generation of C3-arylated pyridine exclusively. Notable features of the present methodology include the use of easily available pyridone precursors in combination with iron catalyst under mild reaction protocols.

RESULTS AND DISCUSSION

Figure 1. Drug molecules with 3-aryl-2-pyridone motifs



Initial studies with *N*-methyl-2-pyridone and phenylboronic acid in the presence of $Fe(NO_3)_3/K_2S_2O_8$ in TFT:H_2O (1:1) (TFT = α,α,α-trifluorotoluene) at 70 ºC led to the formation of *only* one pyridone-arylated product (isolated yield, 9%).[13]

Scheme 1. Pathways for C-3 arylation of *N*-alkyl-2-pyridone

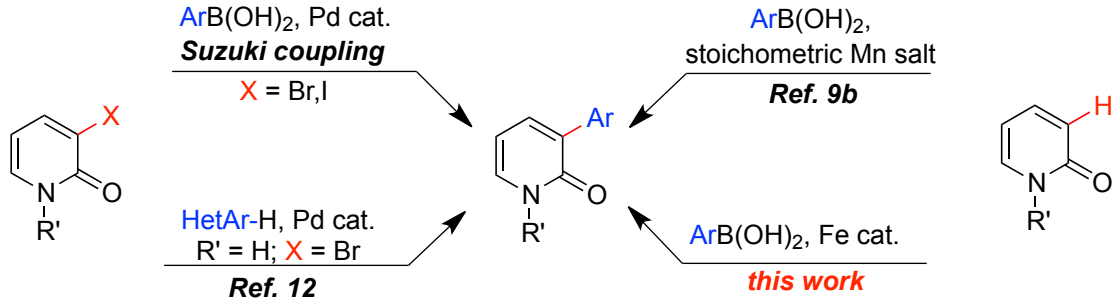
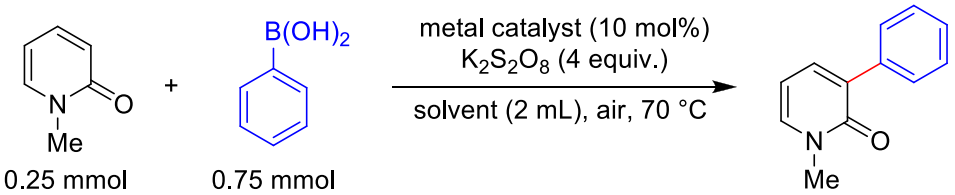


Table 1. C-3 arylation of *N*-methyl-2-pyridone



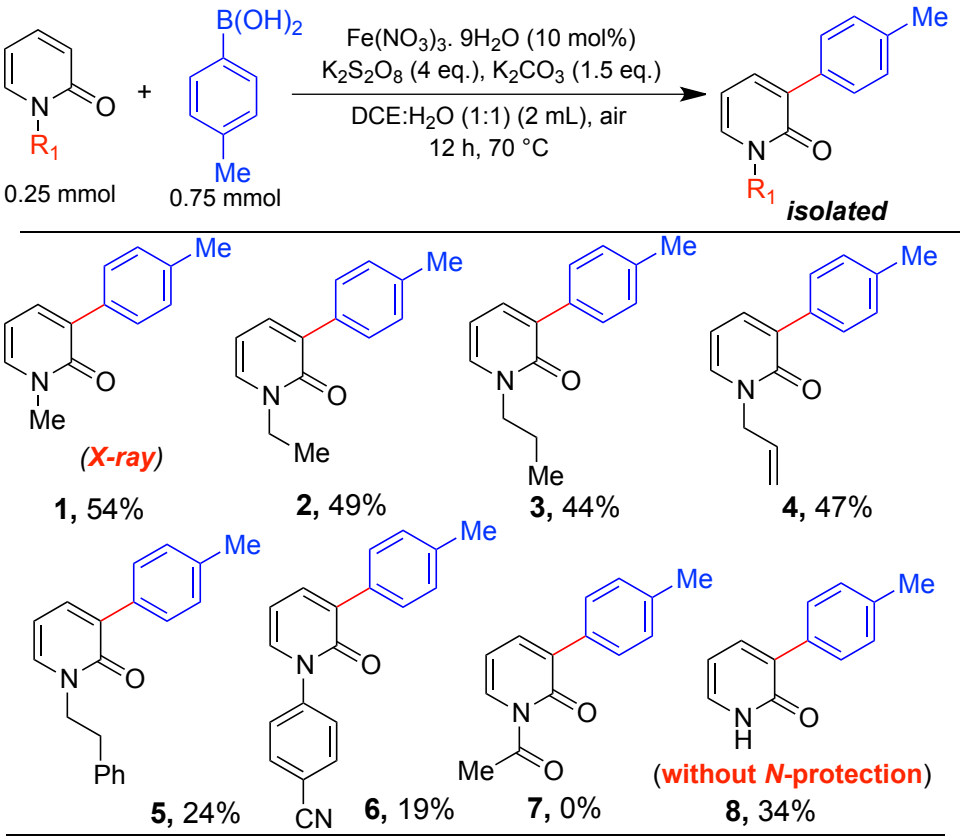
entry	solvent	additive	metal catalyst	time (h)	yield[a] (%)
1	TFT:H_2O (1:1)	TFA	$Fe(NO_3)_3$	24	7
2	TFT:H_2O (1:1)	-	$Fe(NO_3)_3$	24	9
3	DCE:H_2O (1:1)	-	$Fe(NO_3)_3$	24	14
4	DCE:H_2O(1:1)	K_2CO_3	$Fe(NO_3)_3$	24	40
5	DCE:H_2O(1:1)	K_2CO_3	$Fe(NO_3)_3$	24	0*
6	DCE:H_2O (1:1)	K_2CO_3	$Fe(NO_3)_3$	12	40
7	DCE:H_2O(1:1)	K_2CO_3	-	12	22
8	DCE:H_2O(1:1)	K_2CO_3	$AgNO_3$	12	0
9	DCE:H_2O(1:1)	K_2CO_3	$Pd(OAc)_2$	12	<1
10	DCE:H_2O(1:1)	K_2CO_3	$Cu(OAc)_2$	12	13
11	DCE:H_2O(1:1)	K_2CO_3	$Ni(acac)_2$	12	20

*without $K_2S_2O_8$; [a]GC yield.

By NMR and X-ray crystallography (*vide infra*), we confirmed that arylation was occurring at the C-3 position exclusively.[14] These promising initial results had prompted us to explore the reaction with different solvent combinations, iron sources, ligands, additives and bases.[15] A 40% GC yield (isolated, 38%) of C-3 arylated product (Table 1, entry 6) was obtained with $Fe(NO_3)_3.9H_2O/K_2S_2O_8$. The yield of C-3 arylated product, however failed to improve further inspite of our best efforts. Starting materials mostly remained unreacted and homo-coupling of arylboronic acid was obtained as the side product.

The aforesaid optimized reaction protocol was then extended for the reaction of 4-methyl phenylboronic acid (Table 2). Various *N*-alkylated pyridones gave desired arylated product in 44-54% yield (**1**-**3**). By varying the *N*-protecting group from alkyl to allyl, we obtained the C-3 arylated product **4** in 47% yield. In case of *N*-phenethyl-2-pyridone, C3-arylation decreased to 24% (**5**) and *N*-(4-cyanophenyl)-2-pyridone failed to increase the C3-arylation (**6**) as well. Although *N*-acyl-2-pyridone did not deliver any C3-arylation product (**7**), 2-pyridone moiety (without *N*-protection) afforded 34% yield of C-3 arylated product (**8**) selectively.

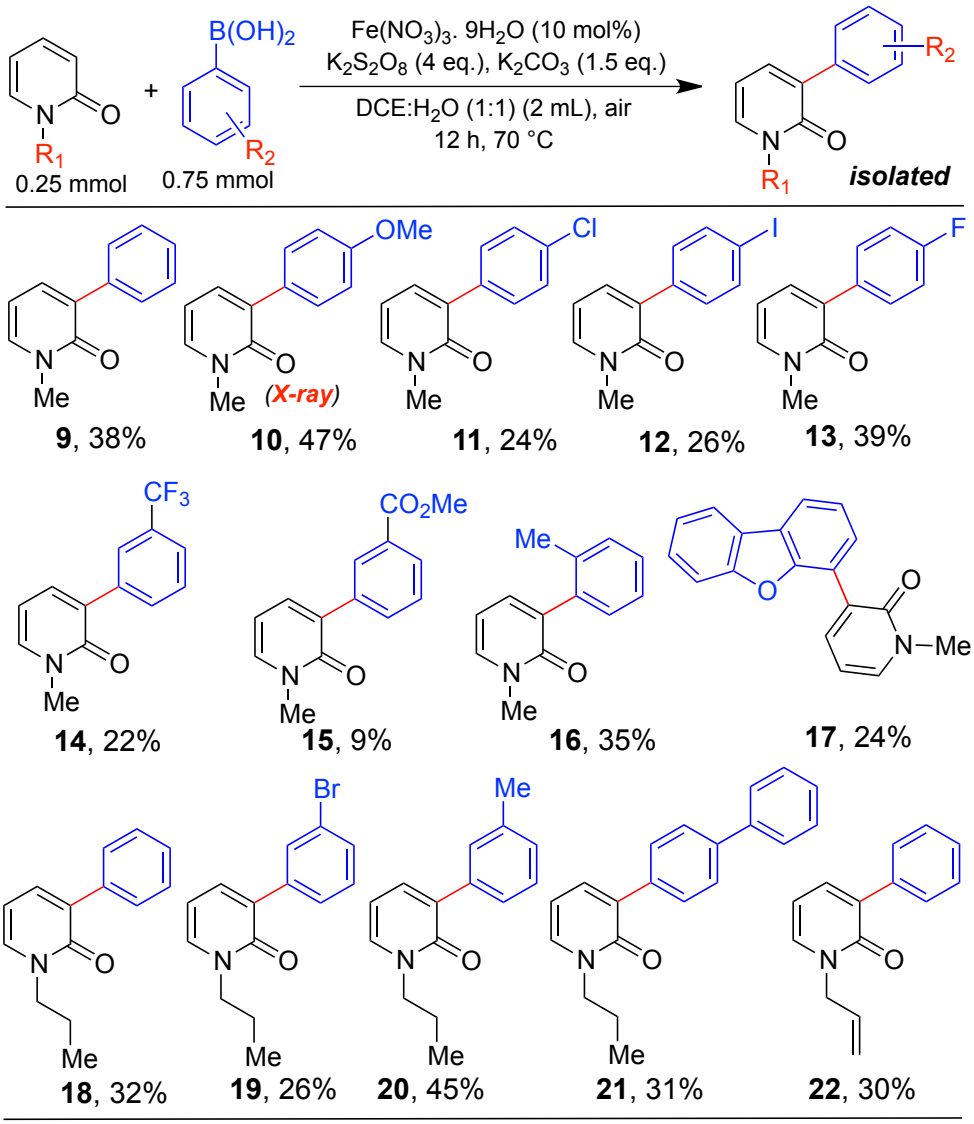
Table 2. C-3 arylation with various *N*-alkyl-2-pyridones



Subsequently, the scope of the selective C-3 arylation on *N*-alkyl-2-pyridone with different arylboronic acids was investigated (Table 3). Electron rich 4-methoxyarylboronic acid provided the desired C-3 arylated product in 47% yield (**10**). Halo-aryl moieties were introduced at the C-

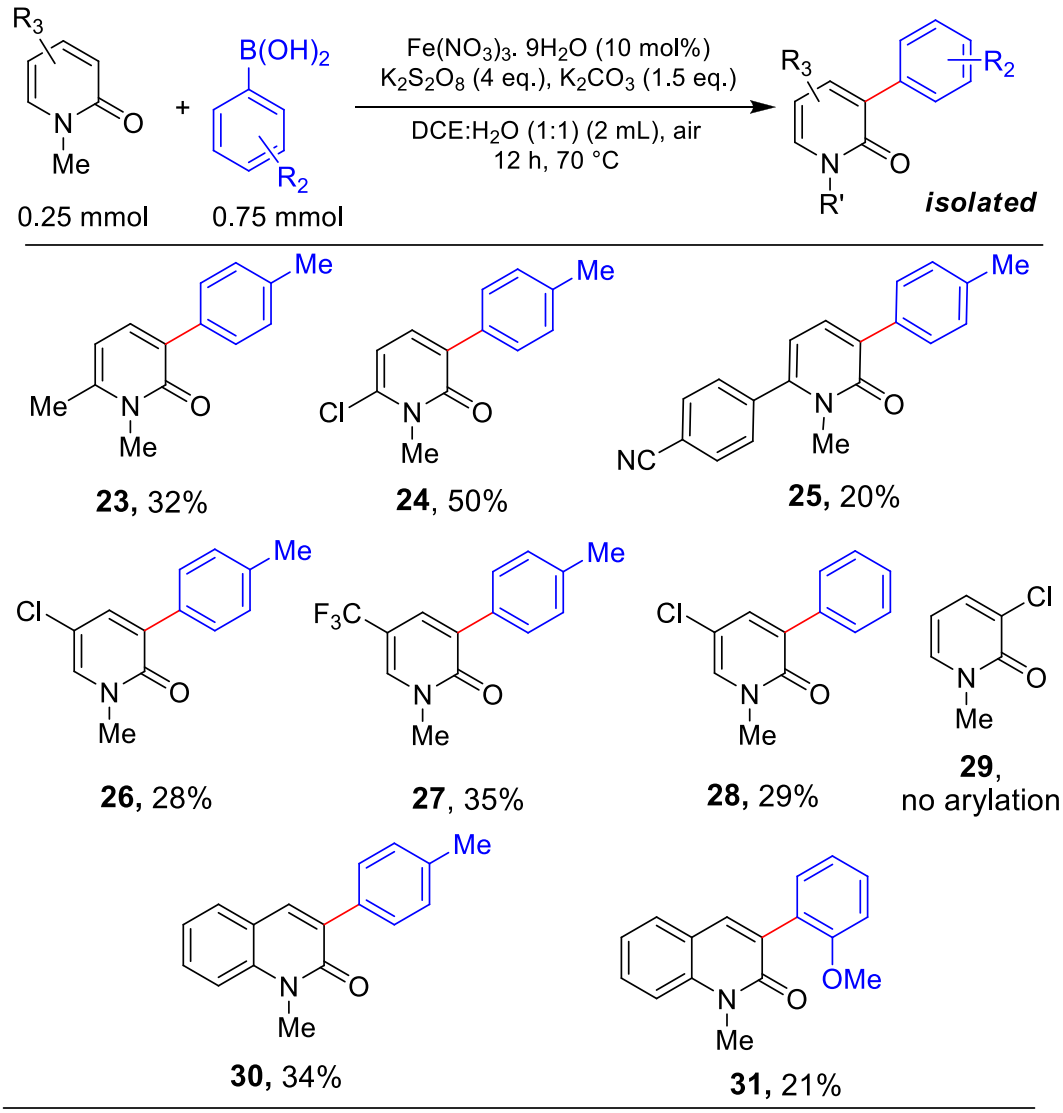
3 position (**11**-**13** and **19**), with the intension of further functionalization. Electron poor boronic acids also afforded arylation exclusively at the C-3 position of pyridone (**13** and **14**). Additionally, sterically constrained *ortho*-tolylboronic acid gave the arylated pyridone **16**. Interestingly, a dibenzofuran moiety can also be coupled at the C-3 position of pyridone using dibenzofuran-4-boronic acid as heterocyclic partner (**17**). Electron-withdrawing arylboronic acids encompassing 4-NO_2, 4-COMe and 4-CO_2Me groups yielded very little C–C coupled product with *N*-methyl-2-pyridone. Nevertheless, 3-(methoxycarbonyl) phenylboronic acid gave the desired product in 9% yield (**15**).

Table 3. C-3 arylation of *N*-alkyl-2-pyridones with arylboronic acids



The applicability of the present method with different functionalized *N*-methyl pyridone entity was also tested (Table 4). The C-6 (**23-25**) and C-5 (**26-28**) substituted *N*-methyl-2-pyridones were successfully arylated. Notably, various chloro substituted pyridones could be employed for C-3 arylation (**24**, **26** and **28**). Expectedly, methylquinolin-2(1H)-one moieties was arylated at the desired C-3 position (**30-31**).

Table 4 C-3 arylation of substituted *N*-methyl-2-pyridones



Furthermore, a 10 mmol scale reaction under reflux conditions afforded the product in 35% yield (Scheme 2; also see Table 3, entry **9**). Anti-inflammatory agent 1-methyl-3-phenylpiperidin-2-one (**32**) was successfully prepared after hydrogenation of **9** (Scheme 2).[15] We have also synthesized 3-(2-methoxyphenyl)quinolin-2(1H)-one (**33**, Scheme 2), which can be further utilized as the precursor in generating pharmaceutically relevant benzofuro[*2,3-b*]quinoline moiety through successive cyclization reaction.[16]

Scheme 2. Large scale reaction and application in pharmaceutically relevant scaffolds

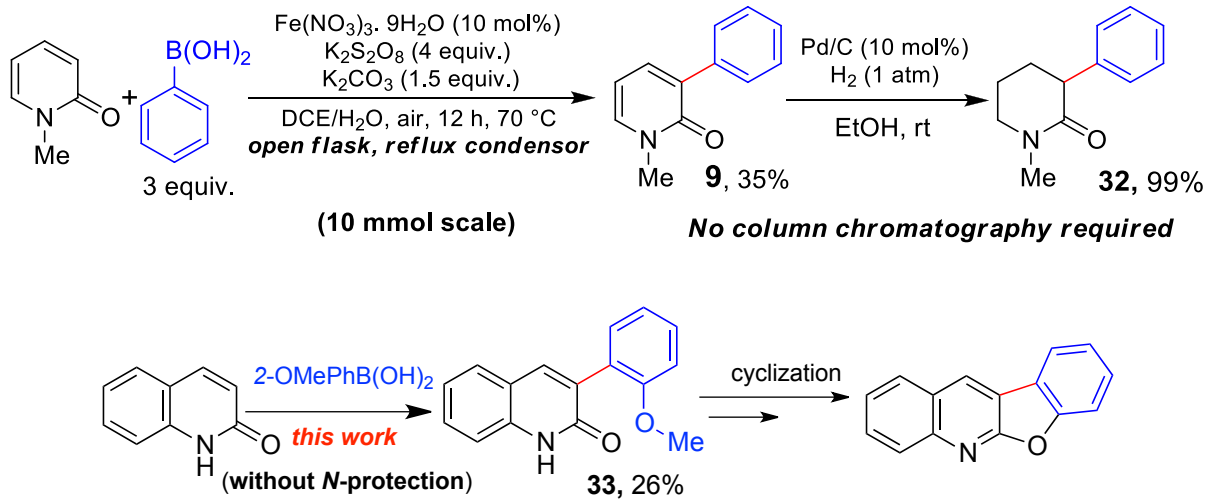
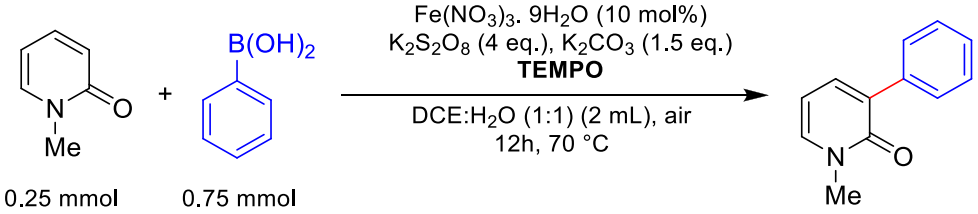


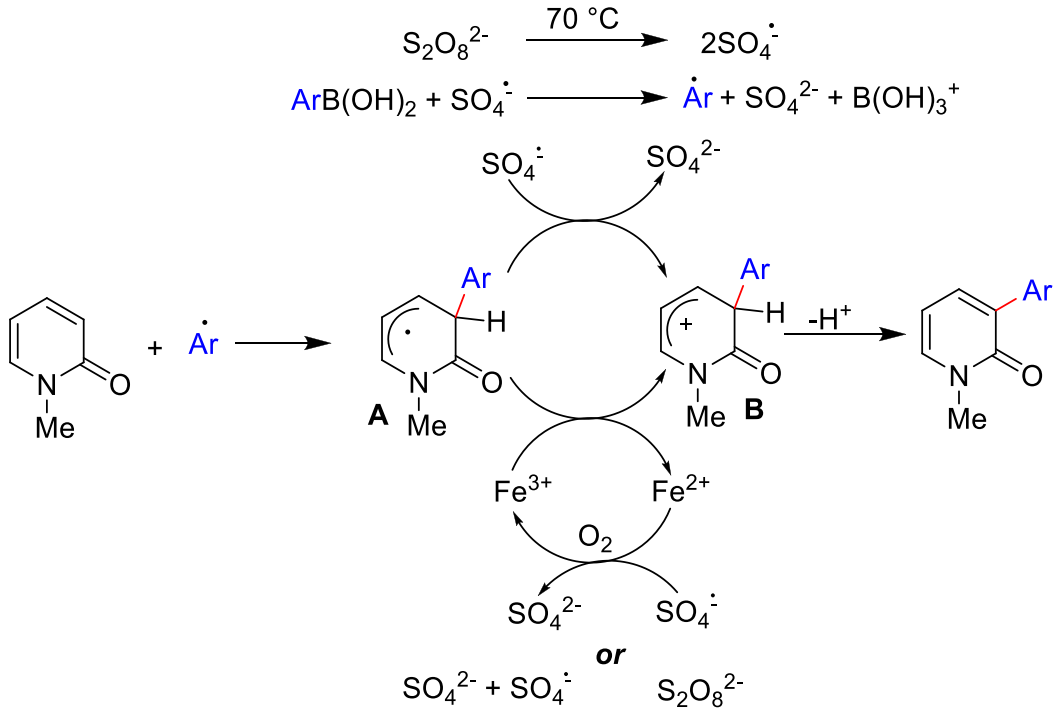
Table 5. Radical scavenger experiments



Entry	Radical Scavenger	Isolated Yield (%)
1	No Scavenger	40%
2	TEMPO (1 equiv)	5%

In order to derive mechanistic insights, the standardized reaction was tested in the presence of TEMPO (2,2,6,6-tetramethylpiperidinyloxy) as the radical scavenger. With stoichiometric amount of TEMPO, yield of the desired arylated product was reduced to 5%, implying the involvement of radical intermediate under the present reaction conditions. However, when we tested a reaction with Bu_3SnPh in place of arylboronic acid, we failed to detect any arylated pyridone product.

Scheme 3. Proposed mechanism for C-3 arylation of 2-pyridone



Based on the literature reports as well as our experimental observations, it is proposed that $K_2S_2O_8$ thermally[17] or in presence of iron (II)[10a,18] decomposes to sulphate radical ($SO_4^{\cdot-}$) which reacts with arylbronic acid to give aryl radical.[19] Subsequently, aryl radical reacts selectively at the C-3 position of 2-pyridone moiety.[9,20] This is likely since C-3 atom possesses a large coefficient of HOMO and LUMO and leading to a resonance stabilized radical adduct **A**.[9] Iron(III)[21] or sulphate radical accepts one electron from **A** (Scheme 5) to make a cationic species **B**,[10c, 21-22] which facilitates the regaining of aromaticity, resulting in the desired C-3 arylated *N*-protected-2-pyridone compound.[9] Under aerobic condition (or in the presence of sulphate radical/persulphate dianion), Fe(II) oxidizes to Fe(III). Therefore, iron may function both as a Lewis acid[19d] and an electron transfer site.

The present iron catalyzed method is compatible with electron rich arylboronic acid. Such an observation is complementary to the findings by Hirano and Miura's C-3 arylation of *N*-protected-2-pyridone with *superstoichiometric* managanese.[9b] The manganese promoted

reaction gave better yields with electron poor arylboronic acids (44-58%) compared to the electron rich analogues (28%). Additionally, the present iron catalyzed protocol can be employed to unprotected 2-pyridone moiety.

CONCLUSION

A direct C-3 arylation of unbiased *N*-alkyl-2-pyridone moiety with environmentally benign and abundant iron catalyst has been developed. A radical mechanism has been proposed based on preliminary studies. This Fe-catalyzed method is expected to be applicable in synthetic chemistry due to its simplicity and easy to handle procedure.

EXPERIMENTAL SECTION

General Procedure A for Iron Catalyzed Direct Arylation of N-protected 2-pyridone with Arylboronic acid. In clean oven-dried screw cap reaction tube charged with magnetic stir-bar, pyridone (0.25 mmol), arylboronic acid (0.75 mmol), $K_2S_2O_8$ (1 mmol, 270 mg), K_2CO_3(0.375 mmol, 52 mg) and $Fe(NO_3)_3.9H_2O$ (0.025 mmol, 10 mg) were taken. 1mL DCE and 1 mL H_2O were added to it. Then the reaction tube was placed on a preheated oil bath at 70˚C. The reaction mixture was stirred at that temperature for 12 h. After cooling the reaction mixture, 2 (N) HCl solution was added dropwise added to neutralize the reaction mixture. After that 5 mL of ethyl acetate was added to the reaction mixture and another 5 mL of ethyl acetate was used for washing the reaction tube. The organic portion was separated by separating funnel and dried over anhyd. Na_2SO_4. Then, the organic solution was concentrated in rotary evaporator and the desired product was purified through neutral aluminium oxide using petroleum ether-ethyl acetate mixture as eluent.

1-Methyl-3-p-tolylpyridin-2(1H)-one (1). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***1*** (27 mg, 54%)

as crystalline solid. m.p 130-133°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.60 (s, 3H), 6.23 (t, *J* = 6.8 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 2H), 7.28 (dd, *J* = 6.8, 2.1 Hz, 1H), 7.46 (dd, *J* = 7.0, 2.1 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 2H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 21.4, 38.4, 106.1, 128.6, 129.0, 131.7, 134.1, 137.3, 137.4, 137.6, 162.2; HRMS (ESI-QTOF) m/z: $[M+K]^+$ calcd.for $C_{13}H_{13}KNO$: 238.0629, found: 238.0625.

1-Ethyl-3-p-tolylpyridin-2(1H)-one (2). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***2*** (26 mg, 49%) as white solid. m.p 81-84°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (t, *J* = 7.2 Hz, 3H), 2.36 (s, 3H), 3.04 (q, *J* = 7.2 Hz, 2H), 6.24 (t, *J* = 6.8 Hz, 1H), 7.20 (d, *J* = 6.8 Hz, 2H), 7.27 (dd, 6.9, 2.1 Hz, 1H), 7.44 (dd, *J* = 6.9, 2.1 Hz, 1H), 7.59 (d, *J* = 6.8 Hz, 2H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 14.8, 21.4, 45.6, 106.2, 128.7, 128.9, 131.9, 134.2, 136.1, 137.1, 137.5, 161.4; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd.for $C_{14}H_{15}NNaO$: 236.1046, found: 236.1046.

1-Propyl-3-p-tolylpyridin-2(1H)-one (3). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***3*** (25 mg, 44%) as brown oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, *J* = 7.4 Hz, 3H), 1.82 (q, *J* = 7.4 Hz, 2H), 2.36 (s, 3H), 3.87 – 4.05 (m, 2H), 6.22 (t, *J* = 6.8 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 2H), 7.25 (dd, *J* = 7.2, 2.6 Hz, 1H), 7.45 (dd, *J* = 6.9, 2.1 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 2H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 11.4, 21.4, 22.6, 52.3, 105.9, 128.7, 128.9, 131.9, 134.2, 136.7, 137.1, 137.5, 161.6. HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd.for $C_{15}H_{17}NNaO$: 250.1202, found: 250.1203.

1-Allyl-3-p-tolylpyridin-2(1H)-one (4). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***4*** (26 mg, 47%) as brown oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 4.63 (dt, *J* = 5.9, 1.5 Hz, 2H),

5.20 – 5.32 (m, 2H), 6.00 (m, 1H), 6.26 (t, *J* = 6.8 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.25 (dd, *J* = 7.1, 2.1 Hz, 1H), 7.46 (dd, *J* = 6.9, 2.1 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 2H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 21.4, 51.9,106.2, 118.7, 128.7, 129.0, 132.1, 132.9, 134.1, 136.1, 137.3, 137.7, 161.5; HRMS (ESI-QTOF) m/z: $[M+K]^+$: calcd.for $C_{15}H_{15}KNO$: 264.0785, found: 264.0783.

1-Phenethyl-3-p-tolylpyridin-2(1H)-one (5). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***5*** (17 mg, 24%) as oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.10 (t, *J* = 7.3 Hz, 2H), 4.20 (t, *J* = 7.2 Hz, 2H), 6.12 (t, *J* = 6.8 Hz, 1H), 6.97 (dd, *J* = 6.7, 2.1 Hz, 1H), 7.15 – 7.35 (m, 7H), 7.45 (dd, *J* = 7.0, 2.1 Hz, 1H), 7.61 (d, *J* = 8.0, 2H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 21.4, 35.3, 53.0, 105.8, 126.8, 128.7, 128.8, 129.0, 129.2, 132.0, 134.1, 136.9, 137.4, 137.7, 138.4, 161.6; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd.for $C_{20}H_{19}NNaO$: 312.1359, found: 312.1359.

4-(2-Oxo-3-p-tolylpyridin-1(2H)-yl)benzonitrile (6). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***6*** (13 mg, 19%) as cryatalline solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 6.40 (t, *J* = 6.9 Hz, 1H), 7.18 – 7.24 (m, 2H), 7.30 (dd, *J* = 6.9, 2.0 Hz, 1H), 7.47 – 7.66 (m, 5H), 7.72 – 7.87 (m, 2H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 21.5, 107.1, 112.5, 118.2, 128.0, 128.7, 129.1, 133.3, 133.3, 133.4, 135.7, 137.9, 138.3, 145.1, 161.3; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd.for $C_{19}H_{14}N_2NaO$: 309.0998, found: 309.1000.

3-p-Tolylpyridin-2(1H)-one (8). The title compound was purified by column chromatography (Silica gel mesh 60-180, ethyl acetate/petroleum ether (50:50 v/v) to get ***8*** (16 mg, 34%) as brown solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 6.39 (t, *J* = 6.7 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 2H), 7.37 (dd, *J* = 6.4, 2.0 Hz, 1H), 7.58 (dd, *J* = 8.5, 6.4 Hz, 3H); $^{13}C\{^{1}H\}$NMR (101 MHz,

$CDCl_3$) δ 21.5, 107.9, 128.6, 129.2, 131.7, 133.5, 133.7, 138.0, 139.9, 163.9; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd.for $C_{12}H_{11}NNaO$: 208.0733, found 208.0732.

1-Methyl-3-phenylpyridin-2(1H)-one (9). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***7*** (17 mg, 38%) as cryatalline solid. m.p 128-131°C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.62 (s, 3H), 6.26 (t, *J* = 6.8 Hz, 1H), 7.30 – 7.35 (m, 2H), 7.38 – 7.43 (m, 2H), 7.49 (dd, *J* = 7.0, 2.1 Hz, 1H), 7.65 – 7.75 (m, 2H); $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 38.4, 106.0, 127.8, 128.3, 128.8, 131.8, 137.0, 137.6, 137.8, 162.1; HRMS (ESI-QTOF) m/z: $[M+H]^+$: calcd.for $C_{12}H_{11}NO$: 186.0919, found: 186.0915.

3-(4-Methoxyphenyl)-1-methylpyridin-2(1H)-one (10). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (10:90 v/v) to get ***8*** (25 mg, 47%) as cryatalline solid. ^1H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 3.84 (s, 3H), 6.24 (t, *J* = 6.8 Hz, 1H), 6.90 – 6.97 (m, 2H), 7.27 (dd, *J* = 6.6, 2.2 Hz, 1H), 7.45 (dd, *J* = 7.0, 2.1 Hz, 1H), 7.62 – 7.72 (m, 2H); $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 38.7, 55.5, 106.1, 113.7, 129.5, 130.0, 131.4, 136. 9, 137.0, 159.4, 162.3; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd.for $C_{13}H_{13}NNaO_2$: 238.0838, found: 238.0834.

3-(4-Chlorophenyl)-1-methylpyridin-2(1H)-one (11). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (12:88 v/v) to get ***9*** (13 mg, 24%) as white solid. m.p 139-143°C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 6.25 (t, *J* = 6.9 Hz, 1H), 7.28 – 7.40 (m, 3H), 7.47 (dd, *J* = 7.0, 2.1 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H); $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 38.5, 106.1, 128.4, 130.1, 130.5, 133.7, 135.4, 137.8, 137.9, 161.9. HRMS (ESI-QTOF) m/z: $[M+K]^+$: calcd.for $C_{12}H_{10}ClKNO$: 258.0082, found: 258.0082.

3-(4-Iodophenyl)-1-methylpyridin-2(1H)-one (12). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (12:88 v/v) to get ***10*** (20 mg, 26%) as yellowish-white solid. m.p 144-147°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.59 (s, 3H), 6.23 (t, *J* = 6.8 Hz, 1H), 7.31 (dd, *J* = 6.7, 2.1 Hz, 1H), 7.38 – 7.50 (m, 3H), 7.70 (d, *J* = 8.4 Hz, 2H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 38.4, 93.6, 106.0, 130. 4, 130.6, 136.4, 137.3, 137.7, 138.0, 161.7; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd.for $C_{12}H_{10}INNaO$: 333.9699, found: 333.9698.

3-(4-Fluorophenyl)-1-methylpyridin-2(1H)-one (13). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (14:86 v/v) to get ***11*** (20 mg, 39%) as brown oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 6.25 (t, *J* = 6.8 Hz, 1H), 7.01 – 7.13 (m, 2H), 7.31 (dd, *J* = 6.7, 2.1 Hz, 1H), 7.46 (dd, *J* = 7.0, 2.1 Hz, 1H), 7.63 – 7.72 (m, 2H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 38.5, 106.1, 115.2 (d, *J* = 21.4 Hz), 130.5, 130.6, 130.8, 133.0, 137.7, 162.1, 162.6 (d, *J* = 245 Hz); ^{19}F NMR (376 MHz, $CDCl_3$, proton coupled) δ -114.51 (tt, *J* = 8.7, 5.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$, proton decoupled) δ -114.51; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd.for $C_{12}H_{10}FNNaO$: 226.0639, found: 226.0635.

1-Methyl-3-(3-(trifluoromethyl)phenyl)pyridin-2(1H)-one (14). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (16:84 v/v) to get ***12*** (14 mg, 22%) as brown oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 (s, 3H), 6.29 (t, *J* = 6.9 Hz, 1H), 7.37 (dd, *J* = 6.7, 2.1 Hz, 1H), 7.47 – 7.61 (m, 3H), 7.91 (d, *J*= 7.7 Hz, 1H), 7.96 (s, 1H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 38.5, 106.1, 123.1, 124.5, 124.6, 125.6, 125.6, 128.7, 130.3, 132.1, 137.7, 138. 3, 138.4, 161. 9; ^{19}F NMR (376 MHz, $CDCl_3$, proton coupled) δ

-62.52 (t, J = 11.3 Hz); $^{19}F\{^{1}H\}$NMR (376 MHz, $CDCl_3$, proton decoupled) δ -62.52; HRMS (ESI-QTOF) m/z: $[M+K]^+$: calcd.for $C_{13}H_{10}F_3KNO$: 292.0346, found:292.0345.

Methyl 3-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)benzoate (15). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (17:83 v/v) to get ***15*** (5 mg, 9%) as brown oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (t, J = 1.6 Hz, 1H), 8.08 – 7.89 (m, 2H), 7.55 (dd, J = 7.0, 2.0 Hz, 1H), 7.47 (t, J = 7.8 Hz, 1H), 7.34 (dd, J = 6.7, 2.0 Hz, 1H), 6.28 (t, J = 6.9 Hz, 1H), 3.92 (s, 3H), 3.62 (d, J = 7.2 Hz, 3H); HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd.for $C_{14}H_{13}NNaO_3$: 266.0788, found:266.0789.

1-Methyl-3-o-tolylpyridin-2(1H)-one (16). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***13*** (17 mg, 35%) as brown oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 3H), 3.63 (s, 3H), 6.25 (t, J = 6.8 Hz, 1H), 7.14 – 7.39 (m, 6H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 20.1, 38.3, 105.6, 125.8, 128.0, 130.1, 130.2, 133.6, 137.1, 137.8, 139.1, 161.9; HRMS (ESI-QTOF) m/z: $[M+K]^+$: calcd. for $C_{13}H_{13}KNO$: 238.0629, found:238.0627.

3-(Dibenzo[b,d]furan-4-yl)-1-methylpyridin-2(1H)-one (17). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (10:90 v/v) to get ***14*** (17 mg, 24%) as white solid. m.p 88-92°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (s, 3H), 6.36 (t, J = 6.8 Hz, 1H), 7.34 (td, J = 7.5, 1.0 Hz, 1H), 7.37 – 7.51 (m, 3H), 7.55 (dt, J = 8.3, 0.8 Hz, 1H), 7.87 – 8.01 (m, 4H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 38.6, 106.0, 111.9, 120.3, 120.8, 121.4, 122.8, 124. 6, 124.7, 126.8, 127.2, 128.7, 129.6, 138.2, 140. 2, 153.9, 156.1, 161.9; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{18}H_{13}NNaO_2$: 298.0838, found: 298.0835.

3-Phenyl-1-propylpyridin-2(1H)-one (18). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***15*** (17 mg,

32%) as oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.4 Hz, 3H), 1.75 – 1.91 (m, 2H), 3.96 (t, *J* = 8.0 Hz, 2H), 6.24 (t, *J* = 6.8 Hz, 1H), 7.25 – 7.34 (m, 2H), 7.36 – 7.42 (m, 2H), 7.47 (dd, *J* = 6.9, 2.1 Hz, 1H), 7.63 – 7.76 (m, 2H). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 11.4, 22.6, 52.3, 105. 9, 127.7, 128.2, 128.8, 131.9, 137.0, 137.1, 137.6, 161.5. HRMS (ESI-QTOF) m/z: $[M+H]^+$: calcd. for $C_{14}H_{15}NO$: 214.1232, found: 214.1238.

3-(3-Bromophenyl)-1-propylpyridin-2(1H)-one (19). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (12:88 v/v) to get ***16*** (19 mg, 26%) as oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, *J* = 7.4 Hz, 3H), 1.83 (h, *J* = 7.4 Hz, 2H), 3.90 – 4.05 (m, 2H), 6.26 (t, *J* = 6.9 Hz, 1H), 7.20 – 7.38 (m, 2H), 7.42 – 7.52 (m, 2H), 7.64 (ddd, *J* = 7.8, 1.7, 1.0 Hz, 1H), 7.87 (t, *J* = 1.8 Hz, 1H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 11.4, 22.7, 52.5, 105.9, 122.3, 127.5, 129.7, 130.4, 130.7, 131.7, 137.6, 138.0, 139.1, 161.3; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{14}H_{14}BrNNaO$: 314.0151, found: 314.0151.

1-Propyl-3-(m-tolyl)pyridin-2(1H)-one (20). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***17*** (26 mg, 45%) as oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, *J* = 7.4 Hz, 3H), 1.82 (q, *J* = 7.4 Hz, 2H), 2.38 (s, 3H), 3.89 – 4.02 (m, 2H), 6.23 (t, *J* = 6.8 Hz, 1H), 7.09 – 7.19 (m, 1H), 7.22 – 7.35 (m, 2H), 7.39 – 7.50 (m, 2H), 7.54 (s 1H). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 11.3, 21.6, 22.6, 52.3, 105.9, 125.8, 128.1, 128.5, 129.5, 132.0, 136.9, 137.0, 137.5, 137.6, 161.5. HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{15}H_{17}NNaO$: 250.1202, found: 250.1202.

3-([1,1'-biphenyl]-4-yl)-1-propylpyridin-2(1H)-one (21). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***18*** (22 mg, 31%) as white solid. m.p 131-134°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (t, *J* = 7.4 Hz, 3H),

1.85 (q, *J* = 7.4 Hz, 2H), 3.90 – 4.05 (m, 2H), 6.26 (t, *J* = 6.8 Hz, 1H), 7.29 (dd, *J* = 6.8, 2.1 Hz, 1H), 7.32 – 7.38 (m, 1H), 7.40 – 7.49 (m, 2H), 7.54 (dd, *J* = 7.0, 2.1 Hz, 1H), 7.58 – 7.68 (m, 4H), 7.74 – 7.86 (m, 2H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 11.4, 22.6, 52.4, 105.9, 127.0, 127.3, 127.4, 128.9, 129.2, 131.4, 136.1, 137.0, 137.4, 140.5, 141.1, 161.6; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{20}H_{19}NNaO$: 312.1359, found: 312.1360.

1-Allyl-3-phenylpyridin-2(1H)-one (22). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***19*** (16 mg, 30%) as oily brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.63 (dt, *J* = 5.9 Hz, 2H), 5.21 – 5.30 (m, 2H), 6.00 (ddt, *J* = 17.2, 10.3, 5.9 Hz, 1H), 6.27 (t, *J* = 6.8 Hz, 1H), 7.24 – 7.36 (m, 2H), 7.36 – 7.42 (m, 2H), 7.48(dd, *J* = 7.0, 2.1 Hz, 1H), 7.63 – 7.72 (m, 2H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 51.9, 106.2, 118.7, 127.8, 128.2, 128.8, 132.0, 132.7, 136.4, 137.0, 137.7, 161.4; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{14}H_{13}NNaO$: 234.0889, found: 234.0882.

1,6-Dimethyl-3-p-tolylpyridin-2(1H)-one (23). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (8:92 v/v) to get ***20*** (17 mg, 32%) as solid. m.p 134-137°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (d, *J* = 2.2 Hz, 6H), 3.58 (s, 3H), 6.11 (d, *J* = 7.1 Hz, 1H), 7.19 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 7.2 Hz, 1H), 7.57 (d, *J* = 8.2 Hz, 2H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 21.3, 21.3, 31.8, 106.6, 128.1, 128.5, 128.9, 134.6, 136.6, 137.1, 145.3, 162.8. HRMS (ESI-QTOF) m/z: $[M+K]^+$: calcd. for $C_{14}H_{15}KNO$: 252.0785, found:252.0786.

6-Chloro-1-methyl-3-p-tolylpyridin-2(1H)-one (24). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (14:86 v/v) to get ***21*** (29 mg, 50%) as white solid. m.p 118-120°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.75 (s, 3H), 6.39 (d, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.9 Hz, 2H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 7.9 Hz,

2H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 21.4, 34.0, 106.8, 128.5, 129.1, 129.4, 133.6, 136.4, 136.5, 137.9, 162.3; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{13}H_{12}ClNNaO$: 256.0500, found:256.0501.

4-(1-Methyl-6-oxo-5-(p-tolyl)-1,6-dihydropyridin-2-yl)benzonitrile (25). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (30:70 v/v) to get ***26*** (16 mg, 20%) as white solid. m.p >200°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.43 (s, 3H), 6.18 (d, *J* = 7.2 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.48 – 7.55 (m, 3H), 7.63(d, *J* = 8.1 Hz, 2H), 7.77 – 7.81 (m, 2H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 21.5, 35.3, 108.3, 113.4, 118.2, 128.7, 129.1, 129.5, 131.1, 132.8, 133.9, 136.1, 138.0, 140.1, 146.7, 162.5; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{20}H_{16}N_2NaO$: 323.1160, found: 323.1161.

5-Chloro-1-methyl-3-p-tolylpyridin-2(1H)-one (26). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (14:86 v/v) to get ***22*** (16 mg, 28%) as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.59 (s, 3H), 7.21 (d, *J* = 7.6 Hz, 2H), 7.33 (d, *J* = 2.9 Hz, 1H), 7.43 (d, *J* = 2.9 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 2H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 21.5, 38.6, 112.3, 128.6, 129.2, 132.6, 132.9, 134.5, 137.9, 138.5, 160.8; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{13}H_{12}ClNNaO$: 256.0500, found:256.0497.

1-Methyl-3-p-tolyl-5-(trifluoromethyl)pyridin-2(1H)-one (27). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (16:84 v/v) to get ***23*** (23 mg, 35%) as white solid. m.p 142 -144°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.64 (s, 3H), 7.17 – 7.31 (m, 2H), 7.53 – 7.62 (m, 3H), 7.68 (dq, *J* = 2.5, 1.3 Hz, 1H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 21.5, 38.9, 109.7 (q, *J* = 34.8 Hz), 123.7 (q, *J* = 269.7 Hz), 128.6, 129.2, 132.5, 132.8, 136.3, 136.3, 138.7, 161.7; $^{19}F\{^{1}H\}$NMR (376 MHz, $CDCl_3$, proton decoupled) δ -

62.25; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{14}H_{12}F_3NNaO$: 290.0763, found: 290.0761.

5-Chloro-1-methyl-3-phenylpyridin-2(1H)-one (28). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (6:94 v/v) to get ***24*** (16 mg, 29%) as white solid. m.p 133 -137°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.59 (s, 3H), 7.34 – 7.43 (m, 4H), 7.45 (d, J = 2.8 Hz, 1H), 7.61 – 7.70 (m, 2H); $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 38.6, 112.3, 128.4, 128.5, 128.8, 132.6, 134.9, 135.7, 138.4, 160.7; HRMS (ESI-QTOF) m/z: $[M+H]^+$: calcd. for $C_{12}H_{10}ClNO$: 220.0529, found: 220.0532.

1-Methyl-3-(p-tolyl)quinolin-2(1H)-one (30). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (16:84 v/v) to get ***27*** (21 mg, 34%) as viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 3.79 (s, 3H), 7.20 – 7.29 (m, 3H), 7.35 – 7.39 (m, 1H), 7.55 (ddd, J = 8.7, 7.2, 1.6 Hz, 1H), 7.58 – 7.63 (m, 3H), 7.78 (s, 1H); $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 21.5, 30.1, 114.1, 121.0, 122.3, 128.9, 129.0, 129.0, 130.3, 132.6, 134.1, 136.5, 138.1, 139.7, 161.8; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{17}H_{15}NNaO$: 272.1046, found: 272.1047.

3-(2-Methoxyphenyl)-1-methylquinolin-2(1H)-one (31). The title compound was purified by column chromatography (neutral alumina, ethyl acetate/ petroleum ether (18:82 v/v) to get ***29*** (14 mg, 21%) as brown oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 3.81 (s, 3H), 6.95 – 7.07 (m, 2H), 7.24 (td, J = 7.5, 1.0 Hz, 1H), 7.30 – 7.42 (m, 3H), 7.52 – 7.60 (m, 2H), 7.73 (s, 1H); $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 30.2, 56.0, 111.4, 114.2, 120.7, 120.8, 122.2, 126.4, 128.9, 129.7, 130.3, 131.1, 131.2, 138.5, 140.0, 157.5, 161.6; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{17}H_{15}NNaO_2$: 288.0995, found: 288.0992.

3-(2-Methoxyphenyl)quinolin-2(1H)-one (33). The title compound was purified by column chromatography (silica gel 60-120-mesh, ethyl acetate/ petroleum ether (50:50 v/v) to get ***33*** (16 mg, 26%) as white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 3H), 7.03 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.06 (td, *J* = 7.5, 1.1 Hz, 1H), 7.19 (ddd, *J* = 8.1, 7.3, 1.1 Hz, 1H), 7.29 – 7.33 (m, 1H), 7.40 (ddd, *J* = 8.3, 7.5, 1.7 Hz, 1H), 7.42 – 7.47 (m, 2H), 7.56 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.84 (s, 1H), 11.52 (s, 1H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 56.0, 111.5, 115.8, 120.3, 120.8, 122.6, 125.7, 127.9, 130.2, 131.0, 131.4, 138.3, 140.3, 157.6, 163.0; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{16}H_{13}NNaO_2$: 274.0838, found 244.0840.

Produre for Large Scale Synthesis of *1-Methyl-3-phenylpyridin-2(1H)-one (8)*: In a 250 mL round-bottom flask, 10.8 gm (40 mmol) $K_2S_2O_8$; 2.07 gm (15 mmol) K_2CO_3; 3.66 gm (30 mmol) phenylboronic acid; 0.403 gm (1 mmol) $Fe(NO_3)_3.9H_2O$ and 1.180 gm (10 mmol) N-methyl-2-pyridone were taken, then 40 mL H_2O and 40 mL DCE were added to it. The total reaction mixture was set with reflux condenser on a preheated 70˚C oil-bath and stirred for 12 h. After cooling the reaction mixture, 2 (N) HCl solution was drop wise added to neutralize the reaction mixture. After that 50 mL of ethyl acetate was added to the reaction mixture and another 25 mL of ethyl acetate was used for washing the round bottom flask. Organic portion was separated by separating funnel and dried over anhyd. Na_2SO_4. Then, the organic solution was concentrated in rotary evaporator and desired product was purified through neutral alumina using ethyl acetate/petroleum ether (8:92 v/v) mixture as eluent. Isolated yield 0.641gm (34%).

1-Methyl-3-phenylpiperidin-2-one (32). In a clean oven-dried screw cap reaction tube charged with magnetic stir-bar, 1-methyl-3-phenyl-2-pyridone (**9**) (0.25 mmol), Palladium in charcoal (10 mol%) were taken. Then the reaction tube was closed tightly. The reaction tube was evacuated and filled with H_2 gas. 2mL H_2 purged EtOH was added to it and stirred at room

temperature for 24 h.[23] After 24 h the reaction mixture was filtered through celite and washed with 20 ml EtOAc. Total organic solution was concentrated and afforded 1-methyl-3-phenylpiperidin-2-one in 99% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.71 – 1.84 (m, 1H), 1.84 – 1.99 (m, 1H), 2.08 – 2.24 (m, 1H), 3.02 (s, 3H), 3.29 – 3.38 (m, 1H), 3.37 – 3.50 (m, 1H), 3.59 – 3.72 (m, 1H), 7.15 – 7.24 (m, 3H), 7.26 – 7.33 (m, 2H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 21.0, 30.7, 35.2, 48.7, 50.5, 126.7, 128.4, 128.6, 141.9, 170.9; HRMS (ESI-QTOF) m/z: $[M+Na]^+$:calcd.for $C_{12}H_{15}NNaO$: 212.1046, found: 212.1050.

General Procedure B for synthesis of N-alkyl-2-pyridone from corresponding 2-hydroxy pyridine[24]. 2-Hydroxy-pyridine (5 mmol), alkyl iodide (1.5 equiv., 7.5 mmol) and K_2CO_3 (1.5 equiv., 7.5 mmol, 1.035 g) were taken in a 50 mL round bottom flask. Then 20 mL MeOH was added to it and set for overnight reflux in a condenser set up at 65˚C. After the reaction the reaction mixture was dried in rota-vap and the residue was diluted with 20 mL ethyl acetate. Organic part was washed with 10 mL brine solution and concentrated in rotary evaporator. Desired N-protected-2-pyridone was isolated through neutral aluminium oxide using petrolium ether-ethyl acetate mixture as eluent.

1-Ethylpyridin-2(1H)-one. The title compound was prepared following general procedure B and was purified by column chromatography (neutral alumina, ethyl acetate) to get as brown oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 – 1.45 (m, 3H), 3.92 – 4.10 (m, 2H), 6.18 (t, J = 6.7 Hz, 1H), 6.57 (d, J = 9.1 Hz, 1H), 7.20 – 7.40 (m, 2H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 14.8, 45.0, 106.3, 121.2, 137.1, 139.5, 162.7. HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for C_7H_9NNaO: 146.0576, found: 146.0577.

1-Propylpyridin-2(1H)-one. The title compound was prepared following general procedure B and was purified by column chromatography (neutral alumina, ethyl acetate) to get as brown oily

liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, *J* = 8 Hz, 3H), 1.81-1.76 (m, 2H), 3.90 (t, *J* = 6 Hz, 2H), 6.15 (t, *J* = 6 Hz, 1H), 6.57 (d, *J* = 7 Hz, 1H), 7.25-7.31(m, 2H). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 11.3, 22.7, 51.6, 106.0, 121.3, 137.8, 139.4, 162.9. HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_8H_{11}NNaO$: 160.0733, found: 160.0732.

1-Allylpyridin-2(1H)-one. The title compound was prepared following general procedure B and was purified by column chromatography (neutral alumina, ethyl acetate) to get as brown oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.54 (dt, *J* = 5.8, 1.5 Hz, 2H), 5.15 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.23 (dq, *J* = 10.3, 1.3 Hz, 1H), 5.93 (ddt, *J* = 17.1, 10.2, 5.8 Hz, 1H), 6.15 (td, *J* = 6.7, 1.4 Hz, 1H), 6.56 (ddd, *J* = 9.2, 1.3, 0.7 Hz, 1H), 7.23 (ddd, *J* = 6.8, 2.1, 0.7 Hz, 1H), 7.30 (ddd, *J* = 9.0, 6.6, 2.1 Hz, 1H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 51.1, 106.2, 118.5, 121.2, 132.6, 137.2, 139.6, 162.5. HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for C_8H_9NNaO: 158.0576, found: 158.0578.

1-Phenethylpyridin-2(1H)-one. The title compound was prepared following general procedure B and was purified by column chromatography (neutral alumina, ethyl acetate) to get as crystalline solid. m.p 106-108°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.06 (t, *J* = 7.1 Hz, 2H), 4.14 (t, *J* = 7.1 Hz, 2H), 5.99 (td, *J* = 6.7, 1.4 Hz, 1H), 6.59 (ddd, *J* = 9.2, 1.4, 0.7 Hz, 1H), 6.88 (ddd, *J* = 6.8, 2.1, 0.7 Hz, 1H), 7.10 – 7.19 (m, 2H), 7.18 – 7.34 (m, 4H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 35.2, 52.3, 105.7, 121.2, 126.9, 128.8, 129.2, 138.1, 138.2, 139.7, 162.8; HRMS (ESI-QTOF) m/z: $[M+Na]^+$: calcd. for $C_{13}H_{13}NNaO$: 222.0889, found: 222.0889.

4-(2-Oxopyridin-1(2H)-yl)benzonitrile. The title compound was prepared following general procedure B and was purified by column chromatography (neutral alumina, ethyl acetate) to get as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30 (td, *J* = 6.8, 1.3 Hz, 1H), 6.67 (ddd, *J* = 9.4, 1.3, 0.8 Hz, 1H), 7.30 (ddd, *J* = 6.9, 2.1, 0.8 Hz, 1H), 7.43 (ddd, *J* = 9.3, 6.6, 2.1 Hz, 1H), 7.52 –

7.59 (m, 2H), 7.78 – 7.83 (m, 2H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 106.9, 112.6, 118.1, 122.5, 127.8, 133.5, 136.9, 140.5, 144.6, 162.0; HRMS (ESI-QTOF) m/z: $[M+H]^+$: calcd. for $C_{12}H_9N_2O$: 197.0709, found: 197.0707.

1,6-Dimethylpyridin-2(1H)-one. The title compound was prepared following general procedure B and was purified by column chromatography (neutral alumina, ethyl acetate) to get as yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.51 (s, 3H), 5.96 – 6.09 (m, 1H), 6.43 (ddd, J = 9.1, 1.5, 0.7 Hz, 1H), 7.19 (dd, J = 9.1, 6.8 Hz, 1H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 21.1, 31.3, 106.7, 117.4, 138.8, 146.5, 164.1; HRMS (ESI-QTOF) m/z: $[M+H]^+$: calcd. for $C_7H_{10}NO$: 124.0757, found: 124.0755.

6-Chloro-1-methylpyridin-2(1H)-one. The title compound was prepared following general procedure B and was purified by column chromatography (neutral alumina, ethyl acetate) to get as white crystalline solid. m.p 59-60°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (s, 3H), 6.32 (dd, J = 7.2, 1.3 Hz, 1H), 6.52 (dd, J = 9.2, 1.2 Hz, 1H), 7.15 – 7.32 (m, 1H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 33.4, 106.8, 118.4, 138.4, 138.7, 163.5. HRMS (ESI-QTOF) m/z: $[M+H]^+$: calcd. for C_6H_7ClNO: 144.0211, found: 144.0210.

5-Chloro-1-methylpyridin-2(1H)-one. The title compound was prepared following general procedure B and was purified by column chromatography (neutral alumina, ethyl acetate) to get as white solid. m.p 60-62°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.50 (s, 3H), 6.52 (dt, J = 9.6, 1.3 Hz, 1H), 7.20 – 7.44 (m, 2H); $^{13}C\{^{1}H\}$NMR (101 MHz, $CDCl_3$) δ 38.0, 112.3, 121.2, 132.9, 142.6, 161.7. HRMS (ESI-QTOF) m/z: $[M+H]^+$: calcd. for C_6H_7ClNO: 144.0211, found: 144.0209.

1-Methyl-5-(trifluoromethyl)pyridin-2(1H)-one. The title compound was prepared following general procedure B and was purified by column chromatography (neutral alumina, ethyl

acetate) to get as white crystalline solid. m.p 78-82°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.58 (s, 3H), 6.62 (dt, *J* = 9.5, 0.8 Hz, 1H), 7.45 (dd, *J* = 9.6, 2.7 Hz, 1H), 7.69 (dt, *J* = 3.1, 1.3 Hz, 1H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 38.3, 109.7 (q, *J* =35 Hz), 123.5 (q, *J* =271 Hz), 135.4, 138.1, 162.5. ^{19}F NMR (376 MHz, $CDCl_3$, proton decoupled) δ -62.34. HRMS (ESI-QTOF) m/z: $[M+H]^+$: calcd. for $C_7H_7F_3NO$: 178.0474, found: 178.0475.

3-Chloro-1-methylpyridin-2(1H)-one. The title compound was prepared following general procedure B and was purified by column chromatography (neutral alumina, ethyl acetate) to get as brown oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (s, 3H), 6.16 (dd, *J* = 7.3, 6.8 Hz, 1H), 7.33(dd, *J* = 6.8, 1.9 Hz, 1H), 7.54 (dd, *J* = 7.3, 1.9 Hz, 1H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 38.6, 105.3, 126.1, 137.1, 137.8, 159.4. HRMS (ESI-QTOF) m/z: $[M+H]^+$: calcd. for C_6H_7ClNO: 144.0211, found: 144.0211.

4-(1-Methyl-6-oxo-1,6-dihydropyridin-2-yl)benzonitrile. The titled compound was prepared by C-C coupling of 6-Chloro-1-methylpyridin-2(1*H*)-one (1 mmol, 143 mg), and 4-cyano-phenylboronic acid (1.5 mmol, 221 mg). The reaction was done in screw cap reaction tube with K_3PO_4 (3 mmol, 690 mg), $Pd(OAc)_2$ (0.03 mmol, 7 mg), X-Phos (0.03 mmol, 7 mg), THF (3 mL). Reaction was carried out in N_2 atmosphere at 110°C for 24h. After the reaction, the mixture was filtered through celite. Pure product was isolated by column chromatography (neutral alumina, ethyl acetate) to get white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.35 (s, 3H), 6.08 (dd, *J* = 8, 2 Hz), 6.64 (dd, *J* = 8, 2 Hz 1H), 7.38-7.34 (m, 1H), 7.48-7.51 (m, 2H), 7.77-7.80 (m, 2H); ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 34.6, 108.2, 113.6, 118.1, 120.4, 129.5, 132.8, 138.6, 139.9, 148.2, 163.6. HRMS (ESI): calcd. for $C_{13}H_{11}N_2O$: 211.0866, found: 211.0865.

ASSOCIATED CONTENTS

Notes

The authors declare no competing financial interest.

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Supporting Information

Figures giving ^{1}H and ^{13}C NMR and all compounds text giving details of the optimization. This material is available free of charge via the Internet at http://pubs.acs.org.

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13. See Supporting Information for details.

14. Experimental details of the structure determination can be found in the Supporting Information. CCDC-947672 (entry 1) and CCDC-947671 (entry 7) contain the supplementary crystallographic data for this paper.These data can be obtained free of charge

from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

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