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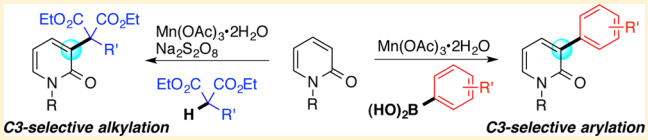
Manganese-Mediated C3-Selective Direct Alkylation and Arylation of 2-Pyridones with Diethyl Malonates and Arylboronic Acids

Akihiro Nakatani, Koji Hirano,* Tetsuya Satoh, and Masahiro Miura*

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan

Supporting Information

ABSTRACT: A manganese-mediated dehydrogenative direct alkylation of 2-pyridones with diethyl malonates has been developed. A similar reaction system is applicable to the direct arylation with arylboronic acids. These manganese-based reactions occur regioselectively at the C3 position of the 2-pyridones. The observed high C3 regioselectivity can complement precedented C−H functionalization protocols of the 2-pyridones in view of the site selectivity.



INTRODUCTION

2-Pyridones frequently occur in pharmaceutical targets and biologically active natural and unnatural products. Such well-known compounds include ciclopirox, milrinone, camptothecin, fredericamycin, and perampanel (Figure 1).[1] The most

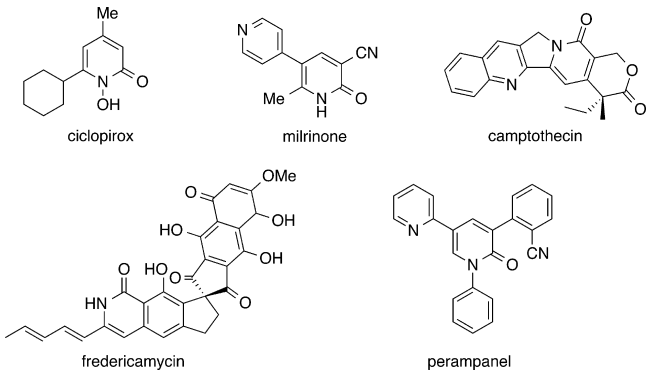


Figure 1. 2-Pyridone rings in biologically active compounds.

powerful and reliable approach to these densely functionalized pyridone cores is considered to be the metal-catalyzed cross-coupling reactions with halogenated pyridone derivatives. On the other hand, recent progress in the metal-mediated C−H functionalization[2] can provide a more straightforward route to the target compounds (Figure 2). So far, palladium-mediated and -catalyzed direct alkenylation and arylation at the C5 position have been reported.[3] On the other hand, the nickel/aluminum bimetallic catalyst system enables direct C6 alkenylation and alkylation.[4] However, despite the relatively high electron density, the selective C−H functionalization at the C3 position remains somewhat of a challenge.[5] In this context, we have recently found the nickel-catalyzed C3-selective alkylation with α-bromocarbonyl compounds (Scheme 1a).[6] Under this nickel catalysis, the otherwise difficult C3-selective direct functionalization was possible through a SOMO/HOMO interaction including an alkyl radical inter-

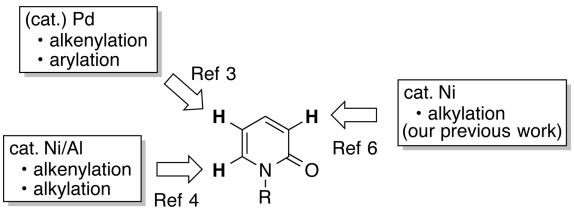


Figure 2. Reactivity profiles of the 2-pyridone ring under metal-mediated C−H functionalization.

mediate generated in situ. The observed unique regioselectivity prompted us to further explore the radical-mediated direct C3 functionalization of 2-pyridones. Here, we report manganese-mediated direct alkylation and arylation with diethyl malonates and arylboronic acids (Scheme 1b,c). The C−C bond formations occur exclusively at the C3 position. Thus, the manganese-based system can complement the above precedents from the viewpoint of site selectivity and directly give C3-decorated 2-pyridones of potential interest in medicinal chemistry.

RESULTS AND DISCUSSION

Mn(III)-Mediated Direct Alkylation with Diethyl Malonates. On the basis of our previous mechanistic insight into the nickel-catalyzed, radical-mediated C3-selective alkylation,[6] we initially focused on a combination of Mn(III) salts and malonic acid esters because it is a well-known system for the generation of the corresponding alkyl radical intermediates, which then undergo smooth addition to electron-rich indoles and pyrroles.[7] Pleasingly, treatment of excess of *N*-methyl-2-pyridone (**1a**; 2.5 mmol) with diethyl 2-methylmalonate (**2a**; 0.50 mmol) in the presence of 1.2 mmol (2.4 equiv) of $Mn(OAc)_3 \cdot 2H_2O$ and 2.5 mmol (5.0 equiv) of NaOAc in hot AcOH (70 °C) afforded the alkylated product **3aa** in 52% GC yield (Table 1, entry 1). Expectedly, the exclusive C3 selectivity

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Scheme 1. Metal-Mediated C3-Selective C−H Functionalization of 2-Pyridones via Radical Species

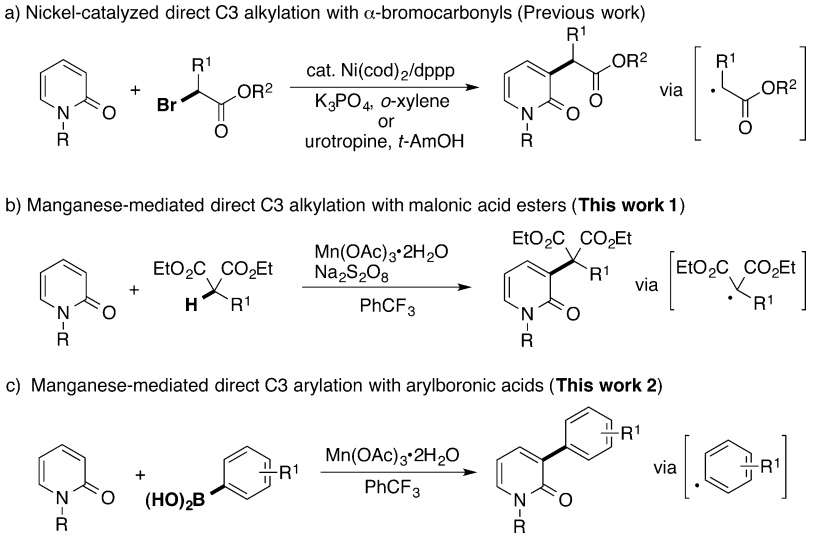
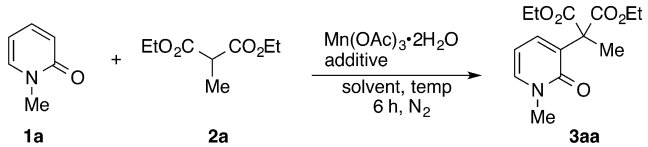


Table 1. Optimization Studies for Manganese-Mediated Direct Alkylation of *N*-Methyl-2-pyridone (1a) with Diethyl 2-Methylmalonate (2a)



1a **2a** **3aa**

entry	1a:2a:Mn(III) (mmol)	additive (amt (mmol))	solvent (amt (mL))	temp (°C)	yield (%)[a]
1	2.5:0.50:1.2	NaOAc (2.5)	AcOH (3.0)	70	52
2	2.5:0.50:1.2	NaOAc (2.5)	$PhCF_3$ (3.0)	90	46
3	2.5:0.50:1.2	none	$PhCF_3$ (3.0)	90	68
4	2.5:0.50:1.2	none	toluene (3.0)	100	55
5	2.5:0.50:1.2	none	PhCl (3.0)	120	66
6	2.5:0.50:1.2	none	1,4-dioxane (3.0)	100	40
7	2.5:0.50:1.2	none	DCE (3.0)	70	24
8	2.5:0.50:1.2	none	DMF (3.0)	140	29
9	2.5:0.50:1.2	none	*t*-AmOH (3.0)	90	20
10	1.5:0.50:1.2	none	$PhCF_3$ (1.0)	90	70
11	1.5:0.50:0.60	$(t\text{-BuO})_2$ (0.60)	$PhCF_3$ (1.0)	90	42
12	1.5:0.50:0.60	*t*-BuOOH (0.60)	$PhCF_3$ (1.0)	90	14
13	1.5:0.50:0.60	MnO_2 (0.60)	$PhCF_3$ (1.0)	90	35
14	1.5:0.50:0.60	oxone (0.60)	$PhCF_3$ (1.0)	90	35
15[b]	1.5:0.50:0.60	$K_2S_2O_8$ (0.60)	$PhCF_3$ (1.0)	90	53
16[b]	1.5:0.50:0.60	$Na_2S_2O_8$ (0.60)	$PhCF_3$ (1.0)	90	70 (75)
17[b]	0.50:1.5:0.60	$Na_2S_2O_8$ (0.60)	$PhCF_3$ (1.0)	90	28

[a]GC yield. Yield after purification is given in parentheses. [b]24 h.

was observed. With this intriguing result in hand, we optimized the reaction conditions. Investigation of some solvents identified aromatic systems to be promising (entries 3−9), with $PhCF_3$ giving a 68% GC yield of **3aa** (entry 3). The benzylic C−H bonds of toluene could be abstracted under current conditions to form the benzylated pyridone as a byproduct (entry 4). Although PhCl showed similar good efficiency (entry 5), in subsequent studies we employed $PhCF_3$ as the best solvent, because it could be evaporated more easily under reduced pressure. Additionally notable is that NaOAc was not necessary in this reaction (entry 2 vs 3). The higher concentration could reduce the amount of **1a** to 1.5 mmol (3.0 equiv) (entry 10). In addition, to cut down the amount of $Mn(OAc)_3{\cdot}2H_2O$, we next tested some co-oxidants. While organic peroxides, MnO_2, and potassium-based persulfates were ineffective (entries 11−15), $Na_2S_2O_8$ showed good performance. Although the catalytic variant in Mn(III) remained unsuccessful, 0.60 mmol (1.2 equiv) of $Mn(OAc)_3{\cdot}2H_2O$ combined with 0.60 mmol (1.2 equiv) of $Na_2S_2O_8$ resulted in a comparable yield (entry 16). Additionally, 3.0 equiv of **1a** was still essential for the satisfactory yield, but about half of the unreactive **1a** could be recovered by simple extraction with chloroform (see the Experimental Section).[8] On the other hand, excess **2a** (3.0 equiv with respect to **1a**) diminished the yield of **3aa** (entry 17).

With the conditions of entry 16 in Table 1, we examined the substrate scope of the 2-pyridone (Scheme 2). Irrespective of the substitution pattern and electronic and steric nature of the substituent, the alkylation reaction occurred exclusively at the C3 position. The 4-, 5-, and 6-methyl-2-pyridones were equally tolerated, and the corresponding alkylated products **3ba**−**3da** were obtained in moderate to good yields, while the introduction of a methyl group at the C3 position completely shut down the reaction (data not shown). Electron-withdrawing trifluoromethyl-, chloro-, and bromo-substituted as well as electron-donating methoxy-substituted substrates also underwent the alkylation to form **3ea**−**3ha**, albeit with somewhat lower yields. The resultant chloride and bromide moieties can be useful synthetic handles for further manipulations under the conventional palladium catalysis. The more readily detachable benzyl protection on the nitrogen was compatible (**3ia**). Additionally, the C3-selective alkylation of 2-quinolinone also proceeded under the standard conditions to furnish **3ja** in an acceptable yield. In some cases of lower product yields, the homocoupling byproducts of **2a**[7c] were detected by GC and GCMS analysis.

An array of malonic acid coupling partners were also evaluated (Scheme 3). The 2-benzylmalonate reacted with **1a** very smoothly to form **3ab** in 83% yield. Notably, the nitrile

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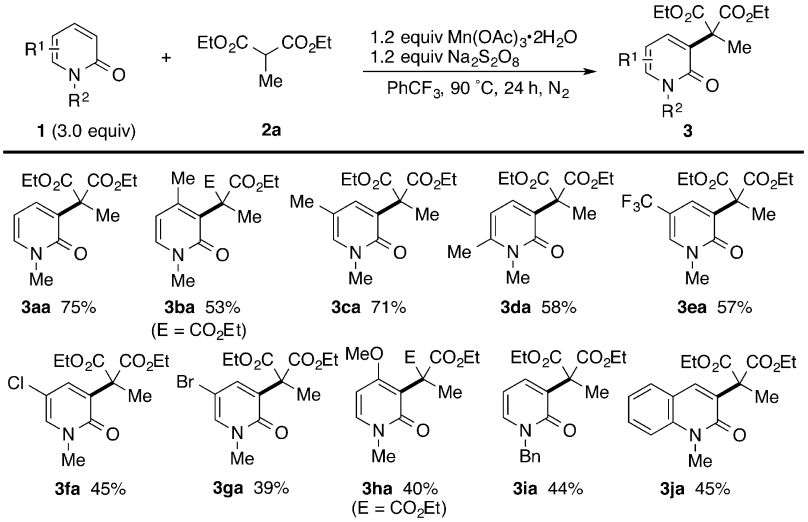
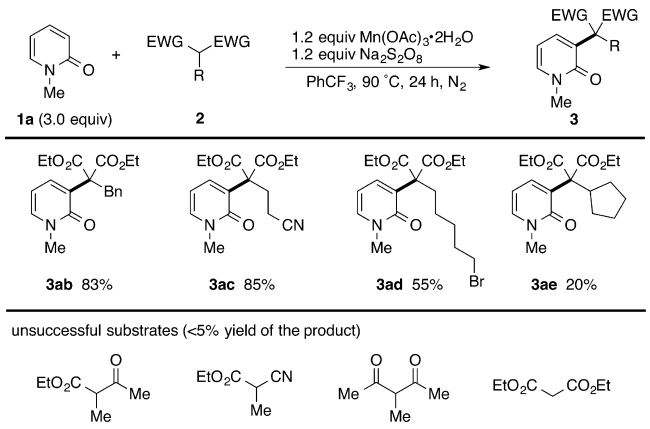
Scheme 2. Manganese-Mediated C3-Selective Direct Alkylation of Various 2-Pyridones 1 with Diethyl 2-Methylmalonate (2a)[a]



[a]The formed C−C bonds are illustrated with a bold line.

Scheme 3. Manganese-Mediated C3-Selective Direct Alkylation of *N*-Methyl-2-pyridone (1a) with Various 1,3-Dicarbonyl Compounds 2[a]

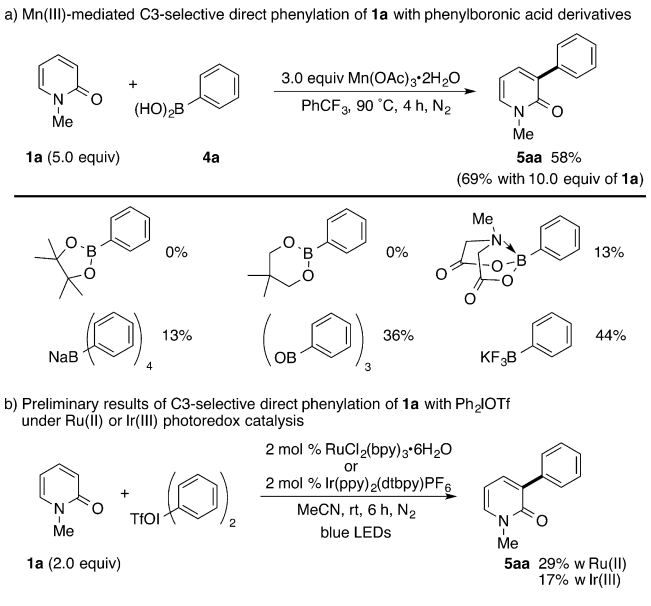


[a]The formed C−C bonds are illustrated with a bold line. EWG = electron-withdrawing group.

and alkyl bromide functionalities remained intact during the reaction course (**3ac** and **3ad**). On the other hand, a secondary alkyl group at the C2 position of the malonate largely decreased the reaction efficiency (**3ae**). The current major limitation of this protocol is the inaccessibility to other 1,3-dicarbonyl compounds: the keto ester, cyano ester, and diketone gave only a <5% yield of the alkylated products. In addition, the simple diethyl malonate was also ineffective. In these cases, similar radical species could be generated but readily decompose under present oxidative conditions, probably through disproportionation, overoxidation, or homocoupling, prior to addition to the pyridone (vide infra). Actually, the Mn(III)-mediated intermolecular aromatic substitution reactions with 1,3-dicarbonyl compounds other than malonates are not trivial in the literature.[7c,d] In addition, α-unsubstituted diethyl malonate cannot form the corresponding radical species, due to its instability associated with the lack of substituents at the α position.[7b] Thus, suitable stability and reactivity of the radical intermediate can be necessary for this transformation.

Mn(III)-Mediated Direct Arylation with Arylboronic Acids. On the basis of the success in Mn(III)-Mediated Direct Alkylation with Diethyl Malonates, we next envisioned the C3-selective direct arylation by using aryl radical species. After the extensive screening of metals, oxidants, and aryl sources, the Mn(III)/ArB(OH)$_2$ system[9] was identified to be optimal. Namely, *N*-methyl-2-pyridone (**1a**; 1.5 mmol) coupled with phenylboronic acid (**4a**; 0.30 mmol) in the presence of 0.90 mmol (3.0 equiv) of Mn(OAc)$_3$·2H$_2$O in hot PhCF$_3$ to produce the C3-phenylated 2-pyridone **5aa** in 58% yield (Scheme 4a). An increase of the amount of **1a** to 3.0 mmol (10 equiv) improved the yield to 69%. As shown in the direct alkylation, unreactive **1a** could be easily recovered after the coupling reaction, although excess **1a** was inevitable (see the Experimental Section). The choice of boryl groups was also critical: the corresponding boronic acid pinacol and neopentylglycol esters, MIDA boronate, and sodium borate were

Scheme 4. Studies for C3-Selective Direct Arylation of *N*-Methyl-2-pyridone (1a)



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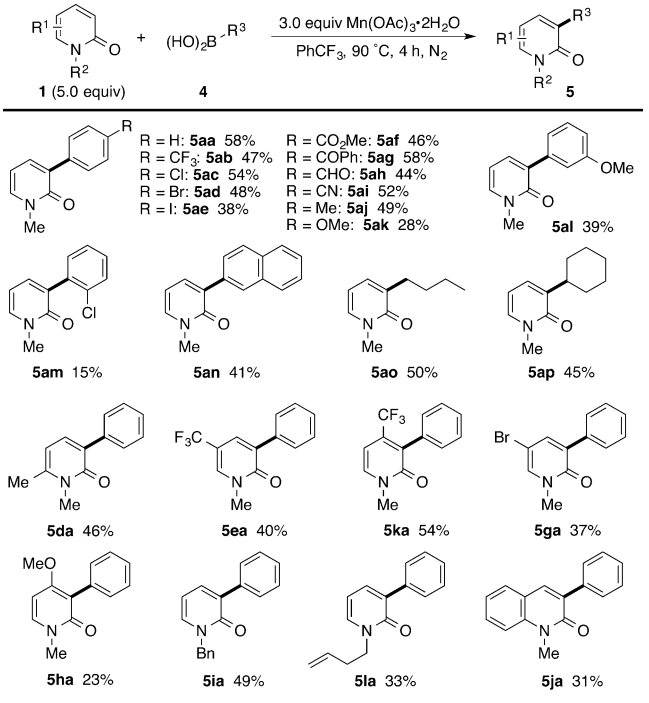
less effective, while the boroxine and potassium trifluoroborate showed comparable reactivities (under conditions with 5.0 equiv of **1a**). We also tested some representative catalytic systems for the generation of the phenyl radical species from **4a**, including $FeCl_3/(t\text{-}BuO)_2$,[10] $CuCl_2/(t\text{-}BuO)_2$,[11] $Ni(acac)_2/(t\text{-}BuO)_2$,[12] and $AgNO_3/K_2S_2O_8$,[13] but the desired **5aa** was not detected at all, and biphenyl was instead formed in 4−46% yields (by GC and GCMS analysis) (see the Supporting Information for details). In contrast, the Mn(III)-based conditions did not form any detectable amounts of the biphenyl byproduct. Only with an excess of **4a** (5.0 equiv to **1a**) did the formation of **5aa** not occur at all, and the biphenyl was detected dominantly in 32% yield (data not shown). On the other hand, while the results were preliminary, we observed the formation of **5aa** under the Ru(II)- or Ir(III)-based photoredox catalysis with Ph_2IOTf as the phenyl source (Scheme 4b).[14]

The Mn(III)-mediated C3-selective arylation was applicable to various electron-poor arylboronic acids that bear trifluoromethyl, ester, ketone, aldehyde, nitrile, chloride, bromide, and iodide functionalities (Scheme 5, **5ab**−**5ai**). The moderately

Scheme 5. Mn(III)-Mediated C3-Selective Direct Arylation and Alkylation of 2-Pyridones with Organoboronic Acids

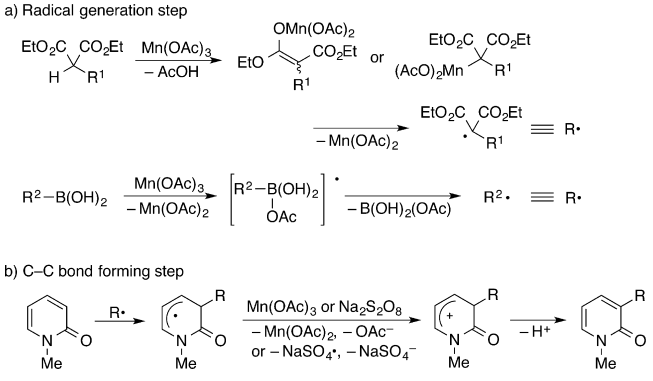


electron-donating methyl substituent was also tolerated (**5aj**). On the other hand, the reaction with electron-rich 4-methoxyboronic acid was sluggish (**5ak**), whereas the 3-methoxyboronic acid afforded a 39% yield of the product (**5al**). Unfortunately, the reaction was sensitive to the steric hindrance around the boron moiety (**5am**). Additionally notable is the accessibility to primary and secondary alkylboronic acids (**5ao** and **5ap**).[15,16]

We then tested some substituted 2-pyridones for the direct arylation with phenylboronic acid (**4a**). All substitution patterns at the C4, C5, and C6 positions were well tolerated, and the C−C bond was formed exclusively at the C3 position (**5da**, **5ea**, **5ka**, **5ga**, and **5ha**). The *N*-benzyl- and *N*-(3-butenyl)-2-pyridones and 2-quinolinone also coupled with **4a** to furnish the corresponding 3-phenylpyridones directly (**5ia**, **5la**, and **5ja**). In most cases of Scheme 5, the yields were somewhat moderate, but this methodology enables the direct introduction of aryl groups at the C3-position of unactivated 2-pyridones, which is otherwise difficult by reported C−H activation protocols[3] as well as traditional procedures. Although all byproducts were not completely identified, the major component was found to be the simple protonated product: e.g., naphthalene in the case of **5an**.

Mechanistic Discussion. Our original working scenario is shown in Scheme 6. Initial alkyl or aryl radical ($R^\bullet$) generation

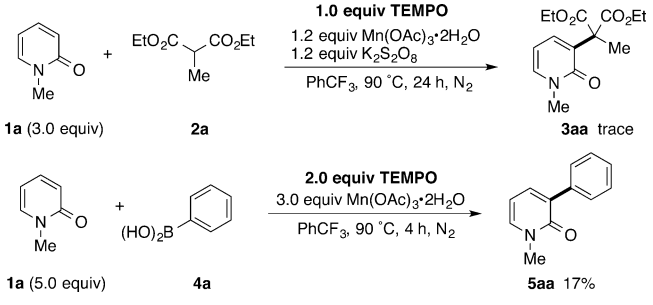
Scheme 6. Plausible Mechanism



is mediated by Mn(III) through the in situ generation of Mn(III) enolates/oxidation sequence[7] or single electron transfer (SET) oxidation of organoboronic acid (radical generation step, Scheme 6a)).[9] Subsequent regioselective addition of $R^\bullet$ to the C3 position of the *N*-methyl-2-pyridone (**1a**) ring forms the allylic radical intermediate, in which the resonance stabilization occurs. Additional SET to Mn(III) (or $Na_2S_2O_8$ in case of the alkylation with malonates) is followed by deprotonation to produce the C3-functionalized 2-pyridone (C−C bond forming step, Scheme 6b)). This mechanistic proposal is analogous to the well-established but recently revisited homolytic radical aromatic substitution (HAS).[18]

The radical inhibitor 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) gave a large negative impact on the reaction efficiency with either diethyl 2-methylmalonate (**2a**) or phenylboronic acid (**4a**), which supports the postulated radical mechanism (Scheme 7). Additional information was available from the experiments in Scheme 8: the xanthate **6**, which generated the corresponding alkyl radical **7** under the conventional peroxide-promoted conditions,[18] coupled with **1a** selectively at the C3 position (Scheme 8a); phenylazo-

Scheme 7. Reactions in the Presence of TEMPO



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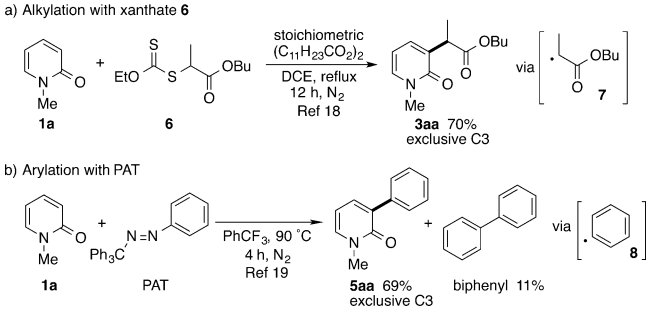
Scheme 8. Attempts at the Direct Alkylation and Arylation of 1a under the Conventional Radical Conditions



(triphenyl)methane (PAT)[19] also gave the C3-phenylated 2-pyridone exclusively through the phenyl radical **8** under pyrolysis, with concomitant formation of 11% of biphenyl (Scheme 8b). These reaction outcomes suggest that an Mn-nonassociated, free radical mechanism is operative at least in the addition step, and the observed high C3 selectivity is attributed to the radical nature of the intermediates. A preliminary DFT calculation revealed the relatively large atomic contributions of both the HOMO and LUMO at the C3 position of **1a** (Figure 3). Thus, the regioselectivity might be

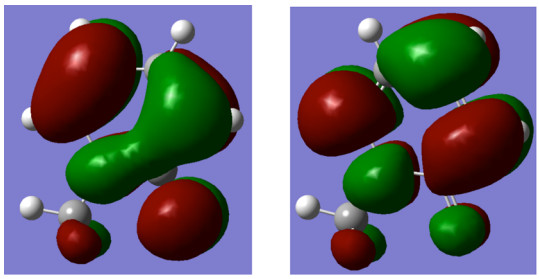


Figure 3. Atomic contributions of HOMO (left) and LUMO (right) in *N*-methyl-2-pyridone (**1a**) calculated by DFT at the RB3LYP/6-31G(d) level of theory.

controlled by a SOMO/HOMO or a SOMO/LUMO interaction between the radical intermediates and the C3 carbon atom on the pyridone as well as a resonance stabilization of the resultant radical adduct. In the case of the malonylation through the electrophilic malonyl radical species, the HOMO is believed to work predominantly, while the LUMO might play a more important role in the butylation and cyclohexylation, including the carbon radicals of nucleophilic characters. Although the exact reason for the arylation activity unique in the Mn(III) system is not clear at present, the relatively slow release of the highly reactive aryl radical species is believed to be beneficial for suppressing the undesired homocoupling leading to the biphenyl byproduct.

However, reactivity trends of 2-pyridones were not always in accord with our proposal; for example, the electron-donating methyl and methoxy groups at the C4 and C6 positions diminished the efficiency of the alkylation reaction (Scheme 2, **3aa** vs **3ba**, **3da**, and **3ha**). Moreover, the possibility of reversibility in the addition process[7c] also needs to be taken into consideration. Thus, neither an Mn-associated radical process nor other organometallic pathways are excluded at this stage. Further efforts are essential for clarification of the detailed mechanism.

CONCLUSION

We have developed Mn(III)-mediated direct C3 alkylation and arylation of 2-pyridones with diethyl malonates and arylboronic acids, respectively.[20] The Mn-based system can provide direct access to C3-alkylated and -arylated 2-pyridone cores, which are conventionally prepared in multiple steps.[1] The observed unique C3 selectivity can complement precedented C−H activation systems of 2-pyridones[3,4] in view of the site selectivity, although excesses of 2-pyridones and Mn(III) salts are essential at present. Further studies on the direct functionalization of the 2-pyridone at other positions are ongoing in our laboratory and will be reported in due course.

EXPERIMENTAL SECTION

Instrumentation and Chemicals. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded at 400, 100, and 376 MHz, respectively, for $CDCl_3$ solutions. HRMS data were obtained by EI or APCI using a double-focusing mass spectrometer or TOF, respectively. GC analysis was carried out using a silicon OV-17 column (i.d. 2.6 mm × 1.5 m) or a CBP-1 capillary column (i.d. 0.5 mm × 25 m). TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck silica gel 60F_{254}. Silica gel was used for column chromatography. Gel permeation chromatography (GPC) was performed with a $CHCl_3$ eluent (3.5 mL/min, UV detector). Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Trifluoromethylbenzene was freshly distilled from CaH_2 prior to use. 2-Pyridone derivatives **1** were prepared from the parent 2-hydroxypyridones (tautomers of NH 2-pyridones) and the appropriate alkylating reagents.[4a,21] PAT was synthesized according to the literature.[22] Unless otherwise noted, all reactions were carried out under N_2 conditions.

Typical Procedure for Mn(III)-Mediated Direct Alkylation of 2-Pyridones with Diethyl Malonates. The synthesis of **3aa** is representative (Table 1, entry 16): $Mn(OAc)_3{\cdot}2H_2O$ (161 mg, 0.60 mmol) and $Na_2S_2O_8$ (143 mg, 0.60 mmol) were placed in a 10 mL Schlenk tube, which was filled with nitrogen by using the standard Schlenk technique. A solution of *N*-methyl-2-pyridone (**1a**; 164 mg, 1.5 mmol) and diethyl 2-methylmalonate (**2a**; 87.1 mg, 0.50 mmol) in $PhCF_3$ (1.0 mL) was added to the tube, and the suspension was stirred for 24 h at 90 °C. The resulting mixture was quenched with water and then extracted four times with ethyl acetate. The combined organic layer was dried over sodium sulfate. Concentration in vacuo and subsequent purification by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent gave diethyl 2-methyl-2-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)malonate (**3aa**; 85 mg, 0.37 mmol) in 75% yield. When the residual water layer was extracted four times again with chloroform, *N*-methyl-2-pyridone (**1a**) left intact was recovered (76 mg, 0.70 mmol).

*Diethyl 2-methyl-2-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-malonate (**3aa**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 85 mg (75%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 6H), 1.81 (s, 3H), 3.53 (s, 3H), 4.23 (dq, J = 7.2, 10.6 Hz, 2H), 4.27 (dq, J = 7.2, 10.6 Hz, 2H), 6.19 (dd, J = 6.9, 6.9 Hz, 1H), 7.26 (dd, J = 1.9, 6.9 Hz, 1H), 7.29 (dd, J = 1.9, 6.9 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 20.9, 37.9, 57.5, 61.8, 105.1, 131.9, 135.6, 137.4, 161.4, 170.8; HRMS (EI) m/z (M^+) calcd for $C_{14}H_{19}NO_5$ 281.1263, found 281.1259.

*Diethyl 2-(1,4-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)-2-methyl-malonate (**3ba**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 78 mg (53%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 6H), 1.71 (s, 3H), 2.05 (s, 3H), 3.45 (s, 3H), 4.19 (dq, J = 7.2, 10.9 Hz, 2H), 4.29 (dq, J = 7.2, 10.9 Hz, 2H), 5.95 (d, J = 6.9 Hz, 1H), 7.09 (d, J = 6.9 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 20.4, 20.9, 37.9, 57.4, 61.9, 110.2, 130.3, 135.3, 147.2, 161.4, 170.8; HRMS (EI) m/z (M^+) calcd for $C_{15}H_{21}NO_5$ 295.1420, found 295.1417.

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*Diethyl 2-(1,5-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)-2-methylmalonate (**3ca**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 106 mg (71%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, J = 7.2 Hz, 6H), 1.80 (s, 3H), 2.07 (s, 3H), 3.49 (s, 3H), 4.23 (dq, J = 7.2, 11.0 Hz, 2H), 4.27 (dq, J = 7.2, 11.0 Hz, 2H), 7.04 (d, J = 2.4 Hz, 1H), 7.15 (d, J = 2.4 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 17.4, 21.0, 37.7, 57.5, 61.7, 113.9, 131.3, 135.0, 138.2, 160.5, 170.8; HRMS (EI) m/z (M^+) calcd for $C_{15}H_{21}NO_5$ 295.1420, found 295.1419.

*Diethyl 2-(1,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)-2-methylmalonate (**3da**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 86 mg (58%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J = 7.1 Hz, 6H), 1.79 (s, 3H), 2.34 (s, 3H), 3.51 (s, 3H), 4.22 (dq, J = 7.1, 10.1 Hz, 2H), 4.26 (dq, J = 7.1, 10.1 Hz, 2H), 6.02 (d, J = 7.3 Hz, 1H), 7.18 (d, J = 7.3 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 20.9, 21.0, 31.6, 57.5, 61.7, 105.6, 128.4, 134.8, 145.5, 162.0, 171.0; HRMS (EI) m/z (M^+) calcd for $C_{15}H_{21}NO_5$ 295.1420, found 295.1421.

*Diethyl 2-methyl-2-[1-methyl-2-oxo-5-(trifluoromethyl)-1,2-dihydropyridin-3-yl]malonate (**3ea**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 99 mg (57%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, J = 7.2 Hz, 6H), 1.81 (s, 3H), 3.58 (s, 3H), 4.24 (dq, J = 7.2, 10.9 Hz, 2H), 4.27 (dq, J = 7.2, 10.9 Hz, 2H), 7.83 (d, J = 2.6 Hz, 1H), 7.68 (d, J = 2.6 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 20.9, 38.5, 57.2, 62.0, 108.9 (q, J = 31.6), 123.5 (q, J = 262.4), 131.4 (q, J = 2.2), 132.7, 136.9 (q, J = 5.1), 161.0, 170.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.17; HRMS (EI) m/z (M^+) calcd for $C_{15}H_{18}F_3NO_5$ 349.1137, found 349.1136.

*Diethyl 2-(5-chloro-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2-methylmalonate (**3fa**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (2/1/0.05 v/v/v) as an eluent; 70 mg (45%), mp 82−83 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, J = 7.1 Hz, 6H), 1.79 (s, 3H), 3.52 (s, 3H), 4.23 (dq, J = 7.1, 10.7 Hz, 2H), 4.27 (dq, J = 7.1, 10.7 Hz, 2H), 7.33 (s, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 21.0, 38.1, 57.3, 62.0, 111.5, 132.8, 134.9, 136.9, 159.9, 170.3; HRMS (EI) m/z (M^+) calcd for $C_{14}H_{18}ClNO_5$ 315.0874, found 315.0876.

*Diethyl 2-(5-bromo-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2-methylmalonate (**3ga**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (2/1/0.05 v/v/v) as an eluent; 70 mg (39%), mp 93−94 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, J = 7.1 Hz, 6H), 1.79 (s, 3H), 3.51 (s, 3H), 4.23 (dq, J = 7.1, 10.7 Hz, 2H), 4.27 (dq, J = 7.1, 10.7 Hz, 2H), 7.39 (d, J = 2.7 Hz, 1H), 7.41 (d, J = 2.7 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 21.0, 38.0, 57.3, 62.0, 97.1, 133.2, 137.3, 138.9, 160.0, 170.3; HRMS (EI) m/z (M^+) calcd for $C_{14}H_{18}BrNO_5$ 359.0368, found 359.0365.

*Diethyl 2-(4-methoxy-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2-methylmalonate (**3ha**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 63 mg (40%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 6H), 1.67 (s, 3H), 3.47 (s, 3H), 3.78 (s, 3H), 4.19 (dq, J = 7.2, 10.8 Hz, 2H), 4.27 (dq, J = 7.2, 10.8 Hz, 2H), 6.03 (d, J = 7.4 Hz, 1H), 7.26 (d, J = 7.4 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.2, 19.7, 37.5, 54.8, 56.1, 61.6, 94.9, 114.9, 137.9, 161.7, 163.3, 170.7; HRMS (APCI) m/z ([M + H]$^+$) calcd for $C_{15}H_{22}NO_6$ 312.1442, found 312.1441.

*Diethyl 2-(1-benzyl-2-oxo-1,2-dihydropyridin-3-yl)-2-methylmalonate (**3ia**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (20:1:0.5, v/v/v) as an eluent; 81 mg (44%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (t, J = 7.2 Hz, 6H), 1.82 (s, 3H), 4.21 (dq, J = 7.2, 10.8 Hz, 2H), 4.24 (dq, J = 7.2, 10.8 Hz, 2H), 5.14 (s, 2H), 6.13 (dd, J = 6.9, 6.9 Hz, 1H), 7.23−7.34 (m, 7H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 21.0, 52.3, 57.6, 61.8, 105.4, 128.1, 128.2, 128.9, 132.5, 135.3, 136.4, 136.6, 161.0, 170.9; HRMS (EI) m/z (M^+) calcd for $C_{20}H_{23}NO_5$ 357.1576, found 357.1578.

*Diethyl 2-methyl-2-(1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)-malonate (**3ja**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (10:1:0.5, v/v/v) as an eluent; 75 mg (45%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, J = 7.1 Hz, 6H), 1.88 (s, 3H), 3.72 (s, 3H), 4.26 (dq, J = 7.1, 10.5 Hz, 2H), 4.30 (dq, J = 7.2, 10.5 Hz, 2H), 7.24 (ddd, J = 1.0, 7.5, 7.5 Hz, 1H), 7.34 (dd, J = 1.0, 8.9 Hz, 1H), 7.55 (dd, J = 1.4, 7.5 Hz, 1H), 7.57 (ddd, J = 1.4, 7.5, 8.9 Hz, 1H), 7.68 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 21.5, 30.0, 57.6, 61.9, 114.0, 120.1, 122.3, 129.3, 130.6, 132.4, 135.2, 139.6, 160.9, 170.8; HRMS (EI) m/z (M^+) calcd for $C_{18}H_{21}NO_5$ 331.1420, found 331.1419.

*Diethyl 2-benzyl-2-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-malonate (**3ab**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (2/1/0.05 v/v/v) as an eluent; 147 mg (83%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 6H), 3.55 (s, 3H), 3.66 (s, 2H), 4.23 (dq, J = 7.2, 10.9 Hz, 2H), 4.26 (dq, J = 7.2, 10.9 Hz, 2H), 5.99 (dd, J = 6.9, 6.9 Hz, 1H), 6.86 (dd, J = 2.1, 6.8 Hz, 2H), 7.10−7.14 (m, 3H), 7.22 (dd, J = 2.0, 6.9 Hz, 1H), 7.30 (dd, J = 2.0, 6.9 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 38.0, 39.2, 61.7, 61.8, 105.1, 126.6, 127.7, 128.7, 130.8, 137.0, 137.1, 139.7, 161.4, 169.5; HRMS (EI) m/z (M^+) calcd for $C_{20}H_{23}NO_5$ 357.1576, found 357.1578.

*Diethyl 2-(2-cyanoethyl)-2-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)malonate (**3ac**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 136 mg (85%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, J = 7.2 Hz, 6H), 2.46 (t, J = 7.5, 2H), 2.73 (t, J = 7.5, 2H), 3.54 (s, 3H), 4.24 (dq, J = 7.2, 10.7 Hz, 2H), 4.29 (dq, J = 7.2, 10.7 Hz, 2H), 6.20 (dd, J = 6.9, 6.9 Hz, 1H), 7.34 (dd, J = 1.8, 6.9 Hz, 1H), 7.43 (dd, J = 1.8, 6.9 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 13.8, 14.1, 28.9, 38.1, 60.1, 62.2, 105.2, 119.5, 128.0, 137.8, 138.3, 161.3, 169.2; HRMS (EI) m/z (M^+) calcd for $C_{16}H_{20}N_2O_5$ 320.1372, found 320.1373.

*Diethyl 2-(5-bromopentyl)-2-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)malonate (**3ad**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 114 mg (55%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, J = 7.1 Hz, 2H), 1.25 (t, J = 7.2 Hz, 6H), 1.41 (tt, J = 7.1, 7.1 Hz, 2H), 1.82 (tt, J = 7.1, 7.1 Hz, 2H), 2.27−2.31 (m, 2H), 3.35 (t, J = 6.9 Hz, 2H), 3.52 (s, 3H), 4.21 (dq, J = 7.2, 10.7 Hz, 2H), 4.25 (dq, J = 7.2, 10.7 Hz, 2H), 6.17 (dd, J = 7.0, 7.0 Hz, 1H), 7.26 (dd, J = 2.1, 7.0 Hz, 1H), 7.61 (dd, J = 2.1, 7.0 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 24.5, 28.4, 32.6, 33.3, 33.9, 37.9, 60.7, 61.6, 105.1, 130.1, 137.2, 137.4, 161.4, 170.1; HRMS (EI) m/z (M^+) calcd for $C_{18}H_{26}BrNO_5$ 415.0994, found 415.099.

*Diethyl 2-cyclopentyl-2-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)malonate (**3ae**):* purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 34 mg (20%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, J = 7.2 Hz, 6H), 1.31−1.42 (m, 2H), 1.45−1.56 (m, 4H), 1.73−1.80 (m, 2H), 3.19 (tt, J = 8.1, 9.1 Hz, 1H), 3.51 (s, 3H), 4.19 (dq, J = 7.2, 10.9 Hz, 2H), 4.24 (dq, J = 7.2, 10.9 Hz, 2H), 6.15 (dd, J = 6.9, 6.9 Hz, 1H), 7.24 (dd, J = 1.8, 6.9 Hz, 1H), 7.70 (dd, J = 1.8, 6.9 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 25.3, 29.2, 37.9, 43.1, 61.2, 63.1, 105.0, 130.5, 136.9, 137.1, 161.7, 170.2; HRMS (EI) m/z (M^+) calcd for $C_{18}H_{25}NO_5$ 335.1733, found 335.1734.

Typical Procedure for Mn(III)-Mediated Direct Arylation of 2-Pyridones with Arylboronic Acids. The synthesis of **5aa** is representative (Scheme 4a): $Mn(OAc)_3{\cdot}2H_2O$ (241 mg, 0.90 mmol) and $PhB(OH)_2$ (**4a**; 36.6 mg, 0.30 mmol) were placed in a 10 mL Schlenk tube, which was filled with nitrogen by using the standard Schlenk technique. A solution of *N*-methyl-2-pyridone (**1a**; 164 mg, 1.5 mmol) in $PhCF_3$ (1.0 mL) was added to the tube, and the suspension was stirred for 4 h at 90 °C. The resulting mixture was quenched with water and then extracted four times with ethyl acetate. The combined organic layer was dried over sodium sulfate. Concentration in vacuo and subsequent purification by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent gave 1-methyl-3-phenylpyridin-2(1*H*)-one (**5aa**; 32 mg, 0.17 mmol) in 58% yield.

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When the residual water layer was extracted four times again with chloroform, *N*-methyl-2-pyridone (**1a**) left intact was recovered (62 mg, 0.57 mmol).

1-Methyl-3-phenylpyridin-2(1H)-one (***5aa***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 32 mg (58%), mp 136−137 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 6.25 (dd, J = 6.8, 6.8 Hz, 1H), 7.30 (dd, J = 2.0, 6.8 Hz, 1H), 7.32 (tt, J = 1.4, 7.4 Hz, 1H), 7.39 (ddd, J = 1.5, 7.4, 7.4 Hz, 2H), 7.48 (dd, J = 2.0, 6.8 Hz, 1H), 7.69 (dd, J = 1.4, 7.4 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.4, 105.9, 127.8, 128.2, 128.8, 131.8, 137.0, 137.5, 137.7, 162.1; HRMS (EI) m/z (M^+) calcd for $C_{12}H_{11}NO$ 185.0841, found 185.0839.

1-Methyl-3-[4-(trifluoromethyl)phenyl]pyridin-2(1H)-one (***5ab***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (2/1/0.05 v/v/v) as an eluent; 36 mg (47%), mp 111−112 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (s, 3H), 6.28 (dd, J = 6.9, 6.9 Hz, 1H), 7.36 (dd, J = 2.0, 6.9 Hz, 1H), 7.53 (dd, J = 2.0, 6.9 Hz, 1H), 7.64 (d, J = 8.2 Hz, 2H), 7.82 (d, J = 8.2 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.4, 105.9, 124.4 (q, J = 272.1 Hz), 125.2 (q, J = 3.9 Hz), 129.0, 129.7 (q, J = 31.6 Hz), 130.2, 138.4, 138.5, 140.5, 161.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.56; HRMS (EI) m/z (M^+) calcd for $C_{13}H_{10}F_3NO$ 253.0714, found 253.0716.

3-(4-Chlorophenyl)-1-methylpyridin-2(1H)-one (***5ac***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (2/1/0.05 v/v/v) as an eluent; 36 mg (54%), mp 142−144 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 6.25 (dd, J = 6.8, 6.8 Hz, 1H), 7.32 (dd, J = 2.0, 6.8 Hz, 1H), 7.36 (d, J = 8.6 Hz, 2H), 7.47 (dd, J = 2.0, 6.8 Hz, 1H), 7.65 (d, J = 8.6 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.4, 106.0, 128.4, 130.0, 130.5, 133.7, 135.4, 137.7, 137.9, 161.9; HRMS (EI) m/z (M^+) calcd for $C_{12}H_{10}ClNO$ 219.0451, found 219.0449.

3-(4-Bromophenyl)-1-methylpyridin-2(1H)-one (***5ad***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (2/1/0.05 v/v/v) as an eluent; 42 mg (48%), mp 146−147 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 3H), 6.24 (dd, J = 6.8, 6.8 Hz, 1H), 7.32 (dd, J = 2.1, 6.8 Hz, 1H), 7.47 (dd, J = 2.1, 6.8 Hz, 1H), 7.50 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 8.3 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.4, 106.0, 121.9, 130.3, 130.4, 131.3, 135.8, 137.7, 137.9, 161.8; HRMS (EI) m/z (M^+) calcd for $C_{12}H_{10}BrNO$ 262.9946, found 262.9943.

3-(4-Iodophenyl)-1-methylpyridin-2(1H)-one (***5ae***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 36 mg (38%), mp 135−137 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 6.25 (dd, J = 6.9, 6.9 Hz, 1H), 7.32 (dd, J = 2.0, 6.9 Hz, 1H), 7.46 (d, J = 8.7 Hz, 2H), 7.47 (dd, J = 2.0, 6.9 Hz, 1H), 7.72 (d, J = 8.7 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.4, 93.6, 106.0, 130.5, 136.5 (two peaks are overlapped), 137.3, 137.7, 138.0, 161.8; HRMS (EI) m/z (M^+) calcd for $C_{12}H_{10}INO$ 310.9807, found 310.9805.

Methyl 4-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)benzoate (***5af***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (2/1/0.05 v/v/v) as an eluent; 34 mg (46%), mp 135−137 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (s, 3H), 3.92 (s, 3H), 6.28 (dd, J = 6.8, 6.8 Hz, 1H), 7.36 (dd, J = 1.9, 6.8 Hz, 1H), 7.55 (dd, J = 1.9, 6.8 Hz, 1H), 7.79 (d, J = 8.7 Hz, 2H), 8.05 (d, J = 8.7 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.4, 52.2, 106.0, 128.6, 129.21, 129.5, 130.5, 138.41, 138.43, 141.6, 161.8, 167.1; HRMS (EI) m/z (M^+) calcd for $C_{14}H_{13}NO_3$ 243.0895, found 243.0893.

3-(4-Benzoylphenyl)-1-methylpyridin-2(1H)-one (***5ag***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (5:1:0.10, v/v/v) as an eluent; 50 mg (58%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 (s, 3H), 6.30 (dd, J = 6.7, 6.7 Hz, 1H), 7.38 (d, J = 6.7 Hz, 1H), 7.49 (dd, J = 7.5, 7.5 Hz, 2H), 7.58 (d, J = 6.7 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.83 (d, J = 7.5 Hz, 2H), 7.84 (s, 4H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.4, 106.0, 128.3, 128.5, 130.0, 130.1, 130.3, 132.4, 136.5, 137.8, 138.4 (two peaks are overlapped), 141.1, 161.7, 196.5; HRMS (EI) m/z (M^+) calcd for $C_{19}H_{15}NO_2$ 289.1103, found 289.1106.

4-(1-Methyl-2-oxo-1,2-dihydropyridin-3-yl)benzaldehyde (***5ah***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 29 mg (44%), mp 111−112 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (s, 3H), 6.30 (dd, J = 6.9, 6.9 Hz, 1H), 7.40 (dd, J = 1.8, 6.9 Hz, 1H), 7.58 (dd, J = 1.8, 6.9 Hz, 1H), 7.90 (s, 4H), 10.03 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.4, 106.0, 129.2, 129.7, 130.1, 135.4, 138.7, 138.8, 143.2, 161.6, 192.1; HRMS (EI) m/z (M^+) calcd for $C_{13}H_{11}NO_2$: 213.0790, found 213.0788.

4-(1-Methyl-2-oxo-1,2-dihydropyridin-3-yl)benzonitrile (***5ai***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (2/1/0.05 v/v/v) as an eluent; 33 mg (52%), mp 130−133 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (s, 3H), 6.31 (dd, J = 6.8, 6.8 Hz, 1H), 7.40 (dd, J = 2.0, 6.8 Hz, 1H), 7.55 (dd, J = 2.0, 6.8 Hz, 1H), 7.68 (d, J = 8.3 Hz, 2H), 7.84 (d, J = 8.3 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.5, 106.0, 111.1, 119.2, 129.3, 129.5, 132.0, 138.7, 139.0, 141.60, 161.50; HRMS (EI) m/z (M^+) calcd for $C_{13}H_{10}N_2O$ 210.0793, found 210.0796.

1-Methyl-3-(4-methylphenyl)pyridin-2(1H)-one (***5aj***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 70 mg (45%), mp 135−137 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.60 (s, 3H), 6.22 (dd, J = 6.9, 6.9 Hz, 1H), 7.20 (d, J = 7.9 Hz, 2H), 7.28 (dd, J = 2.0, 6.9 Hz, 1H), 7.46 (dd, J = 2.0, 6.9 Hz, 1H), 7.59 (d, J = 7.9 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.4, 38.3, 105.9, 128.6, 128.9, 131.7, 134.1, 137.2, 137.2, 137.6, 161.1; HRMS (EI) m/z (M^+) calcd for $C_{13}H_{13}NO$ 199.0997, found 199.0994.

3-(4-Methoxyphenyl)-1-methylpyridin-2(1H)-one (***5ak***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 18 mg (28%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 3.83 (s, 3H), 6.23 (dd, J = 6.9, 6.9 Hz, 1H), 6.93 (dd, J = 2.1, 7.9, 2H), 7.27 (dd, J = 2.1, 6.9 Hz, 1H), 7.45 (dd, J = 2.1, 6.9 Hz, 1H), 7.67 (dd, J = 2.1, 7.9 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.3, 55.5, 106.0, 113.7, 129.4, 129.9, 131.3, 136.7, 136.9, 159.4, 162.2; HRMS (APCI) m/z ([M + H]$^+$) calcd for $C_{13}H_{14}NO_2$ 216.1019, found 216.1017.

3-(3-Methoxyphenyl)-1-methylpyridin-2(1H)-one (***5al***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 26 mg (39%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (s, 3H), 3.84 (s, 3H), 6.23 (dd, J = 6.9, 6.9 Hz, 1H), 6.88 (ddd, J = 1.0, 2.6, 8.1 Hz, 1H), 7.22−7.33 (m, 4H), 7.49 (dd, J = 2.0, 6.9 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.3, 55.4, 105.9, 113.9, 114.1, 121.2, 129.2, 131.5, 137.6, 137.8, 138.3, 159.5, 162.0; HRMS (EI) m/z (M^+) calcd for $C_{13}H_{13}NO_2$ 215.0946, found 215.0947.

3-(2-Chlorophenyl)-1-methylpyridin-2(1H)-one (***5am***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 10 mg (15%), mp 82−83 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (s, 3H), 6.24 (dd, J = 6.8, 6.8 Hz, 1H), 7.27 (dd, J = 1.8, 6.8 Hz, 1H), 7.34−7.37 (m, 1H), 7.28 (d, J = 9.5 Hz, 1H), 7.38 (dd, J = 1.8, 6.8 Hz, 1H), 7.65 (d, J = 8.6 Hz, 1H), 7.42−7.46 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.2, 105.3, 126.7, 129.2, 129.8, 130.7, 131.7, 133.7, 136.0, 138.4, 139.8, 161.5; HRMS (EI) m/z (M^+) calcd for $C_{12}H_{10}ClNO$ 219.0451, found 219.0452.

1-Methyl-3-(naphthalen-2-yl)pyridin-2(1H)-one (***5an***): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (2/1/0.05 v/v/v) as an eluent; 29 mg (41%), mp 159−160 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 (s, 3H), 6.29 (dd, J = 6.8, 6.8 Hz, 1H), 7.33 (dd, J = 1.6, 6.8 Hz, 1H), 7.45−7.48 (m, 2H), 7.61 (dd, J = 1.6, 6.8 Hz, 1H), 7.79−7.88 (m, 4H), 7.23 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.4, 106.1, 126.1, 126.1, 126.7, 127.61, 127.64, 127.8, 128.5, 131.6,

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133.0, 133.5, 134.5, 137.6, 138.1, 162.2; HRMS (EI) m/z (M^+) calcd for $C_{16}H_{13}NO$ 235.0997, found 235.0994.

3-Butyl-1-methylpyridin-2(1H)-one (**5ao**): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (2/1/0.05 v/v/v) as an eluent; 25 mg (50%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, J = 7.3, 3H), 1.38 (tq, J = 7.3, 7.3 Hz, 2H), 1.57 (tt, J = 7.3, 7.4 Hz, 2H), 2.53 (t, J = 7.4 Hz, 2H), 3.54 (s, 3H), 6.09 (dd, J = 6.8, 6.8 Hz, 1H), 7.15 (d, J = 6.8 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.1, 22.7, 30.57, 30.60, 37.8, 105.6, 134.8, 135.6, 135.9, 163.3; HRMS (EI) m/z (M^+) calcd for $C_{10}H_{15}NO$ 165.1154, found 165.1154.

3-Cyclohexyl-1-methylpyridin-2(1H)-one (**5ap**): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 70 mg (45%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16−1.28 (m, 3H), 1.39−1.50 (m, 2H), 1.73−1.83 (m, 3H), 1.86−1.91 (m, 2H), 2.89 (tt, J = 3.1, 11.9, 1H), 3.54 (s, 3H), 6.12 (dd, J = 6.8, 6.8 Hz, 1H), 7.14 (d, J = 6.8 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 26.5, 26.9, 32.6, 37.7, 37.9, 105.7, 133.5, 135.2, 138.9, 162.9; HRMS (EI) m/z (M^+) calcd for $C_{12}H_{17}NO$ 191.1310, found 191.1309.

1,6-Dimethyl-3-phenylpyridin-2(1H)-one (**5da**): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (2/1/0.05 v/v/v) as an eluent; 27 mg (46%), mp 103−105 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.60 (s, 3H), 6.13 (d, J = 7.0 Hz, 1H), 7.29 (tt, J = 1.6, 7.4 Hz, 1H), 7.38 (d, J = 7.0 Hz, 1H), 7.38 (dd, J = 7.4, 7.4 Hz, 2H), 7.67 (dd, J = 1.6, 7.4 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.3, 31.8, 106.5, 127.4, 128.2 (two peaks are overlapped), 128.7, 137.0, 137.5, 145.6, 162.7; HRMS (EI) m/z (M^+) calcd for $C_{13}H_{13}NO$ 199.0997, found 199.0994.

1-Methyl-3-phenyl-5-(trifluoromethyl)pyridin-2(1H)-one (**5ea**): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (10:1:0.5, v/v/v) as an eluent; 30 mg (40%), mp 138−139 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 (s, 3H), 7.38 (tt, J = 1.5, 7.0 Hz, 1H), 7.42 (ddd, J = 1.7, 7.0, 7.0 Hz, 2H), 7.59 (d, J = 2.7 Hz, 1H) 7.67 (dd, J = 1.5, 7.0 Hz, 2H), 7.71 (d, J = 2.7 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.9, 109.6 (q, J = 34.7 Hz), 123.6 (q, J = 269.8 Hz), 128.4, 128.6, 128.7, 132.3, 132.9 (q, J = 2.2 Hz), 135.6, 136.6 (q, J = 5.1 Hz), 161.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.23; HRMS (EI) m/z (M^+) calcd for $C_{13}H_{10}F_3NO$ 253.0714, found 253.0714.

5-Bromo-1-methyl-3-phenylpyridin-2(1H)-one (**5ga**): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (40:1:0.5, v/v/v) as an eluent; 30 mg (37%), mp 135−138 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.59 (s, 3H), 7.35 (tt, J = 1.5, 7.2 Hz, 1H), 7.40 (ddd, J = 1.5, 7.2, 7.2 Hz, 2H), 7.44 (d, J = 2.7 Hz, 1H), 7.53 (d, J = 2.7 Hz, 1H), 7.66 (dd, J = 1.5, 7.2 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.4, 97.8, 128.37, 128.44, 128.7, 133.0, 135.7, 137.2, 140.4, 160.7; HRMS (EI) m/z (M^+) calcd for $C_{12}H_{10}BrNO$ 262.9946, found 262.9943.

4-Methoxy-1-methyl-3-phenylpyridin-2(1H)-one (**5ha**): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (1/1/0.05 v/v/v) as an eluent; 15 mg (23%), mp 139−140 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (s, 3H), 3.78 (s, 3H), 6.15 (d, J = 7.7 Hz, 1H), 7.27 (tt, J = 1.8, 7.2 Hz, 1H), 7.31 (d, J = 7.7 Hz, 1H), 7.38 (ddd, J = 1.7, 7.2, 7.2 Hz, 2H), 7.43 (dd, J = 1.8, 7.2 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 37.7, 56.2, 94.9, 114.8, 127.1, 127.8, 130.8, 133.2, 137.8, 163.0, 163.5; HRMS (APCI) m/z ($[M + H]^+$) calcd for $C_{13}H_{14}NO_2$ 216.1019, found 216.1023.

1-Benzyl-3-phenylpyridin-2(1H)-one (**5ia**): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (5:1:0.1, v/v/v) as an eluent; 39 mg (49%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20 (s, 2H), 6.23 (dd, J = 6.9, 6.9 Hz, 1H), 7.27−7.41 (m, 9H), 7.46 (dd, J = 2.1, 6.9 Hz, 1H), 7.69 (dd, J = 1.3, 7.0 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 52.8, 106.3, 127.8, 128.1, 128.2, 128.4, 128.8, 129.0, 132.2, 136.5, 136.6, 137.0, 137.6, 161.6; HRMS (EI) m/z (M^+) calcd for $C_{18}H_{15}NO$ 261.1154, found 261.1155.

1-Methyl-3-phenylquinolin-2(1H)-one (**5ja**): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (5:1:0.1, v/v/v) as an eluent; 22 mg (31%), mp 138−139 °C (from dichloromethane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H), 7.25 (ddd, J = 2.0, 7.7, 7.7 Hz, 1H), 7.37 (tt, J = 1.3, 7.3 Hz, 1H), 7.38 (dd, J = 2.0, 7.7 Hz, 1H), 7.43 (ddd, J = 1.4, 7.3, 7.3 Hz, 2H), 7.56 (ddd, J = 1.8, 7.7, 7.7 Hz, 1H), 7.60 (dd, J = 1.8, 7.7 Hz, 1H), 7.71 (dd, J = 1.3, 7.3 Hz, 2H), 7.79 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 30.1, 114.1, 120.9, 122.3, 128.2, 128.3, 129.0, 129.1, 130.4, 132.6, 136.9 (two peaks are overlapped), 139.7, 161.7; HRMS (EI) m/z (M^+) calcd for $C_{16}H_{13}NO$ 235.0997, found 235.0996.

1-Methyl-3-phenyl-4-(trifluoromethyl)pyridin-2(1H)-one (**5ka**): purified by column chromatography on silica gel with dichloromethane/ethyl acetate/triethylamine (5:1:0.1, v/v/v) as an eluent; 22 mg (31%), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.59 (s, 3H), 6.43 (d, J = 7.3 Hz, 1H), 7.25 (dd, J = 1.7, 8.6 Hz, 2H), 7.37−7.43 (m, 4H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 38.6, 101.6 (q, J = 3.8 Hz), 122.5 (q, J = 275.8 Hz), 128.0, 128.3, 129.5, 132.8, 133.5, 137.7 (q, J = 30.7 Hz), 138.1, 162.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −59.55; HRMS (EI) m/z (M^+) calcd for $C_{13}H_{10}F_3NO$ 253.0714, found 253.0714.

1-(But-3-en-1-yl)-3-phenylpyridin-2(1H)-one (**5la**): purified by column chromatography on silica gel with hexane/triethylamine (2:1, v/v) as an eluent; 22 mg (33%), mp 82−83 °C (from hexane/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.57 (dt, J = 7.1, 7.1 Hz, 2H), 4.06 (t, J = 7.1 Hz, 2H), 5.07 (dd, J = 1.6, 10.1 Hz, 1H), 5.12 (dd, J = 1.6, 17.1 Hz, 1H), 5.82 (ddt, J = 10.1, 17.1, 7.1 Hz, 1H), 6.24 (dd, J = 6.9, 6.9 Hz, 1H), 7.25 (dd, J = 2.1, 6.9 Hz, 1H), 7.31 (tt, J = 1.3, 7.4 Hz, 1H), 7.39 (ddd, J = 1.5, 7.4, 7.4 Hz, 2H), 7.48 (dd, J = 2.1, 6.9 Hz, 1H), 7.69 (dd, J = 1.3, 7.4 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 33.4, 50.4, 105.8, 118.0, 127.8, 128.2, 128.8, 132.0, 134.3, 137.0, 137.0, 137.6, 161.5; HRMS (EI) m/z (M^+) calcd for $C_{15}H_{15}NO$ 225.1154, found 225.1155.

■ ASSOCIATED CONTENT

Supporting Information

Figures detailing attempts to apply some catalyst systems for C3-selective direct phenylation of **1a** with **4a** and ^{1}H, ^{13}C, and ^{19}F NMR spectra for products. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: k_hirano@chem.eng.osaka-u.ac.jp (K.H.); miura@chem.eng.osaka-u.ac.jp (M.M.).

Notes

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