HIGHLY C3-SELECTIVE DIRECT ALKYLATION AND ARYLATION OF 2-PYRIDONES UNDER VISIBLE-LIGHT-PROMOTED PHOTOREDOX CATALYSIS

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Abstract – An Ir photoredox catalyst-mediated highly site-selective direct alkylation and arylation of 2-pyridones has been developed. Under visible-light-promoted conditions, ethyl 2-bromo-2,2-difluoroacetate couples with various 2-pyridones exclusively at the C3 position. A similar photoredox catalysis is also effective for the direct C3-arylation with diaryliodonium triflates. Thus, these reactions occurs under very mild conditions (blue LEDs irradiation and ambient temperature) to form the corresponding C3-alkylated and arylated 2-pyridones of potential interest in medicinal and pharmaceutical chemistry.

INTRODUCTION

Since 2-pyridones are prevalent structural motifs in many pharmaceutical targets and biologically active natural and unnatural products, as exemplified by ciclopirox, milrinone, camptothecin, perampanel, fredericamycin, and PD180970,1 the C–C forming process on the 2-pyridone ring ranks as one of long-standing important topics in synthetic organic chemistry. While most traditional strategies rely on preactivated halogenated 2-pyridones as starting materials, recent advances in the C–H functionalization2 allow unfunctionalized 2-pyridones to be directly adopted in several types of C–C formations. The biggest challenge in the C–H functionalization of the 2-pyridone is the control of the site-selectivity. In 1984, Itahara and Ouseto reported the Pd-mediated direct alkenylation of the 2-pyridone with acrylates.3 The reaction was stoichiometric in palladium, but the high C5-selectivity was observed. Li then developed the catalytic variant of this process by using a Cu(OAc)₂ terminal oxidant and also succeeded in the related C5-arylation with polyfluoroarenes under Pd/Ag catalysis (Scheme 1a).4 Additionally, Nakao and Hiyama achieved the Ni/Al-catalyzed direct alkenylation and alkylation with alkynes and alkenes, respectively, at the otherwise difficult C6 position.5 Our group also developed the Cu-mediated
or Cu/O₂-catalyzed C6-selective heteroarylation with the aid of a pyridine directing group.\(^6\) Since then, some groups successfully applied the pyridine-directed methodology to the Rh-catalyzed C6-selective alkylation and alkynylation (Scheme 1b).\(^2\) On the other hand, the C3-selective C–H functionalization has been less studied, despite relatively high electron density at the C3 position.\(^5\) In this context, we recently revisited the unique nature of classical carbon-centered radical species and developed the Ni-catalyzed\(^9\) and Mn-mediated\(^10\) radicalic direct C3 alkylation and arylation. Subsequently, Maiti reported a related arylation reaction in the presence of a Fe catalyst (Scheme 1c).\(^11\) However, heating conditions (70–130 °C) and/or excess metallic salts are often necessary for a satisfactory conversion. Thus, despite certain advances mentioned above, there still remains a large demand for further development of the site-selective C–H functionalization of 2-pyridones, particularly at the relatively inaccessible C3 position. Herein, we report an Ir-catalyzed, radical-mediated direct C3-alkylation and arylation of 2-pyridones with ethyl 2-bromo-2,2-difluoroacetate and diaryliodonium triflates,\(^12\) respectively. The reactions proceed smoothly at ambient temperature under visible-light-promoted conditions (Scheme 2).\(^13\)

**RESULTS AND DISCUSSION**

Prompted by recent rapid progress of the radical-mediated, visible-light-promoted photoredox catalysis,\(^14\) we commenced optimization studies with N-methyl-2-pyridone (1a, 1.25 mmol) and ethyl 2-bromo-2,2-difluoroacetate (2a, 0.25 mmol)\(^15\) as model substrates under blue LEDs irradiation (Table 1). Initial catalyst screening identified Ir(ppy)\(_3\) to be a good candidate in MeCN, and the corresponding C3-alkylated 2-pyridone 3aa was isolated in 74\% yield: other representative photoredox catalysts, Ir(ppy)\(_2\)(dtbpy)PF\(_6\), Ru(bpy)\(_3\)Cl\(_2\)•6H\(_2\)O, and Eosin Y (Na), showed no catalytic activity (entries 1–4). Among solvents we tested, MeCN was found to be optimal (entries 5–8). The addition of external inorganic bases gave negligible or negative impact on the reaction efficiency (entries 9–12). A decrease of amount of the pyridone 1a to 0.75 mmol provided a slightly lower but still synthetically useful yield of 3aa (entry 13). The control experiments in the absence of light or catalyst resulted in no conversion (entry 14 and 15). Additionally, an investigation of on/off-switching of the light source revealed that the reaction progressed steady under blue LEDs irradiation and stopped in the dark (see the Experimental section). These outcomes suggest the operation of photoredox catalysis (vide infra).\(^16\) Also note that the difluorinated α-bromo ester 2a did not work at all under previously reported Ni-catalyzed conditions (data not shown).\(^9\)
Scheme 1. Site-selective C–H functionalization approaches to substituted 2-pyridones

Scheme 2. Visible-light-promoted Ir photoredox catalysis for C3-selective direct alkylation and arylation of 2-pyridones at ambient temperature (this work)
Table 1. Optimization studies for C3-selective alkylation of N-methyl-2-pyridone (1a) with ethyl 2-bromo-2,2-difluoroacetate (2a) under visible-light-promoted photoredox catalysisa

<table>
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<th>entry</th>
<th>catalyst</th>
<th>base</th>
<th>solvent</th>
<th>yield of 3aa (%)b</th>
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</tr>
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<td>4</td>
<td>Eosin Y (Na)</td>
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<td>MeCN</td>
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<td>none</td>
<td>MeCN</td>
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a Conditions: 1a (1.3 mmol), 2a (0.25 mmol), catalyst (0.0050 mmol), solvent (3.0 mL), ambient temp, blue LEDs irradiation, 6 h, N₂.  
b Yields are estimated by ¹H NMR or GC analysis. Isolated yields are in parentheses.  
c With 0.75 mmol (3.0 equiv) of 1a.  
d In the dark.
Under the conditions of entry 1 in Table 1, we subsequently performed the direct alkylation of various substituted 2-pyridones 1 with 2a (Scheme 3). Regardless of the substitution pattern of the methyl group, the reaction occurred exclusively at the C3 position, and the corresponding C3-difluoroalkylated products 3ba–3da were formed in substantial yields. The Ir photoredox catalysis was tolerated with electron-donating methoxy and benzyloxy groups (3ea and 3fa) while the electron-withdrawing trifluoromethyl and halogen substituents dropped the yield (3ga–3ia). The observed trend is consistent with the plausible radical mechanism including SOMO/HOMO interaction between the electrophilic difluoromethyl radicals and electron-rich pyridones.\(^2\)\(^,\)\(^10\) We also tested the NH 2-pyridone but the yield was lower (3ja). In most cases, the starting alkyl bromide 2a fully consumed despite the moderate yield of 3. We could not identify any byproducts, but homocoupling and/or reduction of 2a might competitively occur. Although we also tested other fluorinated alkyl halides,\(^17\) only sulfone derivative 4 moderately reacted with 1a under slightly modified conditions using Na\(_2\)S\(_2\)O\(_3\) as an additive (Scheme 4).\(^18\)

**Scheme 3.** C3-Selective direct alkylation of various 2-pyridones 1 with ethyl 2-bromo-2,2-difluoroacetate (2a) under visible-light-promoted Ir(ppy)\(_3\) catalysis. Isolated yields are shown. \(^1\)H NMR yields are in parentheses.
Scheme 4. C3-Selective direct alkylation of N-methyl 2-pyridone (1a) with [(difluoriodomethyl)sulfonyl]benzene (4) under Na2S2O3-modified conditions

Table 2. Optimization studies for C3-selective phenylation of N-methyl-2-pyridone (1a) with diphenyliodonium triflate (6a) under visible-light-promoted photoredox catalysisa

<table>
<thead>
<tr>
<th>entry</th>
<th>base</th>
<th>yield of 7aa (%)b</th>
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<tbody>
<tr>
<td>1</td>
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<td>28</td>
</tr>
<tr>
<td>2</td>
<td>i-Pr2NEt</td>
<td>7</td>
</tr>
<tr>
<td>3</td>
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<td>CsOAc</td>
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<td>7</td>
<td>K3PO4</td>
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<td>11e</td>
<td>KOAc</td>
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</tbody>
</table>

a Conditions: 1a (1.3 mmol), 6a (0.25 mmol), Ir(ppy)3 (0.0050 mmol), MeCN (3.0 mL), ambient temp, blue LEDs irradiation, 6 h, N2. b Yields are estimated by 1H NMR or GC analysis. Isolated yields are in parentheses. c In MeCN (1.0 mL). d In the dark. e Without Ir(ppy)3.

We then turned our attention to the related direct C3-phenylation of N-methyl-2-pyridone (1a) with diphenyliodonium triflate (6a) (Table 2). The conditions same as those in Scheme 3 afforded the desired C3-phenylation product 7aa albeit with 28% yield (entry 1). Given the liberation of strongly acidic TfOH, we investigated basic additives to quench with it (entries 2–8). Gratifyingly, some potassium inorganic bases improved the yield, with KOAc to be optimal (entry 5). Although additional
solvent and catalyst screening gave no further improvement as far as we examined, we finally obtained 55% isolated yield of **7aa** by reducing the amount of MeCN solvent into 1.0 mL (entry 9). Also in the direct alkylation, both visible light and Ir(ppy)$_3$ were essential for the promotion of the reaction (entries 10 and 11).

We next investigated the scope and limitation of the direct arylation reaction. Representative products are shown in Scheme 5. The C3 selectivity was uniformly high, and C4-, C5-, and C6-methylated substrates furnished the corresponding C3-phenylated pyridones **7ba–7da** as the single isomers. In contrast to the difluoroalkylation in Scheme 3, electron-withdrawing trifluoromethyl and chloro substituents were found to be better than electron-donating methoxy group (**7ea–7ga** vs **7ha**). This outcome could arise from an effective SOMO/LUMO interaction between nucleophilic phenyl radical and electron-deficient 2-pyridones.$^{9,10}$ The direct phenylation was compatible with 2-pyridones bearing N-butyl, N-phenyl, and even free N-H substituents (**7ja–7la**). The introduction of 4-methylphenyl, 4-tert-butylphenyl, and 4-bromophenyl groups was also possible, and the corresponding C3-arylated products **7ab–7ad** were formed in moderate yields. In most cases, the yield was moderate probably because the Ir catalyst gradually decomposed during the course of the reaction. Actually, we recovered the starting diaryliodonium triflates **6** in some cases. Additionally, the O-analogue of 2-pyridone, coumarin (**8**), also coupled with **6a** under identical conditions (Scheme 6).

On the basis of the literature information$^{14}$ and our findings, the plausible catalytic cycle of the reaction of **1a** with **2a** or **6a** is illustrated in Scheme 7. Initial visible light irradiation excites the starting Ir(III) catalyst to the active Ir(III)$^*$ species. Subsequent reversible single electron transfer (SET) from Ir(III)$^*$ to **2a** or **6a** delivers the Ir(IV) of the higher oxidation state and anion radical species, which smoothly undergoes the fragmentation to the corresponding alkyl or aryl radical **10**. The 2-pyridone **2a** then reacts with **10** at the C3 position to afford the allylic radical intermediate **11**. The second SET process between **11** and Ir(IV) closes the Ir catalytic cycle and generates the cationic species **12**, which is finally deprotonated to furnish the observed C3-alkylated **3aa** or -arylated **7aa**. The regioselectivity can be determined in the radical addition step and controlled by the inherent nature of radical intermediates: the higher stability associated with the resonance effect of the allylic radical **11** and relatively large contributions of HOMO and LUMO at the C3 position of the 2-pyridone **2a**$^{9,10}$ may be major controlling factors. However, the exact mechanism still remains to be elucidated.$^{16}$

In the above arylation reaction, one aryl group of symmetrical diaryliodonium salts **6** was lost as the aryl iodide. This is problematic and less atom-economical particularly when more complex and highly
functionalized aryl moiety is installed. Thus, we attempted the arylation with unsymmetrical Mes-I(III)-Ar reagent 13 (Mes = mesityl) instead of 6 (Scheme 8a). Although the yield was lower than that with the symmetrical 6, the Mes group did not transfer at all, and the desired aryl group was selectively incorporated to the pyridone molecules. Trifluoromethyl- and ester-containing aromatic rings were also accessible (7ae and 7af). Additionally notable is that the phenyldiazonium salt 14, which is readily available from the corresponding aniline, is a potential alternative to the diaryliodonium salt (Scheme 8b).

Scheme 5. C3-Selective direct arylation of 2-pyridones 1 with diaryliodonium triflates 6 under visible-light-promoted Ir(ppy)$_3$ catalysis. Isolated yields are shown. $^1$H NMR yields are in parentheses.

Scheme 6. C3-Selective direct phenylation of coumarin (8) with diphenyliodonium triflate (6a) under visible-light-promoted Ir(ppy)$_3$ catalysis
Scheme 7. Plausible mechanism for C3-selective direct alkylation and arylation of 2-pyridone 1a with 2a or 6a under visible-light-promoted Ir(ppy)₃ catalysis.

Scheme 8. C3-Selective direct arylation of N-methyl-2-pyridone (1a) with unsymmetrical Mes-I(III)-Ar triflates 13 or phenyldiazonium salt 14 under visible-light-promoted Ir(ppy)₃ catalysis. Isolated yields are shown.

CONCLUSION
We have developed a highly C3-selective difluoroalkylation and arylation of 2-pyridones under visible-light-promoted Ir(ppy)₃ photoredox catalysis. The reactions proceed smoothly at ambient temperature and provide a direct access to the C3-functionalized 2-pyridones of great potential in medicinal and pharmaceutical chemistry, although the reaction efficiency is still moderate. The present
catalysis can complement the known C–H functionalization protocols in view of the site-selectivity. Ongoing work seeks to develop new strategies for the site-selective and diverse C–H functionalization of 2-pyridones.

**EXPERIMENTAL**

**General.** $^1$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 APCI. GC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm x 1.5 m) or a CBP-1 capillary column (i. d. 0.5 mm x 25 m). TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F$_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography. Blue light irradiation was conducted by a blue LED tape light. 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. MeCN was dried on a Glass Contour Solvent dispending system (Nikko Hansen & Co., Ltd.) prior to use. Ir(ppy)$_3$ was synthesized from IrCl$_3$•3H$_2$O and 2-phenylpyridine under the reported conditions. Symmetrical and unsymmetrical diaryliodonium triflates were prepared according to the literature.

**Visible-light-promoted Ir(ppy)$_3$-catalyzed C3-alkylation of 2-pyridones.** The reaction of 1a with 2a is representative (Table 1, entry 1). Ir(ppy)$_3$ (3.3 mg, 0.0050 mmol) was placed in a Schlenk tube. Nitrogen gas displacement was done by using the standard Schlenk technique, and N-methyl-2-pyridone (1a, 136.4 mg, 1.25 mmol) and ethyl bromodifluoroacetate (2a, 50.7 mg, 0.25 mmol) were added using syringe followed by addition of MeCN (3 mL). The mixture was stirred for 6 h under blue light LED irradiation (12 DC/3 W). Water (20 mL) was added, and extraction was done with EtOAc (15 mL x 3). The combined organic phase was dried over sodium sulfate and then concentrated in vacuo. Purification via column chromatography (Wakosil C-200, hexane/EtOAc = 20/1 to EtOAc/CH$_2$Cl$_2$/Et$_3$N = 1/1/0.05) provided pure ethyl 2,2-difluoro-2-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)acetate (3aa, 42.7 mg, 0.19 mmol, 74% yield).

**Visible-light-promoted Ir(ppy)$_3$-catalyzed C3-arylation of 2-pyridones.** The reaction of 1a with 6a is representative (Table 2, entry 9). In a glovebox filled with nitrogen, Ir(ppy)$_3$ (3.3 mg, 0.0050 mmol), Ph$_2$IOTf (6a, 136.4 mg, 0.25 mmol), and potassium acetate (49.1 mg, 0.50 mmol) were placed in a Schlenk tube. The tube was sealed with a septum and then taken out of the glovebox. A solution of N-methyl-2-pyridone (1a, 136.4 mg, 1.25 mmol) in MeCN (1 mL) was added using a syringe. The mixture was stirred for 6 h under blue light LED irradiation (12 DC/3 W). Water (20 mL) was added, and extraction was done with EtOAc (15 mL x 3). The combined organic phase was dried over sodium...
sulfate and then concentrated in vacuo. Purification via column chromatography (Wakosil C-200, hexane/EtOAc = 20/1 to EtOAc/CH2Cl2/ Et3N = 1/1/0.05) followed by GPC provided pure 1-methyl-3-phenylpyridin-2(1H)-one (7aa, 25.4 mg, 0.14 mmol, 55% yield).

**Experiment of ON/OFF Switching of Light Source.** In the glove box filled with nitrogen, Ir(ppy)3 (1.3 mg, 0.0020 mmol), N-methyl-2-pyridone (1a, 54.6 mg, 0.50 mmol), ethyl bromodifluoroacetate (2a, 20.3 mg, 0.10 mmol), dibenzyl ether (internal standard, 12.3 mg), and MeCN-d3 (0.75 mL) were placed in a NMR tube. The tube was sealed with a septum and taken out of the glovebox. After sonication for a few seconds, the on-off switching of light source was performed, and the reaction progress was monitored by 1H NMR. The obtained result is shown in Scheme 9.

![Scheme 9. Reaction progress in on/off switching of the light source](image)

**Characterization Data for Products**

**Ethyl 2,2-difluoro-2-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)acetate (3aa):** 42.7 mg, 74%, yellow oil; IR (neat, cm⁻¹) 767, 1041, 1112, 1276, 1560, 1662, 1772; 1H NMR (400 MHz, CDCl3) δ 1.36 (t, J = 7.2 Hz, 3H), 3.56 (s, 3H), 4.38 (q, J = 7.2 Hz, 2H), 6.29 (t, J = 6.9 Hz, 1H), 7.44 (d, J = 6.9 Hz, 1H), 7.78 (dt, J = 6.9, 1.0 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 13.89, 37.43, 62.98, 104.88, 111.54 (t, J = 247.7 Hz), 124.36 (t, J = 24.5 Hz), 137.60 (t, J = 7.0 Hz), 140.82, 159.96 (t, J = 5.0 Hz), 163.33 (t, J = 32.7 Hz); 19F NMR (376 MHz, CDCl3) δ -105.86; HRMS (APCI) m/z (M+H)+ calecd for C10H12F2NO3: 232.0780, found: 232.0779.

**Ethyl 2-(1,4-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)-2,2-difluoroacetate (3ba):** 26.3 mg, 43%, white solid, mp 83.8-85.9 °C; IR (neat, cm⁻¹) 785, 1114, 1354, 1604, 1654, 1772; 1H NMR (400 MHz, CDCl3) δ 1.36 (t, J = 7.2 Hz, 3H), 2.44 (t, J = 4.0 Hz, 3H), 3.48 (s, 3H), 4.38 (q, J = 7.2 Hz, 2H), 6.07 (d, J = 7.0 Hz, 1H), 7.27 (d, J = 7.0 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 13.92, 20.19 (t, J = 5.4 Hz), 37.35, 62.64,
110.48, 113.86 (t, J = 247.3 Hz), 121.05 (t, J = 24.2 Hz), 138.77, 152.87, 160.57 (t, J = 6.43 Hz), 163.83 (t, J = 32.2 Hz); \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) δ -99.34; HRMS (APCI) m/z (M+H\(^+\)) calcd for C\(_{11}H_{14}F_2NO_3\): 246.0936, found 246.0939.

**Ethyl 2-(1,5-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)-2,2-difluoroacetate (3ca):** 28.2 mg, 46%, yellow oil; IR (neat, cm\(^{-1}\)) 744, 796, 1132, 1568, 1606, 1668, 1772; \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 1.35 (t, J = 7.2 Hz, 3H), 2.15 (s, 3H), 3.52 (s, 3H), 4.38 (q, J = 7.2 Hz, 2H), 7.22 (s, 1H), 7.65 (s, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ 13.89, 17.09, 37.23, 62.96, 111.61 (t, J = 247 Hz), 114.08, 123.72 (t, J = 24.0 Hz), 138.51, 139.90 (t, J = 6.6 Hz), 159.21 (t, J = 4.4 Hz), 163.41 (t, J = 32.0 Hz); \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) δ -105.75; HRMS (APCI) m/z (M+H\(^+\)) calcd for C\(_{11}H_{14}F_2NO_3\): 246.0936, found 246.0931.

**Ethyl 2-(1,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)-2,2-difluoroacetate (3da):** 41.7 mg, 68%, white solid, mp 107.2-108.2 °C; IR (neat, cm\(^{-1}\)) 1112, 1296, 1575, 1653, 1774; \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 1.35 (t, J = 7.2 Hz, 3H), 2.41 (s, 3H), 3.53 (s, 3H), 4.37 (q, J = 7.2 Hz, 2H), 6.17 (d, J = 7.3 Hz, 1H), 7.66 (d, J = 7.3 Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ 13.91, 21.16, 31.09, 62.86, 105.58, 111.89 (t, J = 246.9 Hz), 120.84 (t, J = 24.5 Hz), 136.59 (t, J = 6.6 Hz), 149.75, 160.68 (t, J = 5.3 Hz), 163.60 (t, J = 33.6 Hz); \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) δ -105.70; HRMS (APCI) m/z (M+H\(^+\)) calcd for C\(_{11}H_{14}F_2NO_3\): 246.0936, found: 246.0936.

**Ethyl 2,2-difluoro-2-(4-methoxy-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)acetate (3ea):** 26.8 mg, 41%, yellow solid, mp 104.7-106.5 °C; IR (neat, cm\(^{-1}\)) 788, 1028, 1263, 1363, 1544, 1654, 1772; \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 1.36 (t, J = 7.2 Hz, 3H), 3.47 (s, 3H), 3.92 (s, 3H), 4.38 (q, J = 7.2 Hz, 2H), 6.09 (d, J = 7.8 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ 13.95, 37.18, 56.56, 62.60, 70.57, 94.46, 104.54 (t, J = 24.2 Hz), 113.17 (t, J = 246.2 Hz), 141.48, 161.09, 164.15 (t, J = 32.1 Hz), 168.00; \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) δ -100.17; HRMS (APCI) m/z (M+H\(^+\)) calcd for C\(_{11}H_{14}F_2NO_4\): 262.0885, found: 262.0881.

**Ethyl 2-(4-(benzyloxy)-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-2,2-difluoroacetate (3fa):** 48.0 mg, 57%, white solid, mp 84.5-86.1 °C; IR (neat, cm\(^{-1}\)) 1080, 1109, 1152, 1363, 1541, 1653, 1772; \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 1.34 (t, J = 7.2 Hz, 3H), 3.45 (s, 3H), 4.34 (q, J = 7.2 Hz, 2H), 5.22 (s, 2H), 6.09 (d, J = 7.8 Hz, 1H), 7.32-7.40 (m, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ 13.93, 37.11, 62.57, 70.88, 95.55, 106.07 (t, J = 23.6 Hz), 113.20 (t, J = 246.8 Hz), 126.78, 128.33, 128.74, 135.16, 141.52, 161.10 (t, J = 4.7 Hz), 164.17 (t, J = 31.7 Hz), 167.12; \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) δ -99.90; HRMS (APCI) m/z (M+H\(^+\)) calcd for C\(_{17}H_{18}F_2NO_4\): 338.1198, found: 338.1198.

3-(Difluoro(phenylsulfonyl)methyl)-1-methylpyridin-2(1H)-one (5): 18.3 mg, 24%, white solid, mp 174.2-176.2 °C; IR (neat, cm\(^{-1}\)) 590, 1074, 1165, 1550, 1653; \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 3.58 (s, 3H), 6.28 (t, J = 6.8 Hz, 1H), 7.56 (dd, J = 6.8, 2.0 Hz, 1H), 7.62 (t, J = 8.1 Hz, 2H), 7.76 (tt, J = 7.5, 2.0 Hz, 1H), 7.80 (dd, J = 7.5, 4.1 Hz, 1H), 8.07 (d, J = 7.8 Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ 38.12,
104.35, 116.80 (t, J = 20.5 Hz), 121.52 (t, J = 287.6 Hz), 129.18, 130.92, 133.42, 135.15, 143.00 (t, J = 7.3 Hz), 143.24, 158.71; 19F NMR (376 MHz, CDCl3) δ -99.64; HRMS (APCI) m/z (M+H)+ calcd for C13H12F2NO3S: 300.0500, found: 300.0500.

1-Methyl-3-phenylpyridin-2(1H)-one (7aa): 20.8 mg, 55%, white solid, mp 106.4-108.4 °C; IR (neat, cm⁻¹) 702, 773, 1583, 1647; ¹H NMR (400 MHz, CDCl3) δ 3.62 (s, 3H), 6.25 (t, J = 7.0 Hz, 1H), 7.32 (tt, J = 7.2, 2.1 Hz, 2H), 7.40 (t, J = 7.2 Hz, 2H), 7.49 (dd, J = 7.0, 2.1 Hz, 1H), 7.69 (dd, J = 7.0, 1.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl3) δ 38.24, 105.82, 127.66, 128.10, 128.62, 131.64, 136.83, 137.41, 137.59, 161.95; HRMS (APCI) m/z (M+H)+ calcd for C12H12NO: 186.0913, found: 186.0914.

1-Methyl-3-(p-tolyl)pyridin-2(1H)-one (7ab): 15.0 mg, 30%, white solid, mp 135.2-137.1 °C; IR (neat, cm⁻¹) 825, 1282, 1560, 1585, 1645; ¹H NMR (400 MHz, CDCl3) δ 2.37 (s, 3H), 3.61 (s, 3H), 6.23 (t, J = 6.7 Hz, 1H), 7.20 (d, J = 8.2 Hz, 2H), 7.27 (dd, J = 2.0, 6.7 Hz, 1H), 7.46 (dd, J = 2.0, 7.0 Hz, 1H), 7.59 (d, J = 8.2 Hz, 2H); ¹³C NMR (400 MHz, CDCl3) δ 21.23, 38.20, 105.79, 128.45, 128.80, 131.63, 133.93, 137.06, 137.10, 137.45, 162.02; HRMS (APCI) m/z (M+H)+ calcd for C12H14NO: 200.1070, found: 200.1070.

3-(4-(tert-Butyl)phenyl)-1-methylpyridin-2(1H)-one (7ac): 23.5 mg, 39%, yellowish-brown solid, mp 94.5-96.2 °C; IR (neat, cm⁻¹) 570, 1595, 1647, 2960; ¹H NMR (400 MHz, CDCl3) δ 1.34 (s, 9H), 3.61 (s, 3H), 6.24 (t, J = 6.8 Hz, 1H), 7.29 (dd, J = 6.8, 2.0 Hz, 1H), 7.42 (d, J = 8.7 Hz, 2H), 7.48 (dd, J = 6.8, 2.0 Hz, 1H), 7.64 (d, J = 8.7 Hz, 2H); ¹³C NMR (400 MHz, CDCl3) δ 31.33, 34.58, 38.21, 105.83, 125.08, 128.26, 131.56, 133.88, 137.08, 137.16, 150.60, 162.06; HRMS (APCI) m/z (M+H)+ calcd for C16H20NO: 242.1539, found: 242.1541.

3-(4-Bromophenyl)-1-methylpyridin-2(1H)-one (7ad): 25.1 mg, 38%, white solid, mp 157.0-158.5 °C; IR (neat, cm⁻¹) 1008, 1550, 1583, 1647; ¹H NMR (400 MHz, CDCl3) δ 3.62 (s, 3H), 6.25 (t, J = 6.9 Hz, 1H), 7.33 (dd, J = 6.9, 2.0 Hz, 1H), 7.48 (dd, J = 6.9, 2.0 Hz, 1H), 7.52 (d, J = 8.7 Hz, 2H), 7.59 (d, J = 8.7 Hz, 2H); ¹³C NMR (400 MHz, CDCl3) δ 38.27, 105.83, 121.77, 130.21, 130.36, 131.22, 135.70, 137.55, 137.80, 161.67; HRMS (APCI) m/z (M+H)+ calcd for C16H11BrNO: 264.0019, found: 264.0027.

1-Methyl-3-(4-(trifluoromethyl)phenyl)pyridin-2(1H)-one (7ae): 20.7 mg, 33%, brown solid, mp 98.9-101.0 °C; IR (neat, cm⁻¹) 773, 840, 1112, 1161, 1327, 1554, 1595, 1647; ¹H NMR (400 MHz, CDCl3) δ 3.63 (s, 3H), 6.29 (t, J = 6.9 Hz, 1H), 7.37 (dd, J = 6.9, 2.0 Hz, 1H), 7.53 (dd, J = 6.9, 2.0 Hz, 1H), 7.65 (d, J = 8.2 Hz, 2H), 7.82 (d, J = 8.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl3) δ 38.29, 105.81, 124.26 (q, J = 270.4 Hz), 125.03 (q, J = 3.9 Hz), 128.86, 129.55 (q, J = 32.2 Hz), 130.14, 138.26, 138.35, 140.40, 161.63; ¹⁹F NMR (376 MHz, CDCl3) δ -62.56; HRMS (APCI) m/z (M+H)+ calcd for C13H11F3NO: 254.0787, found: 254.0789.

Methyl 4-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)benzoate (7af): 15.8 mg, 26%, white solid, mp 132.5-134.6 °C; IR (neat, cm⁻¹) 759, 1109, 1290, 1558, 1595, 1653, 1720; ¹H NMR (400 MHz, CDCl3) δ
3.63 (s, 3H), 3.93 (s, 3H), 6.28 (t, J = 6.9 Hz, 1H), 7.36 (dd, J = 6.9, 2.1 Hz, 1H), 7.48 (dd, J = 6.9, 2.1 Hz, 1H), 7.51 (d, J = 8.3 Hz, 2H), 5.59 (d, J = 8.3 Hz, 2H); 13C NMR (400 MHz, CDCl3) δ 38.31, 52.08, 105.84, 128.49, 129.09, 129.40, 130.40, 138.25, 138.30, 141.45, 161.63, 167.02; HRMS (APCI) m/z (M+H)+ calcd for C14H14NO3: 244.0968, found: 244.0968.

1,4-Dimethyl-3-phenylpyridin-2(1H)-one (7ba): 17.4 mg, 35%, white solid, mp 65.0-67.0 °C; IR (neat, cm⁻¹) 771, 1263, 1598, 1647; 1H NMR (400 MHz, CDCl3) δ 2.04 (s, 3H), 3.54 (s, 3H), 6.11 (d, J = 7.0 Hz, 1H), 7.18 (d, J = 7.0 Hz, 1H), 7.25 (d, J = 7.1 Hz, 2H), 7.31 (tt, J = 1.4, 7.1 Hz, 1H), 7.40 (t, J = 7.1 Hz, 2H); 13C NMR (100 MHz, CDCl3) δ 20.44, 37.76, 108.92, 127.20, 128.16, 129.95, 131.02, 135.69, 136.15, 147.03, 162.32; HRMS (APCI) m/z (M+H)+ calcd for C13H14NO: 200.1070, found: 200.1073.

1,5-Dimethyl-3-phenylpyridin-2(1H)-one (7ca): 12.5 mg, 23%, white solid, mp 114.0-115.2 °C; IR (neat, cm⁻¹) 694, 1282, 1419, 1577, 1595, 1653; 1H NMR (400 MHz, CDCl3) δ 2.13 (s, 3H), 3.58 (s, 3H), 7.09 (d, J = 2.3 Hz, 1H), 7.29-7.41 (m, 4H), 7.69 (d, J = 6.0 Hz, 2H); 13C NMR (100 MHz, CDCl3) δ 17.21, 38.04, 114.61, 127.60, 128.06, 128.64, 131.01, 135.04, 136.89, 140.28, 161.15; HRMS (APCI) m/z (M+H)+ calcd for C13H14NO: 200.1070, found: 200.1070.

1,6-Dimethyl-3-phenylpyridin-2(1H)-one (7da): 23.9 mg, 51%, white solid, mp 104.4-106.2 °C; IR (neat, cm⁻¹) 785, 1120, 1259, 1431, 1566, 1587, 1639; 1H NMR (400 MHz, CDCl3) δ 2.40 (s, 3H), 3.60 (s, 3H), 6.38 (d, J = 7.2 Hz, 1H), 7.28 (tt, J = 5.3, 1.3 Hz, 1H), 7.36-7.40 (m, 3H), 7.66-7.69 (m, 2H); 13C NMR (100 MHz, CDCl3) δ 21.15, 31.70, 106.43, 127.28, 128.05, 128.08, 128.55, 136.89, 137.40, 145.49, 162.58; HRMS (APCI) m/z (M+H)+ calcd for C13H14NO: 200.1070, found: 200.1070.

1-Methyl-3-phenyl-4-(trifluoromethyl)pyridin-2(1H)-one (7ea): 33.9 mg, 54%, brown oil; IR (neat, cm⁻¹) 702, 769, 945, 1136, 1184, 1325, 1606, 1659; 1H NMR (400 MHz, CDCl3) δ 3.61 (s, 3H), 6.45 (d, J = 7.2 Hz, 1H), 7.23-7.26 (m, J = 7.1 Hz, 2H), 7.26-7.40 (m, 4H); 13C NMR (100 MHz, CDCl3) δ 38.46, 101.49 (q, J = 4.9 Hz), 122.34 (q, J = 274.3 Hz), 127.93, 128.25, 129.35, 132.80, 133.36, 137.55 (q, J = 30.9 Hz), 137.85, 162.25; 19F NMR (376 MHz, CDCl3) δ -59.5749; HRMS (APCI) m/z (M+H)+ calcd for C13H11F2NO: 254.0785, found: 254.0785.

4-Chloro-1-methyl-3-phenylpyridin-2(1H)-one (7fa): 23.6 mg, 43%, brown oil; IR (neat, cm⁻¹) 696, 758, 1047, 1076, 1259, 1546, 1643; 1H NMR (400 MHz, CDCl3) δ 3.56 (s, 3H), 6.34 (d, J = 7.3 Hz, 1H), 7.23 (d, J = 7.3 Hz,1H), 7.35-7.38 (m, 3H), 7.41-7.45 (m, 2H); 13C NMR (100 MHz, CDCl3) δ 37.94, 108.21, 128.06, 129.12, 130.00, 130.51, 134.07, 136.44, 143.66, 161.62; HRMS (APCI) m/z (M+H)+ calcd for C13H11CINO: 220.0524, found: 220.0522.

6-Chloro-1-methyl-3-phenylpyridin-2(1H)-one (7ga): 23.1 mg, 42%, white solid, mp 99.1-100.8 °C; IR (neat, cm⁻¹) 700, 781, 1047, 1446, 1533, 1596, 1641; 1H NMR (400 MHz, CDCl3) δ 3.76 (s, 3H), 6.41 (d, J = 7.6 Hz, 1H), 7.33 (tt, J = 7.3, 1.3 Hz, 1H), 7.37-7.42 (m, 3H), 7.64 (d, J = 6.2 Hz, 2H); 13C NMR (100 MHz, CDCl3) δ 33.80, 106.58, 127.86, 128.21, 128.51, 129.31, 136.39, 136.67, 136.76, 162.10; HRMS
(APCI) m/z (M+H)^+ calcd for C_{12}H_{11}ClNO: 220.0524, found: 220.0524.

3-Phenylpyridin-2(1H)-one (7ja): 8.6 mg, 20%, white solid, mp 199-201 °C; IR (neat, cm\(^{-1}\)) 1458, 1508, 1541, 1558, 1535, 1653, 1683; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) δ 6.30 (t, J = 6.7 Hz, 1H), 7.26-7.32 (m, 2H), 7.36 (td, J = 7.2, 1.3 Hz, 2H), 7.52 (dd, J = 7.0, 2.0 Hz, 1H), 7.64 (d, J = 7.0 Hz, 2H), 12.66 (bs, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ 106.00, 127.81, 127.28, 127.49, 130.74, 132.68, 135.48, 138.63, 162.74; HRMS (APCI) m/z (M+H)^+ calcd for C\(_{11}\)H\(_{10}\)NO: 172.0757, found: 172.0761.

1-(But-3-en-1-yl)-3-phenylpyridin-2(1H)-one (7ka): 15.2 mg, 27%, brown oil; IR (neat, cm\(^{-1}\)) 698, 754, 918, 1217, 1379, 1460, 1550, 1597, 1645; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) δ 2.57 (q, J = 7.2 Hz, 2H), 4.06 (t, J = 7.2 Hz, 2H), 5.06-6.14 (m, 2H), 5.83 (ddt, J = 15.5, 10.2, 7.0 Hz, 1H), 6.24 (t, J = 7.0 Hz, 1H), 7.2-7.27 (m, 1H), 7.32 (tt, J = 7.3, 1.3 Hz, 1H), 7.40 (t, J = 7.6 Hz, 2H), 7.46-7.53 (m, 2H), 7.58 (dd, J = 6.9, 2.1 Hz, 1H), 7.74 (dd, J = 7.0, 1.2 Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ 33.26, 50.25, 105.67, 117.89, 127.64, 128.08, 128.66, 131.83, 134.19, 136.90, 136.92, 137.49, 161.36; HRMS (APCI) m/z (M+H)^+ calcd for C\(_{15}\)H\(_{16}\)NO: 226.1230, found: 226.1226.

1,3-Diphenylpyridin-2(1H)-one (7la): 24.4 mg, 40%, brown oil; IR (neat, cm\(^{-1}\)) 698, 754, 918, 1217, 1379, 1460, 1550, 1597, 1645; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) δ 6.35 (t, J = 6.9 Hz, 1H), 7.32 (tt, J = 7.3, 1.4 Hz, 1H), 7.38-7.45 (m, 6H), 7.46-7.53 (m, 2H), 7.58 (dd, J = 6.9, 2.1 Hz, 1H), 7.74 (dd, J = 7.0, 1.2 Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ 106.00, 126.72, 127.83, 128.08, 128.43, 128.72, 129.25, 132.56, 136.62, 137.10, 137.86, 141.32, 161.43; HRMS (APCI) m/z (M+H)^+ calcd for C\(_{17}\)H\(_{14}\)NO: 248.1070, found: 248.1073.

3-Phenyl-2(1H)-chromen-2-one (9): 29.4 mg, 53%, white solid, mp 133.0-134.8 °C; IR (neat, cm\(^{-1}\)) 694, 758, 1118, 1454, 1716; \(^1^H\) NMR (400 MHz, CDCl\(_3\)) δ 7.31 (dt, J = 7.5, 1.2 Hz, 1H), 7.32 (tt, J = 7.3, 1.4 Hz, 1H), 7.38-7.45 (m, 6H), 7.46-7.53 (m, 2H), 7.58 (dd, J = 6.9, 2.1 Hz, 1H), 7.74 (dd, J = 7.0, 1.2 Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ 116.50, 119.70, 124.50, 127.91, 128.42, 128.49, 128.55, 128.88, 131.41, 134.73, 139.87, 153.56, 160.60; HRMS (APCI) m/z (M+H)^+ calcd for C\(_{15}\)H\(_{11}\)O\(_2\): 223.0754, found: 223.0754.

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REFERENCES (AND NOTES)


12. We reported a preliminary single example using related photoredox catalysis, see: ref. 10.

13. In the course of this study, Yadav reported the radical-mediated, C3-selective direct arylation of 2-pyridones with arylhydrazines by using K2CO3 and O2 as promoters; P. Chauhan, M. Ravi, S. Singh, P. Prajapati, and P. P. Yadav, *RSC Adv.*, 2016, **6**, 109.


16. The radical chain propagation mechanism cannot be completely excluded; see ref. 14 and 15a.

17. Unsuccessful substrates included diethyl (bromodifluoromethyl)phosphonate, nonafluoriodobutane, and ethyl bromofluoroacetate.

18. Although the exact reason is not clear yet, Na$_2$S$_2$O$_3$ can reduce catalyst poison, molecular I$_2$ into I$^-$.

