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Copper-Catalyzed *N*-Arylation of 2-Pyridones Employing Diaryliodonium Salts at Room Temperature

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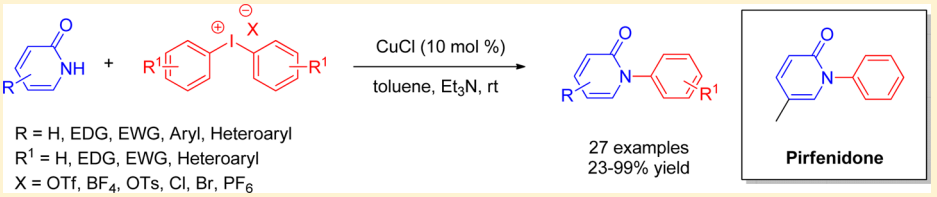
Supporting Information



ABSTRACT: A new and mild synthetic approach for the *N*-arylation of 2-pyridones with diaryliodonium salts has been developed. Most reactions proceed readily at room temperature in the presence of 10 mol % of copper chloride. As a result, a wide range of *N*-arylpyridine-2-ones were synthesized in yields of 23% to 99%. With this method, an antifibrotic drug, Pirfenidone, was successfully synthesized in 99% yield within 30 min at room temperature.

INTRODUCTION

N-Arylpyridine-2-ones are a ubiquitous moiety present in many bioactive compounds and pharmaceutical drugs (Figure 1).[1]

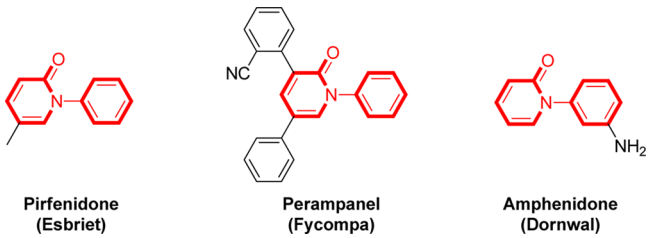
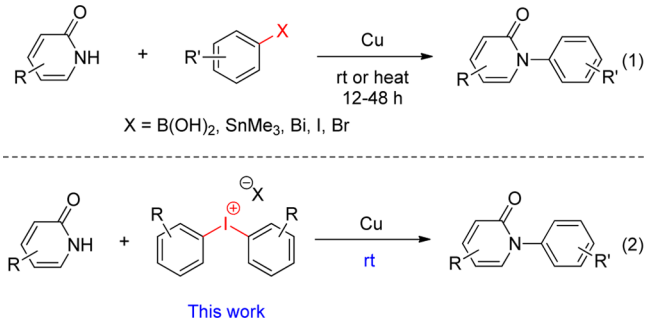


Figure 1. *N*-Arylpyridine-2-ones containing drugs.

Due to their intriguing biological activities such as antifibrotic, anti-inflammatory, anticonvulsant, and sedative activities,[2] several copper-catalyzed coupling reactions for C−N bond formation between 2-pyridones and electrophiles such as aryl boronic acids,[3] aryl stannanes,[4] aryl bismuth,[5] and aryl halides[6] have been previously reported (Scheme 1, eq 1). However, in general, copper-catalyzed coupling reactions for this transformation are relatively slow, requiring more than 12 h due to the low nucleophilicity of 2-pyridones. In particular, the Cu-catalyzed *N*-arylation of 2-pyridones employing aryl halides is generally carried out at elevated temperatures. Therefore, it is still required to develop a mild and expedient method for the preparation of *N*-arylpyridine 2-ones.

More stable, electrophilic, and/or less toxic, compared to the corresponding B, Sn, and Bi electrophiles, diaryliodonium salts have been employed as arylating agents in many coupling reactions.[7] In addition, the electrophilicity of diaryliodonium salts can be increased in the presence of a Cu(I) catalyst by forming a reactive aryl-Cu(III) intermediate.[8] Recently, we demonstrated the use of diaryliodonium salts for the synthesis

Scheme 1. Synthetic Methods for *N*-Arylpyridine-2-ones



of *N*-arylsulfonamides.[9] This reaction was successfully carried out under copper-catalyzed conditions at room temperature. Thus, we hypothesized that the use of diaryliodonium salts could overcome the problems of the current methods and permit the facile production of *N*-arylpyridine-2-ones at room temperature (Scheme 1, eq 2). Furthermore, to the best of our knowledge, the *N*-arylation of 2-pyridones employing diaryliodonium salts has not been reported.

With these considerations in mind, we report herein the preparation of *N*-arylpyridine-2-ones using 2-pyridones and diaryliodonium salts at room temperature.

RESULTS AND DISCUSSION

Optimization of the *N*-arylation of 2-pyridones began at room temperature using 2-hydroxypyridine **1** and bis(4-*tert*-butyl)-phenyl)iodonium triflate **2** (Table 1). Without a copper catalyst, only a low yield of the desired product **3a** was isolated after 24 h (Table 1, entries 1−2). However, when the reactions

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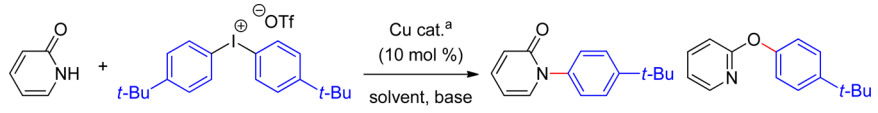
Table 1. Optimization of the *N*-Arylation Reaction of 2-Pyridone 1 with Bis(4-(*tert*-butyl)phenyl)iodonium Triflate 2

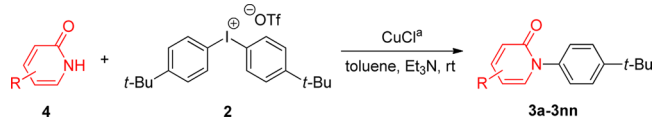


1 2 3a 3aa

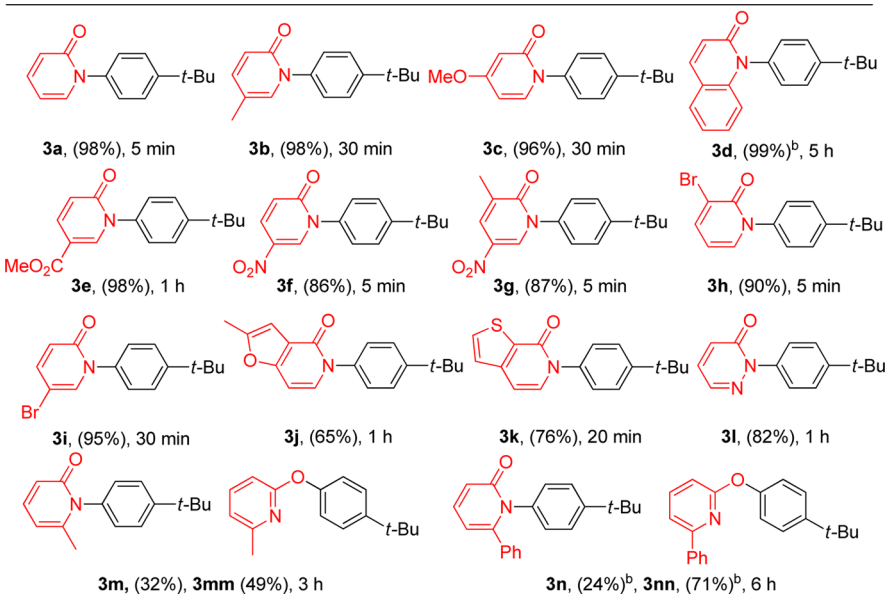
entry	Cu cat.	base	solvent	temp. (°C)	reaction time	yield of **3a** (%)[b]
1	no catalyst	Et_3N	Toluene	25	24 h	13
2	no catalyst	NaH	Toluene	25	24 h	10
3	CuI	Et_3N	Toluene	25	10 min	96
4	CuBr	Et_3N	Toluene	25	10 min	96
5	CuCl	Et_3N	Toluene	25	5 min	98
6	$CuBr{\cdot}SMe_2$	Et_3N	Toluene	25	10 min	96
7	$CuCl_2$	Et_3N	Toluene	25	24 h	27
8	$CuBr_2$	Et_3N	Toluene	25	24 h	76
9	CuO	Et_3N	Toluene	25	24 h	90
10	$CuSO_4$	Et_3N	Toluene	25	24 h	33
11	$Cu(OAc)_2$	Et_3N	Toluene	25	24 h	10
12	CuCl[c]	Et_3N	Toluene	25	5 min	96
13	CuCl[d]	Et_3N	Toluene	25	15 min	89
14	CuCl	Et_3N	THF	25	24 h	0
15	CuCl	Et_3N	CH_2Cl_2	25	5 min	95
16	CuCl	K_2CO_3	Toluene	25	24 h	53
17	CuCl	KO^{t}Bu	Toluene	25	24 h	41
18	CuCl	DIPEA	Toluene	25	5 min	93
19	CuCl	Pyridine	Toluene	25	24 h	14
20	CuCl	K_3PO_4	Toluene	25	24 h	70
21	CuCl	Cs_2CO_3	Toluene	25	5 min	94
22	CuCl	DABCO	Toluene	25	15 min	62 (21)[e]

[a]Reaction conditions: 0.25 mmol of 2-hydroxypyridine, 0.325 mmol of bis(4-(*tert*-butyl)phenyl)iodonium triflate, 0.50 mmol of base, solvent (0.1 M). [b]Isolated yield. [c]5 mol % of CuCl. [d]0.25 mmol of bis(4-(*tert*-butyl)phenyl)iodonium triflate, 0.325 mmol of 2-hydroxypyridine. [e]*O*-arylated product (**3aa**).

Table 2. Cu-Catalyzed *N*-Arylation of Various 2-Pyridones 4 with Bis(4-(*tert*-butyl)phenyl)iodonium Triflate 2



4 2 3a-3nn



3a, (98%), 5 min; **3b**, (98%), 30 min; **3c**, (96%), 30 min; **3d**, (99%)[b], 5 h

3e, (98%), 1 h; **3f**, (86%), 5 min; **3g**, (87%), 5 min; **3h**, (90%), 5 min

3i, (95%), 30 min; **3j**, (65%), 1 h; **3k**, (76%), 20 min; **3l**, (82%), 1 h

3m, (32%), **3mm** (49%), 3 h; **3n**, (24%)[b], **3nn**, (71%)[b], 6 h

[a]Reaction conditions: 0.25 mmol of 2-hydroxypyridine, 0.325 mmol of bis(4-(*tert*-butyl)phenyl)iodonium triflate, 10 mol % of CuCl, 0.50 mmol of Et_3N, toluene (0.1 M). [b]1.5 equiv of bis(4-(*tert*-butyl)phenyl)iodonium triflate.

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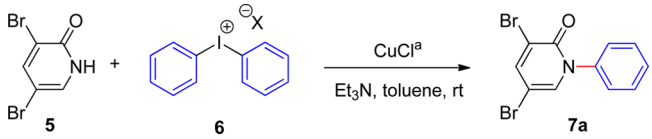
were conducted in the presence of either CuI, CuBr, or CuBr-dimethylsulfide complex, the reactions went to completion within 10 min yielding product **3a** in 96% yield (Table 1, entries 3, 4 and 6). Utilizing CuCl in toluene at room temperature furnished a slightly higher 98% yield in 5 min (Table 1, entry 5). When Cu(II) catalysts such as $CuCl_2$, $CuBr_2$, CuO, $CuSO_4$, and $Cu(OAc)_2$ were employed, prolonged reaction times and lower yields were observed (Table 1, entries 7−11). In particular, when the reaction was conducted with 5 mol % of CuCl, product **3a** was obtained in a slightly lower 96% yield in 5 min (Table 1, entry 12). Also, when bis(4-(*tert*-butyl)phenyl)iodonium triflate **2** was utilized as a limiting reagent, the desired product **3a** was obtained in 89% yield in 15 min (Table 1, entry 13). Next, we examined the solvent effects for *N*-arylation of 2-pyridone (Table 1, entries 14−15). When the reaction was carried out in THF, no desired product was observed. However, utilizing CuCl in CH_2Cl_2 at room temperature provided the desired product in 5 min in 95% yield. Furthermore, when different bases were employed, all proved inferior to Et_3N in terms of yield (Table 1, entries 16−22). Surprisingly, utilizing a bulky base such as DABCO furnished the desired product **3a** in 62% yield along with significant amounts of *O*-arylated product **3aa** (Table 1, entry 22).

With the optimized conditions in hand, we began to investigate the scope of the Cu-catalyzed *N*-arylation of various 2-pyridones with bis(4-(*tert*-butyl)phenyl)iodonium triflate **2**. As shown in Table 2, most 2-pyridones employed provided the desired products in good-to-excellent yields within 1 h at room temperature. However, when 2-hydroxyquinoline was used as a coupling partner, the desired product **3d** was obtained in 99% yield with requiring a longer reaction time, 5 h. It is hypothesized that the increased reaction time is due to the steric hindrance of 2-hydroxyquinoline.[6a] In addition, previous studies have indicated that 2-hydroxypyridine bearing a strong electron-withdrawing nitro group or containing substituents at the 6-position are able to impede Cu-catalyzed coupling reactions.[3a,6b,c] Surprisingly, however, when either 2-hydroxy-5-nitropyridine or 2-hydroxy-3-methyl-5-nitropyridine was respectively employed, the coupled product **3f** and **3g** were obtained in 86% and 87% yield in only 5 min, presumably due to the increased electrophilicity of the diaryliodonium salts. Use of halo-substituted-2-pyridones furnished the desired product **3h** and **3i** in excellent yields. Furthermore, other fused or nonfused nitrogen heterocycles proved effective coupling partners under the optimized conditions, furnishing the desired products **3j**−**3l** in yields ranging from 65 to 82%. Next, we studied the use of 2-hydroxy-6-substituted pyridines which are known as unreactive coupling partners for the preparation of *N*-arylpyridine-2-ones.[3a,6b] Interestingly, the use of 2-hydroxy-6-methylpyridine gave a 1.5:1 ratio of *O*-arylated product **3mm** to *N*-arylated product **3m**. When 2-hydroxy-6-phenylpyridine was used, it showed less reactivity, but provided a 3:1 ratio of *O*-arylated product **3nn** to *N*-arylated product **3n** in 6 h. Presumably, bulky substituents at the 6-position of 2-pyridones hindered coordination at the nitrogen and led to the formation of the *O*-arylated product as the major product.[10]

Encouraged by these cross-coupling results, our attention turned to the effect of the counteranions utilizing 3,5-dibromo-2-hydroxypyridine **5** and various diphenyliodonium salts **6**. As illustrated in Table 3, significant differences in the yield of **7a** were observed. The reactions employing diphenyliodonium salts containing OTf, BF_4, or PF_6 anions provided the coupled

Table 3. Effect of the Counteranions for Cu-Catalyzed *N*-Arylation of 3,5-Dibromo-2-hydroxypyridine 5



entry	X	time	yield (%)[b]
1	OTf	5 min	90
2	BF_4	10 min	95
3	PF_6	10 min	92
4	OTs	24 h	47
5	Cl	24 h	38
6	Br	24 h	15

[a]Reaction conditions: 0.25 mmol of 3,5-dibromo-2-hydroxypyridine, 0.325 mmol of diphenyliodonium salts, 10 mol % of CuCl, 0.50 mmol of Et_3N, toluene (0.1 M). [b]Isolated yield.

product **7a** in excellent yields in a short time. However, the use of diphenyliodonium salts having anions OTs, Cl, and Br furnished a lower yield after 24 h.

To further investigate the scope of the Cu-catalyzed *N*-arylation of 2-pyridones, various symmetrical and unsymmetrical diaryliodonium salts were utilized as a coupling partner under the optimized conditions (Table 4). The use of 3,5-dibromo-2-hydroxypyridine **5** and diaryliodonium salts containing electron-neutral, -donating, and -withdrawing groups furnished the desired products **7a**−**7j** in moderate to excellent yields. In addition, to demonstrate the feasibility of the Cu-catalyzed *N*-arylation of 2-pyridones, the coupling reaction was carried out on a large scale (5.0 mmol), providing **7c** in 99% yield in 5 min. When either the sterically bulky mesityl or trifluoromethoxy- and trifluoromethyl-substituted iodonium salts were used, the reactions were sluggish at room temperature. However, increasing the temperature from rt to 50 °C, furnished full conversion and provided the desired products **7d**, **7e**, and **7i** in 54%, 61% and 53% yield, respectively. Utilizing halo-substituted iodonium triflates at room temperature gave the coupled products **7f**−**7h** in excellent yields within 1 h. Particularly, when unsymmetric mesityl iodonium triflates, used to transfer the other aryl or heteroaryl group selevtively,[11] were employed at 50 °C, the desired products **7k** and **7l** were obtained in 23% and 73% yields along with the significant amounts of **7d**.

Finally, encouraged by the feasibility of the Cu-catalyzed *N*-arylation of 2-pyridones employing diaryliodonium salts, we next attempted to synthesize Pirfenidone **9**, which has been a widely used antifibrotic agent for idiopathic pulmonary fibrosis (IPF) (Scheme 2).[12] Compound **9** was obtained in 99% isolated yield from 2-hydroxy-5-methylpyridine **8** and diphenyliodonium hexafluorophosphate in 30 min at room temperature. This new and mild synthetic approach to Pirfenidone is meaningful compared to its previous preparations in terms of yield, reaction time and temperature.[5b,13]

CONCLUSION

In conclusion, we have described a new synthetic method for the preparation of *N*-arylpyridine-2-ones employing 2-pyridones and diaryliodonium salts. The reaction readily proceeds at room temperature, and large scale preparation of **7c** has been successfully conducted to demonstrate the feasibility of our method. The scope of this method has been investigated

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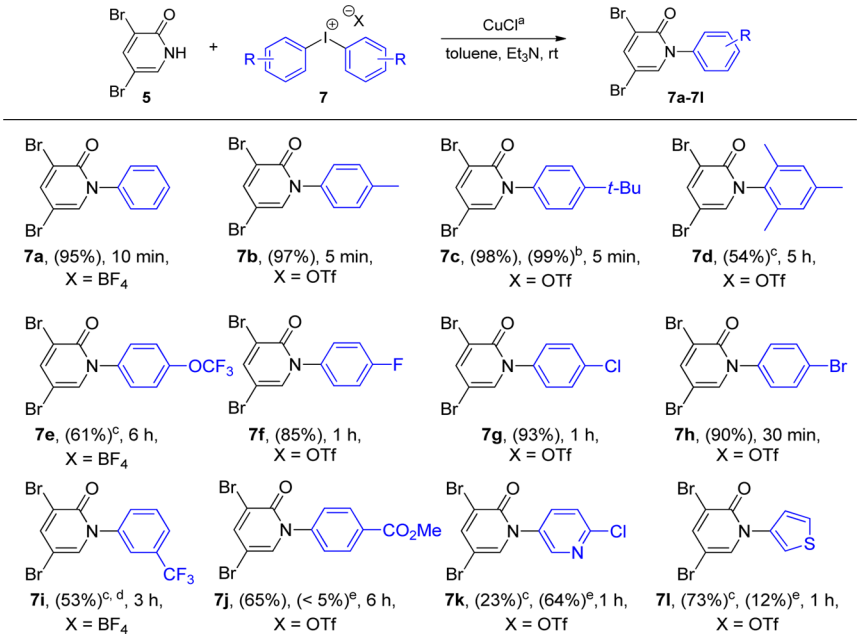
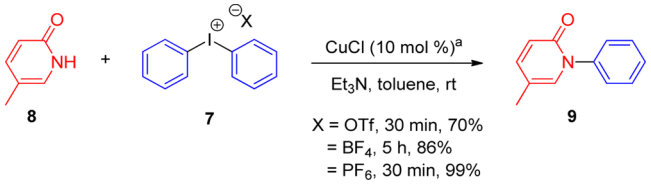
Table 4. Cu-Catalyzed *N*-Arylation of 3,5-Dibromo-2-hydroxypyridine 5 with Various Diaryliodonium Salts 7



[a]Reaction conditions: 0.25 mmol of 3,5-dibromo-2-hydroxypyridine, 0.325 mmol of diaryliodonium salt, 10 mol % of CuCl, 0.50 mmol of Et_3N, toluene (0.1 M). [b]5.0 mmol of 3,5-dibromo-2-hydroxypyridine, 6.5 mmol of bis(4-*tert*-butyl)phenyl)iodonium triflate. [c]The reaction was conducted at 50 °C. [d]1.5 equiv of diaryliodonium salt. [e]Yield of **7d**.

Scheme 2. Synthesis of the Pirfenidone 9



employing various 2-pyridones and diaryliodonium salts. In particular, 2-hydroxypyridines bearing a nitro group proved the effective nucleophile under optimized condition using diaryliodonium salts. In addition, it was found that 2-hydroxypyridines containing substituents at the 6-position can be used to give the *O*-arylated product as the major product. Finally, an antifibrotic drug, Pirfenidone, was easily synthesized in 99% yield in 30 min employing 2-hydroxy-5-methylpyridine and diphenyliodonium hexafluorophosphate. Further applications and developments based on this method are currently ongoing in our laboratory.

EXPERIMENTAL SECTION

General Considerations. Unless otherwise indicated, all chemical reagents were purchased from commercial suppliers and were used without further purification. All reactions were carried out in oven-dried glassware equipped with a magnetic stir bar. Reactions were monitored by thin layer chromatography (TLC) with 0.25 mm precoated silica gel plates (Kieselgel $60F_{254}$). Products were detected by viewing under a UV light, by staining with an anisaldehyde solution composed of acetic acid, sulfuric acid, and MeOH, or by staining with a $KMnO_4$ solution composed of potassium carbonate, sodium hydroxide, and water. Flash column chromatography was performed on silica gel (70−230 mesh). Yields refer to chromatographically and spectroscopically pure compounds unless otherwise noted. ^1H and ^{13}C spectra were recorded on a 300 MHz NMR spectrometer. Chemical shifts are reported as δ values relative to internal $SiMe_4$ (δ 0.00 for ^1H) or chloroform (δ 77.0 for ^{13}C) or DMSO-d_6 (δ 2.50 for ^1H and δ 39.5 for ^{13}C). IR spectra were measured as neat oils and solids on a FT-IR spectrometer. HRMS data were obtained by electron ionization with a double-focusing high-resolution magnetic sector mass analyzer.

Preparation of 2-Pyridones. 4-Methoxypyridin-2(1*H*)-one,[14a] 2-methylfuro[3,2-*c*]pyridin-4(5*H*)-one,[14b] thieno[2,3-*c*]pyridin-7(6*H*)-one[14b] were prepared as according to cited literature procedures.

Preparation of Diaryliodonium Salts. Diphenyliodonium triflate,[15a] diphenyliodonium tetrafluoroborate,[15b] di-*p*-tolyliodonium triflate,[15a] bis(4-(*tert*-butyl)phenyl)iodonium triflate,[15c] dimesityliodonium triflate,[15c] bis(4-(trifluoromethoxy)phenyl)iodonium tetrafluoroborate,[15d] bis(4-fluorophenyl)iodonium triflate,[15c] bis(4-chlorophenyl)iodonium triflate,[15c] bis(4-bromophenyl)iodonium triflate,[15c] bis(3-(trifluoromethyl)phenyl)iodonium tetrafluoroborate,[15b] mesityl(4-(methoxycarbonyl)phenyl)iodonium triflate,[15e] mesityl(2-chloropyridin-5-yl)iodonium triflate[15f] and mesityl(thiophen-3-yl)-iodonium triflate[11d] were prepared as according to cited literature procedures.

General Procedure I for Synthesis of *N*-Arylpyridine-2-ones. A 10 mL round-bottom flask was charged with diaryliodonium salts (0.325 mmol), CuCl (10 mol %), Et_3N (0.5 mmol) and the corresponding pyridin-2-one (0.25 mmol). Toluene (2.5 mL) was then added to the flask. The reaction mixture was stirred at room temperature under Ar. After completion of the reaction as monitored by TLC analysis, the solvent was removed in vacuo and the residue was purified by flash column chromatography on silica gel to obtain the desired product.

*1-(4-(tert-Butyl)phenyl)pyridin-2(1H)-one (**3a**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.325 mmol) and pyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 5 min. Flash chromatography on silica gel using hexane/ethyl acetate (2:1) provided pure **3a** (55.7 mg, 0.245 mmol, 98%) as a white solid. mp 108−110 °C; R_f 0.15 (hexane/ethyl acetate = 2:1); IR (neat) 2957, 1664, 1586, 1524, 1400, 1269, 1127, 838, 761, 592 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, J = 8.4 Hz, 2H), 7.41−7.27 (m, 4H), 6.65 (d, J = 9.3 Hz, 1H), 6.22 (t, J = 6.7 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 151.3, 139.6, 138.2, 138.1, 126.2, 125.8, 121.7, 105.7, 34.6, 31.2; HRMS-EI m/z 227.1310 [M^+; calcd. for $C_{15}H_{17}NO^+$: 227.1310].

*2-(4-(tert-Butyl)phenoxy)pyridine (**3aa**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.325

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mmol), DABCO (instead of Et_3N) and pyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 15 min. Flash chromatography on silica gel using hexane/ethyl acetate (20:1−2:1) provided pure **3a** (35.2 mg, 0.155 mmol, 62%) as a white solid and **3aa** (12.0 mg, 0.053 mmol, 21%) as a colorless oil. R_f 0.64 (hexane/ethyl acetate = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (dd, J = 4.8 Hz and J = 2.1 Hz, 1H), 7.57 (t, J = 7.2 Hz, 1H), 7.43 (d, J = 8.7 Hz, 2H), 7.05 (d, J = 9 Hz, 2H), 6.89 (t, J = 5.1 Hz, 1H), 6.84 (d, J = 8.4 Hz, 1H), 1.31 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 151.5, 147.4, 146.9, 139.0, 126.2, 120.2, 118.0, 111.1, 34.1, 31.2; Data are consistent with those reported in the literature.[16]

*1-(4-(tert-Butyl)phenyl)-5-methylpyridin-2(1H)-one (**3b**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.325 mmol) and 5-methylpyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 30 min. Flash chromatography on silica gel using hexane/ethyl acetate (2:1) provided pure **3b** (59.1 mg, 0.245 mmol, 98%) as a white solid. mp 118−120 °C; R_f 0.13 (hexane/ethyl acetate = 2:1); IR (neat) 3850, 3742, 2957, 2353, 1675, 1526, 1276, 829, 668 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (dd, J = 2.0 Hz and J = 6.6 Hz, 2H), 7.32−7.22 (m, 3H), 7.11 (s, 1H), 6.60 (d, J = 9.3 Hz, 1H), 2.09 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.7, 151.1, 142.3, 138.4, 135.5, 126.2, 125.9, 121.3, 114.6, 34.6, 31.2, 16.9; HRMS-EI m/z 241.1465 [M^+; calcd. for $C_{16}H_{19}NO^+$: 241.1467].

*1-(4-(tert-Butyl)phenyl)-4-methoxypyridin-2(1H)-one (**3c**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.325 mmol) and 4-methoxypyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 30 min. Flash chromatography on silica gel using hexane/ethyl acetate (1:1) provided pure **3c** (61.8 mg, 0.240 mmol, 96%) as a white solid. mp 118−120 °C; R_f 0.1 (hexane/ethyl acetate = 2:1); IR (neat) 3444, 2960, 2348, 1659, 1482, 1347, 1233, 1026, 831, 618 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (dd, J = 1.8 Hz and J = 6.6 Hz, 2H), 7.28 (dd, J = 2.1 Hz and J = 5.7 Hz, 2H), 7.21 (dd, J = 1.5 Hz and J = 6.6 Hz, 1H), 5.98−5.95 (m, 2H), 3.80 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 163.9, 151.1, 138.0, 137.8, 126.2, 126.0, 101.0, 97.5, 55.5, 34.6, 31.2; HRMS-EI m/z 257.1415 [M^+; calcd. for $C_{16}H_{19}NO_2^+$: 257.1416].

*1-(4-(tert-Butyl)phenyl)quinolin-2(1H)-one (**3d**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.375 mmol) and quinolin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 5 h. Flash chromatography on silica gel using hexane/ethyl acetate (2:1) provided pure **3d** (68.7 mg, 0.248 mmol, 99%) as a white solid. mp 156−158 °C; R_f 0.22 (hexane/ethyl acetate = 2:1); IR (neat) 3442, 3049, 2957, 2349, 1657, 1590, 1450, 1249, 1118, 834, 753, 532 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J = 9.6 Hz, 1H), 7.61−7.55 (m, 3H), 7.32 (t, J = 7.9 Hz, 1H), 7.21−7.15 (m, 3H), 6.77 (d, J = 9.6 Hz, 1H), 6.67 (d, J = 8.7 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 151.6, 141.2, 139.6, 134.7, 130.0, 128.1, 128.0, 127.1, 122.13, 122.1, 120.2, 116.0, 34.7, 31.3; HRMS-EI m/z 277.1464 [M^+; calcd. for $C_{19}H_{19}NO^+$: 277.1467].

*Methyl 1-(4-(tert-butyl)phenyl)-6-oxo-1,6-dihydropyridine-3-carboxylate (**3e**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.325 mmol) and methyl 6-oxo-1,6-dihydropyridine-3-carboxylate (0.25 mmol), and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (3:1) provided pure **3e** (69.9 mg, 0.245 mmol, 98%) as a white solid. mp 126−130 °C; R_f 0.36 (hexane/ethyl acetate = 2:1); IR (neat) 3469, 3065, 2959, 1680, 1522, 1445, 1268, 1109, 841, 770, 635 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (dd, J = 0.6 Hz and J = 2.4 Hz, 1H), 7.91 (dd, J = 2.4 Hz and J = 9.6 Hz, 1H), 7.54−7.51 (m, 2H), 7.32−7.29 (m, 2H), 6.63 (dd, J = 0.6 Hz and J = 9.6 Hz, 1H), 3.86 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5, 162.1, 152.0, 143.4, 138.6, 137.4, 126.3, 125.7, 120.4, 109.6, 51.9, 34.6, 31.1; HRMS-EI m/z 285.1362 [M^+; calcd. for $C_{17}H_{19}NO_3^+$: 285.1365].

*1-(4-(tert-Butyl)phenyl)-5-nitropyridin-2(1H)-one (**3f**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.325 mmol) and 5-nitropyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 5 min. Flash chromatography on silica gel using hexane/ethyl acetate (5:1) provided pure **3f** (58.5 mg, 0.215 mmol, 86%) as a white solid. mp 182−185 °C; R_f 0.47 (hexane/ethyl acetate = 2:1); IR (neat) 3073, 2958, 2349, 1682, 1509, 1339, 1272, 1109, 834, 753, 634 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (d, J = 3.0 Hz, 1H), 8.16 (dd, J = 3.0 Hz and J = 10.2 Hz, 1H), 7.56 (d, J = 6.6 Hz, 2H), 7.32 (d, J = 6.6 Hz, 2H), 6.66 (d, J = 9.9 Hz, 1H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.2, 153.0, 139.9, 136.6, 133.4, 130.9, 126.8, 125.6, 120.4, 34.9, 31.2; HRMS-EI m/z 272.1162 [M^+; calcd. for $C_{15}H_{16}N_2O_3^+$: 272.1161].

*1-(4-(tert-Butyl)phenyl)-3-methyl-5-nitropyridin-2(1H)-one (**3g**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)-iodonium triflate (0.325 mmol) and 3-methyl-5-nitropyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 5 min. Flash chromatography on silica gel using hexane/ethyl acetate (9:1) provided pure **3g** (62.3 mg, 0.218 mmol, 87%) as a white solid. mp 152−154 °C; R_f 0.66 (hexane/ethyl acetate = 2:1); IR (neat) 2958, 2349, 1671, 1510, 1341, 1267, 1118, 756, 676 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, J = 2.7 Hz, 1H), 8.04 (dd, J = 1.2 Hz and J = 3.0 Hz, 1H), 7.54 (d, J = 6.9 Hz, 2H), 7.31 (d, J = 6.6 Hz, 2H), 2.25 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 152.8, 137.3, 137.0, 130.4, 130.3, 129.9, 126.6, 125.7, 34.8, 31.2, 17.6; HRMS-EI m/z 286.1316 [M^+; calcd. for $C_{16}H_{18}N_2O_3^+$: 286.1317].

*3-Bromo-1-(4-(tert-butyl)phenyl)pyridin-2(1H)-one (**3h**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.325 mmol) and 3-bromopyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 5 min. Flash chromatography on silica gel using hexane/ethyl acetate (5:1) provided pure **3h** (68.9 mg, 0.225 mmol, 90%) as a white solid. mp 154−155 °C; R_f 0.43 (hexane/ethyl acetate = 2:1); IR (neat) 3448, 2959, 2348, 1660, 1512, 1352, 1265, 1134, 1031, 839, 754, 613 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (dd, J = 1.8 Hz and J = 7.2 Hz, 1H), 7.50−7.47 (m, 2H), 7.36 (dd, J = 2.1 Hz and J = 6.9 Hz, 1H), 7.31−7.26 (m, 2H), 6.14 (t, J = 7.0 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 151.8, 141.7, 138.1, 137.6, 126.2, 125.7, 117.3, 105.7, 34.7, 31.2; HRMS-EI m/z 305.0412 [M^+; calcd. for $C_{15}H_{16}BrNO^+$: 305.0415].

*5-Bromo-1-(4-(tert-butyl)phenyl)pyridin-2(1H)-one (**3i**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.325 mmol) and 5-bromopyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 30 min. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **3i** (72.8 mg, 0.238 mmol, 95%) as a white solid. mp 118−120 °C; R_f 0.79 (hexane/ethyl acetate = 2:1); IR (neat) 3058, 2959, 2349, 1670, 1588, 1516, 1272, 834, 743, 634 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51−7.47 (m, 3H), 7.41 (dd, J = 2.7 Hz and J = 9.6 Hz, 1H) 7.31−7.25 (m, 2H), 6.57 (dd, J = 0.5 Hz and J = 9.6 Hz, 1H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.8, 151.9, 142.7, 137.9, 137.4, 126.4, 125.7, 122.9, 97.9, 34.7, 31.2; HRMS-EI m/z 305.0414 [M^+; calcd. for $C_{15}H_{16}BrNO^+$: 305.0415].

*5-(4-(tert-Butyl)phenyl)-2-methylfuro[3,2-c]pyridin-4(5H)-one (**3j**).* General procedure I was used employing bis(4-(*tert*-butyl)-phenyl)iodonium triflate (0.325 mmol) and 2-methylfuro[3,2-*c*]-pyridin-4(5*H*)-one (0.25 mmol), and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (2:1) provided pure **3j** (45.7 mg, 0.162 mmol, 65%) as a white solid. mp 136−138 °C; R_f 0.23 (hexane/ethyl acetate = 2:1); IR (neat) 3458, 2959, 2349, 1660, 1512, 1265, 1032, 840, 754, 614 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 7.2 Hz, 1H), 6.60 (s, 1H), 6.52 (d, J = 7.5 Hz, 1H), 2.43 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 158.6, 154.0, 151.0, 138.5, 133.6, 126.4, 126.1, 117.7, 103.3, 95.7, 34.6, 31.3, 13.7; HRMS-EI m/z 281.1417 [M^+; calcd. for $C_{18}H_{19}NO_2^+$: 281.1416].

*6-(4-(tert-Butyl)phenyl)thieno[2,3-c]pyridin-7(6H)-one (**3k**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)-iodonium triflate (0.325 mmol) and thieno[2,3-*c*]pyridin-7(6*H*)-one (0.25 mmol), and the reaction was completed in 20 min. Flash chromatography on silica gel using hexane/ethyl acetate (5:1) provided pure **3k** (53.8 mg, 0.190 mmol, 76%) as a white solid. mp 168−172 °C; R_f 0.41 (hexane/ethyl acetate = 2:1); IR (neat) 3099, 2954, 2350, 1650, 1404, 1274, 1136, 839, 768, 706, 575 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J = 5.1 Hz, 1H), 7.49 (d, J = 8.7 Hz, 2H), 7.35−7.21 (m, 3H), 7.22 (d, J = 7.2 Hz, 1H), 6.73 (d, J = 7.2

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J. Org. Chem. 2016, 81, 7717−7724

Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7, 151.0, 147.4, 138.2, 132.7, 131.1, 126.2, 126.1, 125.6, 124.5, 101.7, 34.6, 31.2; HRMS-EI m/z 283.1028 [M^+; calcd. for $C_{17}H_{17}NOS^+$: 283.1031].

*2-(4-(tert-Butyl)phenyl)pyridazin-3(2H)-one (**3l**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.325 mmol) and pyridazin-3(2*H*)-one (0.25 mmol), and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (1:1) provided pure **3l** (46.8 mg, 0.205 mmol, 82%) as a white solid. mp 140−141 °C; R_f 0.08 (hexane/ethyl acetate = 2:1); IR (neat) 3443, 3068, 2956, 2349, 1662, 1583, 1511, 1357, 1139, 1031, 831, 599 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (dd, J = 1.8 Hz and J = 3.9 Hz, 1H), 7.54−7.46 (m, 4H), 7.22 (dd, J = 3.6 Hz and J = 9.3 Hz, 1H), 7.05 (dd, J = 1.8 Hz and J = 9.6 Hz, 1H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 151.3, 138.8, 136.5, 131.1, 131.0, 125.8, 124.7, 34.6, 31.2; HRMS-EI m/z 228.1265 [M^+; calcd. for $C_{14}H_{16}N_2O^+$: 228.1263].

*1-(4-(tert-Butyl)phenyl)-6-methylpyridin-2(1H)-one (**3m**) and 2-(4-(tert-Butyl)phenoxy)-6-methylpyridine (**3mm**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.325 mmol) and 6-methylpyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 3 h. Flash chromatography on silica gel using hexane/ethyl acetate (20:1−2:1) provided pure **3m** (19.3 mg, 0.080 mmol, 32%) as a white solid and **3mm** (29.6 mg, 0.123 mmol, 49%) as a colorless oil. [**3m**] mp 122−124 °C; R_f 0.1 (hexane/ethyl acetate = 2:1); IR (neat) 3074, 2960, 2350, 1662, 1577, 1460, 1258, 1146, 806, 600, 522 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53−7.49 (m, 2H), 7.29 (q, J = 6.7 Hz, 1H), 7.13−7.09 (m, 2H), 6.52 (dd, J = 0.6 Hz and J = 9.3 Hz, 1H), 6.09 (dd, J = 0.9 Hz and J = 6.9 Hz, 1H), 1.95 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.0, 151.4, 146.7, 139.4, 136.0, 127.0, 126.6, 118.3, 105.8, 34.6, 31.2, 21.5; HRMS-EI m/z 241.1465 [M^+; calcd. for $C_{16}H_{19}NO^+$: 241.1467]. [**3mm**] R_f 0.64 (hexane/ethyl acetate = 10:1); IR (neat) 3851, 3742, 3054, 2959, 2353, 1583, 1448, 1234, 1018, 791 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (t, J = 7.8 Hz, 1H), 7.41−7.35 (m, 2H), 7.08−7.02 (m, 2H), 6.84 (d, J = 7.2 Hz, 1H), 6.53 (d, J = 8.4 Hz, 1H), 2.47 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4, 157.6, 152.1, 147.1, 139.4, 126.5, 120.1, 117.7, 107.1, 34.3, 31.4, 24.1; HRMS-EI m/z 241.1463 [M^+; calcd. for $C_{16}H_{19}NO^+$: 241.1467].

*1-(4-(tert-Butyl)phenyl)-6-phenylpyridin-2(1H)-one (**3n**) and 2-(4-(tert-Butyl)phenoxy)-6-phenylpyridine (**3nn**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (0.375 mmol) and 6-phenylpyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 6 h. Flash chromatography on silica gel using hexane/ethyl acetate (20:1−2:1) provided pure **3n** (18.2 mg, 0.060 mmol, 24%) as a white solid and **3nn** (53.9 mg, 0.178 mmol, 71%) as a colorless oil. [**3n**] mp 144−148 °C; R_f 0.14 (hexane/ethyl acetate = 2:1); IR (neat) 3054, 2958, 2349, 1666, 1542, 1389, 1261, 1011, 759, 607 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (q, J = 6.6 Hz, 1H), 7.27−7.22 (m, 2H), 7.18−7.09 (m, 3H), 7.07−7.03 (m, 2H), 6.99−6.96 (m, 2H), 6.68 (dd, J = 1.2 Hz and J = 9.3 Hz, 1H), 6.25 (dd, J = 1.2 Hz and J = 6.9 Hz, 1H), 1.23 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4, 150.8, 149.9, 139.3, 135.8, 135.6, 128.9, 128.3, 128.2, 127.7, 125.6, 120.0, 107.7, 34.5, 31.2; HRMS-EI m/z 303.1620 [M^+; calcd. for $C_{21}H_{21}NO^+$: 303.1623]. [**3nn**] R_f 0.75 (hexane/ethyl acetate = 10:1); IR (neat) 3435, 2348, 1636, 1440, 1242, 753, 539 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (dd, J = 1.8 Hz and J = 8.1 Hz, 2H), 7.70 (t, J = 8.1 Hz, 1H) 7.47−7.35 (m, 6H), 7.17−7.11 (m, 2H), 6.73 (d, J = 8.1 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.6, 155.6, 151.8, 147.2, 140.0, 138.4, 129.0, 128.5, 126.8, 126.3, 120.4, 114.5, 109.0, 34.3, 31.4; HRMS-EI m/z 303.1625 [M^+; calcd. for $C_{21}H_{21}NO^+$: 303.1623].

*3,5-Dibromo-1-phenylpyridin-2(1H)-one (**7a**).* General procedure I was used employing diphenyliodonium tetrafluoroborate (0.325 mmol) and 3,5-dibromopyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 10 min. Flash chromatography on silica gel using hexane/ethyl acetate (5:1) provided pure **7a** (78.1 mg, 0.237 mmol, 95%) as a white solid. mp 122−124 °C; R_f 0.4 (hexane/ethyl acetate = 2:1); IR (neat) 3850, 3741, 3061, 2353, 1665, 1589, 1504, 1338, 1259, 857, 709 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 2.4 Hz, 1H), 7.51−7.42 (m, 4H), 7.37−7.34 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.3, 144.1, 140.0, 137.1, 129.4, 129.1, 126.2, 118.3, 96.9; HRMS-EI m/z 326.8893 [M^+; calcd. for $C_{11}H_7Br_2NO^+$: 326.8894].

*3,5-Dibromo-1-(p-tolyl)pyridin-2(1H)-one (**7b**).* General procedure I was used employing di-*p*-tolyliodonium triflate (0.325 mmol) and 3,5-dibromopyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 5 min. Flash chromatography on silica gel using hexane/ethyl acetate (9:1) provided pure **7b** (83.2 mg, 0.243 mmol, 97%) as a white solid. mp 134−136 °C; R_f 0.62 (hexane/ethyl acetate = 2:1); IR (neat) 3447, 2348, 1664, 1592, 1509, 1261, 845, 748 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 2.4 Hz, 1H), 7.48 (d, J = 2.7 Hz, 1H), 7.30−7.21 (m, 4H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.4, 144.0, 139.2, 137.6, 137.3, 130.0, 125.9, 118.3, 96.7, 21.1; HRMS-EI m/z 340.9052 [M^+; calcd. for $C_{12}H_9Br_2NO^+$: 340.9051].

*3,5-Dibromo-1-(4-(tert-butyl)phenyl)pyridin-2(1H)-one (**7c**).* General procedure I was used employing bis(4-(*tert*-butyl)phenyl)-iodonium triflate (0.325 mmol) and 3,5-dibromopyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 5 min. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7c** (94.3 mg, 0.245 mmol, 98%) as a white solid. For the large scale synthesis, general procedure I was used employing bis(4-(*tert*-butyl)phenyl)iodonium triflate (6.5 mmol) and 3,5-dibromopyridin-2(1*H*)-one (5.0 mmol), and the reaction was completed in 5 min as 99% yield (4.96 mmol, 1.91 g). mp 132−134 °C; R_f 0.78 (hexane/ethyl acetate = 2:1); IR (neat) 3058, 2959, 2414, 1668, 1509, 1353, 1260, 1106, 850, 751, 544 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 2.7 Hz, 1H), 7.51−7.48 (m, 3H), 7.28 (d, J = 9.0 Hz, 2H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 152.3, 144.0, 137.5, 137.3, 126.4, 125.6, 118.3, 96.8, 34.8, 31.2; HRMS-EI m/z 382.9521 [M^+; calcd. for $C_{15}H_{15}Br_2NO^+$: 382.9520].

*3,5-Dibromo-1-mesitylpyridin-2(1H)-one (**7d**).* General procedure I was used employing dimesityliodonium triflate (0.325 mmol) and 3,5-dibromopyridin-2(1*H*)-one (0.25 mmol) at 50 °C, and the reaction was completed in 5 h. Flash chromatography on silica gel using hexane/ethyl acetate (7:1) provided pure **7d** (50.1 mg, 0.135 mmol, 54%) as a white solid. mp 128−130 °C; R_f 0.56 (hexane/ethyl acetate = 2:1); IR (neat) 3854, 3742, 2354, 1664, 1264, 859, 756, 680 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J = 2.7 Hz, 1H), 7.26 (d, J = 2.7 Hz, 1H), 6.97 (s, 2H), 2.31 (s, 3H), 2.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.8, 144.3, 139.2, 137.2, 136.1, 134.0, 129.4, 118.6, 96.9, 21.0, 17.6; HRMS-EI m/z 368.9362 [M^+; calcd. for $C_{14}H_{13}Br_2NO^+$: 368.9364].

*3,5-Dibromo-1-(4-(trifluoromethoxy)phenyl)pyridin-2(1H)-one (**7e**).* General procedure I was used employing bis(4-(trifluoromethoxy)phenyl)iodonium tetrafluoroborate (0.325 mmol) and 3,5-dibromopyridin-2(1*H*)-one (0.25 mmol) at 50 °C, and the reaction was completed in 6 h. Flash chromatography on silica gel using hexane/ethyl acetate (10:1) provided pure **7e** (63.0 mg, 0.153 mmol, 61%) as a white solid. mp 104−106 °C; R_f 0.8 (hexane/ethyl acetate = 2:1); IR (neat) 3851, 3741, 3447, 2353, 1662, 1516, 1258, 852, 751, 670 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, J = 2.7 Hz, 1H), 7.49 (d, J = 2.7 Hz, 1H), 7.46−7.40 (m, 2H), 7.34 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 149.2 (d, J = 1.8 Hz) 144.4, 138.2, 136.6, 128.0, 121.8, 120.3 (q, J = 256.7 Hz), 118.5, 97.3; HRMS-EI m/z 410.8718 [M^+; calcd. for $C_{12}H_6Br_2F_3NO_2^+$: 410.8717].

*3,5-Dibromo-1-(4-fluorophenyl)pyridin-2(1H)-one (**7f**).* General procedure I was used employing bis(4-fluorophenyl)iodonium triflate (0.325 mmol) and 3,5-dibromopyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (5:1) provided pure **7f** (73.7 mg, 0.212 mmol, 85%) as a white solid. mp 148−150 °C; R_f 0.44 (hexane/ethyl acetate= 2:1); IR (neat) 3851, 3742, 3434, 2353, 1656, 1511, 1222, 833, 677, 517 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 2.7 Hz, 1H), 7.48 (d, J = 2.4 Hz, 1H), 7.38−7.32 (m, 2H), 7.17 (t, J = 8.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4 (d, J = 248.3 Hz) 157.3 144.2, 136.9, 135.9, 128.1 (d, J = 8.8 Hz), 118.3, 116.4 (d, J = 23 Hz), 97.1; HRMS-EI m/z 344.8802 [M^+; calcd for $C_{11}H_6Br_2FNO^+$: 344.8800].

*3,5-Dibromo-1-(4-chlorophenyl)pyridin-2(1H)-one (**7g**).* General procedure I was used employing bis(4-chlorophenyl)iodonium triflate

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(0.325 mmol) and 3,5-dibromopyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (6:1) provided pure **7g** (84.5 mg, 0.233 mmol, 93%) as a white solid. mp 160−162 °C; R_f 0.5 (hexane/ethyl acetate = 2:1); IR (neat) 3852, 3743, 2354, 1651, 1566, 1234, 1085, 833, 733; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 2.4 Hz, 1H), 7.47−7.44 (m, 3H), 7.33−7.29 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 144.3, 138.3, 136.6, 135.1, 129.6, 127.6, 118.4, 97.2; HRMS-EI m/z 360.8505 [M^+; calcd. for $C_{11}H_6Br_2ClNO^+$: 360.8505].

*3,5-Dibromo-1-(4-bromophenyl)pyridin-2(1H)-one (**7h**).* General procedure I was used employing bis(4-bromophenyl)iodonium triflate (0.325 mmol) and 3,5-dibromopyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 30 min. Flash chromatography on silica gel using hexane/ethyl acetate (9:1) provided pure **7h** (91.8 mg, 0.225 mmol, 90%) as a white solid. mp 160−162 °C; R_f 0.6 (hexane/ethyl acetate = 2:1); IR (neat) 3854, 3742, 2354, 1659, 1252, 836, 673 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 2.7 Hz, 1H), 7.63 (d, J = 9.0 Hz, 2H), 7.46 (d, J = 2.7 Hz, 1H), 7.26 (d, J = 9.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 144.3, 138.9, 136.5, 132.7, 127.9, 123.2, 118.5, 97.3; HRMS-EI m/z 404.8002 [M^+; calcd. for $C_{11}H_6Br_3NO^+$: 404.7999].

*3,5-Dibromo-1-(3-(trifluoromethyl)phenyl)pyridin-2(1H)-one (**7i**).* General procedure I was used employing bis(3-(trifluoromethyl)-phenyl)iodonium tetrafluoroborate (0.375 mmol) and 3,5-dibromo-pyridin-2(1*H*)-one (0.25 mmol) at 50 °C, and the reaction was completed in 3 h. Flash chromatography on silica gel using hexane/ethyl acetate (9:1) provided pure **7i** (52.6 mg, 0.132 mmol, 53%) as a white solid. mp 128−130 °C; R_f 0.67 (hexane/ethyl acetate = 2:1); IR (neat) 3852, 3740, 3445, 2353, 1651, 1542, 1329, 1128, 667 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J = 2.4 Hz, 1H), 7.75−7.57 (m, 4H), 7.50 (d, J = 2.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 144.5, 140.3, 136.3, 132.1 (q, J = 33.1 Hz), 130.2, 129.8, 126.0 (d, J = 3.6 Hz), 123.5 (d, J = 3.8 Hz), 123.2 (d, J = 271.1 Hz), 118.5, 97.6; HRMS-EI m/z 394.8769 [M^+; calcd. for $C_{12}H_6Br_2F_3NO^+$: 394.8768].

*Methyl 4-(3,5-dibromo-2-oxopyridin-1(2H)-yl)benzoate (**7j**).* General procedure I was used employing mesityl(4-(methoxycarbonyl)-phenyl)iodonium triflate (0.325 mmol) and 3,5-dibromopyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 6 h. Flash chromatography on silica gel using hexane/ethyl acetate (3:1) provided pure **7j** (62.9 mg, 0.163 mmol, 65%) as a pale yellow solid. mp 183−185 °C; R_f 0.3 (hexane/ethyl acetate = 2:1); IR (neat) 3854, 3743, 2354, 1659, 1561, 1281, 1105, 862, 723 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (dd, J = 1.8 Hz and J = 6.9 Hz, 2H), 7.89 (d, J = 2.4 Hz, 1H), 7.51−7.46 (m, 3H), 3.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 157.1, 144.4, 143.5, 136.3, 130.83, 130.77, 126.3, 118.6, 97.5, 52.5; HRMS-EI m/z 384.8948 [M^+; calcd. for $C_{13}H_9Br_2NO_3^+$: 384.8949].

*3,5-Dibromo-6′-chloro-2H-[1,3′-bipyridin]-2-one (**7k**).* General procedure I was used employing mesityl(2-chloropyridin-5-yl)-iodonium triflate (0.325 mmol) and 3,5-dibromopyridin-2(1*H*)-one (0.25 mmol) at 50 °C, and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (7:1−3:1) provided pure **7k** (21.0 mg, 0.058 mmol, 23%) as a white solid and **7d** (59.3 mg, 0.160 mmol, 64%) as a white solid. mp 168−172 °C; R_f 0.36 (hexane/ethyl acetate = 2:1); IR (neat) 3851, 3738, 3445, 2353, 1643, 751, 665 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.57 (d, J = 2.6 Hz, 1H), 8.28 (d, J = 2.5 Hz, 1H), 8.18 (d, J = 2.6 Hz, 1H), 8.06 (dd, J = 2.8 Hz and J = 8.5 Hz, 1H), 7.72 (d, J = 8.5 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 157.2, 150.4, 148.5, 145.4, 139.1, 138.8, 136.5, 125.0, 116.8, 97.1; HRMS-EI m/z 361.8456 [M^+; calcd. for $C_{10}H_5Br_2ClN_2O^+$: 361.8457].

*3,5-Dibromo-1-(thiophen-3-yl)pyridin-2(1H)-one (**7l**).* General procedure I was used employing mesityl(thiophen-3-yl)iodonium triflate (0.325 mmol) and 3,5-dibromopyridin-2(1*H*)-one (0.25 mmol), and the reaction was completed in 1 h. Flash chromatography on silica gel using hexane/ethyl acetate (9:1−7:1) provided pure **7l** (61.1 mg, 0.182 mmol, 73%) as a pale yellow solid and **7d** (11.1 mg, 0.030 mmol, 12%) as a white solid. mp 138−140 °C; R_f 0.67 (hexane/ethyl acetate = 2:1); IR (neat) 3854, 3742, 2354, 1660, 1589, 1403, 1264, 859, 727 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.59 (s, 1H), 7.47 (s, 1H), 7.38 (s, 1H), 7.22 (d, J = 4.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.8, 143.7, 137.4, 136.6, 125.9, 124.3, 120.4, 118.2, 97.0; HRMS-EI m/z 332.8459 [M^+; calcd. for $C_9H_5Br_2NOS^+$: 332.8459].

Procedure for Synthesis of Pirfenidone 9 (5-methyl-1-phenylpyridine-2-(1*H*)-one). A 10 mL round-bottom flask was charged with diphenyliodonium hexafluorophosphate (0.325 mmol), CuCl (10 mol %), Et_3N (0.5 mmol) and 5-methylpyridin-2(1*H*)-one (0.25 mmol). Toluene (2.5 mL) was then added to the flask. The reaction mixture was stirred at room temperature under Ar. After 30 min, the solvent was removed in vacuo and the residue was purified by flash column chromatography on silica gel using dichloromethane/methanol (30:1) provided pure Pirfenidone **9** (45.8 mg, 0.247 mmol, 99%) as a white solid. R_f 0.08 (hexane/ethyl acetate = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.44 (m, 2H), 7.43−7.35 (m, 3H), 7.26 (dd, J = 2.8 Hz and J = 9.3 Hz, 1H), 7.12−7.10 (m, 1H), 6.60 (d, J = 9.6 Hz, 1H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.6, 142.5, 141.0, 135.2, 129.2, 128.2, 126.5, 121.4, 114.7, 16.9; Data are consistent with those reported in the literature.[5b]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01415.

Copies of ^{1}H and ^{13}C spectra for all novel compounds prepared (PDF)

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Notes

The authors declare no competing financial interest.

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