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Palladium-Catalyzed Directed Halogenation of Bipyridine *N*-Oxides

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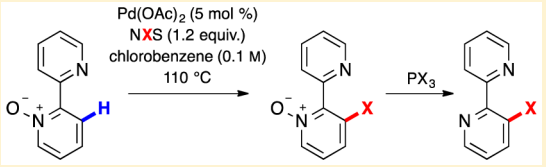
Supporting Information

ABSTRACT: The palladium-catalyzed directed C−H halogenation of bipyridine *N*-oxides was investigated. Using NCS or NBS (*N*-chloro- or *N*-bromosuccinimide) and 5 mol % $Pd(OAc)_2$ in chlorobenzene (0.10 molar) at 110 °C, pyridine-directed functionalization took place and 3-chloro- or 3-bromobipyridine *N*-oxides were obtained in high yields. The reaction is sensitive to steric hindrance by 4- and 6′-substituents. Only in the latter case, where coordination of palladium by the pyridine is hindered, 3′-halogenation directed by the *N*-oxide function was observed. The halogenated products were deoxygenated by PCl_3 or PBr_3.



INTRODUCTION

Halogenated heterocycles are versatile synthetic intermediates, however, 3-halo-2,2′-bipyridines have been underutilized, because they are difficult to access by known methods. Of the three reported preparations (Scheme 1), two involve the *ortho*-directed lithiation of 2,2′-bipyridine under kinetic control at low temperatures followed by halogenation. Thus, intercepting lithiated bipyridine with iodine as an electrophile gave 3-iodo-2,2′-bipyridine in only 11% yield.[1] Using similar conditions, lithiation of 5,5′-bis(trimethylsilyl)bipyridine followed by bromination with $C_2Br_4Cl_2$ occurred in slightly higher yield of 52% (Scheme 1A).[2] A drawback of these reported procedures for the synthesis of 3-halobipyridines is the use of lithiation/quenching sequences. In a different approach, 3-chlorobipyridines were prepared by a palladium-catalyzed Hiyama cross-coupling of 2-trimethylsilyl-3-chloropyridine with 2-bromoypyridine (Scheme 1B).[3] The coupled product was obtained in a good yield of 65% considering that the synthesis of 2,2′-bipyridines by transition-metal catalyzed cross-coupling reactions are generally complicated,[4] because the product is a good chelating ligand and binds to the catalyst, which results in catalyst inhibition or deactivation.

We envisaged transition-metal-catalyzed directed functionalization reactions, which have been demonstrated for substrates with numerous directing groups in the *ortho*-position,[5] might be more efficient for the synthesis of 3-halo-2,2′-bipyridines since the pyridyl ring is a good directing group. Transition-metal-catalyzed pyridyl- or, more general, azine-directed halogenations of 2-arylpyridines, benzo[*h*]quinolines, and related substrates have been achieved with *N*-halosuccinimides,[6] but also with main group metal halides,[7] copper halides,[8] acid chlorides,[9] benzyl chloride,[10] 1,2-DCE (1,2-dichloroethane),[11] or electrochemically with elemental iodine[12] or HBr as a halogen source.[13] Typically palladium catalysts,[6a,b,9a,c,12−14] but also copper(II) salts[6f,h,7a,b,9b] and cobalt,[15] gold,[16] and rhodium catalysts,[6e,7c,11] catalyze directed halogenation reactions.

However, 2,2′-bipyridines are not suitable for such transition-metal-catalyzed directed functionalizations, because they can bind as a bidentate chelating ligand and form a stable, catalytically inactive *N,N*-chelate complex with the transition metal. C−H activation would require energetically unfavorable decomplexation of one of the nitrogen atoms and formation of a *C,N*-chelate, a so-called "roll-over" complex (*cf.* Scheme 1C), which is usually not feasible under catalytic conditions.[17] Only a few examples of roll-over complexes have been reported with iridium,[18] rhodium,[19] platinum,[20] gold,[21] and palladium[22] formed from stoichiometric reactions. As examples for catalytic directed functionalizations of 2,2′-bipyridines, solely rhodium-catalyzed C3-alkylations and alkenylations with terminal olefins,[23] and silylacetylenes have been reported.[24]

Recently, Puddephatt and co-workers reported the synthesis of bipyridine and phenanthroline *N*-oxide *N,O*-chelate platinum(II) complexes and investigated their reactivity under stoichiometric conditions.[25] While a phenanthroline *N*-oxide complex underwent oxidative addition with the N−O bond to give an *N,N*-chelate phenanthroline platinum(IV) complex, the analogous bipyridine *N*-oxide formed a roll-over *C,N*-chelate platinum(II) complex (*cf.* Scheme 1C). C−H bond activation requires decoordination of the *N*-oxide oxygen and rotation of both aromatic planes, which is not possible with metal-bound phenanthroline *N*-oxide due to its rigid structure. Since bipyridine *N*-oxide is able to form roll-over complexes, we envisaged applying them as *N*-protected surrogates for bipyridines in directed halogenations. Here, we demonstrate that bipyridine *N*-oxides undergo catalytic roll-over C−H bond activation to give 3-chloro- and 3-bromobipyridine *N*-oxides in the presence of NXS (*N*-halosuccinimide). The halogenated products were deoxygenated with PX_3 (X = Cl, Br) to the corresponding 3-chloro- and 3-bromobipyridines. Potential palladium intermediates were isolated, and their reactivity investigated.

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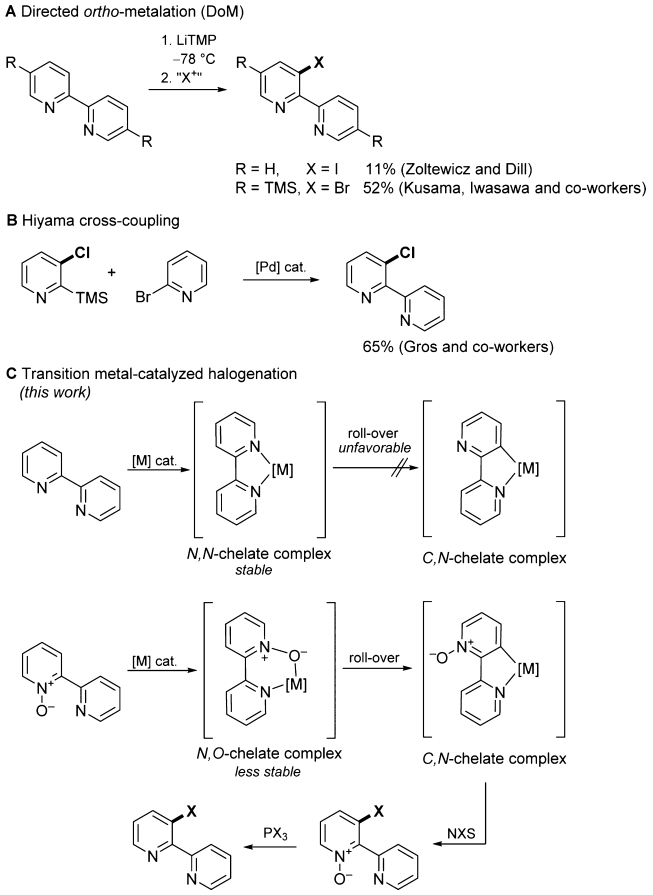
Scheme 1. Approaches for Preparation of 3-Halo-2,2′-bipyridines

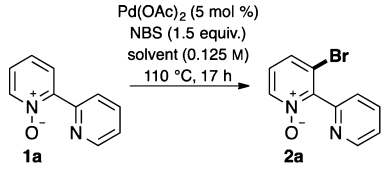


RESULTS AND DISCUSSION

Initially, we tested the conditions previously reported by Sanford and co-workers for directed halogenations of 2-phenylpyridines[6b,14a] and attempted the bromination of bipyridine *N*-oxide **1a** with NBS in AcOH at 120 °C (Table 1, entry 1). However, with the reported conditions only a low yield of the desired product **2a** was observed. When we screened different solvents, the reaction in benzene gave the best yield (entry 9); lower yields were obtained with DCE, CH_3CN, or an AcOH/benzene mixture, DMA, and 2-butanone (entries 2−6), while ethers and alcohols (entries 7, 8) were not suitable. The reaction in Ac_2O did not lead to the brominated product **2a**, but 6-succinimidylbipyridine **3** was found instead (entry 10). This product could arise from a Reissert−Henze-type activation of the *N*-oxide as *N*-acetoxybipyridinium acetate followed by nucleophilic attack of succinimidate (Scheme 2).[26] Indeed, control reactions in the absence of a catalyst with either NBS or succinimide resulted in the same product in 39% and 62% yield, respectively.

Because of the toxicity of benzene and the fact that its atmospheric boiling point is lower than the reaction temperature, we sought a replacement. Toluene, which is often used as a substitute for benzene, proved unsuitable, because, instead of the desired product, only *N*′-benzylated compound **4** was obtained (Table 1, entry 11). Probably, NBS halogenated toluene converted to benzyl bromide,[27] which in turn alkylated the starting material. A control reaction with **1a** and benzyl bromide in CH_3CN provided 94% of a substance with matching spectroscopic properties (Scheme 3). The structural assignment of **4** is further supported by 2D NMR spectroscopy (COESY, HMBC, and HMQC).

Table 1. Optimization of Reaction Conditions



entry	solvent(s)	remarks	yield (%)[a]
1	AcOH	120 °C, cond. ref 14a	10
2	DCE		35
3	CH_3CN		37
4	AcOH/benzene (1:1)		42
5	DMA		14
6	2-butanone		16
7	ethers[b]		0
8	alcohols[c]		0
9	benzene		77
10	Ac_2O		0 (27)[d]
11	toluene		0 (22)[e]
12	benzotrifluoride		56
13	chlorobenzene		77 (22)[f]
14	chlorobenzene	150 °C	0 (52)[f] (19)[g]
15	chlorobenzene	w/o catalyst, 150 °C, w/o NBS	0 (>99)[h]
16	chlorobenzene	w/o catalyst, 110 °C	0 (>99)[h]
17	chlorobenzene	w/o catalyst, 150 °C, 0.2 equiv of NBS	0 (20)[g] (80)[h]
18	chlorobenzene	w/o catalyst, 150 °C, succinimide instead of NBS	0 (>99)[h]
19	benzene	$Pd(OTf)_2$	65
20	benzene	$Pd(OBz)_2$	63
21	benzene	$Pd(OPiv)_2$	68
22	benzene	$PdCl_2$	62
23	benzene	$[Pd(OAc)(tBu_2PCMe_2CH_2)]_2$	56
24	benzene	$[Pd(Br)(tBu_2PCMe_2CH_2)]_2$	23
25	benzene	$[Pd(OAc)(o\text{-}tol_2PC_6H_4CH_2)]_2$	69
26	benzene	$[Pd(Br)(o\text{-}tol_2PC_6H_4CH_2)]_2$	56
27	chlorobenzene	0.37 M in **1a**	21
28	chlorobenzene	0.25 M in **1a**	23
29	chlorobenzene	0.06 M in **1a**	99
30	chlorobenzene	1.2 equiv of NBS	90
31	chlorobenzene	1.0 equiv of NBS	80
32	chlorobenzene	2.5 mol % $Pd(OAc)_2$	59
33	chlorobenzene	1.0 mol % $Pd(OAc)_2$	47

[a]Determined by ^1H NMR vs 1,3,5-trimethoxybenzene as internal standard. [b]Ethers = THF, DME, dioxane, MTBE. [c]Alcohols = EtOH, ^{i}PrOH, ethylene glycol. [d]Yield of 6-succinimidyl-2,2′-bipyridine (**3**). [e]Yield of *N*′-oxo-*N*-benzylbipyridinium bromide (**4**). [f]Yield of 3-bromo-2,2′-bipyridine (**5a**). [g]2,2′-Bipyridine. [h]Yield of recovered **1a**.

Benzotrifluoride as solvent, which is resistant to radical reactions, resulted in a 56% yield, somewhat lower than in the case of benzene (Table 1, entry 12). Finally, chlorobenzene (entry 13), which in contrast to benzene is not carcinogenic or mutagenic, was found to be a suitable replacement for benzene and provided a 77% yield of the desired product **2a** besides 22% of deoxygenated product **5a**. At 150 °C, deoxygenated product **5a** became the main product in 52% yield together with 19% of 2,2′-bipyridine, which results from deoxygenation of the starting material (entry 14). Control experiments (entries 15−18) in the absence of $Pd(OAc)_2$ showed that

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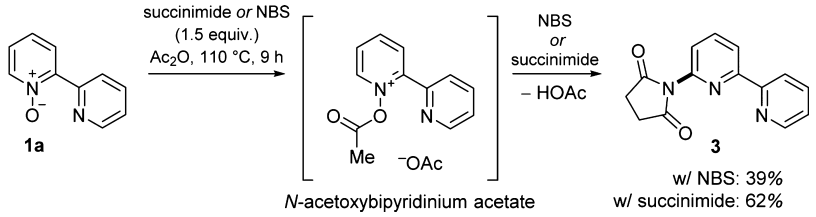
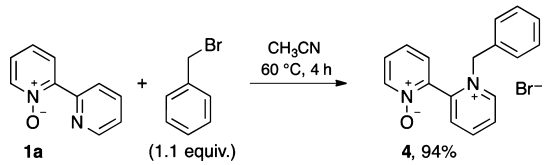
Scheme 2. Formation of 6-Succinimidylbipyridine 3 with Ac_2O



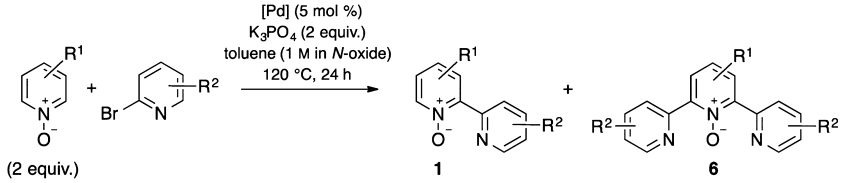
Scheme 3. Formation of *N*-Benzylbipyridinium Bromide 4



NBS and not succinimide is responsible for the deoxygenation. Bipyridine *N*-oxide **1a** on its own is stable at that temperature and was recovered quantitatively after 17 h at 150 °C (entry15).

Simple palladium(II) compounds, such as $Pd(OTf)_2$, $Pd(OBz)_2$, $Pd(OPiv)_2$, and $PdCl_2$, also catalyzed the directed halogenation (Table 1, entries 19−22), albeit in lower yields than $Pd(OAc)_2$. Cyclometalated complexes $[Pd(X)(^tBu_2PCMe_2CH_2)]_2$ and $[Pd(X)(o\text{-}tol_2PC_6H_4CH_2)]_2$ (X = Br, OAc), which are known to be active catalysts in C−H bond arylations of pyridine *N*-oxides,[28] also formed active catalysts, possibly by thermal decomposition of the complex under the reaction conditions, to give the brominated product **2a** (entries 23−26). Some other palladium ($[(tmeda)PdCl_2]$, $[(dppf)PdCl_2]$, $[(CH_3CN)_2Pd(BF_4)_2]$, $[(2,2'\text{-bipyridine})Pd(OAc)_2]$, Buchwald's precatalyst G1) and ruthenium complexes ($RuCl_3\cdot H_2O$, $[(\eta^6\text{-arene})RuX_2]$ with arene = *p*-cymene or benzene, and X = Cl or OAc) either were completely unreactive or produced

Table 2. Preparation of Bipyridine *N*-Oxides 1 by Direct Arylation



[Pd] = [Pd(OAc)(^{t}Bu$_2$PCMe$_2$CH$_2$)]

entry	R^1	R^2		yield of **1** (%)[a]		yield of **6** (%)[a]
1	H	H	**1a**	44 (lit. 23)[b]	**6a**	0
2	6-Me	H	**1b**	8, 22[c]	**6b**	–
3	6-CO_2Et	H	**1c**	59 (lit. 10)[b]	**6c**	–
4	6-CF_3	H	**1d**	49	**6d**	–
5	6-CN	H	**1e**	8 (lit. 58)[b]	**6e**	–
6	5-OMe	H	**1f**	35	**6f**	16
7[c]	5-Me	H	**1g**	20	**6g**	0
8	5-CO_2Me	H	**1h**	72 (lit. 25)[b]	**6h**	0
9	5-NO_2	H	**1i**	13	**6i**	3
10[c]	4-OMe	H	**1j**	15	**6j**	0
11	4-Cl	H	**1k**	41 (lit. 35)[b]	**6k**	12 (lit. 8)[b]
12	4-CO_2Et	H	**1l**	67 (lit. 67)[b]	**6l**	15 (lit. 13)[b]
13	4-CF_3	H	**1m**	87 (lit. 65)[b]	**6m**	10 (lit. 18)[b]
14[c]	4-CN	H	**1n**	27 (lit. 56)[b]	**6n**	5 (lit. 15)[b]
15[c]	H	6′-OMe	**1p**	64	**6p**	13
16[c]	H	6′-Me	**1q**	41	**6q**	5
17	H	6′-CF_3	**1r**	65	**6r**	11
18	H	5′-Me	**1s**	13	**6s**	0
19	H	4′-OMe	**1t**	44	**6t**	7
20	H	4′-Me	**1u**	31	**6u**	4
21[d]	H	4′-F	**1v**	8	**6v**	0
22	H	4′-CO_2Et	**1w**	44	**6w**	11
23[d]	H	4′-CF_3	**1x**	15	**6x**	0
24	2-pyrazine *N*-oxide	H	**1y**	21	**6y**	0
25	2-quinoline *N*-oxide	H	**1z**	19	**6z**	–

[a]Isolated yields. [b]Yields in parentheses reported in ref 28d with $Pd(OAc)_2/P^tBu_3$ as catalyst and K_2CO_3 as base. [c]$Pd(OAc)_2$ (5 mol %) and P^tBu_3 (6 mol %) were used. [d]2-Chloropyridine derivative was used.

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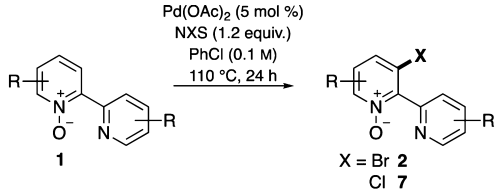
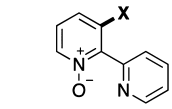
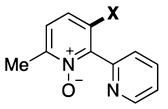
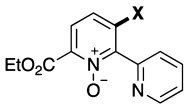
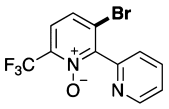
Scheme 4. Scope of Direct Halogenation of 1 with Substituted *N*-Oxide Ring[a]

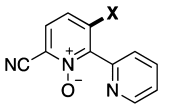


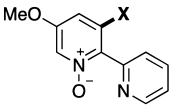

2a, 87%
7a, 95%

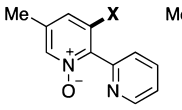

2b, 60%
7b, 68%

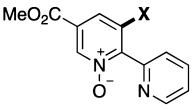

2c, 82%
7c, 91%

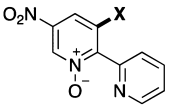

2d, 99%

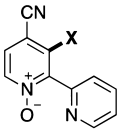

2e, 17% (**1e**, 14%)
7e, 0% (**1e**, 85%)

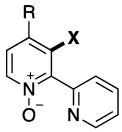

2f, 99%
7f, 97%

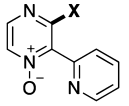

2g, 40% (**5g**, 35%)
7g, 90%

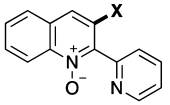

2h, 3%
7h, 64%

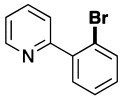

2i, c.m.
7i, 31% (**1j**, 33%)

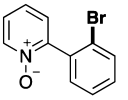

2n, 37% (**1n**, 32%)
7n, 0% (**1n**, 91%)


R = OMe **2j**, 0% (**1k**, 83%)
Cl **2k**, c.m.
CO_2Et **2l**, 0% (**1l**, 99%)
CF_3 **2m**, 0% (**1m**, 53%; **8m**, 36%)
NO_2 **2o**, 0% (**1o**, 72%; **8o**, 12%)[b]

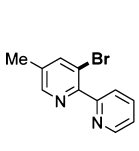

2y, 0% (**1y**, 78%)
7y, 0% (**1y**, 92%)


2z, 49% (**5z**, 9%; **8z**, 8%)
7z, 87%

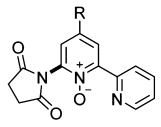

10, 49% (**11**, 13%)

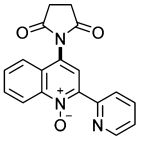

13, 66% (**14**, 10%)
0%[c] (**12**, 45%)

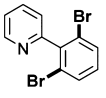
[a]Isolated yields. [b]Obtained as mixture of **1o** and **8o**. [c]Reaction without $Pd(OAc)_2$. c.m. = complex product mixture.

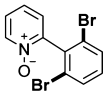

5g


5z


R = CF_3 **8m**
NO_2 **8o**


8z


11


14

exclusively deoxygenated starting material in approximately 50% yield. The combination of NXS with stoichiometric copper(I) chloride or bromide, which has been reported for the halogenation of phenylpyridine,[8c] proved to be unreactive and the starting material was reisolated. We briefly tried other bromine sources (Br_2, Br_2 + $PhI(OAc)_2$, LiBr + oxone, KBr + oxone, $CuBr_2$), but these resulted only in decomposition of the starting material.

The influence of concentration, equivalents of NBS, and catalyst loading was tested (Table 1, entries 27−33). Increasing the concentration of bipyridine *N*-oxide **1a** to more than 0.125 mol/L led to a precipitous drop in the yield (entries 27−29). This observation is in contrast to the arylation of pyridine *N*-oxides, where higher substrate concentrations resulted in higher yields. Adjusting the amount of NBS to 1.2 equiv led to a 90% yield of the desired product **2a** (entry 30). Lowering the catalyst loading unsurprisingly resulted in lower yields (entries 32 and 33). No reaction occurred in the absence of $Pd(OAc)_2$, and the starting material **1a** was quantitatively recovered (entry 16).

To examine the substrate scope of the directed halogenation of bipyridine *N*-oxides **1**, we had to prepare the functionalized starting materials, most of which have not been reported before, by palladium-catalyzed direct arylation of pyridine *N*-oxides with 2-bromopyridines.[28d,e] We used slightly modified conditions (K_3PO_4 instead of K_2CO_3, and cyclometalated dimer $[Pd(OAc)(^tBu_2PCMe_2CH_2)]_2$ as the catalyst instead of $Pd(OAc)_2/P^tBu_3$) and obtained bipyridine *N*-oxides **1** in good to moderate yields (Table 2). With the exception of the cyano (**1e**, **1n**) and nitro (**1i**) substituents, electron-poorer pyridine *N*-oxides (**1a**, **1c**, **1d**, **1h**, **1k**, **1l**, **1m**) were arylated in higher yields (41−87%) than more electron-rich pyridine *N*-oxides (**1b**, **1f**, **1g**, **1j**, 15−35%). This reactivity trend has been previously observed and can be explained by the more polarized C−H undergoing faster C−H bond activation via a concerted metalation−deprotonation (CMD) mechanism.[28a−c]

With respect to the substituent at the bromopyridine, the arylation does not follow an obvious electronic trend. Thus, arylation with the most electron-rich 4-methoxybromopyridine gave the same yield as with the most electron-poor 4-esterbromopyridine (cf. Table 2, entry 19 vs 22). However, the position of the substituent apparently has a stronger influence on the yield, since 6-substituted bromopyridines

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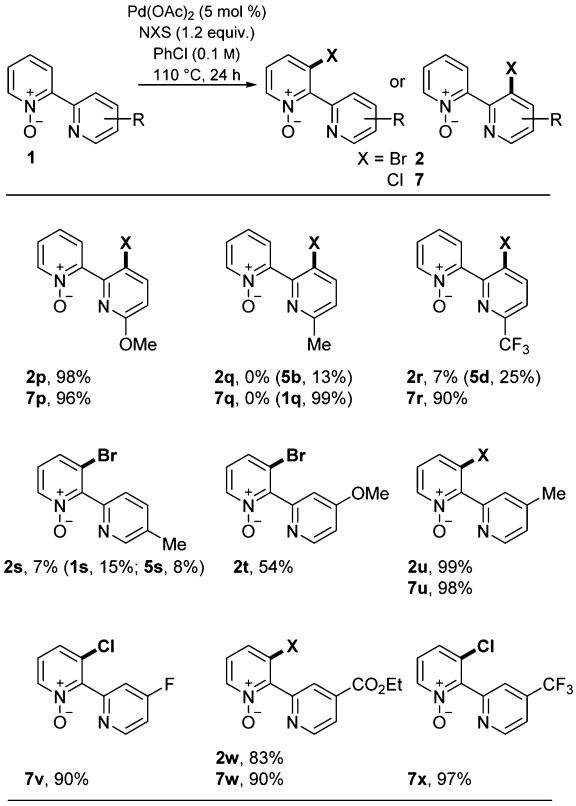
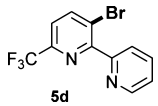
resulted in typically higher yields than the corresponding 4-substituted derivatives (Table 2, entries 15−17 vs 19−23).

With a number of substituted bipyridine *N*-oxides **1** in hand, the scope of the directed halogenation with $Pd(OAc)_2$ as catalyst in chlorobenzene at 110 °C was tested (Schemes 4 and 5). The directed halogenation occurred exclusively in the 3-

Scheme 5. Scope of Direct Halogenation of 1 with Substituted Pyridyl Ring[a]



[a]Isolated yields.



position of the pyridine *N*-oxide ring where cyclometalation, directed by the pyridine ring, is expected. Functionalization of the 6-position, which might conceivably result from activation of the polarized C−H bond neighboring the *N*-oxide in analogy to the arylations of pyridine *N*-oxides,[28a,d,e,29] was not observed. Likewise, no functionalization of the 3′-position, by a possible *N*-oxide directed C−H bond activation,[30] was observed (see however Scheme 5, with **1p**−**r**). Gratifyingly, *N*-chlorosuccinimide (NCS) was also a suitable halogenating reagent, which in several cases gave even better yields than NBS, possibly because of the higher stability of chlorinated compounds compared to their brominated analogues. The same trend had already been observed by Sanford and co-workers.[6b] Substitutions in the 5- or 6-position (CH_3, OCH_3, CF_3, CO_2R) were well tolerated, and the corresponding halogenation products **2** and **7** were obtained in high yields. However, the cyano and nitro substituents were found to be problematic. 6-Cyanobipyridine *N*-oxide **1e** was brominated in only 17% yield, while chlorination did not occur. Bromination of 5-nitro derivative **1i** resulted in an inseparable complex mixture, and chlorination provided **7i** in a low yield of 31%. 4-Substituted bipyridine *N*-oxides **1j**−**o** were generally unreactive, probably because steric hindrance by the substituent prevented cyclometalation, except for 4-cyano bipyridine *N*-oxide **1n**, which was brominated in 37% yield. Here, the linear cyano group is just small enough to allow C−H activation. With the 4-trifluoromethyl derivative **1m**, coupling with succinimide in the 6-position, instead of the desired C-3 halogenation, occurred and provided **8m** in 36% yield (53% starting material recovered). Similarly, succinimide-coupled products **8** were observed with 4-nitrobipyridine *N*-oxide **1o** and 2-pyridylquinoline *N*-oxide **1z**. The structures of brominated products **2a**, **2f**, and **2n** were confirmed by single crystal X-ray diffraction.

For comparison with the conditions developed by Sanford and co-workers, we carried out the bromination of 2-phenylpyridine **9** (Scheme 4). The mono- (**10**) and dibrominated product (**11**) were isolated in 49% and 13% yield, respectively, which corresponds to the expected mixture if the rate constant of the first functionalization is approximately 2.3 times larger than that of the second functionalization (for a derivation of this value, see end of the Experimental Section). From reaction at 120 °C in CH_3CN under otherwise identical conditions, Sanford and co-workers obtained 63% of monobrominated product **10**,[14a] which requires that the rate constant of the first functionalization is at least 4 times larger than that of the second one.

Substitution of the 6′-position remarkably changed the regioselectivity of the reaction to give exclusively 3′-halogenation (Scheme 5, with **1p**−**r**). This observation can be explained by the steric hindrance imposed by the substituent, which prevents coordination of the palladium catalyst to the pyridine moiety and hence prevents activation in the 3-position. Instead, C−H activation directed by the usually less coordinating *N*-oxide takes place, which otherwise cannot compete with coordination by the more donating pyridine nitrogen.[30] To test this hypothesis we subjected 2-phenylpyridine *N*-oxide (**12**) to the catalytic bromination conditions (Scheme 4). Indeed, only *ortho*-brominated product **13** was obtained in 66% yield (besides 10% dibrominated product **14**), which is consistent with *N*-oxide directed functionalization. In a control experiment without $Pd(OAc)_2$ no brominated products were observed.

Substitutions in the 4′-position (CH_3, F, CO_2Et, CF_3) led to the expected pyridine-directed halogenation in the 3-position in high yields (Scheme 5, with **1u**−**x**). However, bromination of 5′-methylbipyridine *N*-oxide **1s** gave only a 7% yield together with the deoxygenated product **5s** in 8% yield. Deoxygenation of products was observed solely in brominations (*cf.* **2g**, **2z** Scheme 4 and **2r** Scheme 5), but not in chlorination reactions. Although speculatory at this point, this particular result might be explained by a palladium-catalyzed pyridyl-directed deoxygenation (as opposed to uncatalyzed deoxygenation at higher temperatures; *cf.* Table 1, entry 17) and subsequent inhibition by the bipyridine product.

The halogenated products were easily deoxygenated by treatment with PCl_3 or PBr_3 (Scheme 6).[28d,31] We used PCl_3 for the deoxygenations of the chlorinated products and PBr_3 for the brominated products to exclude any conceivable halogen exchange reactions. Generally, the reductions with PCl_3 gave better yields than the ones with PBr_3, and the latter reactions usually required purification by flash column chromatography, while reductions with PCl_3 mostly provided pure products directly after extraction. In the case of the halogenated 5-

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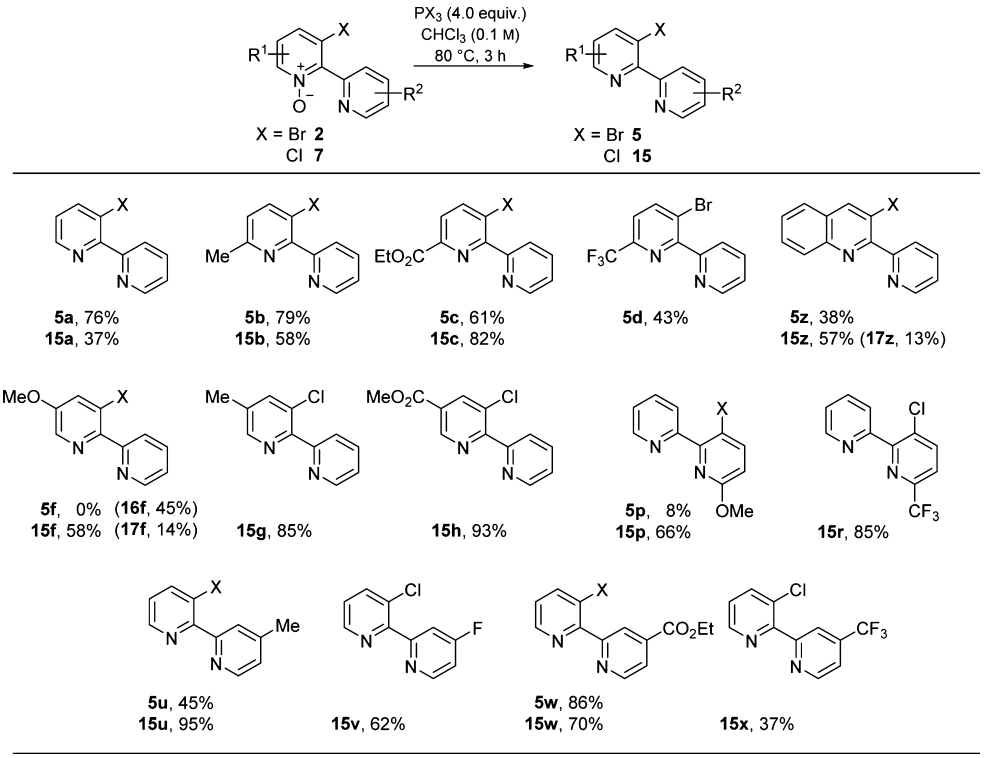
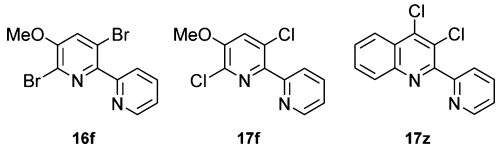
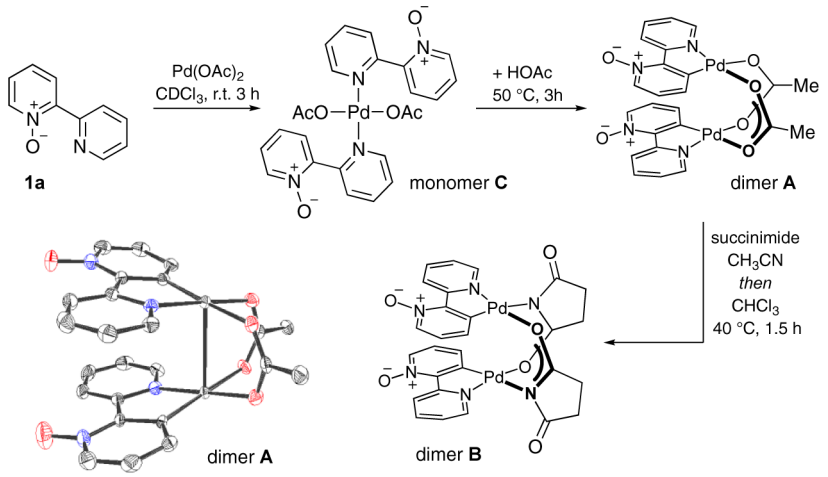
Scheme 6. Deoxygenation of Halogenated Bipyridine *N*-Oxides 2 and 7[a]



[a]Isolated yields.



Scheme 7. Syntheses of Putative Catalyst Intermediates



methoxybipyridine *N*-oxide **2f** and **7f**, additional halogenation in the 6-position by an electrophilic aromatic substitution was observed to give the corresponding dihalogenated bipyridines. Similarly, additional chlorination in the 4-position occurred while deoxygenating chlorinated quinoline *N*-oxide **7z**. In an initial attempt to deoxygenate 3-bromobipyridine *N*-oxide **2a** using Pd/C (10 mol %), NH_4HCO_2 in MeOH,[28a] quantitative dehalogenation was observed and only bipyridine was recovered (see Experimental Section). Using the same conditions, no reaction was observed with chlorinated bipyridine *N*-oxide **7a**.

Recent mechanistic investigations of the azine-directed chlorination by Ritter and co-workers support a catalytic cycle consisting of (i) cyclopalladation of the substrate forming a dimeric palladium(II) succinimidate-bridged complex, (ii) rate-determining acetate-assisted bimetallic oxidation, and (iii) bimetallic reductive elimination.[32] To probe the mechanism of the directed halogenation of bipyridine *N*-oxides **1**, we

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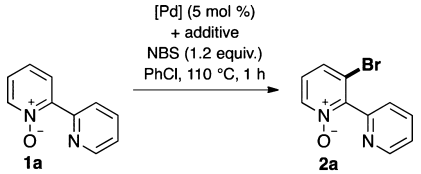
independently prepared two cyclometalated putative catalytic intermediates **A** and **B**. Initially, $Pd(OAc)_2$ and **1a** form a monomeric 1:2 complex **C**, in which the pyridine rings bind *trans* to each other (Scheme 7, crystal structure was obtained for analogous complex with **1l**; for crystal structure, see Supporting Information). Upon heating to 50 °C in the presence of HOAc, the monomeric complex **C** is converted to cyclometalated complex **A**,[33] which has a dimeric structure with bridging acetate ligands and closely resembles the structures of the benzo[*h*]quinoline-derived complexes reported previously.[32b] The acetate ligands were easily exchanged in the presence of succinimide to give analogous dimer **B** with succinimidate as the bridging ligand.

We performed catalytic reactions using $Pd(OAc)_2$, dimer **A**, or dimer **B** as the catalyst (Scheme 8). After 1 h of reaction

Scheme 8. Mechanistic Investigations under Catalytic Conditions[a]



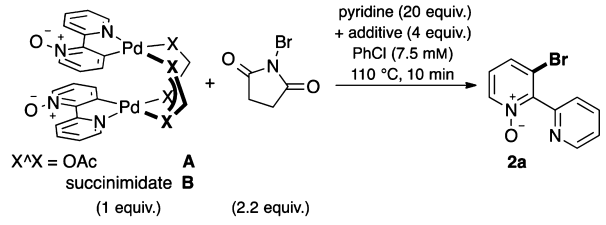
(a)	$Pd(OAc)_2$	66%
(b)	Dimer **A**	93%
(c)	Dimer **B**	41%
(d)	Dimer **B** (+ 10 mol % NBu_4OAc)	25%
(e)	Dimer **B** (+ 10 mol % HOAc)	95%
(f)	$Pd(OAc)_2$ (+ 1 equiv. pyridine)	0%

[a]Yields are based on the ratio **1a**:**2a** in the crude ^{1}H NMR.

time, $Pd(OAc)_2$ provided 66% yield of **2a**, while acetate dimer **A** gave a 93% yield. In contrast, succinimidate dimer **B**, which corresponds to the previously reported catalyst resting state in analogous reactions,[32d] resulted in only 41% yield, which shows **B** itself is not kinetically competent and acetate is required. Indeed, the yield increased to 95% when 10 mol % of HOAc was added; however, it decreased to 25% when 10 mol % of NBu_4OAc was added. Obviously, the rate-determining step either changes or is inhibited in the presence of free acetate anions, but is accelerated with HOAc. This result is in contrast to the reports by Ritter and co-workers, who observed that the directed chlorination of benzo[*h*]quinoline becomes faster in both cases, with HOAc and NBu_4OAc. They concluded that the oxidation step is rate-limiting and mediated by acetate. In the directed bromination of bipyridine *N*-oxide **1a**, the retardation of the reaction by added acetate might be explained by a rate-determining cyclopalladation. Conceivably, excess acetate inhibits the cyclometalation by blocking a free coordination site at the palladium(II) center, which is required for the C–H bond cleavage.[34] The requirement for a free coordination site at the palladium(II) center is further supported by the observation that added pyridine (Scheme 8f), as well as higher substrate concentrations (Table 1, entries 27–29), inhibit the catalytic reaction. The higher yield of **2a**, obtained with added HOAc, might be due to protonation of the *N*-oxide oxygen of **1a** to prevent *N*,*O*-chelate complex formation and to facilitate the desired *C*,*N* coordination mode.

Stoichiometric reactions of dimers **A** and **B** with NBS were performed in the presence of pyridine at 110 °C for 10 min (Scheme 9).[35] Brominated product **2a** was obtained in 66% yield in the reaction with acetate dimer **A**. The reaction with

Scheme 9. Stoichiometric Reactions of Cyclometalated Palladium(II) Dimers[a]



(a)	Dimer **A**	66%
(b)	Dimer **B**	20% (46%)[b]
(c)	Dimer **A** (+ HOAc)	71%
(d)	Dimer **B** (+ HOAc)	51%
(e)	Dimer **B** (+ NBu_4OAc)	81%

[a]Yields were determined by ^{1}H NMR vs 1,3,5-trichlorobenzene as internal standard. [b]Recovered dimer **B**.

succinimidate dimer **B** resulted in a yield of 20%, which increased to 51% in the presence of added HOAc, and further increased to 81%, when NBu_4OAc was added. These observations are essentially consistent with the acetate-assisted bimetallic oxidation outlined in Scheme 10, which was proposed by Ritter for the directed halogenation of 2-phenylpyridine and benzo[*h*]quinoline:[32d] (i) Coordination and cyclopalladation of bipyridine *N*-oxide **1** forms a succinimidate-bridged dimeric palladium(II) complex **B**. This step is probably rate-limiting in the present reaction. (ii) Acetate-assisted bimetallic oxidation leads to a dimeric palladium(III) complex, which (iii) undergoes bimetallic reductive elimination forming the new carbon–halogen bond. Exchange of the palladium-bound product for a molecule of starting material finally closes the catalytic cycle.

CONCLUSION

In conclusion, we described the efficient synthesis of 3-bromo- and 3-chlorobipyridines, which are difficult to access by other methods, via the palladium-catalyzed directed halogenation of bipyridine *N*-oxides followed by deoxygenation of the products with PX_3. The reactivities of isolated dinuclear cyclometalated complexes are consistent with a Pd(II)/Pd(III) mechanism previously proposed for related palladium-catalyzed directed halogenations. Ongoing work on subsequent conversion of the 3-halobipyridines into other functional groups, as well as the extension of the scope for other directed functionalizations of bipyridine *N*-oxides, will be reported in due course.

EXPERIMENTAL SECTION

General Experimental Methods. Unless otherwise noted, direct halogenation reactions were set up in Teflon-lined screw-cap reaction vials (8 or 20 mL) under an air atmosphere and heated in a preheated aluminum block placed on a heater with digital temperature control. The syntheses of bipyridine *N*-oxide starting materials by palladium-catalyzed direct arylation are air and moisture sensitive and were carried out using oven-dried glassware under an argon atmosphere. The reactions were set up in an argon-filled glovebox and heated under stirring outside the glovebox in a preheated oil bath. Commercial and noncommercial pyridine *N*-oxides, which were prepared by literature procedures[28d] and have been described earlier,[28d,36] were dried by azeotropic distillations by means of Dean–Stark distillation from toluene prior to use. Toluene was dried and distilled over sodium/benzophenone and degassed using the freeze–pump–thaw technique. K_3PO_4 was heat-dried at 300–400 °C under vacuum and stored in the glovebox. All other solvents and reagents were used as received from

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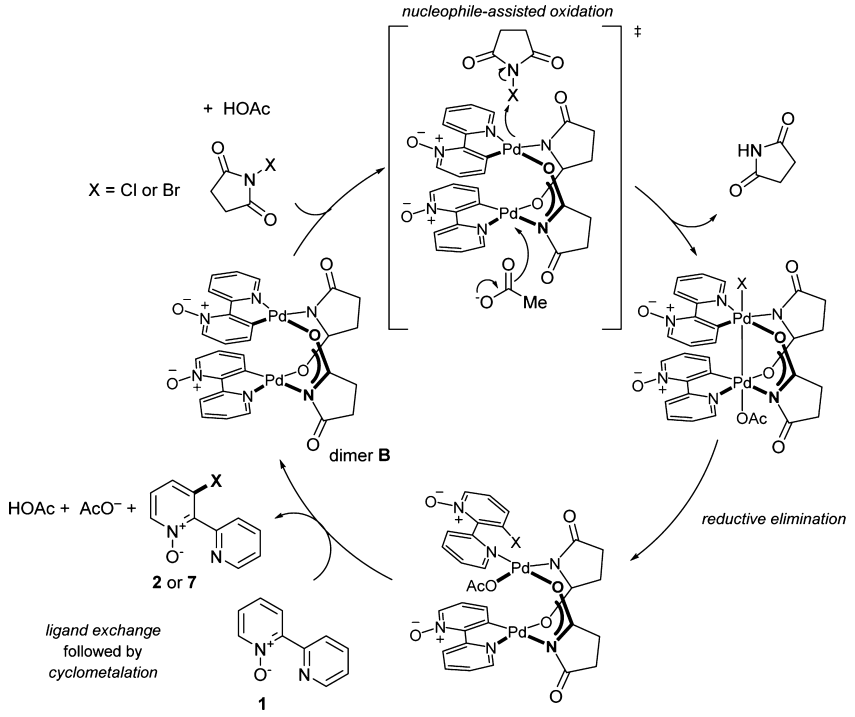
Scheme 10. Mechanism of Palladium-Catalyzed Directed Halogenation of Bipyridine *N*-Oxides 1



commercial suppliers. Cyclometalated catalysts $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$,[28e] $[Pd(^tBu_2PCMe_2CH_2)Br]_2$,[37] Herrmann–Beller catalyst,[38] $Pd(OTf)_2$,[39] $Pd(OBz)_2$,[40] and $Pd(OPiv)_2$,[41] were prepared by reported procedures. Column chromatography was performed on silica gel (230–400 mesh) and monitored by TLC on silica gel using a UV lamb (254 nm) to visualize spots. NMR chemical shifts (δ) are reported in parts per million (ppm) and referenced to residual solvent peak ($CDCl_3$: ^1H δ = 7.26 ppm, ^{13}C δ = 77.16 ppm; C_6D_6: ^1H δ = 7.16 ppm, ^{13}C δ = 128.06 ppm; CD_2Cl_2: ^1H δ = 5.32 ppm, ^{13}C δ = 53.84 ppm; ^{19}F: frequency calibrated log with ±1 ppm deviation). Multiplicities are given as follows: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Coupling constants (J) are reported in hertz (Hz). High resolution mass spectra were recorded on an ESI-TOF (electrospray ionization-time-of-flight) instrument. IR spectra were recorded on an FT/IR with a ZnSe optical window. The absorption bands are given in wave numbers (cm^{-1}). Melting points (mp) are uncorrected. Elemental analyses for contents of carbon, nitrogen, and hydrogen are reported in percentage (%).

General Procedure for Optimization of Palladium-Catalyzed Bromination. A Teflon-lined screw cap vial was charged with bipyridine *N*-oxide **1a** (0.25 mmol), NBS, catalyst, and solvent. After stirring at 110 °C for 17 h, the reaction mixtures were cooled to room temperature, diluted with DCM, and extracted with a 1 M NaOH solution. The combined organic layers were dried with Na_2SO_4 and filtered, and the solvent was removed from the filtrate. The crude products were redissolved in a stock solution of TMB in $CDCl_3$ and transferred into an NMR vial. Yields were calculated by integration of the isolated and fitted signals relative to the aromatic protons of 1,3,5-trimethoxybenzene.

Independent Syntheses of Observed Side Products. *6-(2,5-Pyrrolindion-1-yl)-2,2′-bipyridine (**3**).* Bipyridine *N*-oxide **1a** (86.3 mg, 0.50 mmol) and succinimide (74.8 mg, 0.76 mmol) were dissolved in Ac_2O (4.00 mL). The reaction solution was heated at 110 °C for 9 h before MeOH (4.00 mL) was added. The volatiles were removed in vacuum, and the crude product was purified by column chromatography (SiO_2, MeOH in DCM: 3%) providing **3** (82.8 mg, 0.31 mmol, 62%) as a tan solid. Alternatively, the reaction of bipyridine *N*-oxide **1a** (87.7 mg, 0.51 mmol) and NBS (136.1 mg, 0.77 mmol) in Ac_2O (4.00 mL) provided **3** (49.9 mg, 0.20 mmol, 39%) following the same procedure. The structure was confirmed by COESY, HMBC, and HMQC. Mp 140–150 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.67 (dd, J = 4.8, 1.7 Hz, 1H, ArH-3′), 8.47 (d, J = 7.9 Hz, 1H, ArH-3), 8.34 (d, J = 7.9 Hz, 1H, ArH-5), 7.97 (td, J = 7.9, 0.6 Hz, 1H, ArH-4), 7.78 (td, J = 7.8, 1.8 Hz, 1H, ArH-5′), 7.36–7.26 (m, 2H, ArH-4′, ArH-6′), 2.93 (s, 2H, $-CH_2-$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 175.8, 156.8, 155.1, 149.3, 145.8, 139.4, 137.1, 124.2, 122.0, 121.7, 121.3, 28.8; IR (ν/cm^{-1}): 1704, 1583, 1558, 1452, 1427, 1381, 1173, 993, 774, 743; HRMS (ESI-TOF): $[M + Na]^+$ calcd for $C_{14}H_{11}N_3O_2Na$ 276.0743; found 276.0757.

*N′-Benzyl-N-oxo-2,2′-bipyridinium Bromide (**4**).* Reaction of bipyridine *N*-oxide **1a** (173 mg, 1.00 mmol) and benzyl bromide (0.13 mL, 1.09 mmol) in MeCN (1.00 mL) at 60° for 4 h provided **4** (325 mg, 0.95 mmol, 94%) as a tan oil after removal of the solvent, washing the residue with Et_2O and drying in vacuum. Structure was confirmed by COESY, HMBC, and HMQC. ^1H NMR (500 MHz, $CDCl_3$): δ 9.35 (d, J = 5.2 Hz, 1H, ArH-3′), 8.67 (t, J = 7.7 Hz, 1H, ArH-5′), 8.34 (d, J = 6.4 Hz, 1H, ArH-3), 8.15 (t, J = 6.8 Hz, 1H, ArH-4′), 8.06 (d, J = 7.4 Hz, 1H, ArH-6′), 7.97 (d, J = 6.9 Hz, 1H, ArH-6), 7.56 (t, J = 7.1 Hz, 1H, ArH-4), 7.42 (t, J = 7.8 Hz, 1H, ArH-5), 7.32–7.23 (m, 5H, Ph-H), 5.97 (d, J = 14.5 Hz, 1H, $-CH_2-$), 5.92 (d, J = 14.7 Hz, 1H, $-CH_2-$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 146.9 (C-2′), 146.8 (C-5′), 146.6 (C-3′), 141.0 (C-2), 139.8 (C-3), 131.6 (C-6′), 131.5 (C-1″), 130.6 (C-6), 130.1 (C-4″), 129.7 (C-3″, C-5″), 129.6 (C-2″, C-6″), 129.0 (C-4′), 129.0 (C-4), 127.0 (C-5), 62.9 ($-CH_2-$); IR (ν/cm^{-1}): 3390, 3044, 1621, 1480, 1455, 1422, 1244, 1154, 1031, 847, 771, 745, 725, 696; HRMS (ESI-TOF) m/z: $[M - Br]^+$ calcd for $C_{17}H_{15}N_2O$ 263.1179; found 263.1181.

General Procedure for Synthesis of Bipyridine *N*-Oxides. Based on a reported procedure,[28d] an oven-dried Schlenk flask was charged with pyridine *N*-oxide (2.0 equiv), 2-bromopyridine derivative (1.0 equiv), K_3PO_4 (2.0 equiv), cyclometalated palladium complex $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$ (2.5 mol %) or $Pd(OAc)_2$ (5 mol %) and P^tBu_3 (6 mol %), and toluene (c = 1.0 M) inside the glovebox. The flask was brought outside the glovebox and placed in a preheated oil bath. After stirring at 120 °C for 24–48 h, the reaction mixture was cooled to room temperature and directly subjected to column chromatography (MeOH in DCM mixtures: 0–10%, 1% increments; or acetone in hexane mixtures: 0–100%, 10% increments).

*2,2′-Bipyridine N-Oxide (**1a**).* (150 mg, 44% for 2.0 mmol scale using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, MeOH/DCM mixtures); ^1H NMR

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(400 MHz, $CDCl_3$): δ 8.89 (d, J = 8.1 Hz, 1H), 8.71 (ddt, J = 4.8, 1.7, 0.8 Hz, 1H), 8.30 (ddt, J = 6.5, 1.3, 0.6 Hz, 1H), 8.17 (dd, J = 8.0, 2.2 Hz, 1H), 7.82 (dddd, J = 8.3, 7.7, 1.8, 0.7 Hz, 1H), 7.40−7.29 (m, 2H), 7.30−7.21 (m, 1H). The chemical shifts are in agreement with previous reports.[28d,42] Alternatively, **1a** can be prepared by *N*-oxidation of 2,2′-bipyridine with H_2O_2 in TFA,[42] or with *m*CPBA.[31]

*6-Methyl-2,2′-bipyridine N-Oxide (**1b**).* (711 mg, 8% for 50 mmol scale using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, 1.02 g, 22% for 25 mmol scale using $Pd(OAc)_2/P^tBu_3$, acetone/hexane mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 8.80 (dt, J = 8.1, 1.1 Hz, 1H), 8.71 (ddd, J = 4.8, 1.8, 0.9 Hz, 1H), 7.98 (dd, J = 7.6, 2.7 Hz, 1H), 7.80 (td, J = 7.8, 1.9 Hz, 1H), 7.32 (ddd, J = 7.5, 4.8, 1.2 Hz, 1H), 7.30−7.23 (m, 2H), 2.58 (s, 3H). The chemical shifts are in agreement with previous reports.[43]

*6-Ethoxycarbonyl-2,2′-bipyridine N-Oxide (**1c**).* (5.48 g, 59% for 38 mmol scale using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 8.93 (dt, J = 8.1, 1.1 Hz, 1H), 8.72 (ddd, J = 4.8, 1.9, 0.9 Hz, 1H), 8.28 (dd, J = 8.1, 2.2 Hz, 1H), 7.81 (ddd, J = 8.1, 7.6, 1.9 Hz, 1H), 7.48 (dd, J = 7.7, 2.2 Hz, 1H), 7.38 (t, J = 7.9 Hz, 1H), 7.35 (ddd, J = 7.6, 4.8, 1.2 Hz, 1H), 4.49 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.2 Hz, 3H). The chemical shifts are in agreement with previous reports.[28d]

*6-Trifluoromethyl-2,2′-bipyridine N-Oxide (**1d**).* Yellow oil (518 mg, 49% for 4.4 mmol scale using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 8.85 (ddt, J = 8.1, 2.1, 1.1 Hz, 1H), 8.69 (dtd, J = 4.7, 1.9, 0.9 Hz, 1H), 8.37 (dt, J = 8.2, 2.1 Hz, 1H), 7.78 (ddt, J = 8.1, 7.5, 1.8 Hz, 1H), 7.69 (dt, J = 7.9, 1.9 Hz, 1H), 7.39 (tdd, J = 8.0, 1.7, 0.8 Hz, 1H), 7.33 (dddd, J = 7.7, 4.7, 1.8, 1.1 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 149.6, 148.4, 139.5 (q, J = 32.7 Hz), 136.3, 130.8, 125.7, 124.9, 124.7 (q, J = 4.1 Hz), 124.2, 120.2 (q, J = 272.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ − 68.6;

HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{11}H_8F_3N_2O$ 241.0583; found 241.0597, $[M + Na]^+$ calcd for $C_{11}H_7F_3N_2ONa$ 263.0403; found 263.0442.

*6-Cyano-2,2′-bipyridine N-Oxide (**1e**).* (640 mg, 8% for 40 mmol scale using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 8.91 (dt, J = 8.1, 1.1 Hz, 1H), 8.73 (ddt, J = 4.8, 2.1, 1.0 Hz, 1H), 8.49 (ddd, J = 8.2, 2.2, 1.0 Hz, 1H), 7.86 (td, J = 8.1, 1.8 Hz, 1H), 7.69 (ddd, J = 7.8, 2.1, 0.8 Hz, 1H), 7.46−7.36 (m, 2H). The chemical shifts are in agreement with previous reports.[28d]

*5-Methoxy-2,2′-bipyridine N-Oxide (**1f**).* Brown solid (1.42 g, 35% for 20 mmol scale besides **6f** using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); mp 67 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.81 (dt, J = 8.2, 1.1 Hz, 1H), 8.65 (ddd, J = 4.8, 1.9, 1.0 Hz, 1H), 8.07 (d, J = 9.1 Hz, 1H), 8.01 (d, J = 2.4 Hz, 1H), 7.76 (td, J = 7.8, 1.9 Hz, 1H), 7.26 (ddd, J = 7.6, 4.7, 1.2 Hz, 1H), 6.97 (dd, J = 9.1, 2.4 Hz, 1H), 3.85 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 157.4, 149.7, 149.3, 141.1, 136.3, 127.9, 127.6, 125.2, 123.8, 114.1, 56.3; IR (*ν*/cm^{-1}): 1514, 1462, 1440, 1388, 1312, 1292, 1206, 776; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{11}H_{11}N_2O_2$ 203.0815; found 203.0841, $[M + Na]^+$ $C_{11}H_{10}N_2O_2Na$ 225.0634; found 225.0666, $[M + K]^+$ calcd for $C_{11}H_{10}N_2O_2K$ 241.0374; found 241.0401.

*5′-Methoxy-2,2′:6,2″-terpyridine N-Oxide (**6f**).* Brown solid (459 mg, 16%); mp 143 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.83−8.77 (m, 2H), 8.67 (d, J = 3.9 Hz, 1H), 8.23 (d, J = 9.1 Hz, 1H), 7.83 (td, J = 7.7, 1.8 Hz, 1H), 7.71 (td, J = 7.8, 1.9 Hz, 1H), 7.51 (dt, J = 7.8, 1.1 Hz, 1H), 7.35 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H), 7.30−7.21 (m, 1H), 7.11 (d, J = 9.2 Hz, 1H), 3.83 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 156.0, 150.2, 150.0, 149.2, 141.6, 141.5, 136.6, 136.1, 127.1, 126.2, 125.5, 123.7, 123.6, 120.7, 109.9, 56.7; IR (*ν*/cm^{-1}): 1425, 1360, 1082, 779, 745; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{16}H_{14}N_3O_2$ 280.1081; found 280.1089, $[M + Na]^+$ calcd for $C_{16}H_{13}N_3O_2Na$ 302.0900; found 302.0912, $[M + K]^+$ calcd for $C_{16}H_{13}N_3O_2K$ 318.0639; found 318.0661.

*5-Methyl-2,2′-bipyridine N-Oxide (**1g**).* Off-white solid (1.85 g, 20% for 50 mmol scale using $Pd(OAc)_2/P^tBu_3$, acetone/hexane mixtures); mp 65 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.84 (dt, J = 8.1, 1.1 Hz, 1H), 8.66 (ddd, J = 4.8, 1.9, 1.0 Hz, 1H), 8.13 (dt, J = 1.7, 0.8 Hz, 1H), 8.02 (d, J = 8.2 Hz, 1H), 7.76 (td, J = 7.8, 1.9 Hz, 1H), 7.27 (ddd, J = 7.7, 4.9, 1.3 Hz, 1H), 7.14 (ddd, J = 8.3, 1.7, 0.8 Hz, 1H), 2.29 (d, J = 0.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 149.8, 149.3, 144.7, 140.4, 136.3, 136.1, 127.3, 127.2, 125.4, 124.0, 18.1; IR (*ν*/cm^{-1}): 1377, 1272, 1208, 825, 783, 742; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{11}H_{11}N_2O$ 187.0866; found 187.0888, $[M + Na]^+$ calcd for $C_{11}H_{10}N_2ONa$ 209.0685; found 209.0712, $[M + K]^+$ calcd for $C_{11}H_{10}N_2OK$ 225.0425; found 225.0602.

*5-Methoxycarbonyl-2,2′-bipyridine N-Oxide (**1h**).* (8.14 g, 72% for 49 mmol scale using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 9.00 (dt, J = 8.1, 1.1 Hz, 1H), 8.90 (dd, J = 1.6, 0.6 Hz, 1H), 8.75 (ddd, J = 4.8, 1.8, 0.9 Hz, 1H), 8.33 (dd, J = 8.4, 0.6 Hz, 1H), 7.91 (dd, J = 8.4, 1.6 Hz, 1H), 7.86 (ddd, J = 8.1, 7.6, 1.9 Hz, 1H), 7.40 (ddd, J = 7.6, 4.8, 1.2 Hz, 1H), 3.99 (s, 3H). The chemical shifts are in agreement with previous reports.[28d]

*5-Nitro-2,2′-bipyridine N-Oxide (**1i**).* Yellow solid (209 mg, 13% for 7.3 mmol scale besides **6i** using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); mp 154 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.10 (d, J = 2.2 Hz, 1H), 9.01 (dt, J = 7.9, 1.0 Hz, 1H), 8.75 (dt, J = 4.8, 1.3 Hz, 1H), 8.48 (d, J = 9.0 Hz, 1H), 8.04 (dd, J = 9.0, 2.1 Hz, 1H), 7.86 (td, J = 7.8, 1.8 Hz, 1H), 7.41 (ddd, J = 7.5, 4.7, 1.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 151.9, 149.9, 147.8, 145.6, 137.3, 136.7, 128.0, 125.8, 125.6, 119.2; IR (*ν*/cm^{-1}): 1510, 1352, 1268, 820, 784, 736; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{10}H_8N_3O_3$ 218.0560; found 218.0576, $[M + Na]^+$ calcd for $C_{10}H_7N_3O_3Na$ 240.0380; found 240.0404, $[M + K]^+$ calcd for $C_{10}H_7N_3O_3K$ 256.0119; found 256.0128.

*5′-Nitro-2,2′:6,2″-terpyridine N-Oxide (**6i**).* Yellow oil (28.6 mg, 3%); ^1H NMR (500 MHz, $CDCl_3$): δ 8.87 (dt, J = 8.0, 1.0 Hz, 1H), 8.77 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H), 8.71 (d, J = 5.0 Hz, 1H), 8.44 (d, J = 8.9 Hz, 1H), 7.98−7.87 (m, 3H), 7.81 (td, J = 7.8, 1.8 Hz, 1H), 7.43−7.39 (m, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 150.2, 149.8, 148.4, 148.3, 136.5, 128.04, 128.00, 127.1, 126.2, 125.9, 125.7, 125.4, 124.7, 120.1; IR (*ν*/cm^{-1}): 1540, 1352, 796, 756; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{15}H_{11}N_4O_3$ 295.0826; found 295.0823, $[M + Na]^+$ calcd for $C_{15}H_{10}N_4O_3Na$ 317.0645; found 317.0642.

*4-Methoxy-2,2′-bipyridine N-Oxide (**1j**).* (1.46 g, 15% for 50 mmol scale using $Pd(OAc)_2/P^tBu_3$, MeOH/DCM mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 8.97 (dq, J = 8.1, 1.2 Hz, 1H), 8.68 (ddd, J = 4.8, 1.9, 1.0 Hz, 1H), 8.19 (dd, J = 7.3, 1.0 Hz, 1H), 7.80 (ddt, J = 8.1, 7.5, 1.5 Hz, 1H), 7.69 (dd, J = 3.6, 1.2 Hz, 1H), 7.33 (ddt, J = 7.3, 4.8, 1.2 Hz, 1H), 6.82 (ddd, J = 7.2, 3.6, 1.1 Hz, 1H), 3.90 (s, 3H). The chemical shifts are in agreement with previous reports.[31] Alternatively, **1j** can be prepared by a two-step sequence from **1a**. First nitration with KNO_3/H_2SO_4 to give 4-nitro-2,2′-bipyridine *N*-oxide (**1o**), followed by methoxylation with NaOMe in MeOH.[31]

*4-Chloro-2,2′-bipyridine N-Oxide (**1k**).* (1.27 g, 41% for 15 mmol scale besides **6k** using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 8.96 (dt, J = 8.1, 1.1 Hz, 1H), 8.72 (ddd, J = 4.8, 1.9, 0.9 Hz, 1H), 8.26 (d, J = 3.1 Hz, 1H), 8.22 (d, J = 7.0 Hz, 1H), 7.84 (td, J = 7.8, 1.8 Hz, 1H), 7.37 (ddd, J = 7.6, 4.8, 1.2 Hz, 1H), 7.23 (dd, J = 7.0, 3.1 Hz, 1H). The chemical shifts are in agreement with previous reports.[28d]

*4′-Chloro-2,2′:6,2″-terpyridine N-Oxide (**6k**).* (246 mg, 12%); ^1H NMR (400 MHz, $CDCl_3$): δ 8.77−8.74 (m, 4H), 8.13 (s, 2H), 7.84 (td, J = 7.9, 1.6 Hz, 2H), 7.39 (ddd, J = 7.6, 4.6, 1.3 Hz, 2H). The chemical shifts are in agreement with previous reports.[28d]

*4-Ethoxycarbonyl-2,2′-bipyridine N-Oxide (**1l**).* (326 mg, 67% for 2.0 mmol scale besides **6l** using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 8.82 (dd, J = 8.1, 1.0 Hz, 1H), 8.82−8.73 (m, 2H), 8.35 (d, J = 6.8 Hz, 1H), 7.92−7.79 (m, 2H), 7.38 (ddt, J = 7.0, 4.8, 1.1 Hz, 1H), 4.42 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). The chemical shifts are in agreement with previous reports.[28d]

*4′-Ethoxycarbonyl-2,2′:6,2″-terpyridine N-Oxide (**6l**).* (47.0 mg, 15%); ^1H NMR (400 MHz, $CDCl_3$): δ 8.76 (d, J = 4.8 Hz, 2H), 8.62 (s, 2H), 8.58 (d, J = 8.1 Hz, 2H), 7.80 (td, J = 7.7, 1.5 Hz, 2H), 7.35 (dd, J = 7.5, 4.8, 2H), 4.40 (q, J = 7.1 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H). The chemical shifts are in agreement with previous reports.[28d]

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*4-Trifluoromethyl-2,2′-bipyridine N-Oxide (**1m**).* (420 mg, 87% for 2.0 mmol scale besides **6m** using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 8.90 (dt, J = 8.1, 1.0 Hz, 1H), 8.73 (ddd, J = 4.7, 1.7, 0.8 Hz, 1H), 8.52 (d, J = 2.7 Hz, 1H), 8.35 (d, J = 6.9 Hz, 1H), 7.83 (td, J = 7.8, 1.8 Hz, 1H), 7.44 (dd, J = 6.8, 2.8 Hz, 1H), 7.37 (ddd, J = 7.6, 4.7, 1.1 Hz, 1H). The chemical shifts are in agreement with previous reports.[28d]

*4′-Trifluoromethyl-2,2′:6,2″-terpyridine N-Oxide (**6m**).* (32.0 mg, 10%); ^1H NMR (400 MHz, $CDCl_3$): δ 8.77 (dd, J = 4.8, 0.9 Hz, 2H), 8.72 (d, J = 8.0 Hz, 2H), 8.38 (s, 2H), 7.85 (td, J = 7.8, 1.8 Hz, 2H), 7.40 (ddd, J = 7.6, 4.8, 1.2 Hz, 2H). The chemical shifts are in agreement with previous reports.[28d]

*4-Cyano-2,2′-bipyridine N-Oxide (**1n**).* (2.62 g, 27% for 50 mmol scale besides **6n** using $Pd(OAc)_2/P^tBu_3$, acetone/hexane mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 8.88 (dt, J = 8.1, 1.1 Hz, 1H), 8.76 (ddd, J = 4.8, 1.8, 0.9 Hz, 1H), 8.61 (dd, J = 2.6, 0.6 Hz, 1H), 8.32 (dd, J = 6.8, 0.6 Hz, 1H), 7.87 (ddd, J = 8.2, 7.6, 1.8 Hz, 1H), 7.47 (dd, J = 6.9, 2.6 Hz, 1H), 7.42 (ddd, J = 7.6, 4.8, 1.1 Hz, 1H). The chemical shifts are in agreement with previous reports.[28d]

*4′-Cyano-2,2′:6,2″-terpyridine N-Oxide (**6n**).* (310 mg, 5%); ^1H NMR (400 MHz, $CDCl_3$): δ 8.78 (ddd, J = 4.8, 1.8, 1.0 Hz, 2H), 8.70 (dt, J = 8.1, 1.1 Hz, 2H), 8.42 (s, 2H), 7.86 (td, J = 7.8, 1.8 Hz, 2H), 7.42 (ddd, J = 7.6, 4.8, 1.2 Hz, 2H). The chemical shifts are in agreement with previous reports.[28d]

*6′-Methoxy-2,2′-bipyridine N-Oxide (**1p**).* Colorless solid (3.05 g, 64% for 23 mmol scale besides **6p** using $Pd(OAc)_2/P^tBu_3$, MeOH/DCM mixtures; mp 90−91 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.76 (dd, J = 7.6, 0.8 Hz, 1H), 8.35 (dd, J = 8.1, 2.2 Hz, 1H), 8.31 (dt, J = 6.5, 1.1 Hz, 1H), 7.72 (ddd, J = 8.3, 7.5, 0.8 Hz, 1H), 7.35 (ddt, J = 8.0, 7.3, 1.4 Hz, 1H), 7.23 (dddd, J = 7.5, 6.5, 2.3, 1.1 Hz, 1H), 6.83 (dt, J = 8.3, 0.8 Hz, 1H), 3.99 (d, J = 0.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.3, 147.2 146.1, 141.2, 139.4, 127.7, 125.6, 124.8, 118.9, 112.5, 53.5: IR (ν/cm^{-1}): 1583, 1576, 1466, 1424, 1396, 1335, 1263, 1229, 1208, 1154, 1017, 828, 805, 770, 740; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{11}N_2O_2$ 203.0815; found 203.0803, $[M + Na]^+$ $C_{11}H_{10}N_2O_2Na$ 225.0634; found 225.0647.

*6,6″-Dimethoxy-2,2′:6′,2″-terpyridine N-Oxide (**6p**).* Colorless solid (482 mg, 13%); mp 141 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.53 (dt, J = 7.6, 0.8 Hz, 2H), 8.19 (dd, J = 8.0, 0.7 Hz, 2H), 7.71 (ddd, J = 8.3, 7.5, 0.7 Hz, 2H), 7.44 (td, J = 8.0, 0.7 Hz, 1H), 6.83 (dt, J = 8.3, 0.8 Hz, 2H), 4.01 (d, J = 0.7 Hz, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.5, 148.3, 147.2, 139.1, 127.2, 125.0, 119.0, 111.9, 53.5; IR (ν/cm^{-1}): 1577, 1459, 1422, 1407, 1256, 1237, 1020, 778, 729 (s); HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{16}N_3O_3$ 310.1186; found 310.1169, $[M + Na]^+$ calcd for $C_{17}H_{15}N_3O_3Na$ 332.1006; found 332.1037, $[M + K]^+$ $C_{17}H_{15}N_3O_3K$ 348.0745; found 348.0723.

*6′-Methyl-2,2′-bipyridine N-Oxide (**1q**).* Reddish oil (1.90 g, 41% for 25 mmol scale besides **6q** using $Pd(OAc)_2/P^tBu_3$, MeOH/DCM mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 8.65 (dt, J = 7.9, 0.8 Hz, 1H), 8.30 (ddd, J = 6.5, 1.2, 0.6 Hz, 1H), 8.17 (dd, J = 8.0, 2.2 Hz, 1H), 7.71 (t, J = 7.8 Hz, 1H), 7.35 (ddd, J = 8.1, 7.5, 1.3 Hz, 1H), 7.27−7.22 (m, 1H), 7.20 (ddd, J = 7.8, 1.1, 0.6 Hz, 1H), 2.61 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 158.3, 149.0, 147.8, 140.8, 136.6, 128.1, 125.8, 125.1, 124.0, 122.6, 24.7; IR (ν/cm^{-1}): 1584, 1572, 1453, 1424, 1247, 1221, 880, 825, 800, 764; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{11}N_2O$ 187.0866; found 187.0885.

*6,6″-Dimethyl-2,2′:6′,2″-terpyridine N-Oxide (**6q**).* Tan solid (176 mg, 5%); mp 151−155 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (ddd, J = 7.9, 1.1, 0.6 Hz, 1H), 8.03 (d, J = 7.9 Hz, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.44 (t, J = 7.9 Hz, 1H), 7.21 (ddd, J = 7.6, 1.1, 0.5 Hz, 1H), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 158.3, 150.0, 148.6, 136.4, 127.7, 125.6, 123.8, 122.9, 24.7; IR (ν/cm^{-1}): 1584, 1573, 1446, 1369, 1242, 1218, 810, 772, 733; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{16}N_3O$ 278.1288; found 278.1303.

*6′-Trifluoromethyl-2,2′-bipyridine N-Oxide (**1r**).* Pale yellow solid (838 mg, 65% for 5.4 mmol scale besides **6r** using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); ^1H NMR (400 MHz, $CDCl_3$): δ 9.18 (dt, J = 8.2, 0.8 Hz, 1H), 8.30 (ddd, J = 6.4, 1.3, 0.6 Hz, 2H), 8.27 (dd, J = 8.1, 2.2 Hz, 1H), 7.99 (ddt, J = 8.4, 7.8, 0.7 Hz, 1H), 7.71 (dt, J = 7.7, 0.7 Hz, 1H), 7.43−7.34 (m, 1H), 7.30 (tdd, J = 7.1, 2.2, 0.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 150.1, 148.0 (q, J = 35.2 Hz), 146.1, 140.9, 138.0, 128.3, 128.1, 126.1, 126.0, 121.5 (q, J = 274.3 Hz), 120.8 (q, J = 2.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ −68.0; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{11}H_7F_3N_2ONa$ 263.0403; found 263.0426.

*6,6″-Bis(trifluoromethyl)-2,2′:6′,2″-terpyridine N-Oxide (**6r**).* Pale yellow solid (111 mg, 11%); mp 188−190 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.97 (d, J = 8.1 Hz, 2H), 8.23 (d, J = 8.0 Hz, 2H), 8.01 (t, J = 7.9 Hz, 2H), 7.75 (d, J = 7.7 Hz, 2H), 7.54 (t, J = 8.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 150.7, 148.1 (q, J = 35.1 Hz), 147.1, 137.7, 128.9, 128.3, 126.0, 121.5 (q, J = 274.4 Hz), 120.8 (q, J = 2.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ −67.9; IR (ν/cm^{-1}): 1338, 1239, 1212, 1173, 1111, 1059, 790, 743, 668 (m); HRMS (ESI-TOF) m/z: $[M + H]^+$ $C_{17}H_{10}F_6N_3O$ 386.0723; found 386.0719, $[M + Na]^+$ calcd for $C_{17}H_9F_6N_3ONa$ 408.0542; found 408.0547, $[M + K]^+$ calcd for $C_{17}H_9F_6N_3OK$ 424.0281; found 424.0274.

*5′-Methyl-2,2′-bipyridine N-Oxide (**1s**).* Brown solid (438 mg, 13% for 17 mmol scale using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, MeOH/DCM mixtures); mp 44−45 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.78 (d, J = 8.2 Hz, 1H), 8.52 (d, J = 2.1 Hz, 1H), 8.27 (dd, J = 6.5, 0.8 Hz, 1H), 8.14 (dd, J = 8.1, 2.1 Hz, 1H), 7.61 (ddd, J = 8.2, 2.3, 0.7 Hz, 1H), 7.32 (td, J = 7.8, 1.2 Hz, 1H), 7.22 (ddd, J = 7.4, 6.6, 2.2 Hz, 1H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 150.0, 147.5, 147.0, 140.8, 136.8, 134.4, 127.7, 125.8, 125.0, 18.5; IR (ν/cm^{-1}): 1466, 1424, 1246, 1226, 1026, 846, 767, 716; HRMS (ESI-TOF) m/z: $[M + H]^+$ cald for $C_{11}H_{11}N_2O$ 187.0866; found 187.0873, $[M + Na]^+$ cald for $C_{11}H_{10}N_2ONa$ 209.0691; found 209.0685.

*4′-Methoxy-2,2′-bipyridine N-Oxide (**1t**).* Brown solid (573 mg, 44% for 5.0 mmol scale besides **6t** using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); mp 64 °C, ^1H NMR (500 MHz, $CDCl_3$): δ 8.55 (d, J = 2.6 Hz, 1H), 8.47 (d, J = 5.7 Hz, 1H), 8.26 (ddd, J = 6.5, 1.3, 0.6 Hz, 1H), 8.17 (dd, J = 8.0, 2.2 Hz, 1H), 7.32 (ddd, J = 8.1, 7.5, 1.3 Hz, 1H), 7.23 (ddd, J = 7.5, 6.5, 2.2 Hz, 1H), 6.83 (dd, J = 5.7, 2.6 Hz, 1H), 3.87 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 165.9, 151.1, 150.3, 147.3, 140.8, 128.1, 125.8, 125.3, 111.22, 111.16, 55.4; IR (ν/cm^{-1}): 1585, 1565, 1467, 1442, 1405, 1311, 1273, 1241, 1025, 866, 827, 766, 731; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{11}N_2O_2$ 203.0815; found 203.0841, $[M + Na]^+$ $C_{11}H_{10}N_2O_2Na$ 225.0634; found 225.0666.

*4,4″-Dimethoxy-2,2′:6′,2″-terpyridine N-Oxide (**6t**).* Brown solid (52.8 mg, 7%); mp 167 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.51 (d, J = 5.7 Hz, 2H), 8.27 (d, J = 2.5 Hz, 2H), 8.04 (d, J = 7.9 Hz, 2H), 7.42 (t, J = 7.9 Hz, 1H), 6.86 (dd, J = 5.7, 2.5 Hz, 2H), 3.87 (s, 6H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 165.8, 152.1, 150.4, 148.3, 127.9, 125.5, 111.3, 55.5; IR (ν/cm^{-1}): 2923, 1584, 1561, 1461, 1373, 1292, 1239, 1030, 852, 811; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{16}N_3O_3$ 310.1186; found 310.1185, $[M + Na]^+$ calcd for $C_{17}H_{15}N_3O_3Na$ 332.1006; found 332.1005, $[M + K]^+$ $C_{17}H_{15}N_3O_3K$ 348.0745; found 348.0741.

*4′-Methyl-2,2′-bipyridine N-Oxide (**1u**).* Brown solid (1.46 g, 31% for 25 mmol scale besides **6u** using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); mp 72 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.66 (s, 1H), 8.53 (dd, J = 4.9, 1.2 Hz, 1H), 8.27 (dt, J = 6.4, 1.4 Hz, 1H), 8.09 (dt, J = 8.1, 1.7 Hz, 1H), 7.31 (tt, J = 7.8, 1.3 Hz, 1H), 7.22 (ddt, J = 6.6, 4.4, 1.3 Hz, 1H), 7.12 (d, J = 4.0 Hz, 1H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 149.5, 149.2, 147.5, 140.7, 128.0, 126.3, 125.8, 125.3, 125.2, 21.3; IR (ν/cm^{-1}): 1613, 1597, 1429, 1249, 1184, 876, 835, 754, 722; HRMS (ESI-TOF) m/z: $[M + H]^+$ cald for $C_{11}H_{11}N_2O$ 187.0866; found 187.0881, $[M + Na]^+$ calcd for $C_{11}H_{10}N_2ONa$ 209.0691; found 209.0703, $[M + K]^+$ cald for $C_{11}H_{10}N_2OK$ 225.0425; found 225.0437.

*4,4″-Dimethyl-2,2′:6′,2″-terpyridine N-Oxide (**6u**).* Off-white solid (135 mg, 4%); mp 135 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.57 (dd, J = 5.0, 0.8 Hz, 2H), 8.48 (dt, J = 1.7, 0.8 Hz, 2H), 7.99 (d, J = 7.9 Hz, 2H), 7.42 (t, J = 7.9 Hz, 1H), 7.14 (ddt, J = 4.4, 1.7, 0.8 Hz, 2H), 2.39 (t, J = 0.7 Hz, 6H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 150.4, 149.3, 148.4, 147.3, 127.7, 126.5, 125.6, 125.1, 21.3; IR (ν/cm^{-1}): 1592, 1366, 1248, 863, 829, 796, 761; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{16}N_3O$ 278.1288; found 278.1273, $[M + Na]^+$ calcd

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for $C_{17}H_{15}N_3ONa$ 300.1107; found 300.1087, $[M + K]^+$ calcd for $C_{17}H_{15}N_3OK$ 316.0847; found 316.0823.

*4′-Fluoro-2,2′-bipyridine N-Oxide (**1v**).* Brown solid (276 mg, 8% for 19 mmol scale using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$ and 4-fluoro-2-chloropyridine, acetone/hexane mixtures); mp 94 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.82 (dd, J = 11.0, 2.5 Hz, 1H), 8.64 (dd, J = 8.6, 5.5 Hz, 1H), 8.29 (dd, J = 6.5, 1.3 Hz, 1H), 8.25 (dd, J = 8.0, 2.2 Hz, 1H), 7.34 (td, J = 7.8, 1.3 Hz, 1H), 7.27 (ddd, J = 7.5, 6.5, 2.2 Hz, 1H), 7.07 (ddd, J = 7.9, 5.5, 2.5 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 169.7, 167.7, 152.3 (d, J = 9.1 Hz), 151.3 (d, J = 7.4 Hz), 146.2, 140.9, 128.0, 125.8 (d, J = 2.2 Hz), 113.8 (d, J = 21 Hz), 112.2 (d, J = 17 Hz); ^{19}F NMR (471 MHz, $CDCl_3$): δ − 101.2 (q, J = 8.3 Hz); IR (ν/cm^{-1}): 1594, 1575, 1468, 1431, 1389, 1255, 1176, 894, 841, 768, 729, 719; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_8FN_2O$ 191.0615; found 191.0623, $[M + Na]^+$ calcd for $C_{10}H_7FN_2ONa$ 213.0435; found 213.0447, $[M + K]^+$ calcd for $C_{10}H_7FN_2OK$ 229.0174; found 229.0161.

*4′-Ethoxycarbonyl-2,2′-bipyridine N-Oxide (**1w**).* Brown solid (573 mg, 44% for 5.3 mmol scale besides **6w** using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); mp 68 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.37 (dd, J = 1.6, 0.9 Hz, 1H), 8.82 (dd, J = 4.9, 0.9 Hz, 1H), 8.30 (ddd, J = 6.5, 1.3, 0.6 Hz, 1H), 8.13 (dd, J = 8.0, 2.2 Hz, 1H), 7.88 (dd, J = 4.9, 1.6 Hz, 1H), 7.34 (td, J = 7.7, 1.3 Hz, 1H), 7.27 (ddd, J = 7.4, 6.4, 2.3 Hz, 1H), 4.40 (q, J = 7.2 Hz, 3H), 1.38 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 165.0, 150.9, 150.0, 146.8, 140.8, 138.3, 128.0, 125.7, 124.8, 123.6, 62.0, 14.3; IR (ν/cm^{-1}): 1716, 1426, 1385, 1280, 1219, 1202, 1123, 1024, 897, 887, 781, 765, 715, 682; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{13}N_2O_3$ 245.0921; found 245.0916, $[M + Na]^+$ calcd for $C_{13}H_{12}N_2O_3Na$ 267.0740; found 267.0744.

*4,4″-Bis(ethoxycarbonyl)-2,2′:6′,2″-terpyridine N-Oxide (**6w**).* Brown solid (114 mg, 11%); mp 108 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.18 (dd, J = 1.6, 0.9 Hz, 2H), 8.88 (dd, J = 5.0, 0.9 Hz, 2H), 8.07 (d, J = 7.9 Hz, 2H), 7.92 (dd, J = 5.0, 1.6 Hz, 2H), 7.48 (t, J = 7.9 Hz, 1H), 4.41 (q, J = 7.1 Hz, 4H), 1.38 (t, J = 7.1 Hz, 6H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 165.1, 151.6, 150.2, 147.8, 138.2, 128.3, 125.5, 125.0, 123.6, 62.0, 14.4; IR (ν/cm^{-1}): 1718, 1662, 1590, 1380, 1364, 1260, 1243, 1018, 760; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{20}N_3O_5$ 394.1397; found 394.1424, $[M + Na]^+$ calcd for $C_{21}H_{19}N_3O_5Na$ 416.1217; found 416.1246, $[M + K]^+$ calcd for $C_{21}H_{19}N_3O_5K$ 432.0956; found 432.0979.

*4′-Trifluoromethyl-2,2′-bipyridine N-Oxide (**1x**).* Brown oil (204 mg, 15% for 5.7 mmol scale using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$ and 4-trifluoromethyl-2-chloropyridine, acetone/hexane mixtures); ^1H NMR (500 MHz, $CDCl_3$): δ 9.28 (dt, J = 1.7, 0.8 Hz, 1H), 8.88 (d, J = 5.0 Hz, 1H), 8.34 (dd, J = 6.5, 1.2 Hz, 1H), 8.24 (dd, J = 8.0, 2.2 Hz, 1H), 7.55 (ddd, J = 5.0, 1.7, 0.8 Hz, 1H), 7.39 (ddd, J = 8.0, 7.6, 1.3 Hz, 1H), 7.32 (ddd, J = 7.5, 6.5, 2.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 151.0, 150.2, 146.1, 140.9, 138.8 (q, J = 35 Hz), 136.4, 128.1, 126.09, 126.06, 122.9 (q, J = 273 Hz), 121.5 (q, J = 4.1 Hz), 120.0 (q, J = 3.5 Hz); ^{19}F NMR (471 MHz, $CDCl_3$): δ −64.6; IR (ν/cm^{-1}): 1433, 1394, 1333, 1283, 1227, 1169, 1129, 1085, 851, 766, 666; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_8N_2O$ 241.0583; found 241.0592, $[M + Na]^+$ calcd for $C_{11}H_7N_2ONa$ 263.0403; found 263.0410.

*2-(Pyridin-2-yl)pyrazine N-Oxide (**1y**).* (794 mg, 21% for 22 mmol scale using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, acetone/hexane mixtures); ^1H NMR (400 MHz, DMSO-d_6): δ 9.15 (s, 1H), 8.76 (d, J = 4.1 Hz, 1H), 8.57 (d, J = 8.0 Hz, 1H), 8.52 (d, J = 4.2 Hz, 1H), 8.44 (d, J = 4.1 Hz, 1H), 7.96 (td, J = 7.9, 1.8 Hz, 1H), 7.52 (ddd, J = 7.5, 4.8, 0.9 Hz, 1H). The chemical shifts are in agreement with previous reports.[43]

*2-(Pyridin-2-yl)quinoline N-Oxide (**1z**).* Yellow solid (896 mg, 19% for 21 mmol scale using $[Pd(^tBu_2PCMe_2CH_2)OAc]_2$, MeOH/DCM mixtures); mp 92−93 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 9.12 (d, J = 8.1 Hz, 1H), 8.82 (d, J = 8.8 Hz, 1H), 8.73 (d, J = 4.1 Hz, 1H), 8.23 (d, J = 8.9 Hz, 1H), 7.86−7.77 (m, 2H), 7.77−7.69 (m, 2H), 7.61−7.56 (m, 1H), 7.31 (ddd, J = 7.4, 4.8, 0.9 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 150.3, 149.4, 143.3, 142.4, 136.3, 130.4, 130.0, 128.8, 128.0, 126.0, 125.1, 124.2, 123.2, 120.2; IR (ν/cm^{-1}): 1584, 1563, 1466, 1427, 1348, 1254, 1209, 1065, 992, 922, 892, 822, 773, 736; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{11}N_2O$ 223.0871; found 223.0898, $[M + Na]^+$ calcd for $C_{14}H_{10}N_2ONa$ 245.0691; found 245.0724.

General Procedure for Palladium-Catalyzed Directed Halogenations. A reaction vial was charged with bipyridine *N*-oxide **1** (1.0 equiv), $Pd(OAc)_2$ (5 mol %), NXS (1.2 equiv), and chlorobenzene (0.10 M). After stirring at 110 °C for 24 h, the reaction mixture was cooled to room temperature, diluted with DCM, and extracted with an aqueous NaOH solution (1.0 M). The aqueous layer was extracted with DCM, the combined organic layers were dried with Na_2SO_4 and filtered, and the solvent was removed from the filtrate. In cases of incomplete conversion of the starting material additional purification by column chromatography (MeOH in DCM: 0−10%, 1% increments) was performed. All structures were confirmed by COSEY, HMBC, and HMQC.

*3-Bromo-2,2′-bipyridine N-Oxide (**2a**).* Colorless solid (1.95 g, 87% for 8.9 mmol scale, after extraction); mp 142 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.78 (d, J = 4.7 Hz, 1H, ArH-3′), 8.27 (d, J = 6.5 Hz, 1H, ArH-4), 7.86 (td, J = 7.7, 1.7 Hz, 1H, ArH-5′), 7.56 (d, J = 8.3 Hz, 1H, ArH-6), 7.50 (d, J = 7.8 Hz, 1H, ArH-6′), 7.39 (ddd, J = 7.6, 4.9, 0.9 Hz, 1H, ArH-4′), 7.17 (dd, J = 8.2, 6.6 Hz, 1H, ArH-5); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 151.3 (C-2′), 150.3 (C-3′), 148.7 (C-2), 139.2 (C-4), 136.9 (C-5′), 129.9 (C-6), 125.43 (C-5), 125.35 (C-6′), 124.4 (C-4′), 122.1 (C-3′); IR (ν/cm^{-1}): 1597, 1565, 1454, 1426, 1412, 1282, 1253, 1029, 991, 900, 791, 779, 745, 731; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_8BrN_2O$ 250.9815; found 250.9830, $[M + Na]^+$ calcd for $C_{10}H_7BrN_2ONa$ 272.9634; found 272.9650; Elemental analysis (%): Anal. calcd for $C_{10}H_7BrN_2O$: C, 47.8; H, 2.81; N, 11.2. Found: C, 47.9; H, 2.85; N, 11.2. Single crystals for X-ray diffraction were grown by slow diffusion of pentane into a concentrated solution of **2a** in DCM. CCDC-1476436 contains the crystallographic data for **2a**.

*3-Bromo-6-mtehyl-2,2′-bipyridine N-Oxide (**2b**).* Brown oil (73.5 mg, 50% for 0.56 mmol scale, 2.57 g, 60% for 16.2 mmol scale, after column chromatography with MeOH/DCM mixtures); ^1H NMR (500 MHz, $CDCl_3$): δ 8.79 (ddd, J = 4.9, 1.7, 1.0 Hz, 1H, ArH-3′), 7.86 (td, J = 7.7, 1.7 Hz, 1H, ArH-5′), 7.49−7.46 (m, 2H, ArH-4, ArH-6′), 7.38 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H, ArH-4′), 7.20 (dd, J = 8.4, 0.8 Hz, 1H, ArH-5), 2.48 (d, J = 0.6 Hz, 3H, $-CH_3$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 152.0 (C-2′), 150.2 (C-3′), 149.0 (C-2), 148.4 (C-6), 137.0 (C-5′), 129.0 (C-4), 125.9 (C-5), 125.2 (C-6′), 124.1 (C-4′), 118.7 (C-3), 18.0 ($-CH_3$); IR (ν/cm^{-1}): 1601, 1585, 1567, 1458, 1443, 1426, 1344, 1256, 1146, 1001, 903, 871, 781, 745; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2O$ 264.9971; found 264.9966, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2ONa$ 286.9790; found 286.9794, $[M + K]^+$ calcd for $C_{11}H_9BrN_2OK$ 302.9530; found 302.9534.

*3-Bromo-6-ethoxycarbonyl-2,2′-bipyridine N-Oxide (**2c**).* Brown oil (271 mg, 82% for 1.02 mmol scale, after extraction); ^1H NMR (500 MHz, $CDCl_3$): δ 8.78 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H, ArH-3′), 7.86 (td, J = 7.7, 1.7 Hz, 1H, ArH-5′), 7.58 (d, J = 8.5 Hz, 1H, ArH-4), 7.51 (dt, J = 7.8, 1.1 Hz, 1H, ArH-6′), 7.48 (d, J = 8.6 Hz, 1H, ArH-5), 7.39 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H ArH-4′), 4.42 (q, J = 7.1 Hz, 2H, $-CH_2-$), 1.37 (t, J = 7.1 Hz, 3H, $-CH_3$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 161.3 (C═O), 150.7 (C-2′), 150.2 (C-3′), 149.7 (C-2), 141.6 (C-6), 137.0 (C-5′), 128.8 (C-4), 125.8 (C-5), 125.6 (C-6′), 124.5 (C-4′), 123.8 (C-3), 62.9 ($-CH_2-$), 14.2 ($-CH_3$); IR (ν/cm^{-1}): 1736, 1581, 1369, 1351, 1316, 1247, 1150, 1082, 1011, 992, 917, 780; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{12}BrN_2O_3$ 323.0028; found 323.0042, $[M + Na]^+$ calcd for $C_{13}H_{11}BrN_2O_3Na$ 344.9845; found 344.9851.

*3-Bromo-6-trifluoromethyl-2,2′-bipyridine N-Oxide (**2d**).* Colorless solid (111 mg, quant. for 0.33 mmol scale, after extraction); mp 148 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.80 (d, J = 4.8 Hz, 1H, ArH-3′), 7.88 (td, J = 7.7, 1.7 Hz, 1H, ArH-5′), 7.64 (d, J = 8.7 Hz, 1H, ArH-4), 7.59 (d, J = 8.7 Hz, 1H, ArH-5), 7.52 (dt, J = 7.8, 1.2 Hz, 1H, ArH-6′), 7.42 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H, ArH-4′); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 150.7 (C-2), 150.4 (C-3′), 150.1 (C-2′), 137.0 (C-5′), 128.5 (C-4), 125.7 (C-6), 125.6 (C-6′), 124.7 (C-4′), 124.3 (q, J = 3.8 Hz, C-5), 123.1 (C-3), 119.8 (q, J = 273 Hz, $-CF_3$); ^{19}F NMR

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(376 MHz, $CDCl_3$): δ −68.8; IR (ν/cm^{-1}): 1362, 1339, 1270, 1253, 1148, 1120, 1066, 915, 838, 783; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_8BrF_3N_2O$ 318.9688; found 318.9713, $[M + Na]^+$ calcd for $C_{11}H_7BrF_3N_2ONa$ 340.9508; found 340.9517, $[M + K]^+$ calcd for $C_{11}H_7BrF_3N_2OK$ 358.9247; found 356.9234.

*3-Bromo-6-cyano-2,2′-bipyridine N-Oxide (**2e**).* Colorless solid (48.4 mg, 17% for 1.04 mmol scale besides 14% of **1e**, after column chromatography); mp 178−181 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.78 (ddd, J = 4.9, 1.5, 1.0 Hz, 1H, ArH-3′), 7.88 (td, J = 7.8, 1.8 Hz, 1H, ArH-5′), 7.62 (d, J = 8.7 Hz, 1H, ArH-4), 7.55 (d, J = 8.7 Hz, 1H, ArH-5), 7.49 (dt, J = 7.8, 0.9 Hz, 1H, ArH-6′), 7.43 (ddd, J = 7.7, 4.8, 1.0 Hz, 1H, ArH-4′); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 150.5 (C-3′), 149.9 (C-2), 149.6 (C-2′), 137.1 (C-5′), 130.0 (C-5), 129.0 (C-4), 126.6 (C-6), 125.7 (C-3), 125.4 (C-6′), 125.0 (C-4′), 111.5 (−CN); IR (ν/cm^{-1}): 1579, 1446, 1428, 1347, 1257, 1210, 996, 918, 828, 780, 746, 697; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_8BrN_3O$ 275.9767; found 275.9766, $[M + Na]^+$ calcd for $C_{11}H_7BrN_3ONa$ 297.9586; found 297.9586.

*3-Bromo-5-methoxy-2,2′-bipyridine N-Oxide (**2f**).* Brown solid (281 mg, 99% for 1.01 mmol scale, after extraction); mp 122 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.77 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H, ArH-3′), 8.04 (d, J = 2.3 Hz, 1H, ArH-4), 7.83 (td, J = 7.7, 1.7 Hz, 1H, ArH-5′), 7.48 (dt, J = 7.8, 1.1 Hz, 1H, ArH-6′), 7.36 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H, ArH-4′), 7.20 (d, J = 2.2 Hz, 1H, ArH-6), 3.86 (s, 3H, -OCH_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.9 (C-2), 151.2 (C-2′), 150.1 (C-3′), 142.2 (C-5), 136.8 (C-5′), 127.6 (C-4), 125.9 (C-6′), 124.1 (C-4′), 121.5 (C-3), 117.5 (C-6), 56.6 (−OCH_3); IR (ν/cm^{-1}): 1594, 1539, 1451, 1422, 1384, 1313, 1233, 1214, 1159, 1139, 1020, 891, 853, 821, 790; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2O_2$ 280.9920; found 280.9913, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2O_2Na$ 302.9740; found 302.9727. Single crystals for X-ray diffraction were grown by slow diffusion of pentane into a concentrated solution of **2f** in DCM. CCDC-1476430 contains the crystallographic data for **2f**.

*3-Bromo-5-methyl-2,2′-bipyridine N-Oxide (**2g**).* Tan solid (107 mg, 40% for 1.01 mmol scale besides 3-bromo-5-methyl-2,2′-bipyridine **5g**, after column chromatography): mp 109−112 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73 (d, J = 4.9 Hz, 1H, ArH-3′), 8.09 (s, 1H, ArH-4), 7.79 (td, J = 7.7, 1.7 Hz, 1H, ArH-5′), 7.44 (d, J = 7.8 Hz, 1H, ArH-6′), 7.37 (s, 1H, ArH-6), 7.32 (ddd, J = 7.6, 4.9, 1.1 Hz, 1H, ArH-4′), 2.27 (s, 3H, −CH_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 151.2 (C-2′), 150.0 (C-3′), 145.8 (C-2), 138.9 (C-4), 136.6 (C-5′), 136.2 (C-5), 130.9 (C-6), 125.4 (C-6′), 124.0 (C-4′), 121.1 (C-3), 18.0 (−CH_3); IR (ν/cm^{-1}): 1598, 1537, 1428, 1371, 1280, 1212, 1146, 1020, 986, 854, 789; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2O$ 264.9971; found 264.9991, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2ONa$ 286.9790; found 286.9813, $[M + K]^+$ calcd for $C_{11}H_9BrN_2OK$ 302.9530; found 302.9560.

*3-Bromo-5-methyl-2,2′-bipyridine (**5g**).* Red oil (88.9 mg, 35%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.69 (s, 1H, ArH-3′), 8.43 (s, 1H, ArH-4), 7.79 (dd, J = 1.8, 0.7 Hz, 1H, ArH-6), 7.75 (td, J = 7.7, 1.8 Hz, 1H, ArH-5′), 7.67 (d, J = 7.8 Hz, 1H, ArH-6′), 7.27 (ddd, J = 7.4, 4.8, 1.1 Hz, 1H, ArH-4′), 2.32 (s, 3H, −CH_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 157.1 (C-2′), 153.7 (C-2), 149.1 (C-3′), 148.5 (C-4), 141.8 (C-6), 136.2 (C-5′), 134.5 (C-5), 124.3 (C-6), 123.2 (C-4′), 119.0 (C-3), 17.7 (−CH_3); IR (ν/cm^{-1}): 1584, 1568, 1445, 1424, 1377, 1099, 1086, 1030, 991, 872, 797, 744; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2$ 249.0022; found 249.0040, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2Na$ 270.9841; found 270.9863.

*3-Bromo-5-methoxycarbonyl-2,2′-bipyridine N-Oxide (**2h**).* As reddish oil (9.3 mg, 3% for 1.01 mmol scale, after column chromatography); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.85−8.81 (m, 2H, ArH-4, ArH-3′), 8.13 (d, J = 1.1 Hz, 1H, ArH-6), 7.89 (td, J = 7.8, 1.5 Hz, 1H, ArH-5′), 7.53 (d, J = 7.6 Hz, 1H, ArH-6′), 7.45−7.40 (m, 1H, ArH-4′), 3.99 (s, 3H, −CH_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 162.6 (C═O), 151.6 (C-2), 150.7 (C-3′), 150.4 (C-2′), 140.2 (C-4), 137.0 (C-5′), 130.2 (C-6), 128.9 (C-5), 125.4 (C-6′), 124.8 (C-4′), 122.1 (C-3), 53.5 (−CH_3); IR (ν/cm^{-1}): 1727, 1581, 1538, 1426, 1364, 1301, 1235, 1192, 1106, 928, 850, 786; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{10}BrN_2O_3$ 308.9869; found 308.9878, $[M + Na]^+$ calcd for $C_{12}H_9BrN_2O_3Na$ 330.9689; found 330.9701.

*3-Bromo-5-nitro-2,2′-bipyridine N-Oxide (**2i**).* (101 mg of a complex product mixture for 0.53 mmol scale, after extraction).

*3-Bromo-4-methoxy-2,2′-bipyridine N-Oxide (**2j**).* (0% for 1.02 mmol scale, but 83% of recovered **1j**, after extraction).

*3,4-Dichloro-2,2′-bipyridine N-Oxide (**2k**).* (154 mg of a complex product mixture for 1.00 mmol scale, after extraction).

*3-Bromo-4-ethoxycarbonly-2,2′-bipyridine N-Oxide (**2l**).* (0% for 0.36 mmol scale, but **1l** was quantitatively recovered, after extraction).

*3-Bromo-4-trifluoromethyl-2,2′-bipyridine N-Oxide (**2m**).* (0% for 1.03 mmol scale, but **8m** and 53% of recovered **1m**, after column chromatography).

*4-Trifluoromethyl-6-dioxopyrrolidinyl-2,2′-bipyridine N-Oxide (**8m**).* Brown solid (125 mg, 36%); mp 122 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.82 (dt, J = 8.1, 1.1 Hz, 1H, ArH-6′), 8.75 (ddd, J = 4.8, 1.8, 1.0 Hz, 1H, ArH-3′), 8.65 (dd, J = 2.8, 0.8 Hz, 1H, ArH-5), 7.82 (td, J = 7.8, 1.9 Hz, 1H, ArH-5′), 7.60 (dd, J = 2.8, 0.7 Hz, 1H, ArH-3), 7.39 (ddd, J = 7.6, 4.7, 1.2 Hz, 1H, ArH-4′), 3.12−2.92 (m, 4H, −CH_2CH_2−); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 174.3 (C═O), 149.8 (C-3), 148.9 (C-2′), 147.9 (C-2), 140.6 (C-6), 136.6 (C-5′), 126.1 (q, J = 36.0 Hz, C-4), 125.5 (C-6′), 125.4 (C-4′), 125.2 (q, J = 4.0 Hz, C-5), 122.7 (q, J = 3.9 Hz, C-3), 122.3 (q, J = 272 Hz, CF_3), 29.1 (−CH_2CH_2−); ^{19}F NMR (471 MHz, $CDCl_3$): δ −63.3; IR (ν/cm^{-1}): 1715, 1388, 1327, 1272, 1150, 1134, 1116, 787, 737; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{11}F_3N_3O_3$ 338.0747; found 338.0749, $[M + Na]^+$ calcd for $C_{15}H_{10}F_3N_3O_3Na$ 360.0566; found 360.0573, $[M + K]^+$ calcd for $C_{15}H_{10}F_3N_3O_3K$ 376.0306; found 376.0270.

*3-Bromo-4-cyano-2,2′-bipyridine N-Oxide (**2n**).* Red solid (102 mg, 37% for 1.00 mmol scale besides 32% of recovered **1n**, after column chromatography); mp 157 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.80 (ddd, J = 4.9, 1.7, 1.0 Hz, 1H, ArH-3′), 8.28 (d, J = 7.0 Hz, 1H, ArH-5), 7.91 (td, J = 7.7, 1.7 Hz, 1H, ArH-5′), 7.53 (d, J = 6.9 Hz, 1H, ArH-6), 7.48−7.43 (m, 2H, ArH-4′, ArH-6′); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 150.6 (C-3′), 150.5 (C-2′), 150.0 (C-2), 139.7 (C-5), 137.3 (C-5′), 128.3 (C-6), 125.4 (C-3), 125.3 (C-6′), 125.0 (C-4′), 115.2 (C-4), 112.2 (−CN); IR (ν/cm^{-1}): 2228, 1428, 1403, 1288, 1267, 1080, 821, 738, 727; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_7BrN_3O$ 275.9767; found 275.9788, $[M + Na]^+$ calcd for $C_{11}H_6BrN_3ONa$ 297.9586; found 297.9609. Single crystals for X-ray diffraction were grown by slow diffusion of pentane into a concentrated solution of **2n** in DCM. CCDC-1476429 contains the crystallographic data for **2n**.

*3-Bromo-4-nitro-2,2′-bipyridine N-Oxide (**2o**).* (0% for 1.00 mmol scale, but 75.3 mg of an 1:1.4 mixture of **8o** and **1o**, besides 55% of pure **1o**, after column chromatography).

*4-Nitro-6-dioxopyrrolidinyl-2,2′-bipyridine N-Oxide (**8o**).* (12%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.23 (d, J = 3.3 Hz, 1H), 8.80−8.73 (m, 2H), 8.20 (d, J = 3.3 Hz, 1H), 7.82 (td, J = 7.8, 2.0 Hz, 1H), 7.41 (ddd, J = 7.4, 4.7, 1.1 Hz, 1H), 3.16−2.92 (m, 4H).

*3′-Bromo-6′-methoxy-2,2′-bipyridine N-Oxide (**2p**).* Brown solid (276 mg, 98% for 1.00 mmol scale, after extraction); mp 142 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32−8.28 (m, 1H, ArH-3), 7.78 (d, J = 8.8 Hz, 1H, ArH-5′), 7.37 (dd, J = 5.5, 4.4 Hz, 1H, ArH-4), 7.34−7.30 (m, 2H, ArH-5, ArH-6), 6.72 (d, J = 8.8 Hz, 1H, ArH-4′), 3.87 (s, 3H, −OCH_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 163.1 (C-5′), 148.5 (C-2), 148.2 (C-2′), 142.8 (C-6′), 139.9 (C-3), 127.5 (C-4), 126.0 and 125.1 (C-5, C-6), 113.4 (C-4′), 113.1 (C-3′), 54.1 (−CH_3); IR (ν/cm^{-1}): 1579, 1456, 1423, 1408, 1320, 1247, 1219, 1128, 1119, 1020, 1011, 893, 835, 823, 783, 764; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2O_2$ 280.9920; found 280.9930, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2O_2Na$ 302.9740; found 302.9755, $[M + K]^+$ calcd for $C_{11}H_9BrN_2O_2K$ 318.9479; found 318.9490.

*3′-Bromo-6′-methyl-2,2′-bipyridine N-Oxide (**2q**).* (0% for 0.95 mmol scale, but **5b**, after column chromatography).

*3-Bromo-6-methyl-2,2′-bipyridine (**5b**).* Orange oil (30.9 mg, 13%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (d, J = 4.8 Hz, 1H, ArH-3′), 7.86 (d, J = 8.2 Hz, 1H, ArH-4), 7.79 (td, J = 7.7, 1.8 Hz, 1H, ArH-5′), 7.67 (d, J = 7.8 Hz, 1H, ArH-6′), 7.32 (ddd, J = 7.6, 4.9, 1.2

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Hz, 1H, ArH-4′), 7.06 (d, J = 8.2 Hz, 1H, ArH-5), 2.57 (s, 3H, $-CH_3$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 157.5 and 157.4 (C-6, C2′), 155.8 (C-2), 149.3 (C-3′), 141.6 (C-4), 136.4 (C-5′), 124.5 (C-5), 124.4 (C-6′), 123.4 (C-4′), 116.5 (C-3), 24.2 ($-CH_3$); IR (ν/cm^{-1}): 1561, 1417, 1014, 820, 796, 757; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2$ 249.0022; found 249.0042, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2Na$ 270.9841; found 270.9863.

3′-Bromo-6′-trifluoromethyl-2,2′-bipyridine N-Oxide (**2r**). Tan solid (23.4 mg, 7% for 1.00 mmol scale, besides **5d**, after column chromatography); ^1H NMR (500 MHz, $CDCl_3$): δ 8.31 (d, J = 5.7 Hz, 1H, ArH-3), 8.19 (dt, J = 8.2, 0.7 Hz, 1H, ArH-4′), 7.65 (d, J = 8.3 Hz, 1H, ArH-5′), 7.47 (dd, J = 7.0, 2.8 Hz, 1H, ArH-5), 7.43−7.36 (m, 2H, ArH-4, ArH-6); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 152.5 (C-2′), 147.3 (q, J = 36 Hz, C-6′), 146.9 (C-2), 142.1 (C-4′), 139.9 (C-3), 127.6 (C-5), 126.8 (C-4), 126.1 (C-3′), 125.7 (C-6), 122.0 (q, J = 3.0 Hz, C-5′), 121.2 (q, J = 274 Hz, $-CF_3$); ^{19}F NMR (376 MHz, $CDCl_3$): δ −67.5; IR (ν/cm^{-1}): 1337, 1258, 1106, 1022, 795, 772; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_7BrF_3N_2O$ 318.9688; found 318.9697, $[M + Na]^+$ calcd for $C_{11}H_6BrF_3N_2ONa$ 340.9508; found 340.9520.

3-Bromo-6-trifluoromethyl-2,2′-bipyridine (**5d**). Colorless solid (75.8 mg, 25%); mp 54 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.75 (d, J = 4.8 Hz, 1H, ArH-3′), 8.21 (d, J = 8.2 Hz, 1H, ArH-4), 7.86 (td, J = 7.7, 1.7 Hz, 1H, ArH-5′), 7.77 (d, J = 7.8 Hz, 1H, ArH-6′), 7.58 (d, J = 8.3 Hz, 1H, ArH-5), 7.40 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H, ArH-4′); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 155.5, 155.2, 149.2, 146.1 (q, J = 35.6 Hz), 140.0, 136.9, 133.8, 124.8, 124.1, 121.3 (d, J = 274.3 Hz) 121.0 (q, J = 2.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ − 67.5; IR (ν/cm^{-1}): 1394, 1335, 1185, 1121, 1097, 1082, 1032, 1019, 845, 797, 742; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_7BrF_3N_2$ 302.9739; found 302.9769, $[M + Na]^+$ calcd for $C_{11}H_6BrF_3N_2Na$ 324.9559; found 324.9588.

3-Bromo-5′-methyl-2,2′-bipyridine N-Oxide (**2s**). Brown solid (11.6 mg, 7% for 0.60 mmol scale besides **5s** and 15% of recovered **1s**, after extraction); mp 138 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.62 (dt, J = 1.9, 0.8 Hz, 1H, ArH-6′), 8.27 (dd, J = 6.6, 1.1 Hz, 1H, ArH-4), 7.67 (ddd, J = 7.9, 2.2, 0.9 Hz, 1H, ArH-4′), 7.56 (dd, J = 8.3, 1.0 Hz, 1H, ArH-6), 7.41 (dd, J = 7.9, 0.8 Hz, 1H, ArH-3′), 7.15 (dd, J = 8.3, 6.6 Hz, 1H, ArH-5), 2.42 (s, 3H, $-CH_3$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 150.8 (C-6′), 148.5 (C-2), 139.2 (C-4), 137.4 (C-4′), 134.3 (C-5′), 129.8 (C-6), 125.3 (C-5), 124.8 (C-3′), 122.3 (C-3), 18.7 ($-CH_3$); IR (ν/cm^{-1}): 1451, 1408, 1252, 1026, 903, 828, 797; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2O$ 264.9971; found 264.9977, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2ONa$ 286.9790; found 286.9801, $[M + K]^+$ calcd for $C_{11}H_9BrN_2OK$ 302.9530; found 302.9540.

3-Bromo-5′-methyl-2,2′-bipyridine (**5s**). Brown oil (11.1 mg, 8%); ^1H NMR (500 MHz, $CDCl_3$): δ 8.64 (dd, J = 4.5, 1.5 Hz, 1H, ArH-4), 8.58 (s, 1H, ArH-6′), 8.01 (dd, J = 8.1, 1.5 Hz, 1H, ArH-6), 7.66−7.61 (m, 2H, ArH-3′, ArH-4′), 7.19 (dd, J = 8.1, 4.6 Hz, 1H, ArH-5), 2.41 (s, 3H, $-CH_3$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 156.7 (C-2), 154.6 (C-2′), 149.7 (C-6′), 148.1 (C-4), 141.7 (C-6), 136.9 (C-3′), 132.2 (C-5′), 124.2 (C-5), 124.0 (C-4′), 119.8 (C-3), 18.5 ($-CH_3$); IR (ν/cm^{-1}): 1567, 1459, 1429, 1374, 1093, 1015, 838, 791, 743; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2$ 249.0022; found 249.0030, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2Na$ 270.9841; found 270.9852.

3-Bromo-4′-methoxy-2,2′-bipyridine N-oxide (**2t**). Yellow oil (94.2 mg, 54% for 1.01 mmol scale, after column chromatography); ^1H NMR (500 MHz, $CDCl_3$): δ 8.57 (d, J = 5.8 Hz, 1H, ArH-4), 8.24 (dd, J = 6.6, 1.1 Hz, 1H, ArH-6), 7.53 (dd, J = 8.3, 1.0 Hz, 1H, ArH-6′), 7.15 (dd, J = 8.3, 6.5 Hz, 1H, ArH-5), 6.99 (d, J = 2.5 Hz, 1H, ArH-5′), 6.89 (dd, J = 5.7, 2.5 Hz, 1H, ArH-3′), 3.86 (s, 3H, -OCH_3); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 166.3 (C-2′), 152.6 (C-2), 151.5 (C-6′), 148.8 (C-4′), 139.1 (C-4), 129.7 (C-6), 125.3 (C-5), 122.0 (C-3′), 111.4 (C-3), 110.6 (C-5′), 55.5 ($-OCH_3$); IR (ν/cm^{-1}): 1602, 1563, 1473, 1410, 1312, 1256, 1029, 903, 862, 845, 783; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2O_2$ 280.9920; found 280.9934, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2O_2Na$ 302.9740; found 302.9757, $[M + K]^+$ calcd for $C_{11}H_9BrN_2O_2K$ 318.9479; found 318.9489.

3-Bromo-4′-methyl-2,2′-bipyridine N-Oxide (**2u**). Brown solid (282 mg, quant. for 1.01 mmol scale, after extraction); mp 79 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.63 (dd, J = 5.1, 0.8 Hz, 1H, ArH-6′), 8.26 (dd, J = 6.5, 1.0 Hz, 1H, ArH-4), 7.55 (dd, J = 8.3, 1.0 Hz, 1H, ArH-6), 7.31 (d, J = 0.8 Hz, 1H, ArH-3′), 7.20 (d, J = 5.0 Hz, 1H, ArH-5′), 7.15 (dd, J = 8.3, 6.5 Hz, 1H, ArH-5), 2.42 (s, 3H, $-CH_3$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 151.1 (C-2), 150.0 (C-6′), 148.3 (C-2′), 139.2 (C-4), 129.8 (C-6), 128.7 (C-4′), 126.0 (C-3′), 125.4 (C-5′), 125.3 (C-5), 122.1 (C-3), 21.3 ($-CH_3$); IR (ν/cm^{-1}): 1711, 1605, 1407, 1256, 1182, 904, 829, 779, 720; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2O$ 264.9971; found 264.9991, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2ONa$ 286.9790; found 286.9813, $[M + K]^+$ calcd for $C_{11}H_9BrN_2OK$ 302.9530; found 302.9556.

3-Bromo-4′-ethoxycarbonyl-2,2′-bipyridine N-Oxide (**2w**). Brown solid (272, 83% for 1.01 mmol scale, after extraction); mp 68 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.94 (dd, J = 5.0, 0.9 Hz, 1H, ArH-6′), 8.29 (dd, J = 6.6, 1.0 Hz, 1H, ArH-4), 8.07 (dd, J = 1.6, 0.9 Hz, 1H, ArH-3′), 7.96 (dd, J = 5.1, 1.6 Hz, 1H, ArH-5′), 7.59 (dd, J = 8.3, 1.0 Hz, 1H, ArH-6), 7.21 (dd, J = 8.3, 6.6 Hz, 1H, ArH-5), 4.42 (q, J = 7.2 Hz, 2H, $-CH_2-$), 1.40 (t, J = 7.1 Hz, 3H, $-CH_3$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 164.6 (C═O), 152.2 (C-2′), 151.1 (C-6′), 148.2 (C-2), 139.2 (C-4), 138.9 (C-4′), 129.9 (C-6), 125.7 (C-5), 124.9 (C-3′), 123.6 (C-5′), 122.1 (C-3), 62.2 ($-CH_2-$), 14.3 ($-CH_3$); IR (ν/cm^{-1}): 1722, 1408, 1303, 1289, 1236, 1116, 1101, 1014, 896, 784, 760; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{12}BrN_2O_3$ 323.0028; found 323.0057, $[M + Na]^+$ calcd for $C_{13}H_{11}BrN_2O_3Na$ 344.9845; found 344.9882.

3-Bromo-2-(pyridin-2-yl)pyrazine N-Oxide (**2y**). (0% for 1.02 mmol scale, but 78% recovered **1y**, after extraction).

3-Bromo-2-(pyridin-2-yl)quinoline N-Oxide (**2z**). Brown solid (143 mg, 49% for 0.96 mmol scale besides **5z** and **8z**, after column chromatography); mp 158 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.82 (d, J = 4.4 Hz, 1H, ArH-6′), 8.66 (d, J = 8.9 Hz, 1H, ArH-9), 8.06 (s, 1H, ArH-4), 7.89 (td, J = 7.8, 1.7 Hz, 1H, ArH-4′), 7.80 (d, J = 8.0 Hz, 1H, ArH-6), 7.75 (ddd, J = 8.6, 7.0, 1.4 Hz, 1H, ArH-8), 7.66 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H, ArH-7), 7.58 (d, J = 7.8 Hz, 1H, ArH-3′), 7.42 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H, ArH-5′); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 152.2 (C-2′), 150.2 (C-6′), 144.4 (C-2), 141.3 (C-10), 136.9 (C-4′), 130.8 (C-8), 129.9 (C-7), 129.7 (C-5), 128.5 (C-4), 127.3 (C-6), 125.4 (C-3′), 124.2 (C-5′), 120.4 (C-9), 116.2 (C-3); IR (ν/cm^{-1}): 1324, 1205, 918, 846, 768, 750, 742; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{10}BrN_2O$ 300.9971; found 300.9979, $[M + Na]^+$ calcd for $C_{14}H_9BrN_2ONa$ 322.9790; found 322.9803, $[M + K]^+$ calcd for $C_{14}H_9BrN_2OK$ 338.9530; found 338.9535.

3-Bromo-2-(pyridin-2-yl)quinoline (**5z**). Brown solid (23.6 mg, 9%); mp 86−88 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.79 (d, J = 4.8 Hz, 1H, ArH-6′), 8.52 (s, 1H ArH-4), 8.15 (d, J = 8.5 Hz, 1H ArH-9), 7.86 (td, J = 7.7, 1.7 Hz, 1H, ArH-4′), 7.29 (d, J = 7.9 Hz, 2H, ArH-6, ArH-3′), 7.74 (ddd, J = 8.4, 7.0, 1.4 Hz, 1H, ArH-8), 7.59 (t, J = 7.5 Hz, 1H, ArH-7), 7.39 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H, ArH-5′); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 157.6 (C-2′), 156.4 (C-2), 149.2 (C-6′), 146.5 (C-10), 140.4 (C-4), 136.6 (C-4′), 130.3 (C-8), 129.8 (C-6), 128.8 (C-5), 128.0 (C-7), 126.7 (C-6), 124.5 (C-3′), 123.6 (C-5′), 116.2 (C-3′); IR (ν/cm^{-1}): 1476, 1434, 1396, 1085, 857, 900, 775, 752, 742; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{10}BrN_2$ 285.0022; found 285.0044, $[M + Na]^+$ calcd for $C_{14}H_9BrN_2Na$ 306.9841; found 306.9865.

3-Bromo-4-dioxopyrrolidinyl-2-(pyridin-2-yl)quinoline N-Oxide (**8z**). Brown solid (29.4 mg, 8%); mp 116−120 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 8.83 (d, J = 3.8 Hz, 1H, ArH-6′), 8.72 (d, J = 8.5 Hz, 1H, ArH-6), 7.90 (td, J = 7.7, 1.6 Hz, 1H, ArH-4′), 7.80 (ddd, J = 8.6, 7.0, 1.3 Hz, 1H, ArH-7), 7.69 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H, ArH-8), 7.61−7.54 (m, 2H, ArH-9, ArH-3′), 7.42 (t, J = 6.3 Hz, 1H, ArH-5′), 3.15−3.02 (m, 4H, $-CH_2CH_2-$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 174.8 (C═O), 151.9 (C-2′), 150.4 (C-6′), 144.9 (C-2), 142.2 (C-4), 137.0 (C-4′), 131.3 (C-7), 130.9 (C-8), 126.8 (C-10), 126.6 (C-5), 125.5 (C-3′), 124.5 (C-5′), 123.1 (C-9), 121.2 (C-6), 118.9 (C-3), 29.1 ($-CH_2CH_2-$); IR (ν/cm^{-1}): 1716, 1411, 1320, 1169, 1150,

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1079, 771, 762; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{13}BrN_3O_3$ 398.0135; found 398.0165, $[M + Na]^+$ calcd for $C_{18}H_{12}BrN_3O_3Na$ 419.9954; found 419.9985.

*2-(2-Bromophenyl)pyridine N-Oxide (**13**).* Colorless solid (165 mg, 66% for 1.00 mmol scale besides 2-(3,6-dibromophenyl)pyridine *N*-oxide **14**, after column chromatography with acetone in hexane mixtures 0−100%; 10% increments); mp 113 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.31 (dp, J = 6.9, 2.3 Hz, 1H), 7.67 (dd, J = 8.1, 1.2 Hz, 1H), 7.42−7.39 (m, 1H), 7.37 (dd, J = 7.6, 2.0 Hz, 1H), 7.33−7.27 (m, 4H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 149.3, 140.1, 134.5, 133.0, 131.1, 130.9, 128.1, 127.6, 125.6, 125.2, 123.6; IR (ν/cm^{-1}): 1458, 1411, 1254, 1241, 1230, 1007, 841, 756, 737; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_9BrNO$ 249.9862; found 249.9870, $[M + Na]^+$ calcd for $C_{11}H_8BrNONa$ 271.9681; found 271.9691, $[M + K]^+$ calcd for $C_{11}H_8BrNOK$ 287.9421; found 287.9454. *Uncatalyzed reaction:* Similar to the general procedure, the reaction of 2-phenylpyridine *N*-oxide (175 mg, 1.02 mmol), and NBS (220 mg, 1.24 mmol) in chlorobenzene (10.0 mL) provided only recovered starting material (79.6 mg, 0.46 mmol, 45%) after column chromatography.

*2-(3,6-dibromophenyl)pyridine N-Oxide (**14**).* Brown solid (32.1 mg, 10%); mp 154 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.37 (dd, J = 5.2, 2.4 Hz, 1H, ArH-3), 7.64 (d, J = 8.0 Hz, 2H, ArH-3′, ArH-5′), 7.36−7.32 (m, 2H, ArH-4, ArH-5), 7.30−7.26 (m, 1H, ArH-6), 7.19 (t, J = 8.1 Hz, 1H, ArH-4′); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 149.2 (C-2), 140.1 (C-3), 135.5 (C-1′), 132.0 (C-4′, C-5′), 131.8 (C-4′), 128.2 (C-6), 126.1 and 125.2 (C-4, C-5), 124.6 (C-2′); IR (ν/cm^{-1}): 1419, 1245, 1186, 847, 783, 764, 718; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_8Br_2NO$ 327.8967; found 327.8975, $[M + Na]^+$ calcd for $C_{11}H_7Br_2NONa$ 349.8787; found 349.8797, $[M + K]^+$ calcd for $C_{11}H_7Br_2NOK$ 365.8526; found 365.8583.

*2-(2-Bromophenyl)pyridine (**10**).* Pale yellow oil (119 mg, 49% for 1.03 mmol scale besides 2-(3,6-dibromophenyl)pyridine **11**, after column chromatography with EtOAc in hexane mixtures 0−100%; 10% increments); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H), 7.75 (td, J = 7.7, 1.8 Hz, 1H), 7.67 (dd, J = 8.0, 1.2 Hz, 1H), 7.59 (dt, J = 7.9, 1.1 Hz, 1H), 7.53 (dd, J = 7.6, 1.7 Hz, 1H), 7.40 (td, J = 7.5, 1.2 Hz, 1H), 7.30−7.22 (m, 2H). The chemical shifts are in agreement with previous reports.[44]

*2-(2,6-Dibromophenyl)pyridine (**11**).* Pale yellow solid (41.2 mg, 13%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.75 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H), 7.81 (td, J = 7.7, 1.8 Hz, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.34 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H), 7.30 (dt, J = 7.8, 1.1 Hz, 1H), 7.12 (t, J = 8.1 Hz, 1H). The chemical shifts are in agreement with previous reports.[44]

*3-Chloro-2,2′-bipyridine N-Oxide (**7a**).* Brown solid (3.93 g, 95% for 20.0 mmol scale, after extraction); mp 105 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.79 (ddd, J = 4.9, 1.7, 1.0 Hz, 1H, ArH-6′), 8.24 (dd, J = 6.6, 1.0 Hz, 1H, ArH-4), 7.87 (td, J = 7.8, 1.7 Hz, 1H, ArH-4′), 7.53 (dd, J = 8.5, 1.0 Hz, 1H, ArH-6), 7.42−7.38 (m, 2H, ArH-3′, ArH-5′), 7.23 (dd, J = 8.4, 6.5 Hz, 1H, ArH-5); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 149.6 (C-6′), 148.8 (C-2), 146.8 (C-2′), 138.4 (C-4), 137.4 (C-3), 133.7 (C-4′), 128.5 (C-6), 125.6 (C-5), 125.5 (C-3′), 124.6 (C-5′); IR (ν/cm^{-1}): 1415, 1266, 1247, 1031, 926, 792, 780, 725; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_8ClN_2O$ 207.0320; found 207.0325, $[M + Na]^+$ calcd for $C_{10}H_7ClN_2ONa$ 229.0139; found 229.0147, $[M + K]^+$ calcd for $C_{10}H_7ClN_2OK$ 244.9878; found 244.9869.

*3-Chloro-6-methyl-2,2′-bipyridine N-Oxide (**7b**).* Tan oil (75.1 mg, 68% for 0.49 mmol scale, after column chromatography); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.77 (d, J = 4.8 Hz, 1H, ArH-6′), 7.83 (td, J = 7.8, 1.8 Hz, 1H, ArH-4′), 7.47 (d, J = 7.8 Hz, 1H, ArH-3′), 7.36 (ddd, J = 7.7, 4.9, 1.1 Hz, 1H, ArH-5′), 7.30 (d, J = 8.5 Hz, 1H, ArH-4), 7.24 (d, J = 8.5 Hz, 1H, ArH-5), 2.47 (s, 3H, −CH_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 150.5 (C-2′), 150.2 (C-6′), 148.5 (C-2), 147.2 (C-6), 136.8 (C-4′), 130.5 (C-3), 126.0 (C-4), 125.41 (C-5), 125.36 (C-3′), 124.0 (C-5′), 17.8 (−CH_3); IR (ν/cm^{-1}): 1459, 1443, 1426, 1347, 1260, 1002, 928, 782, 745, 708; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}ClN_2O$ 221.0476; found 221.0491, $[M + Na]^+$ calcd for $C_{11}H_9ClN_2ONa$ 243.0296; found 243.0319.

*3-Chloro-6-ethoxycarbonyl-2,2′-bipyridine N-Oxide (**7c**).* Brown oil (252 mg, 91% for 0.99 mmol scale, after extraction); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.78 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H, ArH-6′), 7.85 (td, J = 7.7, 1.8 Hz, 1H, ArH-4′), 7.57−7.51 (m, 2H, ArH-5, ArH-3′), 7.40 (d, J = 8.7 Hz, 1H, ArH-4), 7.38 (dd, J = 4.9, 1.1 Hz, 1H, ArH-5′), 4.42 (q, J = 7.1 Hz, 2H, −CH_2−), 1.37 (t, J = 7.1 Hz, 3H, −CH_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 161.3 (C═O), 150.3 (C-6′), 149.3 (C-2′), 148.7 (C-2), 141.3 (C-6), 136.8 (C-4′), 135.2 (C-3), 125.89 (C-3′), 125.85 (C-4), 125.5 (C-5), 124.5 (C-5′), 62.9 (−CH_2−), 14.2 (−CH_3); IR (ν/cm^{-1}): 1736, 1583, 1383, 1318, 1248, 1158, 1099, 1084, 1012, 940, 782, 745; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{12}ClN_2O_3$ 279.0531; found 279.0532, $[M + Na]^+$ calcd for $C_{13}H_{11}ClN_2O_3Na$ 301.0350; found 301.0356, $[M + K]^+$ calcd for $C_{13}H_{11}ClN_2O_3K$ 317.0090; found 317.0088.

*3-Chloro-6-cyano-2,2′-bipyridine N-Oxide (**7e**).* (0% for 0.99 mmol scale, but 85% recovered **1e**, after column chromatography).

*3-Chloro-5-methoxy-2,2′-bipyridine N-Oxide (**7f**).* Brown solid (230 mg, 97% for 1.01 mmol scale, after extraction); mp 145 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.76 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H, ArH-6′), 8.01 (d, J = 2.2 Hz, 1H, ArH-4), 7.82 (td, J = 7.7, 1.8 Hz, 1H, ArH-4′), 7.50 (dt, J = 7.8, 1.1 Hz, 1H, ArH-3′), 7.35 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H, ArH-5′), 7.02 (d, J = 2.2 Hz, 1H, ArH-6), 3.85 (s, 3H, −CH_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.7 (C-5), 150.1 (C-6′), 149.8 (C-2′), 141.1 (C-2), 136.7 (C-4′), 133.3 (C-3), 127.1 (C-4), 126.1 (C-3′), 124.1 (C-5′), 114.5 (C-6), 56.6 (−CH_3); IR (ν/cm^{-1}): 1603, 1545, 1460, 1449, 1427, 1376, 1165, 1018, 893, 865, 836, 787, 748; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}ClN_2O_2$ 237.0425; found 237.0449, $[M + Na]^+$ calcd for $C_{11}H_9ClN_2O_2Na$ 259.0245; found 259.0274, $[M + K]^+$ calcd for $C_{11}H_9ClN_2O_2K$ 274.9984; found 275.0009.

*3-Chloro-5-methyl-2,2′-bipyridine N-Oxide (**7g**).* Brown solid (198 mg, 90% for 1.00 mmol scale, after extraction); mp 113 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.78 (d, J = 4.6 Hz, 1H, ArH-6′), 8.11 (s, 1H, ArH-4), 7.85 (td, J = 7.7, 1.7 Hz, 1H, ArH-4′), 7.52 (dt, J = 7.9, 1.1 Hz, 1H, ArH-3′), 7.38 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H, ArH-5′), 7.24 (s, 1H, ArH-6), 2.33 (s, 3H, −CH_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 150.2 (C-6′), 149.9 (C-2′), 144.9 (C-2), 138.7 (C-4), 136.8 (C-4′), 136.0 (C-5), 132.9 (C-3), 128.1 (C-6), 125.9 (C-3′), 124.2 (C-5′), 18.3 (−CH_3); IR (ν/cm^{-1}): 1710, 1599, 1566, 1539, 1427, 1374, 1283, 1217, 1146, 1022, 991, 892, 845, 789, 750; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}ClN_2O$ 221.0476; found 221.0488, $[M + Na]^+$ calcd for $C_{11}H_9ClN_2ONa$ 243.0296; found 243.0313, $[M + K]^+$ calcd for $C_{11}H_9ClN_2OK$ 259.0035; found 259.0319.

*3-Chloro-5-methoxycarbonyl-2,2′-bipyridine N-Oxide (**7h**).* Brown solid (170 mg, 64% for 1.00 mmol scale, after extraction); mp 96 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.80 (dd, J = 5.8, 1.1 Hz, 1H, ArH-6′), 8.79 (s, J = 1.3 Hz, 1H, ArH-4), 7.95 (d, J = 1.4 Hz, 1H, ArH-6), 7.88 (td, J = 7.8, 1.8 Hz, 1H, ArH-4′), 7.55 (dt, J = 7.8, 1.1 Hz, 1H, ArH-3′), 7.42 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H, ArH-5′), 3.98 (s, 3H, −OCH_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 162.6 (C═O), 150.3 (C-2), 149.1 (C-2′), 139.7 (C-4), 137.0 (C-4′), 133.8 (C-3), 128.7 (C-5), 128.6 (C-6′), 127.1 (C-6), 125.6 (C-3′), 124.7 (C-5′), 53.5 (−OCH_3); IR (ν/cm^{-1}): 1724, 1427, 1372, 1318, 1231, 1110, 1008, 958, 879, 757, 744, 728; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{10}ClN_2O_3$ 265.0374; found 265.0379, $[M + Na]^+$ calcd for $C_{12}H_9ClN_2O_3Na$ 287.0194; found 287.0199, $[M + K]^+$ calcd for $C_{12}H_9ClN_2O_3K$ 302.9933; found 302.9945.

*3-Chloro-5-nitro-2,2′-bipyridine N-Oxide (**7i**).* Yellow solid (26.0 mg, 31% for 0.33 mmol scale besides 33% of recovered **1i**, after column chromatography); mp 165−168 °C (decomp.); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.05 (d, J = 2.0 Hz, 1H, ArH-4), 8.83 (d, J = 4.5 Hz, 1H, ArH-3′), 8.15 (d, J = 2.0 Hz, 1H, ArH-6), 7.92 (td, J = 7.8, 1.7 Hz, 1H, ArH-5′), 7.56 (d, J = 7.8 Hz, 1H, ArH-6′), 7.47 (ddd, J = 7.7, 4.9, 1.1 Hz, 1H, ArH-4′); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 152.2 (C-2), 150.6 (C-3′), 148.1 (C-2′), 145.2 (C-5), 137.1 (C-5′), 135.1 (C-4), 134.4 (C-3), 125.6 (C-6′), 125.2 (C-4′), 120.9 (C-6); IR (ν/cm^{-1}): 1514, 1424, 1374, 1351, 1268, 1186, 1101, 994, 778, 743; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_7ClN_3O_3$ 252.0170; found 252.0166, $[M + Na]^+$ calcd for $C_{10}H_6ClN_3O_3Na$ 273.9990; found 273.9990.

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*3-Chloro-4-cyano-2,2′-bipyridine N-Oxide (**7n**).* (0% for 0.82 mmol scale, but 91% recovered **1n**, after extraction).

*3′-Chloro-6′-methoxy-2,2′-bipyridine N-Oxide (**7p**).* Yellow solid (227 mg, 96% for 1.00 mmol scale, after extraction); mp 134 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.29 (dd, J = 4.9, 2.8 Hz, 1H, ArH-3), 7.78 (d, J = 8.7 Hz, 1H, ArH-5′), 7.37 (dd, J = 5.5, 4.4 Hz, 1H, ArH-5), 7.32−7.28 (m, 2H, ArH-4, ArH-6), 6.72 (d, J = 8.7 Hz, 1H, ArH−), 3.88 (s, 3H, $-OCH_3$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 163.1 (C-6′), 148.5 (C-2′), 148.2 (C-2), 142.8 (C-5′), 139.9 (C-3), 127.5 (C-5), 126.0 and 125.10 (C-4, C-6), 113.4 (C-3′), 113.1 (C-4′), 54.1 ($-OCH_3$); IR (ν/cm^{-1}): 1584, 1460, 1410, 1324, 1251, 1226, 1023, 930, 893, 831, 766; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}ClN_2O_2$ 237.0425; found 237.0451, $[M + Na]^+$ calcd for $C_{11}H_9ClN_2O_2Na$ 259.0245; found 259.0276.

*3′-Chloro-6′-methyl-2,2′-bipyridine N-Oxide (**7q**).* (0% for 1.01 mmol scale, but quant. recovered **1q**, after extraction).

*3′-Chloro-6′-trifluoromethyl-2,2′-bipyridine N-Oxide (**7r**).* Colorless solid (234 mg, 90% for 0.95 mmol scale, after extraction); mp 146 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (dd, J = 5.6, 2.0, 1H, ArH-3), 8.01 (dt, J = 8.3, 0.7 Hz, 1H, ArH-4′), 7.74 (d, J = 8.4 Hz, 1H, ArH-5′), 7.50 (dd, J = 7.3, 2.6 Hz, 1H, ArH-6), 7.43−7.36 (m, 2H, ArH-4, ArH-5); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 150.8 (C-2), 146.5 (q, J = 36 Hz, C-6′), 146.6 (C-2′), 139.9 (C-3), 138.8 (C-4′), 136.5 (C-3′), 127.8 (C-6), 126.8 and 125.4 (C-4, C-5), 122.0 (q, J = 2.4 Hz, C-5′), 121.2 (q, J = 275 Hz, $-CF_3$); ^{19}F NMR (471 MHz, $CDCl_3$): δ −67.4; IR (ν/cm^{-1}): 1422, 1336, 1251, 1173, 1160, 1135, 1119, 1105, 1033, 850, 823, 770; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_7ClF_3N_2O$ 275.0194; found 275.0198, $[M + Na]^+$ calcd for $C_{11}H_6ClF_3N_2ONa$ 297.0013; found 297.0025.

*3-Chloro-4′-methyl-2,2′-bipyridine N-Oxide (**7u**).* Brown solid (216 mg, 98% for 0.98 mmol scale, after extraction); mp 129 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.63 (dd, J = 5.0, 0.8 Hz, 1H, ArH-4), 8.23 (dd, J = 6.6, 1.1 Hz, 1H, ArH-6), 7.38 (dd, J = 8.4, 1.1 Hz, 1H, ArH-6′), 7.33 (dt, J = 1.7, 0.8 Hz, 1H, ArH-3′), 7.21 (dd, J = 8.3, 6.6 Hz, 1H, ArH-5′), 7.20 (ddd, J = 5.0, 1.6, 0.7 Hz, 1H, ArH-5), 2.42 (s, 3H, $-CH_3$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 150.0 (C-2), 149.6 (C-2′), 148.2 (C-4), 147.8 (C-4′), 138.7 (C-6), 133.7 (C-3), 126.8 (C-6′), 126.2 (C-3′), 125.4 (C-5), 124.9 (C-5′), 21.2 ($-CH_3$); IR (ν/cm^{-1}): 1605, 1404, 1252, 927, 835, 788, 723; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}ClN_2O$ 221.0476; found 221.0473, $[M + Na]^+$ calcd for $C_{11}H_9ClN_2ONa$ 243.0296; found 243.0317, $[M + K]^+$ calcd for $C_{11}H_9ClN_2OK$ 259.0035; found 259.0030.

*3-Chloro-4′-fluoro-2,2′-bipyridine N-Oxide (**7v**).* Brown solid (204 mg, 90% for 1.01 mmol scale, after extraction); mp 125 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.77 (dd, J = 8.3, 5.7 Hz, 1H), 8.26 (dd, J = 6.6, 1.0 Hz, 1H), 7.42 (dd, J = 8.4, 1.0 Hz, 1H), 7.31 (dd, J = 9.0, 2.4 Hz, 1H), 7.27 (dd, J = 8.4, 6.6 Hz, 1H), 7.15 (ddd, J = 8.2, 5.7, 2.5 Hz, 1H); $^{13}C\{H\}$ NMR (126 MHz, $CDCl_3$): δ 169.0 (d, J = 264 Hz, C-4′), 152.8 (d, J = 7.5 Hz, C-6′), 152.4 (d, J = 8.0 Hz, C-2′), 146.7 (C-2), 138.8 (C-4), 133.7 (C-3), 126.9 (C-6), 125.4 (C-5), 114.2 (d, J = 18 Hz, C-3′), 112.5 (d, J = 16 Hz, C-5′); ^{19}F NMR (471 MHz, $CDCl_3$): δ −100.7; IR (ν/cm^{-1}): 1600, 1575, 1467, 1414, 1395, 1267, 1184, 1046, 900, 932, 894, 839, 829, 783, 724; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_7ClFN_2O$ 225.0225; found 225.0259, $[M + Na]^+$ calcd for $C_{10}H_6ClFN_2ONa$ 247.0045; found 247.0051, $[M + K]^+$ calcd for $C_{10}H_6ClFN_2OK$ 262.9784; found 262.9766.

*3-Chloro-4′-ethoxycarbonyl-2,2′-bipyridine N-Oxide (**7w**).* Brown oil (124 mg, 90% for 0.59 mmol scale, after extraction); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.94 (d, J = 5.0 Hz, 1H, ArH-6), 8.28 (d, J = 6.5 Hz, 1H, ArH-4), 8.11 (t, J = 1.2 Hz, 1H, ArH-3′), 7.97 (dd, J = 5.0, 1.6 Hz, 1H, ArH-5′), 7.43 (d, J = 8.3 Hz, 1H, ArH-6), 7281 (dd, J = 8.6, 6.7 Hz, 1H, ArH-5), 4.43 (q, J = 7.1 Hz, 2H, $-CH_2-$), 1.41 (t, J = 7.1 Hz, 3H, $-CH_3$); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 164.6 (C═O), 151.1 (C-6′), 150.7 (C-2′), 139.0 (C-4), 138.8 (C-4′), 133.8 (C-3), 127.1 (C-6), 125.3 (C-5), 125.2 (C-3′), 123.7 (C-5′), 119.9 (C-2), 62.2 ($-CH_2-$), 14.3 ($-CH_3$); IR (ν/cm^{-1}): 1412, 1303, 1236, 1116, 1100, 1014, 930, 787, 762; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{12}ClN_2O_3$ 279.0531; found 279.0537, $[M + Na]^+$ calcd for $C_{13}H_{11}ClN_2O_3Na$ 301.0350; found 301.0359, $[M + K]^+$ calcd for $C_{13}H_{11}ClN_2O_3K$ 317.0090; found 317.0094.

*3-Chloro-4′-trifluoromethyl-2,2′-bipyridine N-Oxide (**7x**).* Brown oil (155 mg, 97% for 0.58 mmol scale, after extraction); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.98 (d, J = 5.3 Hz, 1H, ArH-6), 8.27 (dd, J = 6.6, 1.1 Hz, 1H, ArH-4), 7.81 (s, 1H, ArH-3′), 7.62 (dd, J = 5.1, 0.9 Hz, 1H, ArH-5′), 7.44 (dd, J = 8.4, 1.1 Hz, 1H, ArH-6), 7.30 (dd, J = 8.4, 6.5 Hz, 1H, ArH-5); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 151.3 (C-6′), 151.1 (C-2′), 146.4 (C-2), 139.2 (q, J = 35 Hz, C-4′), 138.8 (C-4), 133.7 (C-3), 127.0 (C-6), 125.5 (C-5), 122.7 (q, J = 274 Hz, $-CF_3$), 121.9 (q, J = 3.7 Hz, C-3′), 120.1 (q, J = 3.5 Hz, C-5′); ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.6; IR (ν/cm^{-1}): 1414, 1395, 1333, 1244, 1169, 1133, 1083, 1046, 931, 850, 833, 787; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_7ClF_3N_2O$ 275.0194; found 275.0192, $[M + Na]^+$ calcd for $C_{11}H_6ClF_3N_2ONa$ 297.0013; found 297.0013, $[M + K]^+$ calcd for $C_{11}H_6ClF_3N_2OK$ 312.9752; found 312.9748.

*3-Chloro-2-(pyridin-2-yl)pyrazine N-Oxide (**7y**).* (0% for 1.00 mmol scale, but 92% recovered **1y**, after extraction).

*3-Chloro-2-(pyridin-2-yl)quinoline N-Oxide (**7z**).* Brown solid (236 mg, 87% for 1.05 mmol scale, after extraction); mp 127−130 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.83 (ddd, J = 4.9, 1.6, 0.9 Hz, 1H, ArH-6′), 8.69 (d, J = 8.7 Hz, 1H, ArH-9), 7.89 (td, J = 7.8, 1.8 Hz, 1H, ArH-4′), 7.87 (s, 1H, ArH-4), 7.81 (dd, J = 8.1, 1.2 Hz, 1H, ArH-6), 7.75 (ddd, J = 8.6, 7.0, 1.4 Hz, 1H, ArH-8), 7.67 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H, ArH-7), 7.61 (dt, J = 7.8, 1.0 Hz, 1H, ArH-3′), 7.42 (ddd, J = 7.7, 4.9, 1.1 Hz, 1H, ArH-5′); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 150.8 (C-2), 150.3 (C-6′), 143.7 (C-2′), 141.2 (C-10), 136.8 (C-4′), 130.6 (C-8), 129.9 (C-7), 129.1 (C-3), 128.2 (C-5), 127.5 (C-6), 125.7 (C-3′), 125.1 (C-4), 124.2 (C-5′, 120.5 (C-9); IR (ν/cm^{-1}): 1713, 1589, 1556, 1472, 1428, 1328, 938, 847, 821, 769; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{10}ClN_2O$ 257.0476; found 257.0499, $[M + Na]^+$ calcd for $C_{14}H_9ClN_2ONa$ 279.0296; found 279.0326.

General Procedure for Deoxygenation of Halogenated Bipyridine *N*-Oxides. A reaction vial was loaded with halogenated bipyridine *N*-oxide **2** or **7** (1.0 equiv) and $CHCl_3$ (0.10 M). The solution was cooled to 0 °C, and PX_3 (4.0 equiv, X = Br for **2** and X = Cl for **7**) was added. After stirring at 80 °C for 3 h, the reaction mixture was cooled to room temperature, quenched, and neutralized with sat. $NaHCO_3$. The aqueous layer was extracted with DCM, and the combined organic layers were dried with Na_2SO_4, and filtered, and the volatiles were removed from the filtrate. If necessary, flash column chromatography (acetone/hexane 1:9) was performed.

*3-Bromo-2,2′-bipyridine (**5a**).* Pale yellow oil (44.3 mg, 76% for 0.25 mmol scale, after extraction); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (d, J = 4.4 Hz, 1H), 8.64 (d, J = 3.7 Hz, 1H), 8.01 (dd, J = 8.1, 1.5 Hz, 1H), 7.81 (td, J = 7.7, 1.8 Hz, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.34 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H), 7.20 (dd, J = 8.1, 4.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 157.3, 156.7, 149.3, 148.1, 141.7, 136.4, 124.4, 124.3, 123.5, 119.7; IR (ν/cm^{-1}): 1567, 1410, 1101, 1014, 991, 792, 744; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_8BrN_2$ 234.9865; found 234.9890, $[M + Na]^+$ calcd for $C_{10}H_7BrN_2Na$ 256.9685; found 256.9713. *Attempted deoxygenation with Pd/C and NH_4CO_2H:* **2a** (63.6 mg, 0.25 mmol) was dissolved in MeOH (1.30 mL), and NH_4CO_2H (188 mg, 2.99 mmol) and Pd/C (w = 10%, 26.5 mg, 0.025 mmol) were added as solids. The reaction mixture was stirred at room temperature for 5 h, the volatiles were removed, and the residue was extracted with DCM. After removal of the solvent from the extracted solution, 2,2′-bipyridine (35.5 mg, 0.25 mmol, quant.) was obtained.

*3-Bromo-6-methyl-2,2′-bipyridine (**5b**).* Orange oil (38.3 mg, 79% for 0.19 mmol scale, after extraction). NMR data are identical to those of the previous obtained sample (s.a.).

*3-Bromo-6-ethoxycarbonyl-2,2′-bipyridine (**5c**).* Colorless oil (58.8 mg, 61% for 0.31 mmol scale, after extraction); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (d, J = 4.6 Hz, 1H), 8.15 (d, J = 8.3 Hz, 1H), 7.98 (d, J = 8.3 Hz, 1H), 7.84 (td, J = 7.7, 1.7 Hz, 1H), 7.76 (d, J = 7.7 Hz, 1H), 7.36 (ddd, J = 7.4, 4.9, 1.2 Hz, 1H), 4.45 (q, J = 7.1 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.7, 156.7, 149.0, 146.9, 142.7, 136.7, 125.5, 124.7, 123.8, 123.7, 62.3, 14.4; IR (ν/cm^{-1}): 1739, 1715, 1562, 1417, 1392, 1367, 1311, 1281, 1136, 1105, 1015, 992, 856, 798, 785, 744; HRMS (ESI-TOF)

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m/z: $[M + H]^+$ calcd for $C_{13}H_{12}BrN_2O_2$ 307.007; found 307.0107, $[M + Na]^+$ calcd for $C_{13}H_{11}BrN_2O_2Na$ 328.9896; found 328.9937, $[M + K]^+$ calcd for $C_{13}H_{11}BrN_2O_2K$ 344.9635; found 344.9666.

*3-Bromo-6-trifluoromethyl-2,2′-bipyridine (**5d**).* Colorless solid (34.8 mg, 43% for 0.27 mmol scale, after column chromatography). NMR data are identical to those of the previous obtained sample (*v.s.*).

*3,6-Dibromo-5-methoxy-2,2′-bipyridine (**16f**).* Pale yellow solid (83.4 mg, 45% for 0.53 mmol scale, after column chromatography); mp 93−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (d, J = 4.8 Hz, 1H), 7.80 (td, J = 7.8, 1.7 Hz, 1H), 7.73 (d, J = 7.8 Hz, 1H), 7.43 (s, 1H), 7.32 (ddd, J = 7.5, 4.9, 1.3 Hz, 1H), 3.98 (s, 3 H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 155.9, 152.9, 149.1, 148.3, 136.6, 130.7, 124.6, 123.9, 123.5, 118.5, 56.9; IR (ν/cm^{-1}): 1562, 1460, 1410, 1316, 1211, 1119, 1065, 1011, 873, 797, 744; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{11}H_9Br_2N_2O$ 344.9056; found 344.9078, $[M + Na]^+$ calcd for $C_{11}H_8Br_2N_2ONa$ 366.8875; found 366.8899.

*3-Bromo-6-methoxy-2,2′-bipyridine (**5p**).* Pale yellow oil (7.9 mg, 8% for 0.35 mmol scale, after column chromatography); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (d, J = 4.1 Hz, 1H), 7.87−7.77 (m, 2H), 7.73 (dt, J = 7.9, 1.0 Hz, 1H), 7.34 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H), 6.68 (d, J = 8.7 Hz, 1H), 3.95 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 162.7, 157.4, 153.1, 148.9, 144.1, 136.5, 124.5, 123.4, 112.4, 110.3, 77.2, 54.0; IR (ν/cm^{-1}): 1564, 1458, 1408, 1318, 1011, 992, 823, 795, 744; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2O$ 264.9971; found 264.9979, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2ONa$ 286.9790; found 286.9791.

*3-Bromo-4′-methyl-2,2′-bipyridine (**5u**).* Pale yellow solid (65.8 mg, 45% for 0.59 mmol scale, after column chromatography); mp 50−52 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, J = 4.6 Hz, 1H), 8.56 (d, J = 5.0 Hz, 1H), 7.97 (dt, J = 8.1, 1.6 Hz, 1H), 7.50 (s, 1H), 7.18−7.11 (m, 2H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 157.1, 156.7, 148.9, 147.9, 147.6, 141.6, 125.1, 124.4, 124.2, 119.6, 21.2; IR (ν/cm^{-1}): 1603, 1568, 1437, 1384, 1018, 994, 797, 772, 743; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{10}BrN_2$ 249.0022; found 249.0020, $[M + Na]^+$ calcd for $C_{11}H_9BrN_2Na$ 270.9841; found 270.9854.

*3-Bromo-4′-ethoxycarbonyl-2,2′-bipyridine (**5w**).* Brown solid (128 mg, 86% for 0.49 mmol scale, after extraction); mp 78−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.87 (d, J = 5.0 Hz, 1H), 8.65 (dd, J = 4.6, 1.3 Hz, 1H), 8.28 (s, 1H), 8.02 (dd, J = 8.1, 1.4 Hz, 1H), 7.90 (dd, J = 5.0, 1.5 Hz, 1H), 7.22 (dd, J = 8.1, 4.6 Hz, 1H), 4.41 (q, J = 7.1 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.9, 158.2, 155.8, 149.9, 148.2, 141.8, 138.3, 124.6, 123.7, 122.6, 119.7, 62.0, 14.3; IR (ν/cm^{-1}): 1721, 1374, 1307, 1293, 1249, 1232, 1203, 1128, 1015, 899, 912, 750, 733; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{13}H_{11}BrN_2O_2Na$ 328.9896; found 328.9928.

*3-Bromo-2-(pyridin-2-yl)quinoline (**5z**).* Colorless solid (39.6 mg, 38% for 0.37 mmol scale, after column chromatography). NMR data are identical to previous obtained sample (*v.s.*).

*3-Chloro-2,2′-bipyridine (**15a**).* Pale orange oil (34.9 mg, 37% for 0.49 mmol scale, after extraction); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (d, J = 3.2 Hz, 1H), 8.59 (d, J = 3.9 Hz, 1H), 7.78 (dd, J = 8.0, 1.2 Hz, 2H), 7.73 (d, J = 7.8 Hz, 1H), 7.31 (ddd, J = 7.2, 4.9, 1.2 Hz, 1H), 7.25 (dd, J = 8.1, 4.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 156.1, 155.0, 149.3, 147.6, 138.4, 136.4, 130.5, 124.5, 124.2, 123.5; IR (ν/cm^{-1}): 1569, 1412, 1104, 1030, 991, 796, 746; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{10}H_8ClN_2$ 191.0371; found 191.0384, $[M + Na]^+$ calcd for $C_{10}H_7ClN_2Na$ 213.0190; found 213.0208, $[M + K]^+$ calcd for $C_{10}H_7ClN_2K$ 228.9929; found 228.9958. *Attempted deoxygenation with Pd/C and NH_4CO_2H:* **7a** (51.7 mg, 0.25 mmol) was dissolved in MeOH (1.30 mL) and NH_4CO_2H (158 mg, 2.51 mmol) and Pd/C (w = 10%, 26.0 mg, 0.024 mmol) were added as solids. The reaction mixture was stirred at room temperature for 5 h, the volatiles were removed, and the residue was extracted with DCM. After removal of the solvent from the extracted solution, only starting material (53.4 mg, 0.26 mmol, quant.) was recovered.

*3-Chloro-6-methyl-2,2′-bipyridine (**15b**).* Pale yellow oil (46.4 mg, 58% for 0.36 mmol scale, after column chromatography); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (d, J = 4.5 Hz, 1H), 7.77 (td, J = 7.7, 1.8 Hz, 1H), 7.68 (d, J = 7.9 Hz, 1H), 7.65 (d, J = 8.2 Hz, 1H), 7.30 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H), 7.11 (d, J = 8.2 Hz, 1H), 2.57 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 156.8, 156.3, 154.2, 149.4, 138.4, 136.3, 127.5, 124.6, 124.0, 123.3, 24.1; IR (ν/cm^{-1}): 1562, 1448, 1418, 1474, 1234, 1141, 1118, 1027, 992, 821, 797, 745; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{10}ClN_2$ 205.0527; found 205.0549.

*3-Chloro-6-ethoxycarbonyl-2,2′-bipyridine (**15c**).* Orange oil (104 mg, 82% for 0.48 mmol scale, after extraction); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 (d, J = 4.4 Hz, 1H), 8.06 (d, J = 8.3 Hz, 1H), 7.93 (d, J = 8.3 Hz, 1H), 7.83−7.75 (m, 2H), 7.33 (ddd, J = 6.7, 4.8, 1.8 Hz, 1H), 4.43 (q, J = 7.1 Hz, 1H), 1.38 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.4, 155.6, 155.2, 149.1, 146.2, 139.4, 136.6, 134.2, 125.4, 124.8, 123.8, 62.2, 14.3; IR (ν/cm^{-1}): 1739, 1716, 1568, 1418, 1392, 1368, 1313, 1282, 1221, 1140, 1109, 1030, 857, 800, 787, 745; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{13}H_{12}ClN_2O_2$ 263.0582; found 263.0588, $[M + Na]^+$ calcd for $C_{13}H_{11}ClN_2O_2Na$ 285.0401; found 285.0409.

*3-Chloro-5-methoxy-2,2′-bipyridine (**15f**).* Colorless solid (46.4 mg, 58% for 0.36 mmol scale besides 3,6-dichloro-5-methoxy-2,2′-bipyridine, after column chromatography); mp 63 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73 (br s, 1H), 8.33 (br s, 1H), 7.76 (td, J = 7.6, 1.6 Hz, 1H), 7.72 (br d, J = 7.0 Hz, 1H), 7.31 (d, J = 2.5 Hz, 1H), 7.30−7.27 (m, 1H), 3.87 (s, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 156.0, 155.7, 149.2, 147.3, 136.3, 136.0, 130.5, 124.5, 123.1, 122.3, 56.1; IR (ν/cm^{-1}): 1583, 1455, 1424, 1273, 1239, 1206, 1177, 1142, 1097, 1032, 991, 871, 801, 747; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{10}ClN_2O$ 221.0476; found 221.0485.

*3,6-Dichloro-5-methoxy-2,2′-bipyridine (**17f**).* Pale yellow solid (12.5 mg, 14%); mp 66−68 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73 (d, J = 4.4 Hz, 1H), 7.80 (td, J = 7.5, 1.5 Hz, 1H), 7.75 (dt, J = 7.9, 1.1 Hz, 1H), 7.32 (ddd, J = 7.4, 4.8, 1.4 Hz, 1H), 7.33 (s, 1H), 3.98 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 155.0, 151.6, 149.2, 145.9, 138.4, 136.6, 129.5, 124.7, 123.4, 121.5, 56.8; IR (ν/cm^{-1}): 1568, 1456, 1413, 1324, 1213, 1123, 1081, 1016, 867, 798, 745; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{11}H_9Cl_2N_2O$ 255.0086; found 255.0087, $[M + Na]^+$ calcd for $C_{11}H_8Cl_2N_2ONa$ 276.9906; found 276.9908.

*3-Chloro-5-methyl-2,2′-bipyridine (**15g**).* Brown oil (59.8 mg, 85% for 0.32 mmol scale, after extraction); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (d, J = 4.7 Hz, 1H), 8.43 (s, 1H), 7.81 (td, J = 7.6, 1.7 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.63 (s, 1H), 7.33 (ddd, J = 7.2, 4.9, 1.3 Hz, 1H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 155.8, 151.8, 149.0, 148.3, 138.8, 136.7, 134.7, 130.0, 124.7, 123.4, 17.9; IR (ν/cm^{-1}): 1585, 1446, 1426, 1380, 1105, 1034, 898, 799, 746; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{10}ClN_2$ 205.0527; found 205.0542.

*3-Chloro-5-methoxycarbonyl-2,2′-bipyridine (**15h**).* Tan solid (66.4 mg, 93% for 0.29 mmol scale, after extraction); mp 52 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.17 (d, J = 1.8 Hz, 1H), 8.79 (d, J = 4.3 Hz, 1H), 8.42 (dd, J = 1.8, 0.8 Hz, 1H), 7.88 (td, J = 7.8, 1.7 Hz, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.42 (ddd, J = 7.0, 4.9, 1.3 Hz, 1H), 3.98 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.5, 157.7, 154.9, 149.1, 148.4, 139.6, 137.1, 130.6, 126.7, 125.0, 124.2, 52.9; IR (ν/cm^{-1}): 1726, 1584, 1424, 1377, 1279, 1104, 1088, 1033, 992, 958, 761, 742; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{12}H_{10}ClN_2O_2$ 249.0425; found 249.0440, $[M + Na]^+$ calcd for $C_{12}H_9ClN_2O_2Na$ 271.0245; found 271.0261.

*3-Chloro-6-methoxy-2,2′-bipyridine (**15p**).* Colorless oil (35.0 mg, 66% for 0.24 mmol scale, after column chromatography); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (d, J = 4.8 Hz, 1H), 7.80 (td, J = 7.5, 1.6 Hz, 1H), 7.75 (d, J = 7.9 Hz, 1H), 7.65 (d, J = 8.7 Hz, 1H), 7.32 (ddd, J = 6.9, 4.8, 1.1 Hz, 1H), 6.74 (d, J = 8.7 Hz, 1H), 3.95 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 162.1, 156.5, 151.4, 149.0, 141.14, 141.12, 136.4, 124.6, 123.3, 122.3, 112.10, 112.08, 54.0; IR (ν/cm^{-1}): 1583, 1567, 1460, 1408, 1322, 1252, 1129, 823, 797, 745; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{10}ClN_2O$ 221.0476; found 221.0489, $[M + Na]^+$ calcd for $C_{11}H_9ClN_2ONa$ 243.0296; found 243.0308.

*3-Chloro-6-trifluoromethyl-2,2′-bipyridine (**15r**).* Yellow solid (67.8 mg, 85% for 0.31 mmol scale, after extraction); mp 51−53

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°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76 (d, J = 4.9 Hz, 1H), 8.01 (d, J = 8.3 Hz, 1H), 7.86 (td, J = 7.7, 1.8 Hz, 1H), 7.81 (dt, J = 7.9, 1.0 Hz, 1H), 7.67 (d, J = 8.3 Hz, 1H), 7.40 (ddd, J = 7.3, 4.8, 1.3 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 155.6, 155.3, 149.2, 146.1 (q, J = 35.7 Hz), 140.0, 136.9, 133.8, 124.8, 124.1, 121.3 (q, J = 274.3 Hz), 121.0 (q, J = 2.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ −67.5; IR (ν/cm^{-1}): 1395, 1334, 1185, 1122, 1097, 1032, 845, 742; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{11}H_7ClF_3N_2$ 259.0244; found 259.0266, [M + Na]$^+$ calcd for $C_{11}H_6ClF_3N_2Na$ 281.0064; found 281.0083.

*3-Chloro-4′-methyl-2,2′-bipyridine (**15u**).* Tan solid (110 mg, 95% for 0.57 mmol scale, after extraction); mp 61 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (br s, 2H), 7.78 (dd, J = 8.1, 1.4 Hz, 1H), 7.54 (s, 1H), 7.24 (dd, J = 8.1, 4.6 Hz, 1H), 7.14 (d, J = 5.0 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 155.8, 155.0, 148.8, 147.9, 147.5, 138.4, 130.5, 125.3, 124.5, 124.1, 21.2; IR (ν/cm^{-1}): 1604, 1568, 1433, 1385, 1141, 1117, 1099, 1035, 993, 835, 800, 774, 762; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{11}H_{10}ClN_2$ 205.0527; found 205.0532, [M + Na]$^+$ calcd for $C_{11}H_9ClN_2Na$ 227.0346; found 227.0355.

*3-Chloro-4′-fluoro-2,2′-bipyridine (**15v**).* Colorless solid (42.7 mg, 62% for 0.33 mmol scale, after column chromatography); mp 74−76 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (dd, J = 8.5, 5.7 Hz, 1H), 8.62 (d, J = 4.6 Hz, 1H), 7.84 (dd, J = 8.1, 1.4 Hz, 1H), 7.53 (dd, J = 9.6, 2.5 Hz, 1H), 7.32 (dd, J = 8.1, 4.6 Hz, 1H), 7.10 (ddd, J = 8.2, 5.6, 2.5 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 168.8 (d, J = 263 Hz), 159.2 (d, J = 7.1 Hz), 153.9 (d, J = 3.7 Hz), 151.7 (d, J = 7.1 Hz), 147.7, 138.8, 130.7, 124.7, 112.7 (d, J = 18.0 Hz), 111.5 (d, J = 16.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ −101.7 (q, J = 8.8 Hz); IR (ν/cm^{-1}): 1579, 1448, 1388, 1188, 1038, 905, 874, 845, 812, 766; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{10}H_7ClFN_2$ 209.0276; found 209.0293, [M + Na]$^+$ calcd for $C_{10}H_6ClFN_2Na$ 231.0096; found 231.0113, [M + K]$^+$ calcd for $C_{10}H_6ClFN_2K$ 246.9817; found 246.9817.

*3-Chloro-4′-ethoxycarbonyl-2,2′-bipyridine (**15w**).* Orange solid (61.2 mg, 70% for 0.34 mmol scale, after extraction); mp 99−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.91 (br s, 1H), 8.65 (br s, 1H), 8.34 (s, 1H), 7.92 (dd, J = 5.0, 1.3 Hz, 1H), 7.86 (dd, J = 8.1, 1.4 Hz, 1H), 7.33 (dd, J = 8.1, 4.6 Hz, 1H), 4.43 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 164.9, 157.1, 154.2, 150.0, 147.8, 138.7, 138.5, 124.6, 124.0, 122.8, 62.1, 14.3; IR (ν/cm^{-1}): 1720, 1442, 1376, 1308, 1295, 1251, 1228, 1129, 1020, 813, 750; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{13}H_{12}ClN_2O_2$ 263.0582; found 263.0598, [M + Na]$^+$ calcd for $C_{13}H_{11}ClN_2O_2Na$ 285.0401; found 285.0432.

*3-Chloro-4′-trifluoromethyl-2,2′-bipyridine (**15x**).* Colorless solid (22.3 mg, 37% for 0.23 mmol scale, after column chromatography); mp 49−50 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.94 (d, J = 5.0 Hz, 1H), 8.65 (d, J = 4.6 Hz, 1H), 8.05 (s, 1H), 7.87 (dd, J = 8.1, 1.5 Hz, 1H), 7.58 (dd, J = 5.1, 1.0 Hz, 1H), 7.35 (dd, J = 8.1, 4.6 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 157.6, 153.7, 150.2, 147.8, 139.0 (q, J = 34.3 Hz), 138.9, 130.8, 124.9, 122.9 (q, J = 273.4 Hz) 120.5 (d, J = 3.6 Hz), 119.1 (d, J = 3.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.6; IR (ν/cm^{-1}): 1397, 1334, 1277, 1164, 1131, 1086, 1033, 870, 838, 798, 779; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{11}H_7ClF_3N_2$ 259.0244; found 259.0248, [M + Na]$^+$ calcd for $C_{11}H_6ClF_3N_2Na$ 281.0064; found 281.0057.

*3-Chloro-2-(pyridin-2-yl)quinoline (**15z**).* Pale yellow solid (64.9 mg, 57% for 0.47 mmol scale besides 3,4-dichloro-2-(pyridin-2-yl)quinoline, after column chromatography); mp 87−88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (d, J = 4.7 Hz, 1H), 8.28 (s, 1H), 8.16 (d, J = 8.3 Hz, 1H), 7.87−7.78 (m, 2H), 7.76 (d, J = 8.2 Hz, 1H), 7.71 (ddd, J = 8.4, 7.0, 1.4 Hz, 1H), 7.56 (td, J = 7.6, 7.1, 1.0 Hz, 1H), 7.37 (ddd, J = 6.8, 4.9, 1.7 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 156.5, 155.4, 149.3, 146.1, 136.7, 136.5, 130.0, 129.8, 128.3, 128.0, 127.2, 126.6, 124.7, 123.6; IR (ν/cm^{-1}): 1582, 1568, 1479, 1434, 1400, 1370, 1310, 1092, 1047, 994, 971, 952, 900, 860, 772, 750, 734, 711; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{14}H_{10}ClN_2$ 241.0527; found 241.0532, [M + Na]$^+$ calcd for $C_{14}H_9ClN_2Na$ 263.0346; found 263.0350.

*3,4-Dichloro-2-(pyridin-2-yl)quinoline (**17z**).* Pale yellow solid (17.2 mg, 13%); mp 101−103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (d, J = 4.1 Hz, 1H), 8.25 (dd, J = 8.4, 0.7 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.88 (td, J = 7.7, 1.8 Hz, 1H), 7.81−7.76 (m, 2H), 7.70 (ddd, J = 7.9, 7.0, 0.8 Hz, 1H), 7.42 (dd, J = 7.6, 4.9 Hz, 1H, ArH-4′); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 156.7, 156.0, 149.4, 146.2, 141.4, 136.7, 130.7, 130.3, 128.9, 126.8, 126.4, 124.6, 124.5, 123.9; IR (ν/cm^{-1}): 1564, 1476, 1380, 1351, 1335, 1310, 1285, 1111, 905, 851, 792, 760, 736, 711; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{14}H_9Cl_2N_2$ 275.0137; found 275.0144, [M + Na]$^+$ calcd for $C_{14}H_8Cl_2N_2Na$ 296.9957; found 296.9959.

Syntheses of Catalyst Intermediates. *(2,2′-Bipyridin-3-yl-N-oxide)palladium Acetate Dimer (Dimer **A**).* An argon-purged Schlenk flask was charged with Pd_2dba_3·$CHCl_3$ (1.01 g, 0.98 mmol), 3-bromobipyridine N-oxide **2a** (508 mg, 2.02 mmol), and dry toluene (20.0 mL). The mixture was stirred at 50 °C for 1 h and then cooled to room temperature before the flask was opened to air. The volatiles were removed in vacuum, and the solid residue was redissolved in DCM (20.0 mL). AgOAc (1.01 g, 6.06 mmol) was added as a solid, and the resulting mixture was stirred at room temperature for 2.5 h. The reaction mixture was filtered through Celite, the filtrate was concentrated in vacuum, and Et_2O was added, which resulted in the formation of a yellow solid. The clear yellow supernatant solution was decanted, and the solid was washed with Et_2O and dried in vacuum providing dimer **A** (624 mg, 0.93 mmol, 95%) as a yellow solid. Single crystals for X-ray diffraction were grown by slow diffusion of Et_2O into a concentrated solution of **A** in DCM. CCDC-1476427 contains the crystallographic data for dimer **A**. Mp 204 °C (decomp.); ^{1}H NMR (400 MHz, $CDCl_3$, major isomer): δ 9.07 (ddd, J = 8.3, 1.6, 0.7 Hz, 2H), 7.99 (ddd, J = 5.6, 1.7, 0.7 Hz, 2H), 7.75−7.69 (m, 4H), 6.83 (dd, J = 7.7, 1.2 Hz, 2H), 6.76 (ddd, J = 7.4, 5.5, 1.5 Hz, 2H), 6.74 (dd, J = 7.7, 6.4 Hz, 2H), 2.24 (s, 8H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 182.6, 157.6, 149.7, 148.7, 147.6, 139.6, 136.8, 125.5, 123.3, 122.4, 24.8; IR (ν/cm^{-1}): 1559, 1524, 1401, 1253, 1244, 1205, 902, 782, 746, 706; HRMS (ESI-TOF) m/z: [M-OAc]$^+$ calcd for $C_{22}H_{17}N_4O_4Pd_2^+$ 614.9324; found 614.9368, [M + Na]$^+$ calcd for $C_{24}H_{20}N_4NaO_6Pd_2^+$ 696.9354; found 696.9401. Elemental analysis (%): Anal. calcd for $C_{24}H_{20}N_4O_6Pd_2$: C, 42.8; H, 2.99; N, 8.32. Found: C, 42.8; H, 3.34; N, 8.36.

*(2,2′-Bipyridin-3-yl-N-oxide)palladium Succinimidate (Dimer **B**).* A mixture of palladium acetate dimer **A** (336 mg, 0.5 mmol) and succinimide (101 mg, 1.02 mmol) in MeCN (20.0 mL) was stirred at 40 °C for 1.5 h. The volatiles were removed, the residue was redissolved in $CHCl_3$ (20.0 mL), and the resulting solution was stirred at 40 °C for an additional 1.5 h. The reaction solution was concentrated in vacuum, and Et_2O was added, which resulted in formation of a yellow precipitation. The supernatant liquid was decanted, and the solid was washed with Et_2O and dried in vacuum. The dimer **B** (372 mg, 0.50 mmol, quant.) was obtained as a yellow solid. Mp >250 °C (decomp.); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.21 (d, J = 8.3 Hz, 2H), 7.94 (d, J = 5.4 Hz, 2H), 7.78−7.70 (m, 4H), 6.83 (t, J = 6.6 Hz, 2H), 6.61 (dd, J = 7.6, 6.6 Hz, 2H), 6.43 (d, J = 7.7 Hz, 2H), 2.91−2.79 (m, 8H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 195.7, 188.2, 157.1, 149.3, 148.4, 146.7, 140.0, 136.9, 130.5, 125.6, 123.8, 122.8, 32.2, 32.1; IR (ν/cm^{-1}): 1589, 1379, 1244, 1215, 897, 789, 747, 706; HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{28}H_{22}N_6NaO_6Pd_2^+$ 774.9563; found 774.9609, [0.5 M + Na]$^+$ calcd for $C_{14}H_{11}N_3NaO_3Pd^+$ 397.9727; found 397.9751.

*(4-Ethoxycarbonyl-2,2′-bipyridine-N-oxide)palladium(II) Acetate (Monomer **C**).* $Pd(OAc)_2$ (56.3 mg, 0.25 mmol) and 4-ethoxycarbonyl-2,2′-bipyridine N-oxide (122 mg, 0.50 mmol) were dissolved in DCM (3.00 mL) under vigorous stirring. Precipitation occurred within the first 2 min. The mixture was additionally stirred at room temperature for 12 h, before Et_2O (3.00 mL) was added. The supernatant liquid was decanted, the remaining solid was washed with Et_2O, and dried in vacuum. The title complex was obtained as a 2:1 mixture with 4-ethoxycarbonyl-2,2′-bipyridine N-oxide (190 mg). Single crystals for X-ray diffraction were grown by slow diffusion of

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Et_2O into a concentrated solution in $CDCl_3$. CCDC-1476437 contains the crystallographic data for monomer **C**. Mp 154 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.57 (d, J = 1.9 Hz, 2H), 8.71 (d, J = 5.2 Hz, 2H), 8.25 (d, J = 6.8 Hz, 2H), 8.02 (dd, J = 6.8, 2.5 Hz, 2H), 7.89 (dd, J = 8.0, 0.9 Hz, 2H), 7.87−7.79 (m, 2H, overlapping with free noncoordinated *N*-oxide), 7.30 (ddd, J = 7.5, 5.8, 1.6 Hz, 2H), 4.49 (q, J = 7.1 Hz, 4H), 1.57 (s, 6H), 1.46−1.37 (m, 6H, overlapping with noncoordinated *N*-oxide); IR (ν/cm^{-1}): 1718, 1624, 1361, 1304, 1246, 1206, 776; HRMS (ESI-TOF) m/z: [M-OAc]$^+$ calcd for $C_{28}H_{27}N_4O_8Pd^+$ 653.0858; found 653.0964, [M − $(OAc)_2$ + OMe]$^+$ calcd for $C_{27}H_{27}N_4O_7Pd^+$ 625.0909; found 625.1013.

General Procedure for Mechanistic Experiments under Catalytic Conditions. 8 mL reaction vials were charged with **1a** (0.25 mmol), NBS (0.30 mmol), a palladium source (5 mol % based on [Pd]), chlorobenzene (2.50 mL), and if applicable the additive. NBu_4OAc (0.025 mmol, 10 mol %) was directly weighted out together with the substrate, and the liquids were added using Hamilton syringe. Pyridine (20 μL, 0.25 mmol) was added neat, and HOAc was added as stock solution in chlorobenzene (0.25 M, 100 μL, 0.025 mmol, 10 mol %). After stirring at 110 °C for 1 h, the vials were cooled to room temperature, the reaction mixtures were transferred into round-bottom flasks, and the solvent was removed by rotary evaporation. The solid residues were additionally dried in high vacuum for several hours, before being redissolved in $CDCl_3$. The solutions were directly filtered through a short plug of Celite (pipet), and the filtrate was transferred into NMR tubes and analyzed by ^{1}H NMR. Only isolated peaks of the starting material **1a** and brominated product **2a** were used for integration. The average of 3−4 integrals for each compound was used to calculate the ratio **2a** to **1a**.

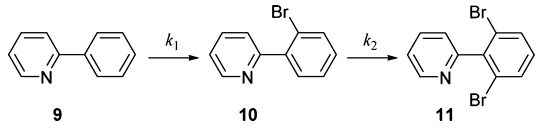
General Procedure for Mechanistic Experiments under Stoichiometric Conditions. 20 mL reaction vials were charged with dimer **A** or **B** (0.075 mmol), NBS (0.17 mmol), pyridine (120 μL, 1.50 mmol), and chlorobenzene (7.5 mM, based on palladium dimer). NBu_4OAc (22.9 mg, 0.075 mmol) was directly weighted out together with the palladium dimer and NBS. HOAc was added as stock solution in chlorobenzene (0.25 M, 1.20 mL, 0.30 mmol). After stirring at 110 °C for 10 min, the vials were cooled to room temperature, the reaction mixtures were transferred into round-bottom flasks, and the solvent was removed by rotary evaporation. The solid residues were additionally dried in high vacuum for several hours, before a stock solution of 1,3,5-trichlorobenzene (TCB) in $CDCl_3$ (0.17 M, 0.25 mL, 0.042 mmol) was added. The mixtures were directly filtered through a short plug of Celite (pipet), and the filtrate was transferred into NMR tubes and analyzed by ^{1}H NMR. Only isolated peaks were used for quantification. The average values of several integrals for each compound were used to calculate the yields.

*Detection of Monomer **C** and Dimer **A**.* A reaction vial was charged with **1a** (51.5 mg, 0.30 mmol), $Pd(OAc)_2$ (68.4 mg, 0.30 mmol), and $CDCl_3$ (0.60 mL) and sealed. After stirring at room temperature for 3 h a precipitation was formed, which was allowed to settle, and the supernatant solution was transferred into an NMR tube and measured by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.13 (dd, J = 8.1, 1.6 Hz, 2H), 8.79 (td, J = 7.9, 1.3 Hz, 2H), 8.54 (dd, J = 6.4, 1.2 Hz, 2H), 8.43 (dd, J = 5.7, 1.1 Hz, 2H), 8.12 (d, J = 7.3 Hz, 2H), 7.87 (td, J = 7.8, 1.6 Hz, 2H), 7.65 (ddd, J = 8.0, 6.4, 1.7 Hz, 2H), 7.48 (ddd, J = 7.6, 5.7, 1.4 Hz, 2H), 1.98 (s, 6H); then, the reaction mixture was treated with one drop of HOAc resulting in formation of a clear solution. The solution was stirred under heating at 50 °C for an additional 3 h before again being measured by ^{1}H NMR. The spectrum showed besides the formation of dimer **A** an additional set of signals.

Estimation of Relative Rate Constants for Formation of 10 and 11. The bromination of **9** to **10** and **11** (Scheme 11) is a sequential reaction. Hence, the molar fractions a, b, and c of the three components can be derived from the integrated rate laws and are given by eqs 1, 2, and 3, respectively.[45]

$$a = \frac{[\mathbf{9}]_t}{[\mathbf{9}]_0} = e^{-k_1 t} \tag{1}$$

Scheme 11. Bromination of phenylpyridine



$$b = \frac{[\mathbf{10}]_t}{[\mathbf{9}]_0} = \frac{k_1}{k_2 - k_1}(e^{-k_1 t} - e^{-k_2 t}) \tag{2}$$

$$c = \frac{[\mathbf{11}]_t}{[\mathbf{9}]_0} = 1 - \frac{1}{k_2 - k_1}(k_2 e^{-k_1 t} - k_1 e^{-k_2 t}) \tag{3}$$

The product fractions b and c can be expressed independent of time by inserting eq 1 into eqs 2 and 3, respectively, where s is the ratio of the rate constants according to eq 4.

$$s = \frac{k_2}{k_1} \tag{4}$$

$$b = \frac{a - a^s}{s - 1} \tag{5}$$

$$c = 1 - \frac{sa - a^s}{s - 1} \tag{6}$$

$$a + b + c = 1 \tag{7}$$

The values of a, b, and c are obtained directly from the yields of **9**, **10**, and **11**. If the starting material is not reisolated, a can be calculated by eq 7. The ratio of the rate constants s can in principle be obtained from eq 5. However, eq 5 cannot be solved for s by using elementary functions. Therefore, it is easier to find the solution for s numerically by a simple iterative search. In the case of the bromination of **9** under our conditions, b = 0.49 and c = 0.13 are found experimentally, from which a = 0.38 is calculated. For these values, s = 0.4323 solves eq 5, meaning that k_1 is approximately 2.3 times larger than k_2 (Figure 1).

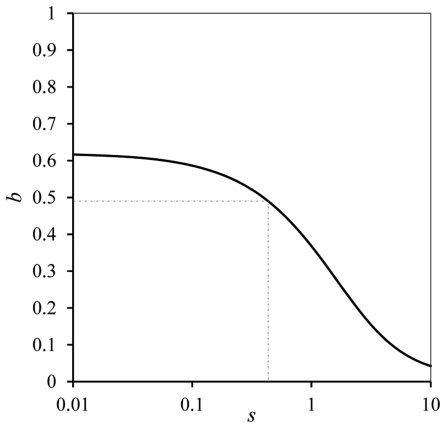


Figure 1. Plot of b as a function of s according to eq 5 for a = 0.38.

The literature[14a] reports the yield of **10**, but not the conversion or the amount of **11**; only b = 0.63 is known, which is not sufficient to calculate s. However, the concentration of **10** passes through a maximum during the course of the reaction. By treating b as a function of a, the maximum is easily found and the respective values for a and b are given in eqs 8 and 9.

$$a_{max} = s^{1/(1-s)} \tag{8}$$

$$b_{max} = \frac{1}{1 - s}(s^{1/(1-s)} - s^{s/(1-s)}) \tag{9}$$

With b_{max} = 0.63, s = 0.2499 (i.e., k_1 is at least 4.0 times larger than k_2) can be numerically found as a solution of eq 9 (Figure 2). This

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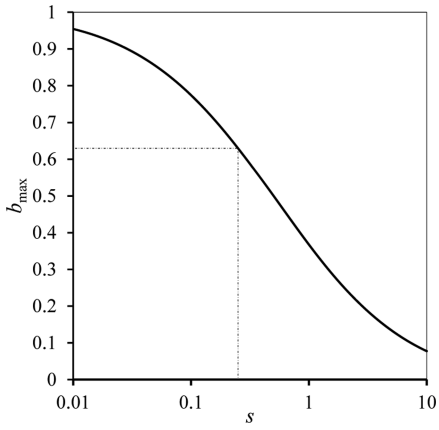

Figure 2. Plot of b_{max} as a function of s according to eq 9.

value for s is the upper limit for the ratio of the rate constants under the assumption that the concentration of monobrominated product **10** passed the maximum in the moment, when the reaction was stopped. If the same approach is applied to our result with b_{max} = 0.48, one obtains s = 0.5265 (i.e., k_1 is at least 1.9 times larger than k_2) as the upper limit for s, which is close to the value obtained above.

Clearly, eq 5 is not applicable for s = 1. In this case, b is given by eq 5a and its maximum value by eqs 8a and 9a.

$$b = -a \cdot \ln a \tag{5a}$$

$$a_{max} = e^{-1} \tag{8a}$$

$$b_{max} = e^{-1} \tag{9a}$$

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00444.

^{1}H, ^{13}C, and ^{19}F NMR spectra for all new compounds (PDF)

Compounds **2a**, **2f**, **2n**, dimer **A**, and monomer **C** (CIF)

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Notes

The authors declare no competing financial interest.

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