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Palladium-Catalyzed C–H Bond Direct Alkynylation of 5-Membered Heteroarenes: A Well-Defined Synthetic Route to Azole Derivatives Containing Two Different Alkynyl Groups

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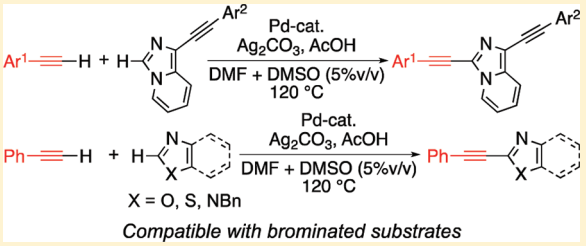
Supporting Information

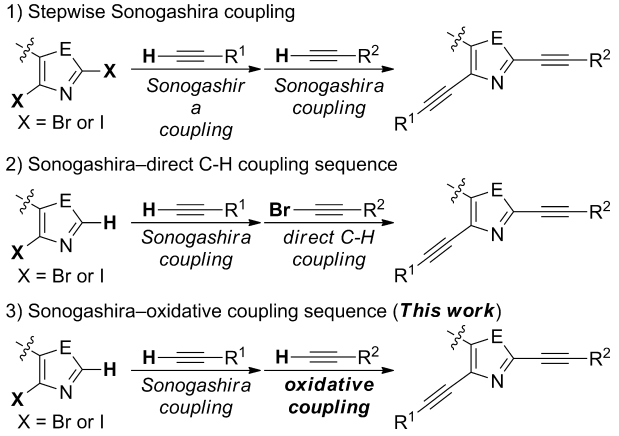
ABSTRACT: A widely applicable oxidative coupling of 5-membered heteroarenes and terminal alkynes that uses a combination of palladium and silver salts was developed. Under suitable conditions, imidazole and benzimidazole, which are sluggish under similar previously reported oxidative coupling conditions, as well as imidazo[1,5-*a*]pyridines, oxazole, benzoxazole, thiazole, and benzothiazole could be alkynylated. In addition, the bromine atom on the substrates was intact under the reaction conditions, and conventional Sonogashira coupling did not occur at all. With these reactivities in hand, a well-defined synthetic route to imidazo[1,5-*a*]pyridines and thiazole containing two different alkynyl groups was achieved in a simple manner. In addition, linear correlations were observed between the fluorescence wavelength and the Hammett substituent constants of aryl groups, not only on the C1- but also on the C3-alkynyl group of the obtained 1,3-bis(arylethynyl)imidazo [1,5-*a*]pyridines.



INTRODUCTION

Ethynylene-bridged π-conjugated systems are widely found in functional materials since the ethynylene moiety acts as a π-conjugated spacer.[1] Sonogashira coupling has been used to introduce such alkynyl moieties to π-conjugated systems.[2] However, it has been difficult to introduce two or more different alkynyl groups to (hetero)arenes by conventional Sonogashira coupling because of the low chemo- and regioselectivities of the reaction of polyhalogenated (hetero)arenes, such as dihaloarenes (Scheme 1, upper). For selective reactions, arenes bearing bromine and iodine atoms have usually been used as substrates, but a multistep synthesis is needed to obtain these substrates.[3,4]

Scheme 1. Approaches to Heteroarenes Containing Two Different Alkynyl Groups by Coupling Reactions



To obtain such bisalkynylated compounds, the direct C–H coupling of monoalkynylated products and haloalkynes is a promising approach (Scheme 1, middle),[5] but commercially available haloalkynes are still limited. The direct dehydrogenative coupling (oxidative coupling) of terminal alkynes and monoalkynylated (hetero)arenes is an alternative route to such dialkynylated compounds (Scheme 1, lower).[6] However, the previously reported reaction systems have usually been suitable only for highly acidic (low pK_a) C–H bonds, such as those of C2 in benzoxazole and oxadiazole.

We recently found that 1-arylethynylated 3-arylimidazo[1,5-*a*]pyridines show linear correlations between the Hammett substituent constants σ of aryl groups on the C1-alkynyl group and the fluorescence wavelength (Figure 1).[7,8] In contrast, there is no noticeable correlation between the constants σ of a directly bonded C3-aryl group and the fluorescent wavelength, perhaps due to the formation of distorted π-conjugated systems on the biaryl moieties as a result of steric hindrance. Our subsequent interest in the electronic influence of the arylalkynyl group on fluorescence prompted us to investigate the synthesis of 1,3-bis(arylalkynyl)imidazo[1,5-*a*]pyridines. Initially, we attempted the oxidative coupling of 1-(arylalkynyl)imidazo[1,5-*a*]pyridines and terminal alkynes under previously reported conditions,[6] but the reaction did not occur at all, perhaps because of the relatively low acidity of the C–H bond on C3 of the imidazo[1,5-*a*]pyridines. Therefore, we then sought to identify conditions under which such C–H bonds could participate in the reaction. We report herein a widely

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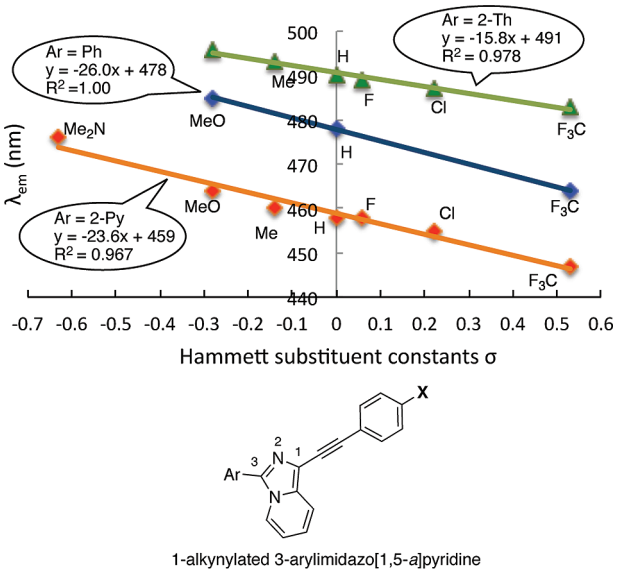


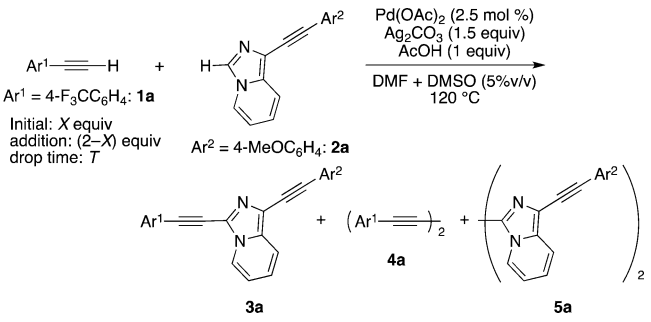
Figure 1. Correlation between the fluorescence wavelength and the Hammett substituent constants σ of the substituents on the aryl group on the C1 alkynyl group of 1-alkynylated 3-arylimidazo[1,5-*a*]-pyridines.

applicable oxidative coupling of 5-membered heteroarenes and terminal alkynes that uses a combination of palladium and silver salts. This catalytic system allowed the reaction to proceed even at C−H bonds with a large pK_a, such as in an imidazole derivative, with good efficiency. Furthermore, the transformation realized a well-defined synthetic route to imidazo[1,5-*a*]-pyridines and thiazole containing two different alkynyl groups. In addition, linear correlations were observed between the fluorescence wavelength and the Hammett substituent constants σ of aryl groups, not only on the C1- but also on the C3-alkynyl group of the obtained 1,3-bis(arylethynyl)imidazo[1,5-*a*]-pyridines.

RESULTS AND DISCUSSION

The use of less-expensive metals such as copper, nickel, and iron as a catalyst for C−H bond functionalization reactions of aromatic compounds is attractive, but reported examples of these reactions, particularly of the oxidative coupling of heteroarenes and terminal alkynes, with those metals have usually occurred at highly acidic C−H bonds on the substrates.[6] On the other hand, palladium catalysts have often participated in related direct C−H bond functionalization reactions at nucleophilic C−H bonds that show a large pK_a.[8b,9] Thus, we focused on palladium systems to develop the target oxidative coupling at the C3 position of imidazopyridines. During our initial survey of the reaction conditions, we found that a combination of palladium and silver salts showed good catalytic activity for the reaction of imidazopyridines and terminal alkynes,[10] while the reaction scarcely occurred under previously reported Pd salt−*t*BuOLi−air[6b] and Pd salt−Cs_2CO_3−O_2 systems.[6c] For example, the reaction of 4-trifluoromethylphenylacetylene (**1a**, 2 equiv) and 1-(4-methoxyphenylethynyl)-imidazo[1,5-*a*]pyridine (**2a**) with $Pd(OAc)_2$ (2.5 mol %), Ag_2CO_3 (1.5 equiv), and acetic acid (1 equiv) as an additive in a mixture of DMF and DMSO (5%) gave the desired bisalkynylated imidazopyridine **3a** in 11% yield (Table 1, entry 1). However, most of the alkyne **1a** underwent a homocoupling reaction, and the dimer **4a** was recovered in 77% yield

Table 1. Optimization of the Oxidative Coupling of 1a and 2a[a]



entry	X	T (min)	total reaction time (h)	yields (%)[b] 3a[c]	5a[c]	recovered alkyne as 4a (%)[d]
1	2	–	3	11	11	77
2	0	30	3	15	30	32
3	0.5	40	3	52	ND	46
4	0.5	20	1	80	14	41
5	0.5	90	3	18	21	26
6[e]	0.5	20	1	no reaction		–
7[f]	0.5	20	1	21	trace	74
8[g]	0.5	20	1	no reaction		–
9[h]	0.5	20	1	54	14	39
10[i]	0.5	20	1	50	trace	49

[a]Reaction conditions: To a solution of alkyne **1a** (*X* equiv), imidazo[1,5-*a*]pyridine **2a** (0.4 mmol), $Pd(OAc)_2$ (2.5 mol %), Ag_2CO_3 (1.5 equiv), and AcOH (1 equiv) in a mixture of DMF (0.9 mL) and DMSO (0.1 mL) was added dropwise a solution of **1a** (2−*X* equiv) in DMF (1 mL) over the indicated time period (*T*) at 120 °C. [b]Isolated yields. [c]Based on imidazopyridine **2a**. ND: not determined. [d]Based on alkyne **1a**. [e]The reaction was carried out in the absence of $Pd(OAc)_2$. [f]In the absence of AcOH. **2a** was recovered in 66% yield after the reaction. [g]In the absence of Ag_2CO_3. [h]In the absence of DMSO. [i]In DMSO.

under these conditions. The homocoupling of **1a** was suppressed when all of **1a** was added dropwise over 30 min, whereas the competitive homocoupling of imidazopyridine **2a** significantly took place to result in no improvement in the yield of **3a** (Table 1, entry 2). Meanwhile, those results implied that competitive homocouplings may be controlled by the concentration of the alkyne monomer **1a** in the reaction solution. In fact, we found that the initial amount and the rate of addition of the alkyne strongly influenced the yield of the cross-coupling product **3a**, and the best yield (80%) of **3a** was achieved when half an equivalent of the alkyne **1a** was used in the reaction mixture as an initial amount and 1.5 equiv of **1a** was added dropwise over 20 min (Table 1, entry 4). The slower addition of **1a** was ineffective, and the yield of **3a** decreased (Table 1, entry 5). Each additive was essential for obtaining satisfactory yields (Table 1, entries 6−10). In particular, the catalytic activity significantly dropped in the absence of acetic acid (Table 1, entry 7). Furthermore, no reaction occurred in the absence of silver carbonate (Table 1, entry 8). The former result suggests that the reaction may proceed via a concerted metalation−deprotonation (CMD) pathway at the stage of the palladation of imidazopyridine, which may allow it to react at relatively low acidic C−H bonds.[11]

Although the conditions required further optimization for each combination of the substrates, cross-coupling products **3b−g** were obtained in moderate to good yields (Chart 1).

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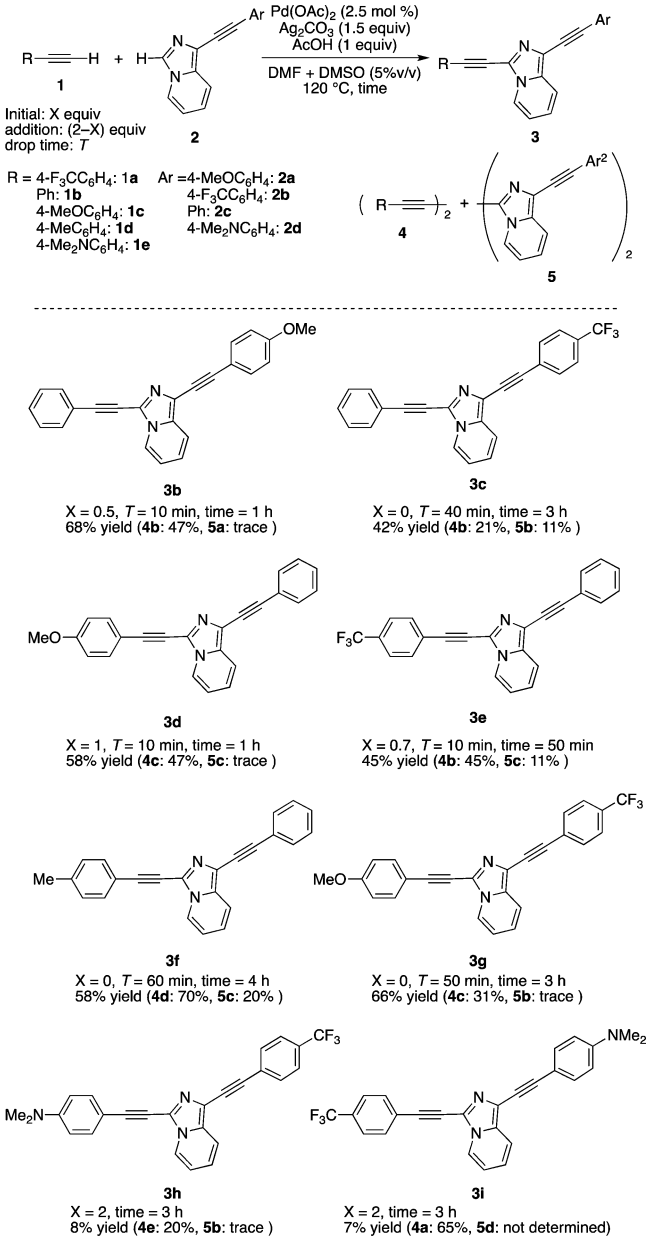
Chart 1. Scope of Substrates



In contrast, the cross-coupling reactions did not proceed well with substrates bearing a dimethylamino group (**1e** and **2d**) and gave a complex mixture.

The UV/vis and fluorescence spectra of the resulting 1,3-bis(arylethynyl)imidazo[1,5-*a*]pyridines were measured.[12] The results are summarized in Table S1 (Supporting Infomation). The photophysical properties of the imidazo[1,5-*a*]pyridines indicated that the arylethynyl groups clearly influence the emission maxima λ_{em}, though the influence of those on the absorption wavelength is unclear. In fact, the λ_{em} values of the 1,3-bis(arylethynyl)imidazo[1,5-*a*]pyridine derivatives still show linear correlations with the Hammett substituent constants σ of the substituents on the arylethynyl group on C1, as shown in Figure 2.[7] Gratifyingly, the arylethynyl groups on C3 also showed similar correlations, as we expected (Figure 3). The dual linear correlations may make it possible to obtain predictable photofunctional materials by careful selection of the substituents.

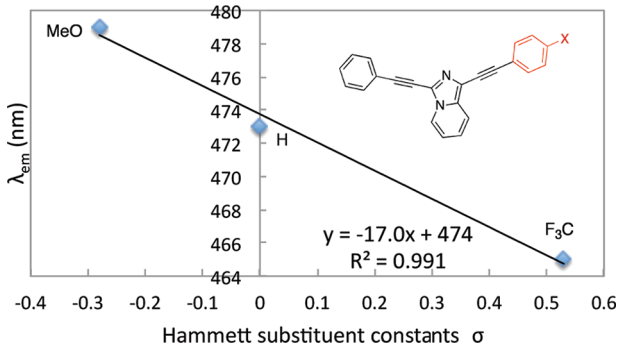


Figure 2. Correlation between fluorescence spectra and the Hammett substituent constants σ of the substituents on the arylethynyl group on C1 of bisalkynylated imidazo[1,5-*a*]pyridines.

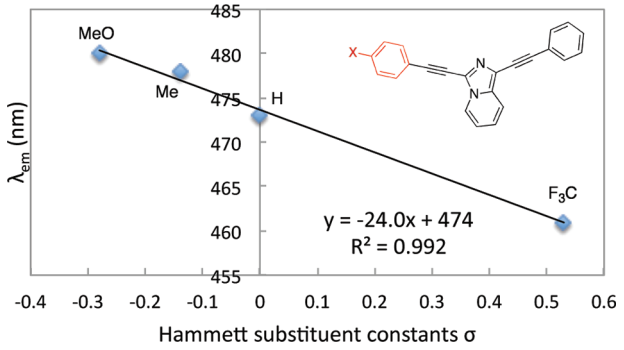
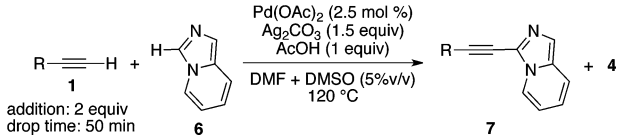


Figure 3. Correlation between fluorescence spectra and the Hammett substituent constants σ of the substituents on the arylethynyl group on C3 of bisalkynylated imidazo[1,5-*a*]pyridines.

Next, the reaction of unsubstituted imidazo[1,5-*a*]pyridine (**6**), which has two potentially reactive C–H bonds, was investigated. The results are summarized in Table 2. The reaction of **6** with arylacetylenes proceeded at C3 selectively to give the corresponding alkynylated products **7** in good yields regardless of the arylacetylenes (Table 2, entries 1–4). In this case, trace amounts of the imidazopyridine dimers were observed by GC mass analysis, whereas most of the remaining alkynes were recovered as their dimers. In addition, the reaction also coupled **6** and enyne **1f** in 53% yield (Table 2, entry 5).

Table 2. Oxidative Coupling of 6 and Terminal Alkynes[a]



entry	R	yields (%)[b] 7[c]		4[d]	
1	4-$F_3CC_6H_4$	**7a**	60	**4a**	44
2	Ph	**7b**	63	**4b**	42
3	4-$MeOC_6H_4$	**7c**	78	**4c**	18
4	4-MeC_6H_4	**7d**	67	**4d**	51
5	1-cyclohexenyl	**7f**	53	**4f**	21

[a]Reaction conditions: To a solution of imidazo[1,5-*a*]pyridine (**6**) (0.4 mmol), $Pd(OAc)_2$ (2.5 mol %), Ag_2CO_3 (1.5 equiv), and AcOH (1 equiv) in a mixture of DMF (0.9 mL) and DMSO (0.1 mL) was added dropwise a solution of **1** (2 equiv) in DMF (1 mL) over 50 min at 120 °C. [b]Isolated yields. [c]Based on imidazopyridine **2a**. [d]Based on alkyne **1**.

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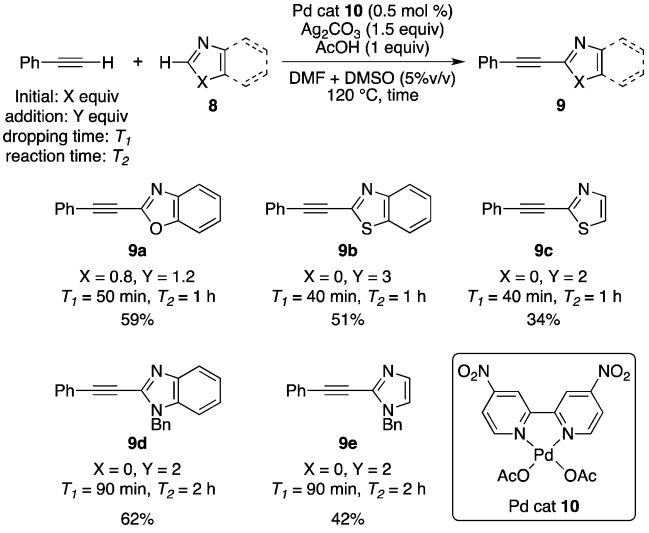
The scope of azoles was then investigated to probe the generality of the present catalytic system. The results are summarized in Chart 2. Prior to the investigations, we briefly

Chart 2. Oxidative Coupling of Phenylacetylene and Azoles 8

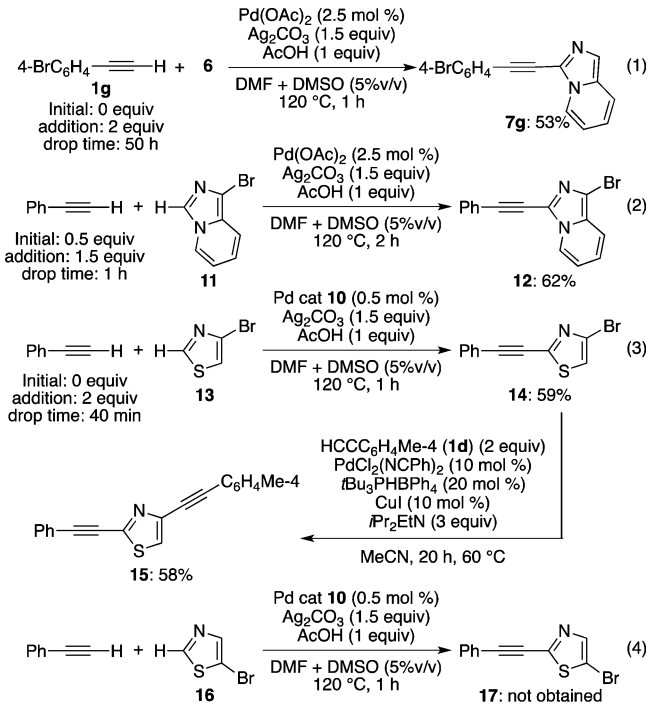


screened the catalyst as shown in Table S2 (Supporting Information)[13] and found that bi(4-nitropyridinyl)-Pd complex **10** was an efficient catalyst for the reaction even under low catalyst loading conditions, although the reaction conditions were not yet fully optimized. Under these conditions, the reaction proceeded at C−H bonds with relatively large pK_a values, which are sluggish or inert under previously reported conditions, such as *N*-benzylbenzimidazole (**9d**: pK_a of related *N*-methylbenzimidazole at C2: 32.5) and *N*-benzimidazole (**9e**: pK_a of *N*-methylimidazole at C2: 35.1), as well as benzoxazole (**9a**: pK_a at C2: 24.8), benzothiazole (**9b**: pK_a at C2: 27.3), and thiazole (**9c**: pK_a at C2: 29.5).[14]

Notably, the reaction tolerates halogen substituents on both substrates such as 4-bromophenylacetylene (**1g**), 1-bromoimidazo[1,5-*a*]pyridine (**11**), and 4-bromothiazole (**13**) to give the corresponding cross-coupling products **7g**, **12**, and **14** in good yields. The bromine atom remained intact under the reaction conditions, and no conventional Sonogashira coupling products were observed (eqs 1−3), although 5-bromothiazole (**16**) was inert and the starting **16** was recovered quantitatively (eq 4). The results probably indicated that reoxidation of the reduced Pd catalyst by the Ag salt is much faster than the oxidative addition of the halides under these conditions. Regarding chemoselectivity, an alternative synthetic route to the bisalkynylated compounds can also be achieved. For example, the obtained monoalkynylated bromothiazole **14** was readily alkynylated by conventional Sonogashira coupling conditions to give the bisalkynylated **15** in 58% yield (eq 3, lower).

CONCLUSION

In conclusion, a widely applicable direct oxidative coupling of azole derivatives and terminal alkynes has been developed through the use of a combination of Pd and Ag salts under the finely tuned dropwise addition of terminal alkynes. This catalytic system allowed us to easily access imidazo[1,5-*a*]-pyridines and thiazole containing two different alkynyl groups.



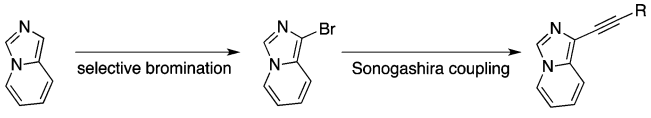
Further investigations of oxidative C−C bond-forming reactions and the application of bisalkynylated heteroarenes as functional materials are underway in our group.

EXPERIMENTAL SECTION

General Methods. The ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), and ^{19}F NMR (376 MHz) spectra were recorded in $CDCl_3$. Chemical shifts of ^{1}H and ^{13}C were reported in δ values referred to tetramethylsilane and $CDCl_3$ as an internal standard, respectively. The ^{19}F chemical shifts are expressed in δ value deshielded with respect to CF_3COOH as an external standard. The mass spectra (MS) and high resolution mass spectra (HRMS) were obtained by ionizing samples via electron ionization (EI) or fast atom bombardment (FAB) in positive mode with magnetic sector analyzer. All reactions were carried out in argon atmosphere.

Materials. Unless otherwise noted, reagents were commercially available and were used without further purifications. Complex **10**[15] was prepared according to the literature. Silica gel 60N (Spherical, Neutral, 40−50 mm) from Kanto Chemical Co., Inc. was used on flash column chromatography.

Synthesis of 1-Alkynylimidazo[1,5-*a*]pyridines (2).



Selective Bromination of Imidazo[1,5-*a*]pyridine (6). To a solution of imidazo[1,5-*a*]pyridine (**6**) (2.4 g, 3.1 mmol) in CH_2Cl_2 was added NBS (3.6 g, 1 equiv) at −78 °C under Ar atmosphere. The resulting mixture was stirred for 1.5 h at room temperature. The reaction mixture was quenched with $Na_2S_2O_3$ aq and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 4:1 then 2:1) to give 1-bromoimidazo[1,5-*a*]pyridine (**11**) (2.5 g, 60%), 3-bromoimidazo[1,5-*a*]pyridine (**18**) (0.92 g, 23%), and 1,3-dibromoimidazo[1,5-*a*]pyridine (**19**) (0.53 g, 17%).

1-Bromoimidazo[1,5-*a*]pyridine (11). Brownish solid: mp 79−80 °C, R_f = 0.20 (hexane/AcOEt = 4:1); IR (KBr) 3136, 3076, 3033,

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2363, 1770, 1632, 1266, 1003, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.53 (dd, J = 7.1, 6.6 Hz, 1H), 6.70 (dd, J = 9.2, 6.6 Hz, 1H), 7.29 (d, J = 9.2 Hz, 1H), 7.81 (d, J = 7.1 Hz, 1H), 7.96 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 113.6, 117.5, 117.6, 119.8, 119.8, 122.3, 126.5; MS (EI) m/z 196 (96, M^+), 198 (100, M^+ + 2); HRMS (EI) m/z calcd for $C_7H_5BrN_2$ (M^+), 195.9636, found 195.9631.

3-Bromoimidazo[1,5-*a*]pyridine (18). Yellow solid: mp 30−32 °C, R_f = 0.45 (hexane/AcOEt = 4:1); IR (KBr) 3445, 3087, 2360, 1928, 1776, 1739, 1632, 1505, 1396, 1261, 1026, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.65 (dd, J = 7.8, 7.3 Hz, 1H), 6.75 (dd, J = 8.8, 7.3 Hz, 1H), 7.40 (d, J = 8.8 Hz, 1H), 7.43 (s, 1H), 7.85 (d, J = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 107.9, 113.2, 118.0, 119.0, 120.5, 121.2, 132.5; MS (EI) m/z 196 (96, M^+), 198 (100, M^+ + 2); HRMS (EI) m/z calcd for $C_7H_5BrN_2$ (M^+), 195.9636, found 195.9638.

1,3-Dibromoimidazo[1,5-*a*]pyridine (19). Brownish solid: mp 129 °C, R_f = 0.55 (hexane/AcOEt = 4:1); IR (KBr) 2361, 1631, 1396, 1260, 1026, 955, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.71 (dd, J = 7.3, 6.3 Hz, 1H), 6.82 (dd, J = 9.3, 6.3 Hz, 1H), 7.35 (d, J = 9.3 Hz, 1H), 7.83 (d, J = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 104.7, 106.3, 114.3, 117.4, 120.0, 121.6, 130.5; MS (EI) m/z 274 (51, M^+), 276 (100, M^+ + 2); HRMS (EI) m/z calcd for $C_7H_4Br_2N_2$ (M^+), 273.8741, found 273.8735.

General Procedure for Sonogashira Coupling of 1-Bromoimidazo[1,5-*a*]pyridine. To a solution of 1-bromoimidazo-[1,5-*a*]pyridine (**11**) in MeCN (0.25 M) was added $PdCl_2(NCPh)_2$ (10 mol %), t-$Bu_3PH{\cdot}BPh_4$ (10 mol %), CuI (10 mol %), terminal alkyne (2 equiv), and i-Pr_2NEt (3 equiv) under Ar atmosphere. The resulting mixture was stirred at 60 °C for 24 h. The resulting mixture was cooled at room temperature and directly separated by flash column chromatography on silica gel (hexane/EtOAc = 2:1 then 1:1) to give 1-alkynylated imidazo[1,5-*a*]pyridine **2**.

1-(4-Methoxyphenylethynyl)imidazo[1,5-*a*]pyridine (2a). On 3 mmol scale, 86% yield (0.64 g), yellow solid: mp 70−79 °C, R_f = 0.20 (hexane/AcOEt = 1:1); IR (KBr) 3389, 2836, 2202, 1631, 1604, 1504, 1244, 1049 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.75 (s, 3H), 6.54 (dd, J = 8.0, 7.1, Hz, 1H), 6.76 (dd, J = 7.1, 6.8 Hz, 1H), 6.82 (d, J = 8.3 Hz, 2H), 7.46 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 6.8, 1H), 7.99 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 55.1, 81.1, 91.7, 113.4, 113.8, 114.5, 115.5, 118.2, 120.6, 122.6, 127.3, 132.6, 159.2 (some of peaks are overlapped); MS (EI) m/z 248; HRMS (EI) m/z calcd for $C_{16}H_{12}N_2O$ (M^+), 248.0950, found 248.0953.

1-(4-Trifluoromethylphenylethynyl)imidazo[1,5-*a*]pyridine (2b). On 3 mmol scale, quantitative yield (0.86 g), yellow solid: mp 127−129 °C, R_f = 0.28 (hexane/AcOEt = 1:1); IR (KBr) 3437, 3129, 3068, 2204, 1611, 1322, 1105, 1066 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.68 (dd, J = 7.1, 6.3 Hz, 1H), 6.92 (dd, J = 7.8, 7.1 Hz, 1H), 7.58 (d, J = 8.3 Hz, 2H), 7.65 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 6.3 Hz, 1H), 7.95 (d, J = 7.8 Hz, 1H), 8.10 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 85.4, 90.9, 113.6, 113.8, 118.1, 121.5, 122.8, 123.9 (q, J = 271.8 Hz), 125.1 (q, J = 3.3 Hz), 127.3, 127.8 (Ar), 129.2 (q, J = 32.2 Hz), 131.2, 133.; ^{19}F NMR ($CDCl_3$) −63.0; MS (EI) m/z 286 (M^+); HRMS (EI) m/z calcd for $C_{16}H_9F_3N_2$ (M^+), 286.0718, found 286.0727.

1-(Phenylethynyl)imidazo[1,5-*a*]pyridine (2c). On 2 mmol scale, 80% yield (0.35 g), yellow solid: mp 89−91 °C, R_f = 0.18 (hexane/AcOEt = 1:1); IR (KBr) 3124, 2202, 1597, 1487, 1335, 1239, 1047 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.63 (dd, J = 6.8, 6.6 Hz, 1H), 6.85 (dd, J = 9.0, 6.6 Hz, 1H), 7.32 (m, 3H), 7.56 (dd, J = 6.8 Hz, 2H), 7.64 (d, J = 9.0 Hz, 1H), 7.91 (d, J = 6.8 Hz, 1H), 8.05 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 82.7, 92.1, 113.7, 114.5, 118.4, 121.0, 122.7, 123.5, 127.5, 127.7, 127.8, 128.3, 131.3; MS (EI) m/z 218 (M^+); HRMS (EI) m/z calcd for $C_{15}H_{10}N_2$ (M^+), 218.0844, found 218.0836.

1-(4-*N*,*N*-Dimethylphenylethynyl)imidazo[1,5-*a*]pyridine (2d). On 1 mmol scale, quantitative yield (0.26 g), orange solid: mp 175−181 °C, R_f = 0.18 (hexane/AcOEt = 1:1); IR (KBr) 3466, 3114, 3036, 2919, 2359, 2199, 1603, 1515, 1358, 1048 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.92 (s, 6H), 6.54 (dd, J = 6.8, 6.6, Hz, 1H), 6.60 (d, J = 8.8 Hz, 2H), 6.74 (dd, J = 8.8, 6.6 Hz, 1H), 7.39 (d, J = 8.8 Hz, 2H), 7.57 (d, J = 8.8 Hz, 1H), 7.83 (d, J = 6.8 Hz, 1H), 7.98 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 40.2, 80.2, 92.9, 110.4, 111.8, 113.5, 115.3, 118.6, 120.2, 122.6, 127.2, 132.3, 132.5, 149.9; MS (EI) m/z 261 (M^+); HRMS (EI) m/z calcd for $C_{17}H_{15}N_3$ (M^+), 261.1266, found 261.1269.

General Procedure for the Oxidative Coupling of 1-Alkynylimidazo[1,5-*a*]pyridines and Terminal Alkynes (Table 1 and Chart 1). To a solution of 1-arylethynylimidazo[1,5-*a*]pyridines (0.4 mmol), $Pd(OAc)_2$ (2.5 mol %), Ag_2CO_3 (150 mol %), AcOH (100 mol %), and terminal alkynes (X equiv) in a mixture of DMF (0.6 mL) and DMSO (0.08 mL) was added dropwise a solution of terminal alkynes (2−X equiv) in DMF (1.0 mL) over T min at 120 °C. The resulting mixture was cooled at room temperature, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to give bisalkynylated imidazo[1,5-*a*]pyridines **3**.

1-(4-Methoxyphenyl)ethynyl)-3-(4-trifluoromethylphenylethynyl)imidazo[1,5-*a*]pyridine (3a). 80% yield (0.133 g), yellow solid: mp 211−214 °C, R_f = 0.24 (hexane/AcOEt = 4:1); IR (KBr) 3445, 3069, 3001, 2934, 2834, 2360, 2342, 2204, 1605, 1499, 1321, 1244, 1126, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.81 (s, 3H), 6.82 (t, J = 6.8 Hz, 1H), 6.86 (d, J = 8.8 Hz, 2H), 6.98 (dd, J = 8.3, 6.8 Hz, 1H), 7.49 (d, J = 8.8 Hz, 2H), 7.61 (d, J = 8.3 Hz, 2H), 7.66 (d, J = 8.3 Hz, 2H), 7.69 (d, J = 8.3 Hz, 1H), 8.20 (d, J = 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.3, 80.0, 80.4, 92.2, 94.4, 114.0, 114.9, 115.2, 116.5, 118.7, 121.4, 122.3, 123.1, 123.8 (q, J = 271.8 Hz), 125.4, 125.5 (q, J = 4.1 Hz), 130.5 (q, J = 33.0 Hz), 131.6, 132.9, 133.4, 159.6; ^{19}F NMR ($CDCl_3$) δ −63.2; MS (EI) m/z 416 (M^+); HRMS (EI) m/z calcd for $C_{25}H_{15}F_3N_2O$ (M^+), 416.1136, found 416.1123.

1-(4-Methoxyphenylethynyl)-3-(phenylethynyl)imidazo[1,5-*a*]pyridine (3b). 68% yield (0.095 g), orange solid: mp 181−183 °C, R_f = 0.22 (hexane/AcOEt = 4:1); IR (KBr) 3451, 2925, 2853, 2204, 1603, 1500, 1248 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.80 (s, 3H), 6.78 (dd, J = 7.1, 6.3 Hz, 1H), 6.86 (d, J = 8.8 Hz, 2H), 6.94 (dd, J = 8.8, 6.3 Hz, 1H), 7.35−7.37 (m, 3H), 7.50 (d, J = 8.8 Hz, 2H), 7.57−7.60 (m, 2H), 7.66 (d, J = 8.8 Hz, 1H), 8.17 (d, J = 7.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.3, 77.6, 80.7, 92.0, 95.7, 113.9, 114.5, 115.3, 115.9, 118.5, 121.7, 121.9, 122.1, 123,1, 128.5, 129.1, 131.6, 132.9, 133.1, 159.5; MS (EI) m/z 348 (M^+); HRMS (EI) m/z calcd for $C_{24}H_{16}N_2O$ (M^+), 348.1263, found 348.1258.

3-(Phenylethynyl)-1-(4-trifluoromethylphenylethynyl)-imidazo[1,5-*a*]pyridine (3c). 42% yield (0.065 g), yellow solid: mp 196−199 °C, R_f = 0.32 (hexane/AcOEt = 4:1); IR (KBr) 3451, 3049, 2924, 2854, 2204, 1613, 1322, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.85 (dd, J = 7.0, 6.6 Hz, 1H), 7.04 (dd, J = 9.0, 6.6 Hz, 1H), 7.38−7.39 (m, 3H), 7.58−7.62 (m, 3H), 7.65 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 9.0 Hz, 2H), 8.23 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 77.3, 84.9, 91.0, 95.9, 114.7, 114.8, 118.3 121.5, 122.7, 122.8, 123.4, 124.0 (q, J = 270.9 Hz), 125.3 (q, J = 4.1 Hz), 127.1, 128.6, 129.3, 129.5 (q, J = 32.1 Hz), 131.4, 131.7, 133.9; ^{19}F NMR ($CDCl_3$) δ −63.1; MS (EI) m/z 386 (M^+); HRMS (EI) m/z calcd for $C_{24}H_{13}F_3N_2$ (M^+), 386.1031, found 386.1031.

3-(4-Methoxyphenylethynyl)-1-(phenylethynyl)imidazo[1,5-*a*]-pyridine (3d). 58% yield (0.081 g), yellow solid: mp 182−184 °C, R_f = 0.20 (hexane/AcOEt = 4:1); IR (KBr) 3458, 2930, 2838, 2360, 2341, 2201, 1603, 1513, 1294, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.83 (s, 3H), 6.79 (dd, J = 7.0, 6.6 Hz, 1H), 6.90 (d, J = 8.7 Hz, 2H), 6.97 (dd, J = 9.0, 6.6 Hz, 1H), 7.33 (m, 3H), 7.54 (d, J = 8.7 Hz, 2H), 7.56 (d, J = 8.1 Hz, 2H), 7.69 (d, J = 9.0 Hz, 1H), 8.19 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.3, 76.3, 82.3, 92.1, 95.8, 113.7, 114.2, 114.4, 115.3, 118.4, 122.0, 123.2, 123.3, 128.0, 128.3, 128.3, 131.3, 131.4, 133.3, 160.3; MS (EI) m/z 348 (M^+); HRMS (EI) m/z calcd for $C_{24}H_{16}N_2O$ (M^+), 348.1263, found 348.1281.

1-(Phenylethynyl)-3-(4-trifluoromethylphenylethynyl)-imidazo[1,5-*a*]pyridine (3e). 45% yield (0.070 g), Yellow solid: mp 187−191 °C, R_f = 0.35 (hexane/AcOEt = 4:1); IR (KBr) 3454, 3044, 2361, 2206, 1611, 1514, 1323, 1126, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.86 (dd, J = 7.0, 6.6 Hz, 1H), 7.03 (dd, J = 9.0, 6.6 Hz, 1H), 7.29−7.37 (m, 3H), 7.57 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 8.3 Hz, 2H), 7.69 (d, J = 8.3 Hz, 2H), 7.73 (d, J = 9.0 Hz, 1H), 8.22 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 79.9, 81.9, 92.3, 94.4, 114.9, 116.2, 118.7, 121.6, 122.6, 123.1, 123.2, 123.8 (q, J = 272.0 Hz), 122.5, 122.5 (q, J = 3.9 Hz), 128.2, 128.4, 130.6 (q, J = 33.0 Hz), 131.4, 131.7, 133.7; ^{19}F NMR

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($CDCl_3$) δ −63.2; MS (EI) m/z 386 (M^+); HRMS (EI) m/z calcd for $C_{24}H_{13}F_3N_2$ (M^+), 386.1031, found 386.1033.

1-(Phenylethynyl)-3-(*p*-tolylethynyl)imidazo[1,5-*a*]pyridine (3f). 58% (0.077 g), Yellow solid: mp 173−175 °C, R_f = 0.35 (hexane/AcOEt = 4:1); IR (KBr) 3448, 3048, 2915, 2360, 2205, 1751, 1628, 1512, 1309, 1246, 746 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.29 (s, 3H), 6.81 (dd, J = 6.8, 6.6 Hz, 1H), 6.99 (dd, J = 8.8, 6.6 Hz, 1H), 7.10 (d, J = 7.8 Hz, 2H), 7.32−7.38 (m, 3H), 7.51 (d, J = 7.8 Hz, 2H), 7.58 (d, J = 7.3 Hz, 2H), 7.71 (d, J = 8.8 Hz, 1H), 8.21 (d, J = 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.6, 76.8, 82.2, 92.1, 96.0, 114.4, 115.4, 118.4, 118.5, 122.1, 122.5, 123.1, 123.3, 128.0, 128.2, 129.2, 131.3, 131.5, 133.4, 139.5; MS (FAB) m/z 333 (M + H^+); HRMS (FAB) m/z calcd for $C_{24}H_{17}N_2$ (M + H^+), 333.1393, found 333.1378.

3-(4-Methoxyphenylethynyl)-1-(4-trifluoromethylphenylethynyl)imidazo[1,5-*a*]pyridine (3g). 66% yield (0.110 g), yellow solid: mp 230−233 °C, R_f = 0.23 (hexane/AcOEt = 4:1); IR (KBr) 3445, 2924, 2854, 2204, 1606, 1517, 1322, 1118, 1064 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.83 (s, 3H), 6.82 (dd, J = 7.0, 6.7 Hz, 1H), 6.90 (d, J = 8.8 Hz, 2H), 7.01 (dd, J = 9.0, 6.7 Hz, 1H), 7.54 (d, J = 8.8 Hz, 2H), 7.58 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 8.3 Hz, 2H), 7.70 (d, J = 9.0 Hz, 1H), 8.21 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.4, 76.1, 85.0, 91.0, 96.0, 113.5, 114.2, 114.2, 114.6, 118.3, 122.6, 123.1, 123.4, 124.0 (q, J = 271.8 Hz), 125.3 (q, J = 4.1 Hz), 127.2, 129.5 (q, J = 32.5 Hz), 131.4, 133.4, 133.8, 160.4; ^{19}F NMR ($CDCl_3$) δ −63.1; MS (EI) m/z 416 (M^+); HRMS (EI) m/z calcd for $C_{25}H_{15}F_3N_2O$ (M^+), 416.1136, found 416.1134.

3-(4-*N*,*N*-Dimetylethynyl)-1-(4-trifluoromethylphenylethynyl)-imidazo[1,5-*a*]pyridine (3h). 8% yield (0.014 g), yellow solid: mp 238−242 °C, R_f = 0.18 (hexane/AcOEt = 4:1); IR (KBr) 3455, 2925, 2359, 2341, 2198, 1606, 1532, 1321, 1118, 1064 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.00 (s, 6H), 6.66 (d, J = 8.8 Hz, 2H), 6.89 (dd, J = 6.8, 6.4 Hz, 1H), 6.99 (dd, J = 8.8, 6.4 Hz, 1H), 7.47 (d, J = 8.8 Hz, 2H), 7.58 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 8.8 Hz, 1H), 8.20 (d, J = 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 40.1, 75.4, 85.3, 90.9, 97.5, 107.8, 111.7, 114.2, 114.3, 118.3, 122.4, 123.5, 123.8, 124.0 (q, J = 271.8 Hz), 125.2 (q, J = 4.1 Hz), 127.3, 129.4 (q, J = 32.2 Hz), 131.3, 133.1, 133.7, 150.7; ^{19}F NMR ($CDCl_3$) δ −63.1; MS (EI) m/z 429 (M^+); HRMS (EI) m/z calcd for $C_{26}H_{18}F_3N_3$ (M^+), 429.1453, found 429.1454.

1-(4-*N*,*N*-Dimetylphenylethynyl)-3-(4-trifluoromethylphenylethynyl)imidazo[1,5-*a*]pyridine (3i). 7% yield (0.012 g), yellow solid: mp 231−235 °C, R_f = 0.33 (hexane/AcOEt = 4:1); IR (KBr) 3437, 2924, 2201, 1606, 1532, 1321, 1231, 1166 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.98 (s, 6H), 6.66 (d, J = 8.5 Hz, 2H), 6.82 (dd, J = 6.8, 6.3 Hz, 1H), 6.97 (dd, J = 8.8, 6.3 Hz, 1H), 7.45 (d, J = 8.5 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H), 7.68 (d, J = 8.3 Hz, 2H), 7.71 (d, J = 8.8 Hz, 1H), 8.19 (d, J = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 40.2, 79.6, 80.2, 93.4, 94.4, 109.8, 111.8, 114.8, 117.2, 118.9, 121.2, 121.9, 123.0, 123.8 (q, J = 271.8 Hz), 125.5 (q, J = 3.7 Hz), 125.7, 130.5 (q, J = 33.0 Hz), 131.6, 132.7, 133.1, 150.1; ^{19}F NMR ($CDCl_3$) δ −63.2; MS (EI) m/z 429 (M^+); HRMS (EI) m/z calcd for $C_{26}H_{18}F_3N_3$ (M^+), 429.1453, found 429.1445.

1,1′-Bis(4-methoxyphenylethynyl)-3,3′-biimidazo[1,5-*a*]-pyridinyl (5a). 14% yield (0.014 g), brownish solid: mp 257−264 °C, R_f = 0.3 (hexane/AcOEt = 4:1); IR (KBr) 3436, 3113, 2924, 2853, 2202, 1605, 1499, 1250, 827 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.83 (s, 6H), 6.85 (dd, J = 6.8, 6.6, Hz, 2H), 6.90 (d, J = 8.8 Hz, 4H), 7.03 (dd, J = 9.0, 6.6 Hz, 2H), 7.56 (d, J = 8.8 Hz, 4H), 7.75 (d, J = 9.0 Hz, 2H), 9.92 (d, J = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 55.3, 81.1, 92.6, 114.0, 114.4, 115.4, 117.9, 122.2, 126.3, 129.0, 129.9, 133.0, 133.8, 159.5; MS (EI) m/z 494 (M^+); HRMS (EI) m/z calcd for $C_{32}H_{22}N_4O_2$ (M^+), 494.1743, found 494.1744.

1,1′-Bis(4-trifluoromethylphenylethynyl)-3,3′-biimidazo-[1,5-*a*]pyridinyl (5b). 11% yield (0.013 g), yellow solid: mp 268−269 °C, R_f = 0.53 (hexane/AcOEt = 4:1); IR (KBr) 3446, 3110, 2925, 2201, 1611, 1499, 1328, 1171, 1119, 756 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.93 (dd, J = 7.6, 6.1 Hz, 2H), 7.11 (dd, J = 9.3, 6.1 Hz, 2H), 7.62 (d, J = 8.3 Hz, 4H), 7.71 (d, J = 8.3 Hz, 4H), 7.78 (d, J = 9.3 Hz, 2H), 9.95 (d, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 85.3, 91.7, 113.6, 114.8, 117.8, 123.1 (Ar), 124.0 (q, J = 271.8 Hz), 125.3 (q, J = 3.3 Hz), 126.5, 127.2, 129.2, 129.3 (q, J = 31.9 Hz), 131.4, 134.7; ^{19}F NMR ($CDCl_3$) δ −63.0; MS (FAB) m/z 571 (M + H^+); HRMS (FAB) m/z calcd for $C_{32}H_{17}F_6N_4$ (M + H^+), 571.1357, found 571.1344.

1,1′-Bis(phenylethynyl)-3,3′-biimidazo[1,5-*a*]pyridinyl (5c). 20% yield (0.017 g), yellow solid: mp 226−227 °C, R_f = 0.33 (hexane/AcOEt = 4:1); IR (KBr) 3465, 3103, 3077, 2359, 2341, 2203, 1627, 1510, 1488, 1329, 1242, 749 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.88 (dd, J = 6.8, 6.6, Hz, 2H), 7.06 (dd, J = 8.8, 6.8 Hz, 2H), 7.35 (m, 6H), 7.63 (d, J = 6.8 Hz, 4H), 7.78 (d, J = 8.8 Hz, 2H), 9.94 (d, J = 6.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 82.6, 92.8, 114.2, 114.5, 117.8, 122.5, 123.3, 126.3, 128.1, 128.4, 129.1, 131.5, 134.1; MS (FAB) m/z 435 (M + H^+); HRMS (FAB) m/z calcd for $C_{30}H_{19}N_4$ (M + H^+), 435.1610, found 435.1630.

General Procedure for the Oxidative Coupling of Unsubstituted Imidazo[1,5-*a*]pyridine and Terminal Alkynes (6) (Table 2). To a solution of imidazo[1,5-*a*]pyridine (**6**) (0.5 mmol), $Pd(OAc)_2$ (2.5 mol %), Ag_2CO_3 (150 mol %), and AcOH (100 mol %) in a mixture of DMF (1.0 mL) and DMSO (0.010 mL) was added dropwise a solution of terminal alkyne (2 equiv) in the DMF (1.0 mL) over 50 min at 120 °C. The resulting mixture was cooled at room temperature, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to give 3-alkynylated imidazo[1,5-*a*]pyridines **7**.

3-(4-Trifluoromethylphenylethynyl)imidazo[1,5-*a*]pyridine (7a). 60% yield (0.086 g), colorless solid: mp 115−118 °C, R_f = 0.15 (hexane/AcOEt = 4:1); IR (KBr) 3446, 3068, 2359, 2199, 1611, 1501, 1321, 1114, 1067, 736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.77 (dd, J = 7.1, 6.6 Hz, 1H), 6.88 (dd, J = 8.8, 6.6 Hz, 1H), 7.52 (s, 1H), 7.52(d, J = 8.8 Hz, 1H), 7.62 (d, J = 8.3 Hz, 2H), 7.69 (d, J = 8.3 Hz, 2H), 8.20 (d, J = 7.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 80.6, 94.4, 114.0, 118.6, 120.8, 121.8, 121.9, 122.7, 123.8 (q, J = 271.8 Hz), 125.4 (q, J = 3.9 Hz), 125.9, 130.3 (q, J = 32.8 Hz), 131.5, 131.5; ^{19}F NMR ($CDCl_3$) δ −63.2; MS (EI) m/z 286 (M^+); HRMS (EI) m/z calcd for $C_{16}H_9F_3N_2$ (M^+), 286.0718, found 286.0719.

3-(Phenylethynyl)imidazo[1,5-*a*]pyridine (7b). 63% yield (0.069 g), orange solid: mp 99−102 °C, R_f = 0.18 (hexane/AcOEt = 4:1); IR (KBr) 3457, 3107, 3086, 2929, 2214, 1920, 1786, 1631, 1497, 1348, 1246, 1049, 766 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.72 (dd, J = 7.3, 6.8 Hz, 1H), 6.82 (dd, J = 9.3, 6.8 Hz, 1H), 7.34−7.37 (m, 3H), 7.48 (d, J = 6.8 Hz, 2H), 7.58−7.60 (m, 2H), 8.18 (d, J = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 78.1, 95.6, 113.6, 118.3, 120.3, 121.1, 121.9, 122.5, 128.3, 128.7, 131.0, 131.3, 131.4; MS (EI) m/z 218 (M^+); HRMS (EI) m/z calcd for $C_{15}H_{10}N_2$ (M^+), 218.0844, found 218.0837.

3-(4-Methoxyphenylethynyl)imidazo[1,5-*a*]pyridine (7c). 78% yield (0.097 g), brownish solid: mp 107−110 °C, R_f = 0.30 (hexane/AcOEt = 4:1); IR (KBr) 3447, 3094, 2844, 2543, 2359, 2203, 1884, 1604, 1519, 1254, 1024, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.80 (s, 3H) 6.67 (dd, J = 7.1, 6.8 Hz, 1H), 6.78 (dd, J = 7.8, 7.1 Hz, 1H), 6.87 (d, J = 8.8 Hz, 2H), 7.44 (d, J = 8.8 Hz, 2H), 7.50 (s, 1H), 7.51 (d, J = 7.8 Hz, 1H), 8.14 (d, J = 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.3, 76.8, 95.6, 113.4, 114.0, 114.1, 118.3, 120.1, 121.0, 122.6, 122.7, 130.9, 133.1, 160.1; MS (EI) m/z 248 (M^+); HRMS (EI) m/z calcd for $C_{16}H_{12}N_2O$ (M^+), 248.0950, found 248.0949.

3-(*p*-Tolylethynyl)imidazo[1,5-*a*]pyridine (7d). 67% yield (0.078 g), orange solid: mp 105−110 °C, R_f = 0.18 (hexane/AcOEt = 4:1); IR (KBr) 3444, 2916, 2198, 1631, 1519, 1502, 1353, 1248, 807 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.32 (s, 3H) 6.65 (dd, J = 6.6, 5.6 Hz, 1H), 6.76 (dd, J = 7.3, 6.6 Hz, 1H), 7.13 (d, J = 7.8 Hz, 2H), 7.41−7.47 (m, 4H), 8.11 (d, J = 5.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.5, 77.5, 95.8, 113.5, 118.3, 118.9, 120.2, 121.1, 122.5, 129.1, 130.9, 131.3, 131.3, 139.1; MS (EI) m/z 232 (M^+); HRMS (EI) m/z calcd for $C_{16}H_{12}N_2$ (M^+), 232.1000, found 232.1008.

3-(Cyclohex-1-en-1-ylethynyl)imidazo[1,5-*a*]pyridine (7f). 53% yield (0.059 g), brown oil: R_f = 0.30 (hexane/AcOEt = 4:1); IR (KBr) 3402, 2931, 2858, 2168, 1631, 1503, 1349, 1247, 797, 740, 678 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.59−1.72 (m, 4H), 2.14−2.19 (m, 2H), 2.25−2.30 (m, 2H), 6.33−6.35 (m, 1H), 6.68 (dd, J = 7.1, 5.9 Hz, 1H), 6.80 (dd, J = 9.3, 5.9 Hz, 1H), 7.45−7.47 (m, 2H), 8.07 (d, J = 7.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.4, 22.2, 25.8, 28.8, 75.5, 97.5, 113.3, 118.3, 119.9, 120.0, 120.9, 122.6, 122.9, 130.8, 136.7; MS

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(EI) m/z 222 (M^+); HRMS (EI) m/z calcd for $C_{15}H_{14}N_2$ (M^+), 222.1157, found 222.1147.

3-(4-Bromophenylethynyl)imidazo[1,5-*a*]pyridine (7g). 62% yield (0.092 g), brownish solid: mp 127−130 °C, R_f = 0.23 (hexane/AcOEt = 4:1); IR (KBr) 3443, 2924, 2853, 2203, 1631, 1503, 1454, 1351, 1249, 823 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.78 (t, J = 6.8 Hz, 1H), 6.89 (dd, J = 8.8, 6.8 Hz, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.50−7.54 (m, 4H), 8.19 (d, J = 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 79.3, 94.7, 113.8, 118.5, 120.5, 121.0, 121.5, 122.6, 123.1, 131.7, 132.7 (some of peaks are overlapped); MS (EI) m/z 296 (100, M^+), 298 (98, M^+ + 2); HRMS (EI) m/z calcd for $C_{15}H_9BrN_2$ (M^+), 295.9949, found 295.9948.

General Procedure for the Oxidative Coupling of Azoles and Phenylacetylene (Chart 2). To a solution of azoles (0.5 mmol), Pd cat **10** (0.5 mol %), Ag_2CO_3 (150 mol %), AcOH (100 mol %), and phenylacetylene (X equiv) in a mixture of DMF (1.0 mL) and DMSO (0.1 mL) was added dropwise a solution of terminal alkyne (2−X equiv) in DMF (1.0 mL) in T min at 120 °C. The resulting mixture was cooled at room temperature, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to give coupling products.

2-(Phenylethynyl)benzo[*d*]oxazole (9a). The compound was identified by comparison with ^1H NMR data of previous report.[16] 59% yield (0.065 g): ^1H NMR ($CDCl_3$) δ 7.35−7.47 (m, 5H), 7.53 (d, J = 7.3 Hz, 2H), 7.65 (d, J = 8.3 Hz, 1H), 7.74 (d, J = 8.5 Hz, 1H).

2-(Phenylethynyl)benzo[*d*]thiazole (9b). The compound was identified by comparison with ^1H NMR data of previous report.[16] 51% yield (0.060 g): ^1H NMR ($CDCl_3$) δ 7.38−7.53 (m, 5H), 7.63 (dd, J = 7.8 Hz, 2H), 7.85 (d, J = 8.3 Hz, 1H), 8.06 (d, J = 7.8 Hz, 1H).

2-(Phenylethynyl)thiazole (9c). The compound was identified by comparison with ^1H NMR data of previous report.[17] 34% yield (0.031 g): ^1H NMR ($CDCl_3$) δ 7.36−7.39 (m, 4H), 7.63 (dd, J = 7.8 Hz, 2H), 7.56−7.59 (m, 2H), 7.84 (d, J = 2.9 Hz, 1H).

1-Benzyl-2-(phenylethynyl)-1*H*-benzo[*d*]imidazole (9d). 62% yield (0.095 g), colorless solid: mp 175−177 °C, R_f = 0.20 (hexane/AcOEt = 4:1); IR (KBr) 3436, 3059, 3030, 2925, 2360, 1675, 1596, 1496, 1450, 1398, 745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.53 (s, 2H), 7.26−7.43 (m, 11H), 7.59 (d, J = 6.3 Hz, 2H), 7.80 (d, J = 6.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 48.3, 78.8, 95.1, 110.1, 120.2, 121.0, 123.0, 124.0, 127.0, 128.0, 128.5, 128.8, 129.7, 132.0, 134.1, 135.7, 137.4, 143.1; MS (EI) m/z 308 (M^+); HRMS (EI) m/z calcd for $C_{22}H_{16}N_2$ (M^+), 308.1313, found 308.1311.

1-Benzyl-2-(phenylethynyl)-1*H*-imidazole (9e). 42% yield (0.054 g), colorless solid: mp 59−61 °C, R_f = 0.38 (hexane/AcOEt = 1:1); IR (KBr) 3437, 3137, 3031, 2928, 2353, 2218, 1956, 1886, 1810, 1513, 1454, 1281, 1119, 755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.28 (s, 2H), 6.94 (s, 1H), 7.13 (s, 1H), 7.24−7.26 (m, 2H), 7.33−7.39 (m, 6H), 7.51−7.54 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 50.5, 78.6, 92.8, 120.4, 121.6, 127.4, 128.1, 128.3, 128.8, 129.0, 130.0, 131.6, 132.1, 136.0; MS (EI) m/z 258 (M^+); HRMS (EI) m/z calcd for $C_{18}H_{14}N_2$ (M^+), 258.1157, found 258.1158.

4-Bromo-2-(phenylethynyl)thiazole (14). The compound was identified by comparison with ^1H NMR data of previous report.[4b] 59% yield (0.087 g): ^1H NMR ($CDCl_3$) δ 7.24 (s, 1H), 7.34−7.40 (m, 3H), 7.55−7.57 (m, 2H).

2-(Phenylethynyl)-4-(*p*-tolylethynyl)thiazole (15). To a solution of 4-bromo-2-(phenylethynyl)thiazole (**14**) (0.080 g, 0.3 mmol) in MeCN (1.2 mL) were added $PdCl_2(NCPh)_2$ (0.012 g, 10 mol %), tBu$_3$PH·BPh$_4$ (0.031 g, 20 mol %), CuI (0.0060 g, 10 mol %), 4-ethynyltoluene (0.076 mL, 2 equiv), and iPr$_2$NEt (0.16 mL, 3 equiv) under Ar atmosphere. The resulting mixture was stirred at 60 °C for 20 h. The resulting mixture was cooled at room temperature and purified by flash column chromatography on silica gel (hexane/EtOAc = 20:1 then 10:1) to give 2-(phenylethynyl)-4-(*p*-tolylethynyl)thiazole (**15**) (0.052 g, 58%) as a colorless solid: mp 140−142 °C, R_f = 0.35 (hexane/AcOEt = 10:1); IR (KBr) 3466, 3105, 2924, 2854, 2359, 2211, 1518, 1468, 1091, 818 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.35 (s, 3H), 7.15 (d, J = 7.8 Hz, 2H), 7.35−7.40 (m, 3H), 7.44 (d, J = 7.8 Hz, 2H), 7.48 (s, 1H), 7.58 (d, J = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.5, 81.9, 82.2, 89.6, 94.3, 119.0, 121.1, 123.3, 128.5, 129.1, 129.7, 131.7, 132.0, 138.5, 139.1, 148.2; MS (EI) m/z 299 (M^+); HRMS (EI) m/z calcd for $C_{20}H_{13}NS$ (M^+), 299.0769, found 299.0776.

Synthesis of 1,3-Bis(phenylethynyl)imidazo[1,5-*a*]pyridine (20) That Appeared in Figures 2 and 3. To a solution of 1,3-dibromoimidazo[1,5-*a*]pyridine (**19**) (0.5 mmol, 0.138 g) in MeCN (4 mL) were added $PdCl_2(NCPh)_2$ (0.038 g, 20 mol %), tBu$_3$PH·BPh$_4$ (0.105 g, 40 mol %), CuI (0.019 g, 20 mol %), phenylacetylene (0.220 mL, 4 equiv), and iPr$_2$NEt (0.522 μL, 6 equiv) under Ar atmosphere. The resulting mixture was stirred at 60 °C for 24 h. The resulting mixture was cooled at room temperature and directly purified by flash column chromatography on silica gel (hexane/EtOAc = 2:1 then 1:1) to give a 1,3-bis(phenylethynyl)imidazo[1,5-*a*]pyridine (**20**) (0.040 g, 25%) as a yellow solid: mp 160−162 °C, R_f = 0.38 (hexane/AcOEt = 4:1); IR (KBr) 3448, 3050, 2924, 2854, 2204, 1627, 1596, 1487, 1309, 1243, 753, 689 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.82 (t, J = 6.8 Hz, 1H), 7.00 (dd, J = 9.0, 6.8 Hz, 1H), 7.33−7.39 (m, 6H), 7.56−7.62 (m, 4H), 7.72 (d, J = 9.0 Hz, 1H), 8.22 (d, J = 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 77.5, 82.2, 92.2, 95.8, 114.6, 115.6, 118.5, 121.7, 122.2, 123.2, 123.3, 128.1, 128.3, 128.5, 129.2, 131.4, 131.6 (some of peaks are overlapped); MS (EI) m/z 318 (M^+); HRMS (EI) m/z calcd for $C_{23}H_{14}N_2$ (M^+), 318.1157, found 318.1148.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Tables S1 and S2, copies of NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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