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Zinc-Mediated One-Pot Tandem Reaction of Nitriles with Propargyl Bromides: An Access to 3-Alkynylpyridines

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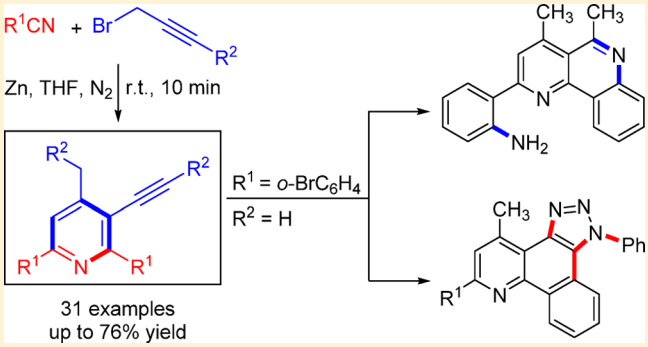
Supporting Information

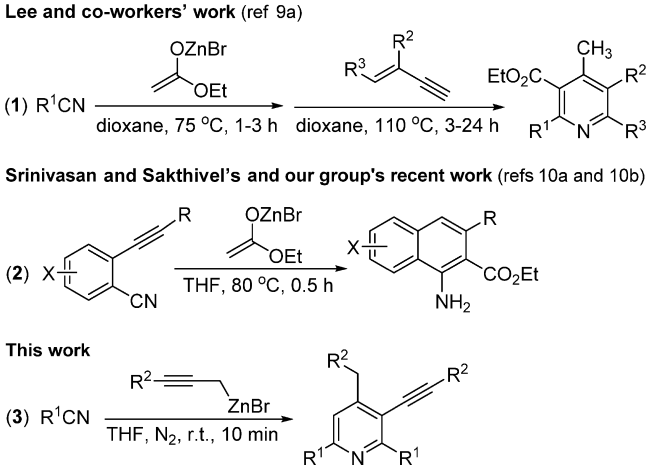
ABSTRACT: A one-pot procedure for the synthesis of 3-alkynylpyridines via a zinc-mediated tandem reaction of nitriles with propargyl bromides under extremely mild reaction conditions has been developed. This reaction exhibits high efficiency, broad substrate scope, and good functional group tolerance. In addition, the 3-alkynylpyridines obtained herein were found to be versatile and convenient intermediates for the preparation of fused-heterocyclic compounds with potential biological and material interests.



Pyridine derivatives possess a wide range of biological activities and often act as versatile building blocks in a plethora of natural products and pharmaceuticals.[1−3] Moreover, pyridines have also been utilized as transition-metal ligands[4] and highly sensitive analytical agents.[5] As a result, numerous methods for the construction of the pyridine skeleton have been developed, which include the classical Hantzsch reaction,[6] aza-Diels−Alder reaction of 1- or 2-azadiene with dienophiles,[7] and [2 + 2 + 2] cycloaddition of nitriles with alkynes.[8] While these methods are generally effective and reliable, some of them still suffer from harsh reaction conditions, prolonged reaction time, use of precious metal catalysts, and/or low yields. Therefore, the development of more efficient and convenient synthetic routes toward functionalized pyridines still remains a hot topic.

Organozinc compounds have attracted much attention in the development of novel tandem reactions due to their versatile reactivity and good functional group tolerance.[9] In this regard, Lee and co-workers have developed an elegant methodology for the synthesis of polysubstituted pyridines through a one-pot, three-component reaction of nitriles with Reformatsky reagent and 1,3-enynes (Scheme 1, eq 1).[9a] Very recently, Srinivasan and Sakthivel[10a] and our group[10b] have independently disclosed an efficient tandem reaction of 2-alkynylbenzonitriles with Reformatsky reagent leading to naphthalene amino esters (Scheme 1, eq 2). As a continuation of our study in this aspect, we found that the zinc-mediated four-component reaction of two nitriles with two propargyl bromides led to an efficient and straightforward access to 3-alkynylpyridines (Scheme 1, eq 3). It is noteworthy that this one-pot cascade reaction involved the formation of three C−C and one C−N bonds with good selectivity. Moreover, compared with Lee and co-workers' pyridine synthesis and Srinivasan and Sakthivel's and our naphthalene amino ester synthesis, the formation of 3-alkynylpyridines could be realized under much milder reaction conditions, indicating that propargylzinc reagents possess higher reactivity toward nitriles than Reformatsky reagent.

Scheme 1. Reactions of Nitriles with Organozinc Reagents



Initially, benzonitrile (**1a**) and 3-bromoprop-1-yne (**2a**) were employed as model substrates to optimize the reaction conditions (Table 1). Treatment of a mixture of **1a** (0.5 mmol) and **2a** (0.5 mmol) with activated zinc (0.5 mmol) in THF (1 mL) at room temperature under a nitrogen

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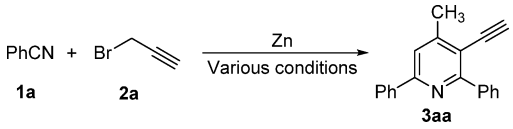
Table 1. Optimization Studies of Zinc-Mediated One-Pot Synthesis of 3aa[a]



1a 2a 3aa

entry	2a (mmol)	Zn (mmol)	T (°C)	solvent	t (min)	yield (%)[b]
1	0.5	0.5	r.t.	THF	10	58
2	0.5	1	r.t.	THF	10	63
3	0.5	1.5	r.t.	THF	10	61
4	0.75	0.75	r.t.	THF	10	68
5	0.75	1	r.t.	THF	10	65
6	**1**	**1**	**r.t.**	**THF**	**10**	**74**
7	1	1.5	r.t.	THF	10	69
8	1	1	60	THF	10	68
9	1	1	r.t.	DCM	30	20
10	1	1	r.t.	DMF	30	30
11	1	1	r.t.	EtOH	30	25

[a]Reaction conditions: **1a** (0.5 mmol), **2a**, activated Zn, solvent (1 mL), N_2, 10 min. [b]Isolated yield.

atmosphere for 10 min gave 3-ethynyl-4-methyl-2,6-diphenylpyridine (**3aa**) in 58% yield (entry 1). With 0.5 mmol of **1a** and 0.5 mmol of **2a**, the effect of different amounts of zinc on this reaction was examined, and a yield of 63% was obtained when 1 mmol of zinc was used (entry 2). A higher dosage of zinc did not benefit this reaction (entry 3). Next, it was found that a further increase of the amounts of **2a** and zinc could improve the yield of **3aa** (entries 4 and 5). Encouragingly, reacting 0.5 mmol of **1a** and 1 mmol of **2a** with 1 mmol of zinc resulted in the highest yield of 74% (entry 6). Elevating the reaction temperature from room temperature to 60 °C did not give a higher yield of **3aa** (entries 6 vs 8). When another solvent, such as DCM, DMF, or EtOH, was used to replace THF as the reaction medium, the yield of **3aa** decreased dramatically (entries 6 vs 9−11).

With the optimized conditions (Table 1, entry 6) in hand, the scope and generality of this zinc-mediated one-pot, four-component tandem reaction leading to highly substituted pyridines were investigated. First, the reaction of different nitriles (**1**) was studied. The results included in Table 2 showed that aryl-substituted nitriles with various substituents (from electron-donating alkyl or alkoxyl to electron-withdrawing halides) on the aryl ring underwent this tandem reaction smoothly to afford the desired pyridines **3aa**−**3qa** in moderate to good yields without showing obvious electronic and steric effects. With 1-naphthonitrile and thiophene-2-carbonitrile, the corresponding products **3ra** and **3sa** were obtained in 76% and 50% yield, respectively. The zinc-mediated tandem reaction of cinnamonitrile with **2a** proceeded smoothly to give **3ta** in 55% yield. In addition, alkyl-substituted nitriles were found to be suitable for this reaction to provide the desired pyridines **3ua** and **3va** in 60% and 67% yield, respectively. Interestingly, we were delighted to find that (*E*)-methyl 3-(4-cyanophenyl)-acrylate bearing an active acrylate unit was also compatible with this reaction to afford the corresponding product **3wa** in 60% yield.

Next, the scope of propargyl bromides (**2**) was screened. It turned out that, under the optimized conditions, both alkyl- (methyl and ethyl) and aryl- (phenyl and 4-fluorophenyl) substituted propargyl bromides reacted well with various **1** to generate the expected pyridines **3ab**−**3pe** in 40−65% yields. These results together with those included in Table 2 indicate that this zinc-mediated tandem reaction of nitriles with propargyl bromides could be used as an efficient and general method for the preparation of diversely substituted pyridines.

It was then noticed that the pyridine products included in Tables 2 and 3 had same substituents attached on the 2- and 6-position, and homologous substituents on the 3- and 4-position of the pyridine ring. The reason behind this regular substitution pattern is that these pyridines were formed from two identical nitriles and two identical propargyl bromides. On the basis of this fact, we predicted that, if two different nitriles or propargyl bromides were used, pyridines with different substituents attached on the 2,6-, or 3,4-positions might be obtained. If so, the scope and applicability of this new synthetic strategy would be further expanded. Thus, propargyl bromide (**2a**) was treated with benzonitrile (**1a**) and 4-methylbenzonitrile (**1b**) in the presence of zinc. NMR study of the resulting mixture indicated that this reaction gave four products, **3aa**, **3ba**, 3-ethynyl-4-methyl-6-phenyl-2-(*p*-tolyl)pyridine (**3aba**), and 3-ethynyl-4-methyl-2-phenyl-6-(*p*-tolyl)pyridine (**3baa**), with a ratio of about 1:1:1:1 (Scheme 2). This reaction confirmed our prediction as described above and provided pyridines with diverse substitution patterns. Unfortunately, it did not show any chemoselectivity, most likely owing to the close structural similarity of the two nitrile substrates **1a** and **1b**.

In the following study, we chose **1a** and acetonitrile (**1u**) as substrates to react with **2a** and zinc. Interestingly, this reaction selectively gave **3aa** and 3-ethynyl-4,6-dimethyl-2-phenylpyridine (**3uaa**), a pyridine derivative with different substituents attached on the 2- and 6-position. The other two possible products (**3ua** and **3aua**) were not obtained (Scheme 3).

Encouraged by the above results, we then studied the reaction of two different propargyl bromides, **2a** and (3-bromoprop-1-yn-1-yl)benzene (**2d**), with **1a** and zinc. It turned out that this reaction could also selectively afford two of the four possible products, **3ad** and 4-benzyl-3-ethynyl-2,6-diphenylpyridine (**3ada**), a pyridine derivative with non-homologous substituents attached on the 3- and 4-position. The other two possible products (**3aa** and **3aad**) were not obtained (Scheme 4).

Having established a simple and efficient synthesis of 3-alkynylpyridines, we were then interested in exploring their synthetic applications by taking advantage of the versatile reactivity of the alkynyl unit. As a first example, the acetylenyl unit embedded in **3pa** was easily transformed into an acetyl group by treating **3pa** with $H_2SO_4/HgSO_4$ in AcOH to give 1-(2,6-bis(2-bromophenyl)-4-methylpyridin-3-yl)ethanone (**4**). Treatment of **4** with aqueous ammonia in the presence of CuI afforded 2-(4,5-dimethylbenzo[*h*][1,6]naphthyridin-2-yl)-aniline (**5**) in a yield of 65% (Scheme 5). This is a promising transformation since 1,6-naphthyridine is a widely found scaffold in naturally occurring products[11] and synthetic compounds displaying significant pharmacological and biological activities, including antiherpes,[12a] anticancer,[12b] antimicrobial,[12c] anti-HIV-1,[12d,e] and adrenoceptor blocking.[12f]

In a second example, we noticed that Ackermann et al. recently reported a one-pot synthesis of fully substituted triazoles through a CuI-catalyzed "click" reaction and direct arylation sequence.[13] On the basis of this elegant strategy, we designed and developed an efficient one-pot procedure for the construction of [1,2,3]triazolo[4,5-*f*]quinoline derivatives, which have proved to be quite active in three human cell lines (HeLa, Hep-G2, and Aou-373).[14] As illustrated in Scheme

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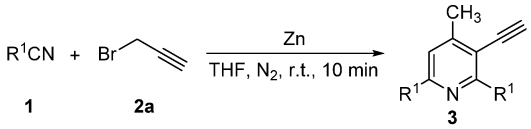
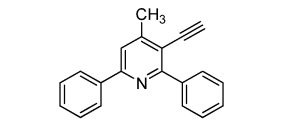
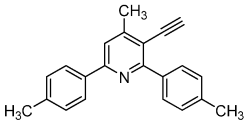
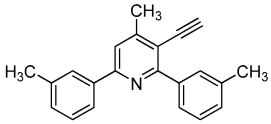
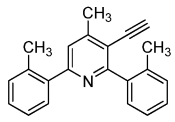
Table 2. Scope of the Tandem Reaction Leading to 3-Alkynylpyridines (I)[a,b]

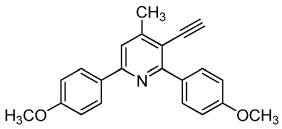


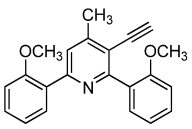

3aa, 74%

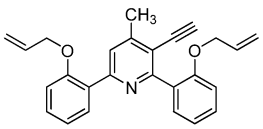

3ba, 62%

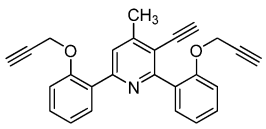

3ca, 71%

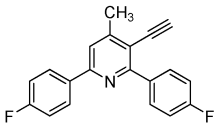

3da, 67%

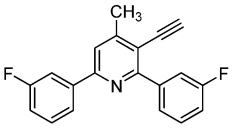

3ea, 60%

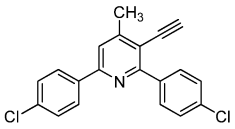

3fa, 75%

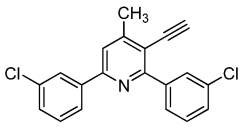

3ga, 60%

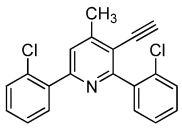

3ha, 53%


3ia, 65%


3ja, 68%


3ka, 64%


3la, 72%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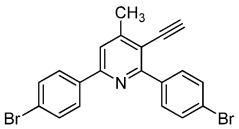
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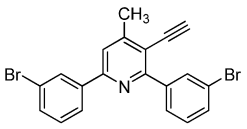
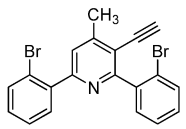
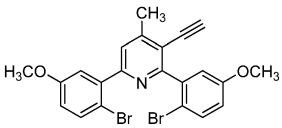
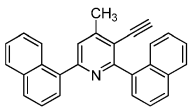
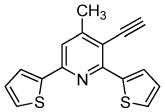
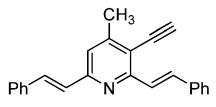

3oa, 67%

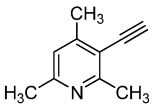

3pa, 60%

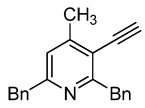

3qa, 58%

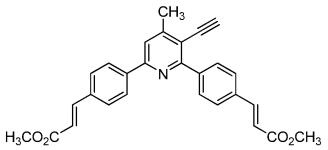

3ra, 76%


3sa, 50%


3ta, 55%


3ua, 60%


3va, 67%


3wa, 60%

[a]Reaction conditions: **1** (1.0 mmol), **2a** (2.0 mmol), activated Zn (2.0 mmol), THF (2 mL), r.t., N_2, 10 min. [b]Isolated yields.

6, tetracyclic [1,2,3]triazolo[4,5-*f*]quinoline (**6**) could be efficiently prepared in 40% overall yield through the click chemistry of pyridine **3pa** with NaN_3, followed by a base-promoted intramolecular cross-coupling through C−H activation. It is noteworthy that, in Ackermann et al.'s *intermolecular* couplings, aryl iodides were employed as substrates. In our *intramolecular* version of a similar cascade process, aryl bromide was found to be reactive enough for the coupling reaction, albeit the yield was moderate.

In summary, we have developed a zinc-mediated tandem reaction of nitriles with propargyl bromides leading to diversely substituted pyridines under extremely mild reaction conditions. This unprecedented procedure enabled the construction of 3-alkynylpyridine through the reaction of up to four components with the formation of three C−C bonds and one C−N bond. Various nitriles and propargyl bromides were well tolerated with the reaction conditions. Moreover, the versatile applicability of the 3-alkynylpyridines obtained herein was well showcased by the convenient synthesis of 2-(4,5-dimethylbenzo[*h*][1,6]naphthyridin-2-yl)aniline and [1,2,3]triazolo[4,5-*f*]quinolone derivatives.

EXPERIMENTAL SECTION

General Methods. Commercial reagents were used without further purification, and solvents were dried prior to use. Melting points were recorded with a micro melting point apparatus and uncorrected. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts were reported in ppm (parts per million) from tetramethylsilane (TMS) as internal standard in $CDCl_3$ solutions. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet), q (quadruplet), dd (doublet of

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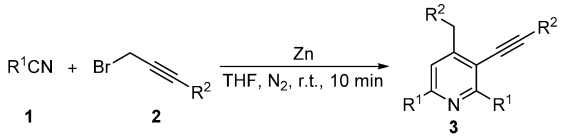
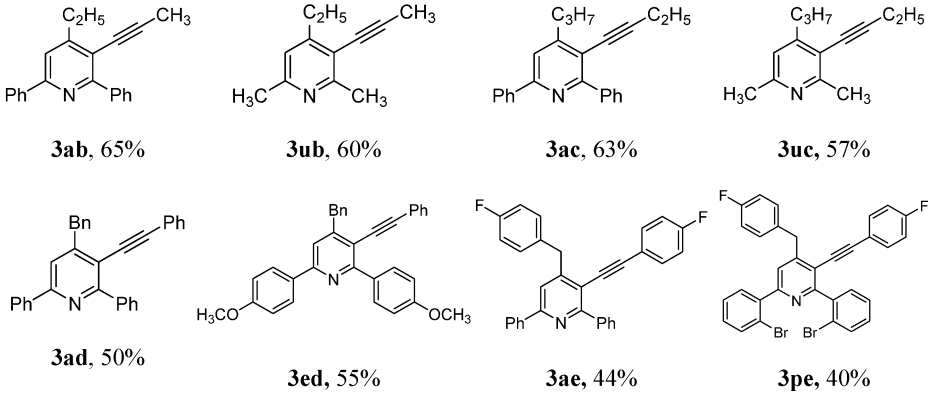
Table 3. Scope of the Tandem Reaction Leading to 3-Alkynylpyridines (II)[a,b]



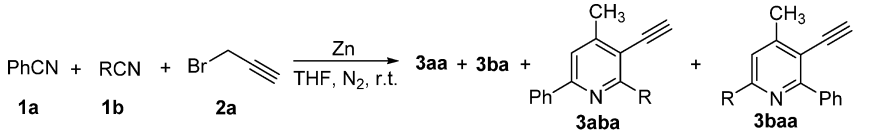


3ab, 65% **3ub**, 60% **3ac**, 63% **3uc**, 57%

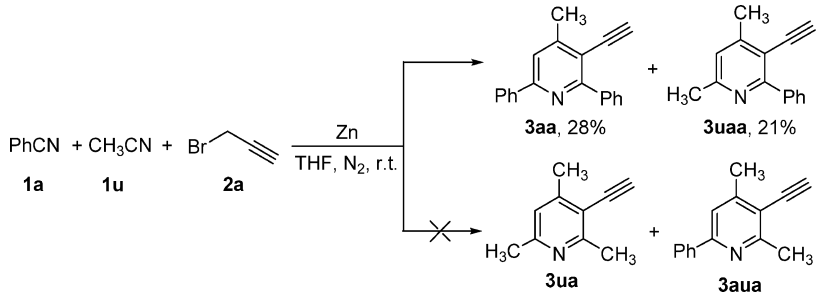
3ad, 50% **3ed**, 55% **3ae**, 44% **3pe**, 40%

[a]Reaction conditions: **1** (1.0 mmol), **2** (2.0 mmol), activated Zn (2.0 mmol), THF (2 mL), r.t., N_2, 10 min. [b]Isolated yields.

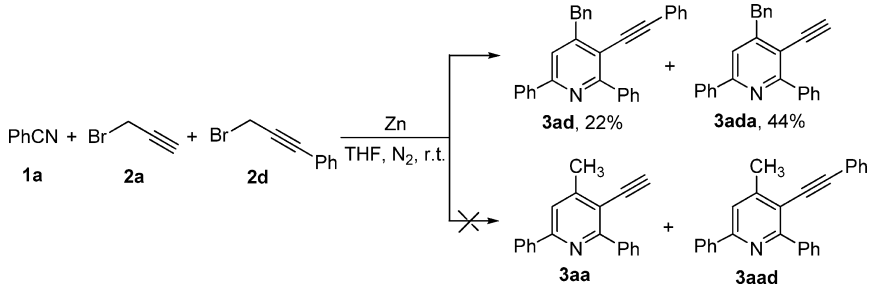
Scheme 2. Reaction of 1a, 1b with 2a Affording 3aa, 3ba, 3aba, and 3baa



Scheme 3. Reaction of 1a, 1u with 2a Affording 3aa and 3uaa



Scheme 4. Reaction of 1a with 2a, 2d Affording 3ad and 3ada



doublets). Coupling constants were given in Hz. High-resolution mass spectra (HRMS) were obtained by using a MicrOTOF mass spectrometer. All the reactions were monitored by thin-layer chromatography (TLC) using silica gel plates (silica gel 60 F_{254} 0.25 mm).

Typical Procedure for the Synthesis of 3aa and Spectroscopic Data of 3aa–3pe. To a flask containing benzonitrile (**1a**, 1 mmol), THF (2 mL), and 3-bromoprop-1-yne (**2a**, 2 mmol) was added activated zinc dust (2 mmol) with stirring. The mixture was then stirred at room temperature under a nitrogen atmosphere. Upon completion, it was diluted with saturated aqueous NH_4Cl (10 mL) and the excess zinc was filtered. The filtrate was concentrated, and to the residue was added water (10 mL). The aqueous phase was extracted with EtOAc (10 mL × 3). The combined organic phase was dried with anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel with EtOAc/hexane (2.5%) to

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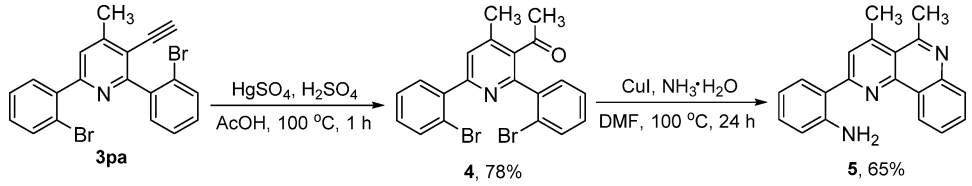
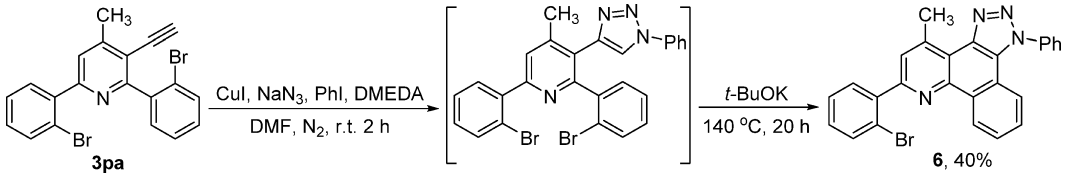
Scheme 5. Synthesis of 1,6-Naphthyridine Derivative (5) from 3pa



Scheme 6. One-Pot Synthesis of [1,2,3]Triazolo[4,5-*f*]quinoline (6) from 3pa



give 3-ethynyl-4-methyl-2,6-diphenylpyridine (**3aa**) in 74% yield. **3ba**–**3ada** were obtained in a similar manner.

3-Ethynyl-4-methyl-2,6-diphenylpyridine (***3aa***). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (100 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.60 (s, 3H), 3.50 (s, 1H), 7.42–7.50 (m, 6H), 7.61 (s, 1H), 8.05 (d, J = 6.0 Hz, 2H), 8.12 (d, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.4, 80.3, 87.4, 115.4, 119.2, 127.2, 127.8, 128.7, 128.8, 129.3, 129.6, 138.8, 139.8, 151.9, 155.3, 160.3. HRMS calcd for $C_{20}H_{16}N$: 270.1283 [M + H], found: 270.1287.

3-Ethynyl-4-methyl-2,6-di-p-tolylpyridine (***3ba***). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (92 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.42 (s, 3H), 2.44 (s, 3H), 2.58 (s, 3H), 3.50 (s, 1H), 7.28–7.31 (m, 4H), 7.57 (s, 1H), 7.98 (d, J = 7.6 Hz, 2H), 8.03 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.35, 21.45, 80.6, 87.1, 114.8, 118.6, 127.0, 128.5, 129.4, 129.6, 136.0, 137.1, 138.6, 139.3, 151.8, 155.3, 160.2. HRMS calcd for $C_{22}H_{20}N$: 298.1596 [M + H], found: 298.1602.

3-Ethynyl-4-methyl-2,6-di-m-tolylpyridine (***3ca***). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (105 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.48 (s, 3H), 2.50 (s, 3H), 2.61 (s, 3H), 3.51 (s, 1H), 7.28 (t, J = 8.0 Hz, 2H), 7.40 (t, J = 8.0 Hz, 2H), 7.61 (s, 1H), 7.87–7.92 (m, 3H), 7.97 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.3, 21.6, 80.4, 87.3, 115.4, 119.3, 124.4, 126.8, 127.7, 127.9, 128.6, 129.5, 130.1, 130.3, 137.4, 138.4, 138.8, 139.9, 151.8, 155.6, 160.6. HRMS calcd for $C_{22}H_{20}N$: 298.1596 [M + H], found: 298.1603.

3-Ethynyl-4-methyl-2,6-di-o-tolylpyridine (***3da***). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (99 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.44 (s, 3H), 2.57 (s, 3H), 2.59 (s, 3H), 3.31 (s, 1H), 7.28–7.43 (m, 7H), 7.48 (t, J = 7.6 Hz, 1H), 7.62 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.8, 20.5, 20.9, 79.4, 86.6, 123.1, 125.3, 125.80, 125.84, 126.2, 128.2, 128.4, 129.3, 129.6, 130.0, 130.2, 130.8, 132.5, 136.0, 140.0, 150.6, 158.3. HRMS calcd for $C_{22}H_{20}N$: 298.1596 [M + H], found: 298.1608.

3-Ethynyl-2,6-bis(4-methoxyphenyl)-4-methylpyridine (***3ea***). Eluent: ethyl acetate/hexane (5%); yellow syrup (99 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.55 (s, 3H), 3.50 (s, 1H), 3.86 (s, 3H), 3.87 (s, 3H), 6.97–7.01 (m, 4H), 7.49 (s, 1H), 8.03–8.08 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.4, 55.3, 55.4, 80.8, 86.9, 113.2, 114.0, 117.9, 128.4, 131.0, 131.5, 132.5, 134.0, 151.8, 154.8, 159.6, 160.1, 160.7. HRMS calcd for $C_{22}H_{20}NO_2$: 330.1494 [M + H], found: 330.1498.

3-Ethynyl-2,6-bis(2-methoxyphenyl)-4-methylpyridine (***3fa***). Eluent: ethyl acetate/hexane (5%); yellow syrup (123 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.54 (s, 3H), 3.26 (s, 1H), 3.81 (s, 3H), 3.88 (s, 3H), 6.95–7.04 (m, 5H), 7.50–7.56 (m, 3H), 7.71 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.0, 55.5, 55.6, 85.2, 101.7, 111.1, 111.3, 120.4, 120.7, 121.0, 124.0, 129.7, 130.0, 130.9, 131.6, 133.7, 134.4, 154.2, 157.0, 157.2, 161.2. HRMS calcd for $C_{22}H_{20}NO_2$: 330.1494 [M + H], found: 330.1499.

2,6-Bis(2-(allyloxy)phenyl)-3-ethynyl-4-methylpyridine (***3ga***). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (114 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.55 (s, 3H), 3.27 (s, 1H), 4.58–4.63 (m, 4H), 5.17 (dd, J_1 = 14.4 Hz, J_2 = 1.6 Hz, 1H), 5.27–5.32 (m, 2H), 5.42 (dd, J_1 = 14.8 Hz, J_2 = 1.6 Hz, 1H), 5.97–6.10 (m, 2H), 6.98 (d, J = 8.0 Hz, 2H), 7.03–7.07 (m, 2H), 7.30–7.38 (m, 2H), 7.47 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 7.80 (s, 1H), 7.90 (dd, J_1 = 7.6 Hz, J_2 = 2.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.0, 69.31, 69.33, 80.3, 85.4, 112.6, 112.9, 116.6, 117.1, 117.4, 120.7, 121.4, 124.1, 129.1, 129.6, 129.9, 131.0, 131.8, 133.2, 133.7, 149.3, 154.1, 156.1, 156.4, 159.4. HRMS calcd for $C_{26}H_{24}NO_2$: 382.1807 [M + H], found: 382.1815.

3-Ethynyl-4-methyl-2,6-bis(2-(prop-2-ynyloxy)phenyl)pyridine (***3ha***). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (100 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.53–2.57 (m, 5H), 3.28 (s, 1H), 4.70 (d, J = 2.4 Hz, 2H), 4.75 (d, J = 2.4 Hz, 2H), 7.06–7.17 (m, 3H), 7.33–7.56 (m, 4H), 7.74 (s, 1H), 7.88 (d, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.4, 56.5, 56.6, 75.3, 75.7, 78.7, 79.0, 80.0, 85.8, 112.9, 113.0, 117.6, 121.5, 121.7, 122.2, 124.2, 129.6, 129.9, 131.2, 131.3, 131.9, 134.0, 134.2, 149.6, 153.9, 155.1. HRMS calcd for $C_{26}H_{20}NO_2$: 378.1494 [M + H], found: 378.1501.

3-Ethynyl-2,6-bis(4-fluorophenyl)-4-methylpyridine (***3ia***). Eluent: ethyl acetate/hexane (2.5%); yellow solid (99 mg, 65%), mp 135–136 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.58 (s, 3H), 3.51 (s, 1H), 7.13–7.17 (m, 4H), 7.55 (s, 1H), 8.01–8.09 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.3, 80.0, 87.6, 114.6, 114.8, 115.1, 115.5, 115.7, 118.8, 128.9, 129.0, 131.4, 131.5, 134.69, 134.71, 135.65, 135.69, 152.2, 154.2, 159.1, 162.0, 164.4, 164.9. HRMS calcd for $C_{20}H_{14}F_2N$: 306.1094 [M + H], found: 306.1098.

3-Ethynyl-2,6-bis(3-fluorophenyl)-4-methylpyridine (***3ja***). Eluent: ethyl acetate/hexane (2.5%); yellow solid (104 mg, 68%), mp 122–123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.60 (s, 3H), 3.56 (s, 1H), 7.13 (d, J = 8.4 Hz, 2H), 7.41–7.45 (m, 2H), 7.60 (s, 1H), 7.76–7.85 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.3, 79.7, 88.3, 113.9, 114.2, 115.6, 115.8, 116.0, 116.1, 116.3, 116.5, 116.7, 119.6, 122.56, 122.59, 125.3, 129.26, 129.34, 130.2, 130.3, 140.9, 152.4, 153.9, 158.8, 162.1, 163.7. HRMS calcd for $C_{20}H_{14}F_2N$: 306.1094 [M + H], found: 306.1097.

2,6-Bis(4-chlorophenyl)-3-ethynyl-4-methylpyridine (***3ka***). Eluent: ethyl acetate/hexane (2.5%); yellow solid (108 mg, 64%), mp 149–150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.57 (s, 3H), 3.54 (s, 1H), 7.43 (d, J = 6.4 Hz, 2H), 7.45 (d, J = 6.8 Hz, 2H), 7.55 (s, 1H), 7.99 (d, J = 8.0 Hz, 2H), 8.02 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.3, 79.9, 88.1, 115.6, 119.1, 128.1, 128.3, 128.9, 131.0, 135.0, 135.5, 136.9, 138.0, 152.3, 154.1, 159.0. HRMS calcd for $C_{20}H_{14}Cl_2N$: 338.0503 [M + H], found: 338.0508.

2,6-Bis(3-chlorophenyl)-3-ethynyl-4-methylpyridine (***3la***). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (121 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.58 (s, 3H), 3.55 (s, 1H), 7.40–7.42 (m, 4H), 7.59 (s, 1H), 7.91–7.96 (m, 2H), 8.02 (s, 1H), 8.08 (d, J = 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.3, 79.6, 88.4, 116.1, 119.7, 125.2, 127.2, 127.8, 128.9, 129.1, 129.4, 129.7, 130.0, 133.8, 134.9,

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140.3, 141.2, 152.4, 153.9, 158.9. HRMS calcd for $C_{20}H_{14}Cl_2N$: 338.0503 [M + H], found: 338.0512.

2,6-Bis(2-chlorophenyl)-3-ethynyl-4-methylpyridine (**3ma**). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (103 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.59 (s, 3H), 3.33 (s, 1H), 7.30−7.37 (m, 4H), 7.45−7.52 (m, 3H), 7.57−7.59 (m, 1H), 7.63−7.68 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.9, 78.8, 87.3, 118.0, 124.4, 126.5, 127.1, 129.57, 129.64, 129.8, 130.1, 131.0, 131.8, 132.2, 133.1, 138.6, 139.0, 150.4, 155.0, 159.7. HRMS calcd for $C_{20}H_{14}Cl_2N$: 338.0503 [M + H], found: 338.0511.

2,6-Bis(4-bromophenyl)-3-ethynyl-4-methylpyridine (**3na**). Eluent: ethyl acetate/hexane (2.5%); yellow solid (130 mg, 61%), mp 152−153 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.58 (s, 3H), 3.53 (s, 1H), 7.58−7.61 (m, 5H), 7.91 (d, J = 8.4 Hz, 2H), 7.96 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.3, 79.8, 88.1, 115.6, 119.1, 123.3, 123.9, 128.6, 131.0, 131.2, 131.9, 137.3, 138.4, 152.3, 154.2, 159.1. HRMS calcd for $C_{20}H_{14}Br_2N$: 425.9493 [M + H], found: 425.9499.

2,6-Bis(3-bromophenyl)-3-ethynyl-4-methylpyridine (**3oa**). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (142 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.58 (s, 3H), 3.55 (s, 1H), 7.32−7.37 (m, 2H), 7.54−7.58 (m, 3H), 7.95 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 8.16 (s, 1H), 8.23 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.3, 79.6, 88.4, 116.1, 119.7, 122.0, 123.1, 125.7, 128.2, 129.4, 130.1, 130.3, 131.8, 132.3, 132.5, 140.5, 141.5, 152.4, 153.8, 158.8. HRMS calcd for $C_{20}H_{14}Br_2N$: 425.9493 [M + H], found: 425.9502.

2,6-Bis(2-bromophenyl)-3-ethynyl-4-methylpyridine (**3pa**). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (128 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.58 (s, 3H), 3.33 (s, 1H), 7.22−7.26 (m, 1H), 7.35−7.48 (m, 3H), 7.51 (s, 1H), 7.58−7.66 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.9, 78.8, 87.4, 117.8, 121.7, 122.6, 124.4, 127.1, 127.6, 129.9, 130.9, 131.7, 132.7, 133.3, 133.9, 134.4, 140.7, 150.5, 156.4, 160.9. HRMS calcd for $C_{20}H_{14}Br_2N$: 425.9493 [M + H], found: 425.9495.

2,6-Bis(2-bromo-5-methoxyphenyl)-3-ethynyl-4-methylpyridine (**3qa**). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (141 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.59 (s, 3H), 3.17 (s, 1H), 3.80 (s, 3H), 3.81 (s, 3H), 6.81−6.84 (m, 2H), 7.03 (d, J = 2.8 Hz, 1H), 7.16 (d, J = 2.8 Hz, 1H), 7.51−7.54 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.9, 55.6, 78.7, 87.6, 112.1, 113.1, 116.2, 116.5, 116.7, 117.7, 124.3, 133.4, 134.0, 141.3, 141.4, 150.6, 156.2, 158.5, 159.0, 160.7. HRMS calcd for $C_{22}H_{18}Br_2NO_2$: 485.9704 [M + H], found: 485.9708.

3-Ethynyl-4-methyl-2,6-di(naphthalen-1-yl)pyridine (**3ra**). Eluent: ethyl acetate/hexane (2.5%); yellow solid (140 mg, 76%), mp 156−157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.68 (s, 3H), 3.20 (s, 1H), 7.49−7.60 (m, 7H), 7.71 (d, J = 7.2 Hz, 2H), 7.83−7.94 (m, 5H), 8.26 (d, J = 2.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.1, 79.4, 87.4, 118.1, 124.4, 125.1, 125.3, 125.6, 125.7, 125.9, 126.0, 126.1, 126.6, 127.5, 127.8, 128.3, 128.4, 128.8, 129.1, 131.2, 131.7, 133.7, 134.0, 137.9, 138.0, 151.0, 157.6, 161.4. HRMS calcd for $C_{28}H_{20}N$: 370.1596 [M + H], found: 370.1608.

3-Ethynyl-4-methyl-2,6-di(thiophen-2-yl)pyridine (**3sa**). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (70 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.54 (s, 3H), 3.82 (s, 1H), 7.11−7.14 (m, 2H), 7.38−7.46 (m, 3H), 7.63 (d, J = 3.2 Hz, 1H), 8.42 (d, J = 3.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.2, 80.4, 89.5, 111.8, 116.8, 125.3, 127.6, 128.0, 128.4, 128.5, 128.8, 144.3, 144.4, 150.4, 152.35, 152.38. HRMS calcd for $C_{16}H_{12}NS_2$: 282.0411 [M + H], found: 282.0414.

3-Ethynyl-4-methyl-2,6-distyrylpyridine (**3ta**). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (88 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.48 (s, 3H), 3.75 (s, 1H), 7.16 (s, 1H), 7.17−7.43 (m, 7H), 7.62−7.82 (m, 6H), 8.04 (d, J = 16.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.7, 79.4, 88.5, 116.1, 120.9, 125.3, 127.3, 127.6, 127.9, 128.4, 128.46, 128.50, 128.7, 128.8, 133.9, 135.0, 136.7, 137.0, 153.8, 156.1. HRMS calcd for $C_{24}H_{20}N$: 322.1596 [M + H], found: 322.1599.

3-Ethynyl-2,4,6-trimethylpyridine (**3ua**). Eluent: ethyl acetate/hexane (2.5%); yellow liquid (44 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.34 (s, 3H), 2.44 (s, 3H), 2.61 (s, 3H), 3.52 (s, 1H), 6.82 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.3, 23.5, 24.2, 79.5, 86.5, 115.3, 121.4, 150.1, 156.5, 160.1. HRMS calcd for $C_{10}H_{12}N$: 146.0970 [M + H], found: 146.0977.

2,6-Dibenzyl-3-ethynyl-4-methylpyridine (**3va**). Eluent: ethyl acetate/hexane (2.5%); yellow solid (99 mg, 67%), mp 166−167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.39 (s, 3H), 3.62 (s, 1H), 4.19 (s, 2H), 4.47 (s, 2H), 6.86 (s, 1H), 7.28−7.37 (m, 8H), 7.48 (d, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.7, 42.9, 44.6, 79.8, 87.1, 116.0, 121.6, 126.2, 126.5, 128.3, 128.7, 129.2, 129.3, 139.4, 139.6, 151.0, 159.7, 162.2. HRMS calcd for $C_{22}H_{20}N$: 298.1596 [M + H], found: 298.1601.

(2E,2′E)-Dimethyl 3,3′-(4,4′-(3-ethynyl-4-methylpyridine-2,6-diyl)bis(4,1-phenylene))diacrylate (**3wa**). Eluent: ethyl acetate/hexane (10%); colorless solid (131 mg, 60%), mp 196−197 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.61 (s, 3H), 3.57 (s, 1H), 3.82 (s, 3H), 3.84 (s, 3H), 6.52 (d, J = 16.0 Hz, 1H), 6.53 (d, J = 16.0 Hz, 1H), 7.63−7.65 (m, 5H), 7.75 (d, J = 16.0 Hz, 1H), 7.78 (d, J = 16.4 Hz, 1H), 8.09 (d, J = 8.0 Hz, 2H), 8.14 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.4, 51.8, 79.9, 88.3, 115.9, 118.3, 118.4, 119.5, 127.5, 127.6, 128.5, 130.1, 134.8, 135.3, 140.2, 141.4, 144.2, 144.5, 152.3, 154.3, 159.3, 167.4, 167.5. HRMS calcd for $C_{28}H_{24}NO_4$: 438.1705 [M + H], found: 438.1709.

4-Ethyl-2,6-diphenyl-3-(prop-1-ynyl)pyridine (**3ab**). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (97 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.34−1.38 (m, 3H), 2.06 (s, 3H), 2.93−2.94 (m, 2H), 7.40−7.49 (m, 6H), 7.59 (s, 1H), 8.06 (d, J = 7.6 H, 2H), 8.12 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 4.7, 13.8, 27.9, 76.2, 95.8, 117.5, 127.0, 127.5, 127.6, 128.4, 128.6, 128.8, 128.9, 139.2, 140.5, 154.6, 156.5, 159.6. HRMS calcd for $C_{22}H_{20}N$: 298.1596 [M + H], found: 298.1599.

4-Ethyl-2,6-dimethyl-3-(prop-1-ynyl)pyridine (**3ub**). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (52 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.15 (t, J = 8.0 Hz, 3H), 2.07 (s, 3H), 2.42 (s, 3H), 2.57 (s, 3H), 2.66 (q, J = 8.0 Hz, 2H), 6.77 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 4.5, 13.6, 23.5, 24.2, 27.2, 75.2, 94.9, 116.4, 119.6, 154.9, 155.3, 159.3. HRMS calcd for $C_{12}H_{16}N$: 174.1283 [M + H], found: 174.1288.

3-(But-1-ynyl)-2,6-diphenyl-4-propylpyridine (**3ac**). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (102 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.06 (t, J = 7.2 Hz, 3H), 1.21 (t, J = 7.2 Hz, 3H), 1.79 (q, J = 7.2 Hz, 2H), 2.43 (q, J = 7.2 Hz, 2H), 2.88 (t, J = 7.2 Hz, 2H), 7.41−7.50 (m, 6H), 7.57 (s, 1H), 8.07−8.12 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.49, 13.53, 14.1, 22.9, 36.9, 101.3, 116.7, 118.4, 127.0, 127.5, 128.3, 128.6, 128.9, 129.7, 139.2, 140.4, 154.3, 155.0, 159.5. HRMS calcd for $C_{24}H_{24}N$: 326.1909 [M + H], found: 326.1916.

3-(But-1-ynyl)-2,6-dimethyl-4-propylpyridine (**3uc**). Eluent: ethyl acetate/hexane (2.5%); yellow syrup (57 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.86 (t, J = 7.2 Hz, 3H), 1.16 (t, J = 7.6 Hz, 3H), 1.54 (q, J = 7.6 Hz, 2H), 2.36−2.42 (m, 5H), 2.50−2.57 (m, 5H), 6.69 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.3, 13.9, 14.0, 22.7, 23.6, 24.2, 36.1, 75.6, 100.6, 116.5, 120.3, 153.2, 155.1, 159.3. HRMS calcd for $C_{14}H_{20}N$: 202.1596 [M + H], found: 202.1599.

4-Benzyl-2,6-diphenyl-3-(phenylethynyl)pyridine (**3ad**). Eluent: ethyl acetate/hexane (2.5%); yellow solid (105 mg, 50%), mp 128−129 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.38 (s, 2H), 7.26−7.53 (m, 17H), 8.06 (d, J = 7.6 Hz, 2H), 8.13 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 40.5, 93.6, 99.2, 118.8, 118.9, 123.2, 126.6, 127.1, 127.6, 127.7, 128.3, 128.4, 128.5, 128.6, 128.7, 129.1, 129.2, 129.7, 131.2, 138.79, 138.84, 144.1, 153.3, 160.0. HRMS calcd for $C_{32}H_{24}N$: 422.1909 [M + H], found: 422.1918.

4-Benzyl-2,6-bis(4-methoxyphenyl)-3-(phenylethynyl)pyridine (**3ed**). Eluent: ethyl acetate/hexane (5%); yellow solid (132 mg, 55%), mp 148−149 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.85 (s, 3H), 3.90 (s, 3H), 4.36 (s, 2H), 6.97 (d, J = 8.8 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 7.33−7.42 (m, 11H), 8.03 (d, J = 8.8 Hz, 2H), 8.15 (d, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 40.5, 55.3, 55.4, 87.1, 98.8, 113.1, 114.0, 114.8, 117.6, 123.3, 126.5, 128.2, 128.4, 128.7, 129.1, 131.15, 131.20, 131.5, 132.8, 139.0, 153.2, 154.7, 159.2, 160.1, 160.6. HRMS calcd for $C_{34}H_{28}NO_2$: 482.2120 [M + H], found: 482.2129.

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*4-(4-Fluorobenzyl)-3-((4-fluorophenyl)ethynyl)-2,6-diphenylpyridine (**3ae**).* Eluent: ethyl acetate/hexane (2.5%); yellow solid (101 mg, 44%), mp 120−121 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.35 (s, 2H), 7.01−7.08 (m, 5H), 7.28−7.54 (m, 10H), 7.07−8.13 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 39.8, 86.2, 98.4, 115.4, 115.45, 115.50, 115.6, 115.7, 115.9, 116.1, 118.8, 127.2, 127.8, 128.7, 128.9, 129.4, 129.8, 130.5, 130.6, 133.1, 133.2, 134.39, 134.42, 138.5, 139.8, 153.1, 155.3, 160.0, 161.6, 163.0, 164.1. HRMS calcd for $C_{32}H_{22}F_2N$: 458.1720 [M + H], found: 458.1723.

*2,6-Bis(2-bromophenyl)-4-(4-fluorobenzyl)-3-((4-fluorophenyl)-ethynyl)pyridine (**3pe**).* Eluent: ethyl acetate/hexane (2.5%); yellow syrup (123 mg, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.31 (s, 2H), 6.97 (t, J = 8.4 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 7.12−7.15 (m, 2H), 7.22−7.31 (m, 4H), 7.36−7.44 (m, 3H), 7.55 (d, J = 7.6 Hz, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.71 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 39.7, 83.8, 100.0, 115.71, 115.75, 115.9, 116.0, 118.4, 121.9, 123.0, 125.0, 127.2, 127.8, 130.6, 130.8, 130.9, 131.5, 132.1, 132.3, 132.7, 133.3, 133.41, 133.45, 133.49, 154.8, 160.7, 163.1, 164.2, 165.1. HRMS calcd for $C_{32}H_{20}Br_2F_2N$: 613.9931 [M + H], found: 613.9939.

Procedure for the Reaction of 1a, 1u with 2a and Spectroscopic Data of 3uaa. To a flask containing benzonitrile (**1a**, 1 mmol), acetonitrile (**1u**, 1 mmol), THF (4 mL), and 3-bromoprop-1-yne (**2a**, 4 mmol) was added activated zinc dust (4 mmol) with stirring. The mixture was then stirred at room temperature under a nitrogen atmosphere. Upon completion, it was diluted with saturated aqueous NH_4Cl (10 mL) and the excess zinc was filtered. The filtrate was concentrated, and to the residue was added water (10 mL). The aqueous phase was extracted with EtOAc (10 mL × 3). The combined organic phase was dried with anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel with EtOAc/hexane (2.5%) to give 3-ethynyl-4-methyl-2,6-diphenylpyridine (**3aa**) in a yield of 28% and 3-ethynyl-4,6-dimethyl-2-phenylpyridine (**3uaa**) in a yield of 21%.

*3-Ethynyl-4,6-dimethyl-2-phenylpyridine (**3uaa**).* Eluent: ethyl acetate/hexane (2.5%); yellow solid (43 mg, 21%), mp 93−94 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.48 (s, 3H), 2.58 (s, 3H), 3.37 (s, 1H), 7.02 (s, 1H), 7.40−7.44 (m, 3H), 7.86 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.9, 24.5, 80.0, 86.4, 114.3, 122.5, 127.9, 128.6, 129.4, 139.6, 151.5, 157.2, 160.2. HRMS calcd for $C_{15}H_{14}N$: 208.1126 [M + H], found: 208.1133.

Procedure for the Reaction of 1a with 2a, 2d and Spectroscopic Data of 3ada. To a flask containing benzonitrile (**1a**, 1 mmol), THF (2 mL), 3-bromoprop-1-yne (**2a**, 1 mmol), and (3-bromoprop-1-yn-1-yl)benzene (**2d**, 1 mmol) was added activated zinc dust (2 mmol) with stirring. The mixture was then stirred at room temperature under a nitrogen atmosphere. Upon completion, it was diluted with saturated aqueous NH_4Cl (10 mL) and the excess zinc was filtered. The filtrate was concentrated, and to the residue was added water (10 mL). The aqueous phase was extracted with EtOAc (10 mL × 3). The combined organic phase was dried with anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel with EtOAc/hexane (2.5%) to give 4-benzyl-2,6-diphenyl-3-(phenylethynyl)pyridine (**3ad**) in a yield of 22% and 4-benzyl-3-ethynyl-2,6-diphenylpyridine (**3ada**) in a yield of 44%.

*4-Benzyl-3-ethynyl-2,6-diphenylpyridine (**3ada**).* Eluent: ethyl acetate/hexane (2.5%); yellow syrup (76 mg, 44%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.49 (s, 1H), 4.32 (s, 2H), 7.26−7.50 (m, 12H), 8.01−8.05 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 40.3, 80.2, 87.7, 118.8, 126.7, 127.3, 127.8, 128.7, 128.9, 129.2, 129.4, 129.7, 131.3, 132.2, 132.8, 138.6, 139.5, 154.7, 155.6, 160.7. HRMS calcd for $C_{26}H_{20}N$: 346.1596 [M + H], found: 346.1599.

Procedure for the Synthesis of 4 and Spectroscopic Data of 4. To a flask containing 2,6-bis(2-bromophenyl)-3-ethynyl-4-methylpyridine (**3pa**, 0.5 mmol) and AcOH (2.5 mL) were added concentrated sulfuric acid (1 mmol) and $HgSO_4$ (0.5 mmol). The mixture was stirred at 100 °C. Upon completion as monitored by TLC, the reaction was quenched with aqueous $NaHCO_3$. Then, the mixture was extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with water and brine, and then dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum, and the crude product was purified by column chromatography on silica gel to afford **4** in 78% yield.

*1-(2,6-Bis(2-bromophenyl)-4-methylpyridin-3-yl)ethanone (**4**).* Eluent: ethyl acetate/hexane (5%); yellow syrup (173 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.10 (s, 3H), 2.42 (s, 3H), 7.22−7.41 (m, 5H), 7.51 (s, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.66 (t, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.6, 31.6, 121.7, 122.8, 125.8, 127.4, 127.7, 130.0, 130.4, 131.6, 131.7, 133.25, 133.29, 136.2, 139.9, 140.6, 144.3, 154.4, 157.8, 204.4. HRMS calcd for $C_{20}H_{16}Br_2NO$: 443.9599 [M + H], found: 443.9606.

Procedure for the Synthesis of 5 and Spectroscopic Data of 5. To a tube containing 1-(2,6-bis(2-bromophenyl)-4-methylpyridin-3-yl)ethanone (**4**, 0.2 mmol) and CuI (0.02 mmol) in DMF (1 mL) was added 26% aqueous ammonia (0.6 mL). Then, the tube was sealed and the mixture was stirred at 100 °C for 24 h. The reaction was quenched with NH_4Cl solution and extracted with ethyl acetate (8 mL × 3). The combined organic layer was washed with water and brine, and then dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum, and the crude product was purified by column chromatography on silica gel to afford **5** in 65% yield.

*2-(4,5-Dimethylbenzo[h][1,6]naphthyridin-2-yl)aniline (**5**).* Eluent: ethyl acetate/hexane (5%); yellow solid (39 mg, 65%), mp 184−185 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.96 (s, 3H), 3.15 (s, 3H), 6.24 (s, 2H), 6.84 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 7.6 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.69−7.77 (m, 3H), 8.04 (d, J = 7.6 Hz, 1H), 8.86 (d, J = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.8, 30.0, 117.5, 117.6, 119.0, 123.5, 123.9, 124.8, 126.7, 127.2, 128.3, 130.0, 130.1, 131.0, 132.8, 147.0, 147.6, 148.9, 158.2, 160.7. HRMS calcd for $C_{20}H_{18}N_3$: 300.1501 [M + H], found: 300.1512.

Procedure for the Synthesis of 6 and Spectroscopic Data of 6. To a suspension of CuI (0.025 mmol) and NaN_3 (0.3 mmol) in DMF (2.5 mL) were added 2,6-bis(2-bromophenyl)-3-ethynyl-4-methylpyridine (**3pa**, 0.25 mmol), iodobenzene (0.25 mmol), and *N*,*N*′-dimethylethylenediamine (0.0375 mmol). The resulting mixture was stirred at ambient temperature under N_2 for 2 h. Then, potassium *tert*-butoxide (0.5 mmol) was added. The resulting suspension was stirred at 140 °C under N_2 for 20 h. Upon completion, diethyl ether (5 mL) and water (5 mL) were added. The separated aqueous layer was extracted with diethyl ether (8 mL × 3). The combined organic layer was washed with aqueous NH_4Cl, water and brine, then dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by column chromatography on silica gel with EtOAc/hexane (5%) to give 6-(2-bromophenyl)-4-methyl-1-phenyl-1*H*-benzo[*h*]-[1,2,3]triazolo[4,5-*f*]quinoline (**6**) in 40% yield.

*6-(2-Bromophenyl)-4-methyl-1-phenyl-1H-benzo[h][1,2,3]-triazolo[4,5-f]quinoline (**6**).* Eluent: ethyl acetate/hexane (5%); yellow solid (46 mg, 40%), mp 230−231 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.41 (s, 3H), 7.35 (t, J = 7.6 Hz, 1H), 7.48−7.54 (m, 2H), 7.59 (d, J = 7.6 Hz, 1H), 7.72−7.82 (m, 8H), 7.77−7.82 (m, 1H), 7.87 (s, 1H), 9.59 (d, J = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 23.3, 118.6, 121.1, 121.9, 122.2, 125.9, 127.0, 127.56, 127.58, 128.1, 128.5, 129.8, 130.0, 130.6, 132.1, 132.6, 133.6, 138.0, 141.3, 141.5, 144.9, 145.7, 156.1. HRMS calcd for $C_{26}H_{18}BrN_4$: 465.0715 [M + H], found: 465.0719.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra. 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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