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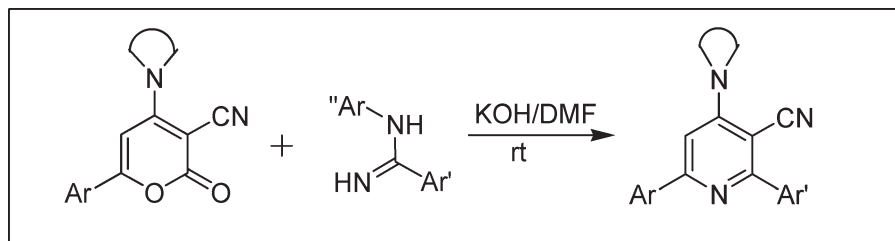
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The ring transformation of 2*H*-pyran-2-one by *N*-aryl amidine in the presence of KOH in DMF at room temperature resulted in a facile synthesis of the 2,6-diaryl-4-secondary aminonicotinitrile and highly substituted unsymmetrical 2,2'-bipyridines in moderate yield.

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INTRODUCTION

2*H*-pyran-2-ones are extensively used for the synthesis of a wide variety of heterocyclic compounds via ring transformation [1]. Ram and coworkers applied this strategy for the synthesis of various organic compounds like pyrimidine, fused heterocycles, congested benzene [1j], and pyridine [2]. The pyridine ring is one of the fundamental heterocycle present in many biologically active natural products. The compounds containing pyridine ring possess a broad range of biological activities [3]. Kawamura et al. have synthesized 4-substituted 2,6-diphenyl pyridines and reported their bleaching herbicidal activity [3b]. It was also found that 2-(*p*-aminobenzamido) pyridines exhibit a powerful inhibiting effect on gastric ulcers in rats [3g]. The pyridines 2,2'-bi- and 2,2',2''-ter-pyridine were used as metal chelating ligands with various substituents [4a]. Similarly, pyridine derivatives are of growing relevance in material science and supramolecular chemistry [4b]. Therefore, there is a continuous interest to develop the new synthetic methods for pyridines and their derivatives. Classical routes to pyridine preparation are Hantzsch [5], Chichibabin [6], Petrenko-Kritschenko and Zonoff [7], Krohnke [8], and Guareschi-Thorpe [9] condensation reactions. The condensation of 1,5-diketone with ammonia followed by nitric acid oxidation is a common approach for the synthesis of pyridines [10]. The reaction of dieneamine and ketone in the presence of Vilsmeier type 1-substituted-1,2,3-benzotriazole reagent results in the formation of nicotinonitriles [11]. The construction of unsymmetrically substituted pyridines was achieved by the reaction

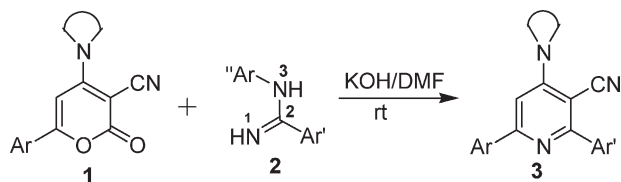
of 1,3-dicarbonyl compounds and 3-aminoenones or nitriles [12]. Saikai et al. reported indium trichloride catalyzed synthesis of tetrasubstituted pyridines [13]. Penieres et al. have synthesized pyridine by using microwave irradiated Hantzsch reaction [14]. A transition metal mediated 6-endo-dig cyclization of *N*-propargylamine derivative was carried out by Abbiati et al. to generate a pyridine ring [15]. Combinatorial approach also has been used for the synthesis of pyridine derivatives [16]. 2,4,6-trisubstituted pyridine derivatives were prepared from aroylketene dithioacetal by Potts et al. [17]. Recently, Ram and coworkers [18] have described the use of 2*H*-pyran-2-one for the synthesis of substituted pyridines, prompted us to carry out the synthesis of novel pyridines.

RESULT AND DISCUSSION

We investigated that compound **3** in moderate yield can be constructed from 2*H*-pyran-2-one **1** and the *N*-aryl amidine **2** via a ring transformation reaction using KOH in DMF at room temperature (Scheme 1).

Pyridine **3** isolated in this study could arise by nucleophilic attack of amidine N-1 at C-6 position of 2*H*-pyran-2-one. The intermediate **4** formed is unstable and it undergoes cyclization with a retro [2 + 2] process to yield **3a–i** with the loss of carbon dioxide. In the event of ring transformation of 2*H*-pyran-2-one **1** (Scheme 2) with *N*-aryl amidine **2**, the N-1 takes part in the reaction as a nucleophile rather than N-3. It might be due to the lone pair electrons on N-3 are delocalized over the

Scheme 1. Preparation of 2,6-diaryl-4-secondary aminonicotinonitriles **3** from 2*H*-pyran-2-one **1** and *N*-aryl amidine **2**.



benzene nucleus by orbital overlap with the π -orbital of the aromatic ring; therefore, they are less available for nucleophilic attack.

To generalize our strategy, we examined this method for the reaction of 2*H*-pyran-2-one **1** with *N*-heteroaryl amidine **6** in the presence of KOH/DMF catalytic system (Scheme 3). The reaction of 2*H*-pyran-2-one with *N*-heteroaryl amidine furnished the corresponding 2,6-disubstituted nicotinonitrile **3** in the poor yields (Table 1). The structure of the newly synthesized compounds was confirmed by spectroscopic data. It was observed that there is no improvement of yield even after 48 h also. The plausible mechanistic pathway is shown in Scheme 4.

In 2*H*-pyran-2-one **1**, three electrophilic centers are present C-3, C-4, and C-6, in which C-6 is more electrophilic in nature due to presence of an electron withdrawing group (—CN) at C-3 position of the ring system. The synthesis of 2,6-diaryl nicotinonitrile involves the nucleophilic attack by more basic N-1 of amidine **6** at C-6 of 2*H*-pyran-2-one. The attack of amidine N-1 leads to form unstable intermediate **7** followed by ring closure and a retro [2 + 2] process with the elimination of carbon dioxide to form 2,6-diaryl nicotinonitrile **3**. It is noteworthy that the pyridine ring nitrogen of amidine does not involve in ring transformation reaction. The structures of compounds **3a–i** (Table 2) were determined based on the spectroscopic data and elemental analysis.

Thus, in both cases (Schemes 1 and 3), the 2,6-diaryl nicotinonitriles were formed exclusively without any side product.

Finally, we used our strategy to synthesize highly substituted unsymmetrical 2,2-bipyridines (Scheme 5) in presence of powdered KOH and DMF at room temperature. The results show that the yield of obtained bipyridine was moderate (Table 2). We believe that the reaction proceeds with the same mechanistic pathway as depicted in Scheme 2.

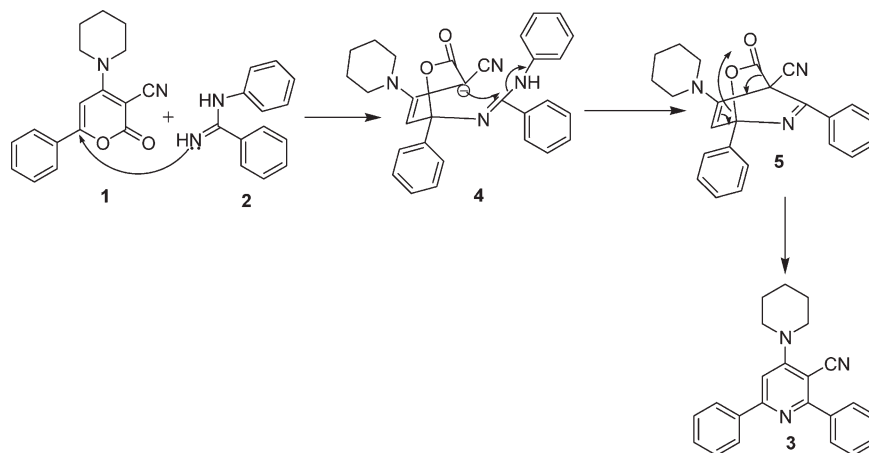
CONCLUSIONS

In summary, this study demonstrates that the ring system proposed for nicotinonitrile is correct with the substitution pattern. An additional finding is that the ring transformation of 2*H*-pyran-2-one by *N*-pyridyl amidine provides useful information for construction of the nicotinonitrile ring system with 2,6-diaryl substituent. Furthermore, we synthesized highly substituted unsymmetrical bipyridine using this method. Further studies on the applications of this method for the synthesis of nicotinonitrile with the 2,6-heteryl substituent are underway.

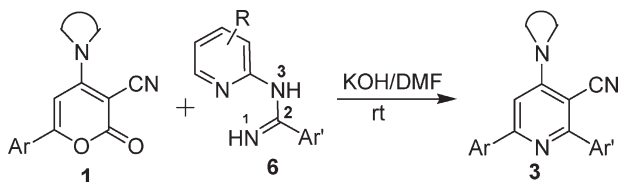
EXPERIMENTAL

General procedures. Melting points were determined in open capillaries and are uncorrected. Progress of the reaction was monitored by TLC (visualization was effected by exposure to UV light). Commercial reagents were used without purification. IR spectra were recorded on a Perkin-Elmer Spectrum One spectrometer. Mass spectra were recorded under ESI mode, on Thermo Finnigan (model-LCQ Advantage MAX) mass spectrometer. ^1H NMR and ^{13}C NMR were recorded in CDCl_3 on a Bruker Spectrometers, operating at 300 MHz and 75 MHz for ^1H NMR and ^{13}C NMR, respectively, and shifts are given in ppm downfield from TMS as an internal standard.

Scheme 2. The plausible mechanism [18] for the formation of substituted compounds **3**.



Scheme 3. Reaction between 2*H*-pyran-2-one **1** and *N*-heteroaryl amine **6** for synthesis of 2,6-disubstituted nicotinonitrile.



Elemental analysis was carried out on Thermo Quest micro-analysis instrument, Whitehouse, NJ.

General experimental procedure for the synthesis of 3a-1. The mixture of 2*H*-pyran-2-one-3-carbonitrile (1.0 mmol), *N*-phenyl/heteroaryl benzamidine (1.0 mmol) and powdered KOH (2.0 mmol) in 5 mL DMF was stirred for 5–6 h at room temperature. The reaction was monitored by TLC. After completion of the reaction, excess DMF was removed under reduced pressure. Then the residue was poured into crushed

ice with vigorous stirring. The aqueous solution was neutralized with 10% HCl, the precipitate obtained was filtered, and the obtained residue was purified by column chromatography on silica gel 60–120 by eluting 5% ethyl acetate:hexane.

2,6-Diphenyl-4-(piperidin-1-yl)pyridine-3-carbonitrile (3a). White solid, IR (KBr): 2209 (C≡N), 1568 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ = 1.73 (d, *J* = 5.7 Hz, 2H, CH₂), 1.83 (d, *J* = 3.3 Hz, 4H, 2CH₂), 3.54 (t, *J* = 9.9 Hz, 4H, 2CH₂N), 6.91 (s, 1H, CH), 7.5 (m, 5H, ArH), 7.84 (d, *J* = 4.7 Hz, 2H, ArH), 8.05 (t, *J* = 9.5 Hz, 3H, ArH). ¹³C NMR (75 MHz, CDCl₃) δ = 24.2, 26.1, 52.1, 96.4, 106.7, 118.7, 124.4, 125.3, 127.6, 128.5, 128.9, 129.6, 130.1, 138.9, 159.8, 162.9, 164.2. MS (ESI, 70 eV) *m/z* (%) = 340 (100) [M⁺], 341(27) [(M+H)⁺]. Anal. Calcd. for C₂₃H₂₁N₃: C, 81.38; H, 6.24; N, 12.38. Found: C, 81.42; H, 6.20; N, 12.38.

6-(4-Bromophenyl)-2-phenyl-4-(piperidin-1-yl)pyridine-3-carbonitrile (3b). White solid, IR (KBr): 2212 (C≡N), 1568 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ = 1.72 (d, 2H, CH₂), 1.8 (d, *J* = 5 Hz, 4H, 2CH₂), 3.54 (t, *J* = 10.6 Hz, 4H, 2CH₂N), 7.12 (s, 1H, CH), 7.51 (m, 3H, ArH), 7.59 (s,

Scheme 4. The plausible mechanism [18] for the formation of substituted 2,6-disubstituted nicotinonitrile.

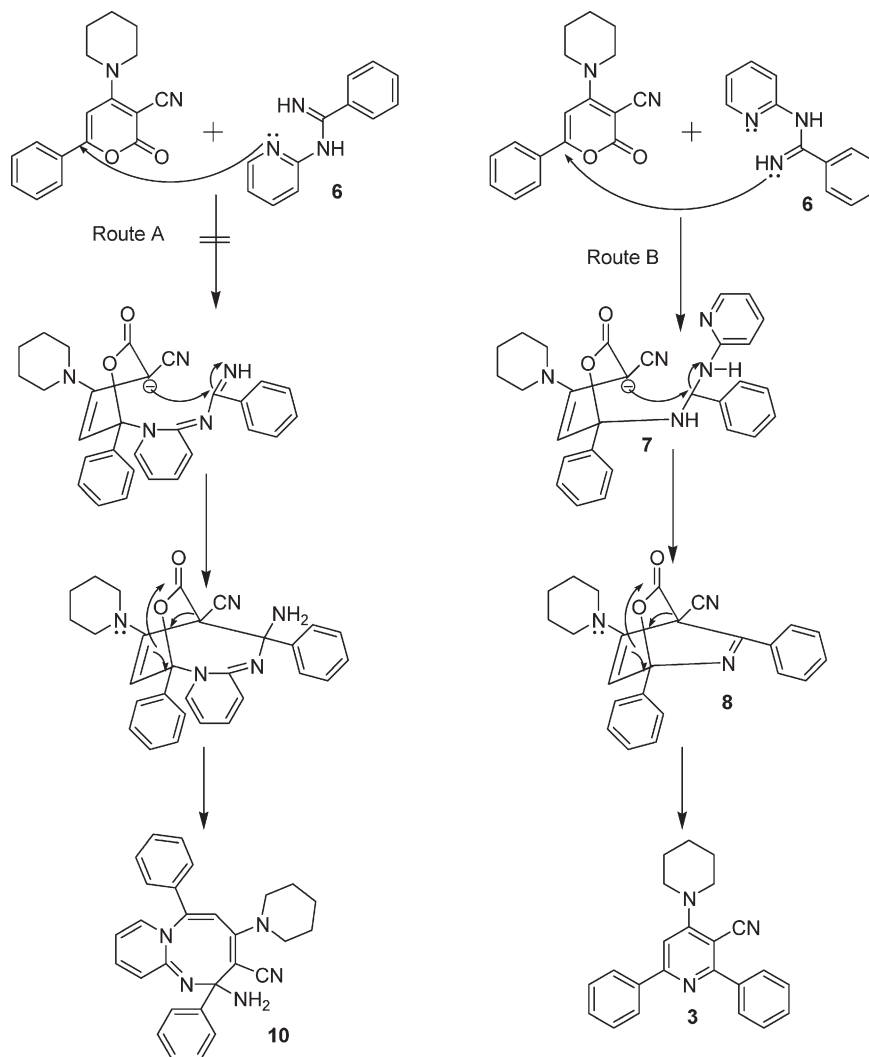


Table 1

Preparation of 2,6-diaryl-4-secondary aminonicotinonitriles **3^a** from 2*H*-pyran-2-one **1** and *N*-aryl amidine **2^b**.

Entry	Ar		Ar'	Ar''	Yields ^c (%)	m.p.
3a	C ₆ H ₅	Piperidine	C ₆ H ₅	4-F-C ₆ H ₄	48%	160°C
3a	C ₆ H ₅	Piperidine	C ₆ H ₅	C ₆ H ₅	48%	161°C
3b	4-Br-C ₆ H ₄	Piperidine	C ₆ H ₅	C ₆ H ₅	48%	173°C
3b	4-Br-C ₆ H ₄	Piperidine	C ₆ H ₅	4-F-C ₆ H ₄	42%	173°C
3c	4-Br-C ₆ H ₄	Morpholine	C ₆ H ₅	4-F-C ₆ H ₄	46%	172°C
3c	4-Br-C ₆ H ₄	Morpholine	C ₆ H ₅	C ₆ H ₅	44%	172°C
3d	4-Cl-C ₆ H ₄	Morpholine	C ₆ H ₅	4-F-C ₆ H ₄	39%	198°C

^a All products were characterized by using I.R., ¹H, ¹³C NMR, mass spectroscopy, and elemental analysis.^b 2*H*-pyran-2-one **1** (1.0 mmol), *N*-aryl amidine **2** (1.0 mmol), KOH (2.0 mmol), and DMF (5 mL), room temperature.^c Isolated yield.

1H, ArH), 7.62 (s, 1H, ArH), 7.93 (m, 4H, ArH). ¹³C NMR (75 MHz, CDCl₃) δ = 24.2, 26.1, 52.0, 96.8, 106.4, 118.6, 124.7, 128.6, 129.2, 129.6, 130.1, 132.1, 137.7, 138.7, 158.5, 162.9, 163.9. MS (ESI, 70 eV) *m/z* (%) = 418 (100) [M⁺], 420 (92) [(M+2H)⁺]. Anal. Calcd. for C₂₃H₂₀BrN₃: C, 66.04; H, 4.82; N, 10.04. Found: C, 66.01; H, 4.77; N, 10.08.

6-(4-Bromophenyl)-4-(morpholin-4-yl)-2-phenylpyridine-3-carbonitrile (3c). White solid, IR (KBr): 2210 (C≡N), 1582 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ = 3.55 (q, *J* = 13.5 Hz, 4H, 2CH₂N), 3.94 (q, *J* = 14 Hz, 4H, 2CH₂O), 6.73 (s, 1H, CH), 7.51 (q, *J* = 9.9 Hz, 3H, ArH), 7.59 (s, 1H, ArH), 7.63 (s, 1H, ArH), 7.92 (m, 3H, ArH), 7.97 (s, 1H, ArH). ¹³C NMR (75 MHz, CDCl₃) δ = 50.9, 66.8, 97.3, 106.3, 118.2, 125.1, 128.6, 129.2, 129.5, 130.3, 132.2, 137.3, 138.3, 159.1, 162.6, 164.2. MS (ESI, 70 eV) *m/z* (%) = 420 (28%) [M⁺], 422 (12%) [(M+2H)⁺], 393 (8). Anal. Calcd. for C₂₂H₁₈BrN₃O: C, 62.87; H, 4.32; N, 10.00. Found: C, 62.82; H, 4.37; N, 10.11.

6-(4-Chlorophenyl)-4-(morpholin-4-yl)-2-phenylpyridine-3-carbonitrile (3d). White solid, IR (KBr): 2216 (C≡N), 1583 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ = 3.54 (q,

J = 14.1 Hz, 4H, 2CH₂N), 3.94 (q, *J* = 13.9 Hz, 4H, 2CH₂O), 7.14 (s, 1H, CH), 7.51 (m, 5H, ArH), 7.89 (m, 2H, ArH), 8.00 (s, 1H, ArH), 8.04 (s, 1H, ArH). ¹³C NMR (75 MHz, CDCl₃) δ = 50.9, 66.8, 97.2, 106.3, 118.2, 128.6, 128.9, 129.3, 129.5, 130.3, 136.7, 136.9, 138.3, 159.0, 162.7, 164.2. MS (ESI, 70 eV) *m/z* (%): 376 (100) [M⁺], 378 (33) [(M+2H)⁺]. Anal. Calcd. for C₂₂H₁₈ClN₃O: C, 70.30; H, 4.83; N, 11.18. Found: C, 70.34; H, 4.94; N, 11.23.

2,6-Bis(4-bromophenyl)-4-(piperidin-1-yl)pyridine-3-carbonitrile (3e). White solid, IR (KBr): 2214 (C≡N), 1580 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ = 1.79 (m, 6H, 3CH₂), 3.53 (t, *J* = 15 Hz, 4H, 2CH₂N), 7.12 (s, 1H, CH), 7.62 (m, 4H, ArH), 7.77 (d, *J* = 4.7 Hz, 1H, ArH), 7.81 (d, *J* = 3 Hz, 1H, ArH), 7.89 (d, *J* = 3 Hz, 1H, ArH), 7.93 (s, 1H, ArH). MS (ESI, 70 eV) *m/z* (%) = 497.8 (25) [M⁺], 499 (12) [(M+2H)⁺]. Anal. Calcd. for C₂₃H₁₉Br₂N₃: C, 55.56; H, 3.85; N, 8.45. Found: C, 55.59; H, 3.81; N, 8.48.

6-(4-Chlorophenyl)-2-phenyl-4-(piperidin-1-yl)pyridine-3-carbonitrile (3f). White solid, IR (KBr): 2214 (C≡N), 1568 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ = 1.73 (d, *J* = 532 Hz, 2H, CH₂), 1.82 (d, *J* = 5.0 Hz, 4H, 2CH₂), 3.55

Table 2

Reaction conditions with yields and m.p. for products^a **3**.

Entry	Ar		Ar'	R	Yields ^b (%)	m.p.
3a	C ₆ H ₅	Piperidine	C ₆ H ₅	H	13%	160°C
3b	4-Br-C ₆ H ₄	Piperidine	C ₆ H ₅	H	26%	173°C
3c	4-Br-C ₆ H ₄	Morpholine	C ₆ H ₅	H	24%	172°C
3d	4-Cl-C ₆ H ₄	Morpholine	C ₆ H ₅	H	24%	198°C
3e	4-Br-C ₆ H ₄	Piperidine	4-Br-C ₆ H ₄	H	22%	168°C
3f	4-Cl-C ₆ H ₄	Piperidine	C ₆ H ₅	H	16%	172°C
3g	4-Cl-C ₆ H ₄	Pyrolidine	C ₆ H ₅	H	19%	156°C
3g	4-Cl-C ₆ H ₄	Pyrolidine	C ₆ H ₅	4-Br	22%	156°C
3h	4-CH ₃ O-C ₆ H ₄	Piperidine	C ₆ H ₅	H	38%	166°C
3i	4-Cl-C ₆ H ₄	Pyrolidine	4-Br-C ₆ H ₄	H	44%	122°C

^a All products were characterized by using I.R., ¹H, ¹³C NMR, mass spectroscopy, and elemental analysis.^b Isolated yield.

Table 3
Reaction conditions with yields and m.p. for products^a 3.

Entry	Ar		Ar''	Yields ^b (%)	m.p.
3j	4-Br-C ₆ H ₄	Pyrolidine	4-Br-C ₆ H ₄	43%	206–208°C
3k	4-Cl-C ₆ H ₄	Morpholine	4-Br-C ₆ H ₄	48%	164–166°C
3l	C ₆ H ₅	Morpholine	3,4-Cl-C ₆ H ₃	52%	152–154°C

^a All products were characterized by using I.R., ¹H, ¹³C NMR, mass spectroscopy, and elemental analysis.

^b Isolated yield.

(t, $J = 10.6$ Hz, 4H, 2CH₂N), 7.13 (s, 1H, CH), 7.44 (m, 5H, ArH), 7.93 (q, $J = 9.68$ Hz, 2H, ArH), 8.00 (s, 1H, ArH), 8.03 (s, 1H, ArH). MS (ESI, 70 eV) m/z (%) = 374 (100) [M⁺], 376 (35) [(M+H)⁺]. Anal. Calcd. for C₂₃H₂₀ClN₃: C, 73.89; H, 5.39; N, 11.24. Found: C, 73.97; H, 5.35; N, 11.36.

6-(4-Chlorophenyl)-2-phenyl-4-(pyrrolidin-1-yl)pyridine-3-carbonitrile (3g). White solid, IR (KBr): 2199 (C≡N), 1590 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ 2.09 (m, 4H, 2CH₂), 3.81 (t, $J = 13.2$ Hz, 4H, 2CH₂N), 6.85 (s, 1H, CH), 7.48 (m, 5H, ArH), 7.86 (q, $J = 9.6$ Hz, 2H, ArH), 7.98 (d, $J = 8.66$ Hz, 2H, ArH). ¹³C NMR (75 MHz, CDCl₃) δ = 25.9, 50.5, 96.1, 106.5, 118.6, 128.4, 128.6, 129.0, 129.6, 129.8, 135.9, 137.5, 139.3, 158.6, 162.8, 163.1. MS (ESI, 70 eV) m/z (%) = 360 (100) [M⁺], 362 (32) [(M+2H)⁺]. Anal. Calcd. for C₂₂H₁₈ClN₃: C, 73.43; H, 5.04; N, 11.68. Found: C, 73.42; H, 5.04; N, 11.03.

6-(4-Methoxyphenyl)-2-phenyl-4-(piperidin-1-yl)pyridine-3-carbonitrile (3h). White solid, IR (KBr): 2209 (C≡N), 1607 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ = 1.72 (d, $J = 5.1$ Hz, 2H, CH₂), 1.83 (d, $J = 4.6$ Hz, 4H, 2CH₂), 3.52 (t, $J = 10.5$ Hz, 4H, 2CH₂N), 3.88 (s, 3H, CH₃O), 6.98 (s, 1H, CH), 7.01 (s, 1H, ArH), 7.12 (s, 1H, ArH), 7.50 (m, 3H, ArH), 7.94 (q, $J = 9.6$ Hz, 2H, ArH), 8.04 (s, 1H, ArH), 8.06 (s, 1H, ArH). ¹³C NMR (75 MHz, CDCl₃) δ = 24.3, 25.1, 52.1, 55.6, 95.9, 105.7, 114.3, 124.7, 124.9, 129.1, 131.2, 131.8, 131.8, 132.2, 137.5, 159.4, 161.5, 163.0. MS (ESI, 70 eV) m/z (%) = 370 (100) [M⁺], 371 (32) [(M+2H)⁺]. Anal. Calcd. for C₂₄H₂₃N₃O: C, 78.02; H, 6.27; N, 11.37. Found: C, 78.06; H, 6.29; N, 11.34.

2-(4-Bromophenyl)-6-(4-chlorophenyl)-4-(pyrrolidin-1-yl)pyridine-3-carbonitrile (3i). White solid, IR (KBr): 2115 (C≡N), 1590 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ = 2.08 (brs, 4H), 3.79 (brs, 4H), 6.84 (s, 1H), 7.43 (s, 2H), 7.63 (s, 2H), 7.73 (s, 2H), 7.96 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ = 25.2, 50.1, 88.5, 103.6, 119.5, 123.2, 128.6, 128.9, 131.1, 131.3, 134.3, 134.6, 136.7, 138.1, 155.1, 155.4, 162.7. MS (ESI, 70 eV) m/z (%) = 438 [M⁺, 43%], 440

[(M+2H)⁺, 55%]. Anal. Calcd. for C₂₂H₁₇BrClN₃: C 60.22; H 3.91; N 9.58. Found: C, 60.42; H, 3.83; N, 9.42.

6-(4-Bromophenyl)-2-(pyridine-2-yl)-4-(pyrrolidin-1-yl)pyridine-3-carbonitrile (3j). Yellowish red solid, IR (KBr): 2190 (C≡N), 1566 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ = 2.07 (bs, 4H, CH₂), 3.82 (bs, 4H, 2NCH₂), 6.91 (s, 1H, CH), 7.39 (s, 1H, ArH), 7.59 (s, 2H, ArH), 7.91 (bs, 3H, ArH), 8.02 (bs, 1H, ArH), 8.77 (bs, 1H, ArH). ¹³C NMR (125 MHz, CDCl₃) δ = 25.7, 50.4, 94.4, 103.9, 116.4, 123.9, 124.3, 128.8, 131.8, 136.7, 137.6, 146.7, 148.7, 158.3. MS (ESI, 70 eV) m/z (%) = 405 (100) [M⁺]. Anal. Calcd. for C₂₁H₁₇BrN₄: C, 62.23; H, 4.23; N, 13.82. Found: C, 62.43; H, 4.364; N, 13.87.

6-(4-Chlorophenyl)-4-morpholino-2-(pyridine-2-yl)pyridine-3-carbonitrile (3k). Yellowish red solid, IR (KBr): 2225 (C≡N), 1566 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ = 3.55–3.58 (t, 4H, 2NCH₂), 3.94–3.97 (t, 4H, 2OCH₂), 7.21 (s, 1H, CH), 7.41–7.49 (m, 3H, ArH), 7.85–7.91 (m, 1H, ArH), 8.02–8.05 (q, 2H, ArH), 8.17–8.19 (d, $J = 7.8$ Hz, 1H, ArH), 8.78–8.79 (dd, 1H, ArH). ¹³C NMR (125 MHz, CDCl₃) δ = 50.8, 66.6, 97.4, 107.3, 117.5, 123.7, 124.8, 128.8, 129.2, 136.7, 148.8, 155.4, 158.3, 162.8. MS (ESI, 70 eV) m/z (%) = 377 [M⁺, 100%], 379 [(M+2H)⁺, 35%]. Anal. Calcd. for C₂₁H₁₇ClN₄O: C, 66.93; H, 4.55; N, 14.87. Found: C, 66.83; H, 4.64; N, 14.94.

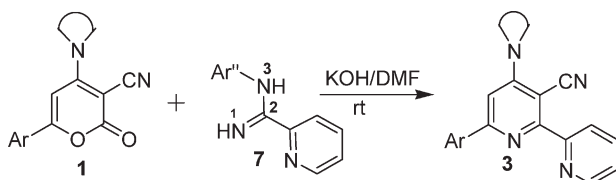
4-Morpholino-6-phenyl-2-(pyridin-2-yl)pyridine-3-carbonitrile (3l). Yellowish red solid, IR (KBr): 2215 (C≡N), 1574, 1538 (C=N) cm⁻¹. ¹H NMR (300 MHz, CDCl₃, 25°C) δ = 3.55–3.58 (t, 4H, 2NCH₂), 3.94–3.97 (t, 4H, 2OCH₂), 7.25 (s, 1H, CH), 7.40–7.51 (m, 4H, ArH), 7.85–7.91 (m, 1H, ArH), 8.07–8.09 (t, 2H, ArH), 8.20–8.23 (d, $J = 7.8$ Hz, 1H, ArH), 8.77–8.79 (d, $J = 4.2$ Hz, 1H, ArH). ¹³C NMR (125 MHz, CDCl₃) δ = 50.7, 66.6, 97.3, 107.5, 117.6, 123.7, 124.7, 127.4, 128.8, 130.2, 136.8, 138.1, 148.6, 155.5, 159.5, 161.3, 162.7, 165.3. MS (ESI, 70 eV) m/z (%) = 343 [(M+H)⁺, 78%]. Anal. Calcd. for C₂₁H₁₈N₄O: C, 73.67; H, 5.30; N, 16.36. Found: C, 73.88; H, 5.42; N, 16.44.

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Scheme 5. Synthesis of highly substituted unsymmetrical bipyridine.



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