Facile and Efficient Synthesis of a New Class of Indole-Substituted Pyridine Derivatives via One-Pot Multicomponent Reactions

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Abstract: A new series of indole-containing pyridine derivatives, 4-aryl-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitriles, were synthesized via one-pot multicomponent reactions of 3-(cyanoacetyl)indoles, aldehydes, heterocyclic ketones, and ammonium acetate. Particularly valuable features of this method include high yields of products, broad substrate scope, and straightforward procedures.

Key words: pyridine derivatives, indole, one-pot synthesis, multicomponent reactions, heterocycles

Pyridine derivatives have long been the focus of considerable attention for their abundant existence in numerous nature products as well as their extensive applications in biological, pharmic, and supramolecular science.[1–3] In particular, bipyridines, along with higher oligopyridines, have attracted widespread attention as key building blocks in the formation of discrete metallosupramolecular species having well-defined geometries and stoichiometries because of their π-stacking ability, directional hydrogen bonding, and excellent coordination properties to various of transition metals.[4] Moreover, bipyridines and related complexes have also found numerous applications in asymmetric catalysis,[5] photoinduced electron transfer,[6] artificial photosynthesis,[7] and polymer and dendrimer science.[8] With all these fascinating potential applications, much research has been devoted to the development of directed synthetic routes to suitable bipyridine units, as well as effective functionalization strategies.[9]

Indole fragments are featured in a wide variety of pharmacologically and biologically active compounds,[10] the fluorescent amino acid tryptophan, the plant growth regulator indole-3-acetic acid, the neurotransmitter serotonin, and a variety of marine alkaloids containing indole units, such as the meridianins A–E, are all of crucial importance in plant, animal, and human physiology (Figure 1).[11] Thus, synthetic methods and the structure decoration of indole derivatives have received increased attention in recent years.[12]

Drawn by the extraordinary capacity of bipyridines to chelated transition metals and the brilliant physiological and biological activities of indole derivatives, a great

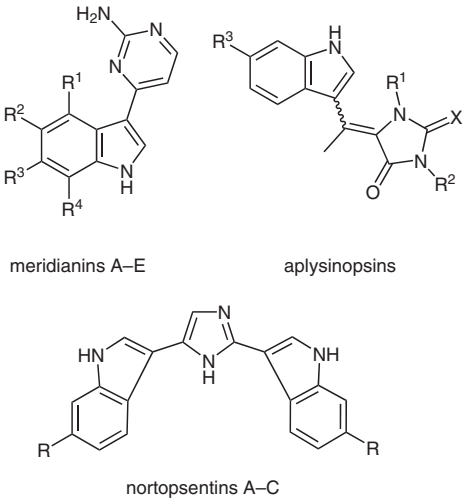

Figure 1 Some typical indole-substituted heterocycles

number of efforts have been devoted to the synthesis of indole-containing bipyridine complexes in order to design suitable labels or probes for indole-binding proteins, such as serum albumins and tryptophanase. Whereas the indole moiety serves as the biological recognition unit for these proteins, the polypyridine units coordinating with a luminescent transition metal play a role as the environment-sensitive emitter, which assist in the detection, monitoring, and isolation of these important biomolecules.[13]

Base on the remarkable range of applications of bipyridines and indole derivatives, we became interested in introducing an indole unit into the bipyridine skeleton. However, many existing methods for the synthesis of substituted bipyridines have drawbacks, such as restriction of the functionalization positions in the well-known Kröhnke procedure,[14] the increasing isomeric mixture when using Raney nickel catalysts in the Rode procedure,[15] and the creation of organophosphorus[16] or organosulfur compounds[17] in other synthetic strategies. Even modern synthetic routes such as the Suzuki[18] or Negishi cross-coupling[19] suffered from narrow scope of substrates, harsh reaction conditions, generality, and operational complexity due to the occurrence of several side reactions. Additionally, to the best of our knowledge, there have been few reports on the synthesis of bipyridine derivatives incorporated indole moieties. Therefore, inspired by our previous work, the synthesis of a series of bisindoles derivatives containing 3,5-dicyanopyridine

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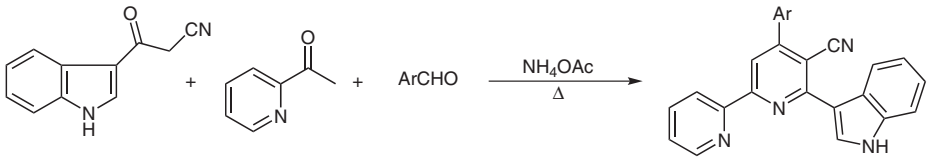
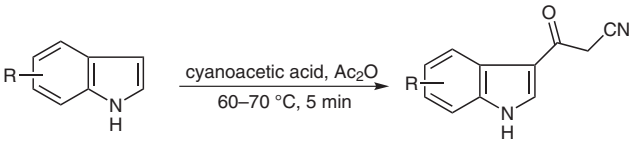


Scheme 1

units,[20] we devised a simple, efficient, and straightforward protocol for the synthesis of a new series of indole-substituted bipyridines via a one-pot, multicomponent reaction between an aldehyde, 3-(cyanoacetyl)indole, 2-acetylpyridine, and ammonium acetate (Scheme 1).

The starting material 3-(cyanoacetyl)indoles **1** were previously prepared by Kreher and Wagner[21] and recently by Bergman[22] via a new facile approach starting from indoles and cyanoacetic acid (Scheme 2).



1

Scheme 2

In our initial studies, the one-pot reaction of 4-chlorobenzaldehyde (**2a**), 3-(cyanoacetyl)-1*H*-indole (**1a**), 2-acetylpyridine (**3**), and ammonium acetate (Table 1) was chosen as the model reaction to optimize the reaction conditions.

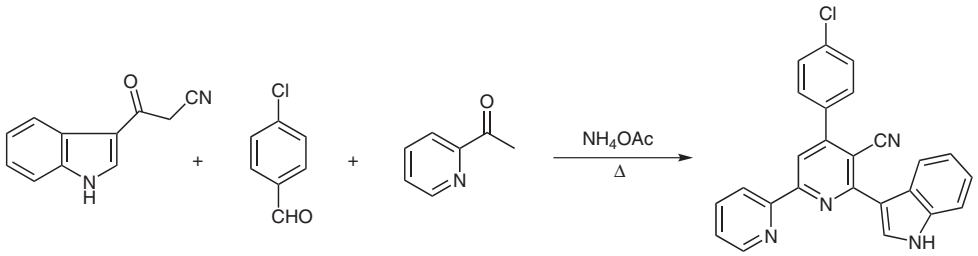
Firstly, the synthesis of **4a** was carried out in different solvents, such as anhydrous ethanol, methanol, acetic acid, acetonitrile, *N*,*N*-dimethylformamide, glycol, and butan-1-ol, to investigate their effects on the synthetic procedure. The results are shown in Table 1 (entries 1–6), from which we can see that the best yield was obtained when butan-1-ol was used as the solvent.

The temperature screening was also carried out for the range 80–110 °C in butan-1-ol (Table 1, entries 7–10), elevation of the temperature had some positive effects and improved the yield of the target product; 100 °C was the most appropriate temperature that gave acceptable results.

Under these optimal conditions (*n*-BuOH, 100 °C), a series of 4-aryl-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitriles **4** were synthesized (Table 2).

During the experiments, the desired products **4a**–**w** were isolated in moderate to good yields, however, monitoring

Table 1 Solvent and Temperature Optimization for the Synthesis of **4a**

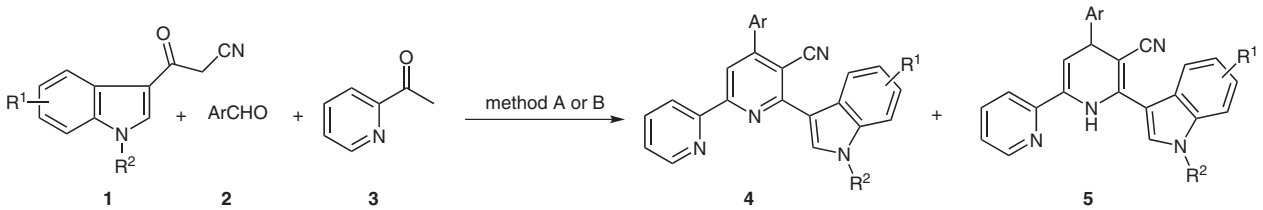


1a **2a** **3** **4a**

Entry	Solvent	Temp (°C)	Time (h)	Yield[a] (%)
1	MeOH	80	10	43
2	EtOH	80	8	58
3	MeCN	80	10	52
4	glycol	80	9	60
5	DMF	80	8	50
6	AcOH	80	12	35
7	*n*-BuOH	80	9	68
8	*n*-BuOH	90	8	70
9	*n*-BuOH	100	8	78
10	*n*-BuOH	110	8	71

[a] Isolated yields.

Table 2 Synthesis of 4-Aryl-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitriles **4**



1 2 3 4 5

Entry	Product	Ar	R^1	R^2	Method A[a]		Method B[a]		Mp (°C)
					Yield[b] (%)	Time (h)	Yield[b] (%)	Time (h)	
1	**4a**	4-ClC_6H_4	H	H	78	8	95	5	>300
2	**4b**	4-BrC_6H_4	H	H	72	9	90	5	>300
3	**4c**	4-$O_2NC_6H_4$	H	H	80	6	93	4	>300
4	**4d**	3-$O_2NC_6H_4$	H	H	82	6	91	4	272–273
5	**4e**	2,4-$Cl_2C_6H_3$	H	H	73	10	88	6	275–277
6	**4f**	Ph	H	H	66	9	87	5	294–296
7	**4g**	4-MeC_6H_4	H	H	62	11	81	7	288–290
8	**4h**	4-$MeOC_6H_4$	H	H	58	11	87	8	266–268
9	**4i**	2-MeC_6H_4	H	H	60	10	88	6	271–273
10	**4j**	2-$MeOC_6H_4$	H	H	55	12	79	9	283–285
11	**4k**	3,4-$OCH_2OC_6H_3$	H	H	65	10	89	6	258–260
12	**4l**	2-thienyl	H	H	60	10	82	8	275–277
13	**4m**	3-thienyl	H	H	60	12	80	9	253–255
14	**4n**	2-furyl	H	H	58	13	86	8	258–259
15	**4o**	1-naphthyl	H	H	70	10	90	8	270-271
16	**4p**	2-naphthyl	H	H	76	11	88	7	262–264
17	**4q**	2-ClC_6H_4	H	H	75[c] (**5a**)	3	85	8	>300
18	**4r**	2-BrC_6H_4	H	H	80[c] (**5b**)	3	83	9	>300
19	**4s**	Ph	5-Me	H	65	7	89	4	256–258
20	**4t**	Ph	6-Me	H	66	7	93	5	>300
21	**4u**	Ph	7-Me	H	63	8	90	5	298–299
22	**4v**	Ph	H	Me	58	9	80	5	243–244
23	**4w**	Ph	5-Br	H	70	8	92	6	>300

[a] Method A: NH_4OAc (3 equiv), *n*-BuOH, 100 °C; Method B: 1. NH_4OAc (3 equiv), *n*-BuOH, 100 °C, 2. DDQ (50 mol%).
[b] Isolated yields.
[c] The non-aromatized 4-aryl-6-(1*H*-indol-3-yl)-1,4-dihydro-2,2′-bipyridine-5-carbonitriles **5a**,**b** were isolated.

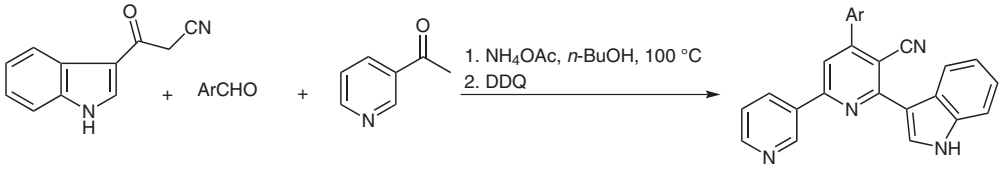
the synthetic procedure by thin layer chromatography showed that the desired aromatized products **4** were obtained together with non-aromatized products (Table 2, Method A). In order to further improve the yield of the final products, a powerful oxidant 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was added in order to promote aromatization. To our great delight, the use of DDQ led to an obvious increase in the yields of the target compounds **4** as well as a decrease of the reaction time (Table 2, Method B).

To examine the efficiency and the applicability of this new multi-component reaction, different aldehydes and indoles were tested. As shown in Table 2, this protocol was readily available to aromatic aldehydes bearing either electron-withdrawing functional groups, such as nitro and

halo substituents (Table 2, entries 1–5), or electron-donating ones, such as alkyl and alkoxy (Table 2, entries 7–11), as well as heterocyclic aldehydes, such as thiophene-2-carbaldehyde, thiophene-3-carbaldehyde, and furan-2-carbaldehyde (Table 2, entries 12–14). In addition, sterically bulky 1- and 2-naphthaldehyde (Table 2, entries 15 and 16) gave the target compounds **4o**,**p** in high yields. During the experiments, subtle electronic effects were observed in the substituents, for example, arylaldehydes with electron-withdrawing groups reacted rapidly and gave better yields of final products, while the electron-rich groups might decrease the reactivities of the substrates, so that they required longer reaction times and the yields were a little lower. Moreover, reactions of substituted 3-(cyanoacetyl)indoles **1** were smooth and gave the anticipated products in excellent yields. Interestingly, when the aldehydes bearing a halide substituent at the 2-position (Table 2, entries 17 and 18) were applied, the non-aromatized 1,4-dihydropyridine derivatives **5a**,**b** were sufficiently stable to be isolated from the reaction system in good yields, which indicated that substitution at the 2-position of the aldehydes might have some subtle effects, which would prevent the further aromatization observed in other cases in Table 2. However, **5a** and **5b** were transformed into the aromatized products **4q** and **4r** with the addition of a stoichiometric amount of DDQ. To our disappointment, aliphatic aldehydes did not take part in related reactions effectively.

In order to further expand the scope of application of this protocol, 2-acetylpyridine (**3**) was replaced by 3-acetylpyridine (**6**) (Table 3) and 2-acetylthiophene (**8**) (Table 4) and these reacted smoothly to give the corresponding indole-containing pyridine derivatives **7** and **9**, respectively. Aliphatic ketones were also tested, however, no target compounds were obtained because of their deficient reactivities.

Table 3 Synthesis of 4-Aryl-6-(1*H*-indol-3-yl)-2,3′-bipyridine-5-carbonitriles **7**

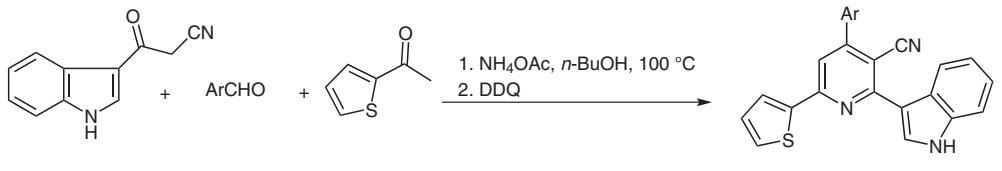


1a **2** **6** **7**

Entry	Product	Ar	Time (h)	Yield[a] (%)	Mp (°C)
1	**7a**	4-ClC_6H_4	12	72	278–280
2	**7b**	4-$O_2NC_6H_4$	10	75	>300
3	**7c**	Ph	14	70	282–284
4	**7d**	4-$MeOC_6H_4$	16	70	233–235
5	**7e**	2-furyl	12	68	293–294

[a] Isolated yields.

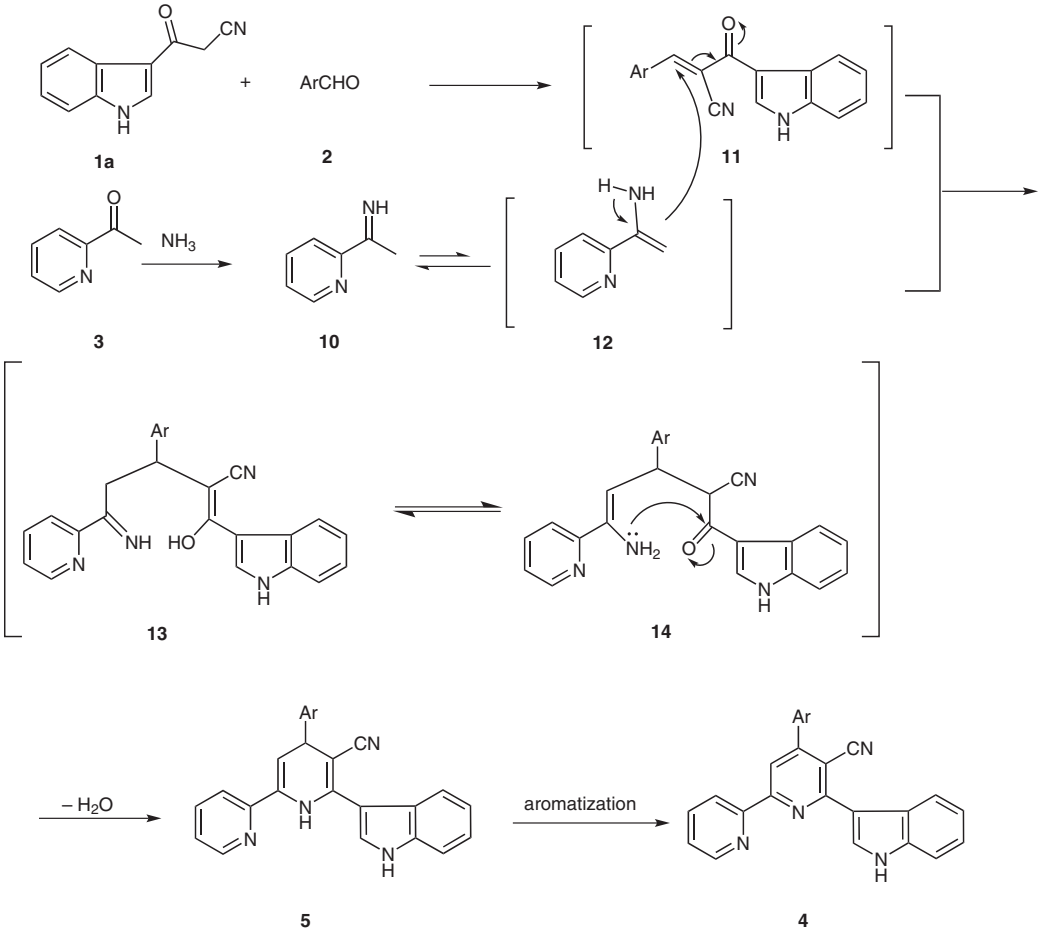
Table 4 Synthesis of 4-Aryl-2-(1*H*-indol-3-yl)-6-(2-thienyl)nicotinonitriles **9**



1a **2** **8** **9**

Entry	Product	Ar	Time (h)	Yield[a] (%)	Mp (°C)
1	**9a**	4-ClC_6H_4	13	68	>300
2	**9b**	4-BrC_6H_4	12	70	>300
3	**9c**	4-$O_2NC_6H_4$	10	73	>300
4	**9d**	3-$O_2NC_6H_4$	10	69	285–286
5	**9e**	Ph	16	65	283–285

[a] Isolated yields.



Scheme 3

Although the detailed mechanism of the above reaction remains to be fully clarified, formation of the final products, 4-aryl-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitriles **4** for instance, might undergo a sequential procedure containing a typical Knoevenagel condensation following by a Hantzsch condensation (Scheme 3).

Firstly, condensation between 3-(cyanoacetyl)indole **1a** and aldehyde **2** gave intermediate **11** and 2-acetylpyridine (**3**) and ammonium acetate gave intermediate **12**. Then, **11** was attacked by **12** via a Michael addition to give **13**, which could isomerize to intermediate **14**. Intramolecular cyclization of **14** gave the dihydro intermediate **5**, which could further undergo dehydrogenation to afford the fully aromatized products **4** (Scheme 3). This type of dehydrogenation is well precedented.[23]

In this study, all the products were characterized by melting point, IR, NMR, and HRMS data. Furthermore, the structures of **4f**[24] and **5b**[25] were confirmed by X-ray crystallographic analysis (Figures 2 and 3).

In conclusion, we have demonstrated a simple and efficient approach to the synthesis of a series of indole-substituted pyridine derivatives via multicomponent reactions of aldehydes, 3-(cyanoacetyl)indoles, heterocyclic ketones, and ammonium acetate in butan-1-ol at 100 °C, which incorporates an indole, a pyridine, and another (het)arene into a single molecule in just one-step. The most fascinating characteristics of this procedure are the excellent yields of the target compounds, the broad scope of the substrates, the short reaction time, and the convenient and straightforward synthetic routes.

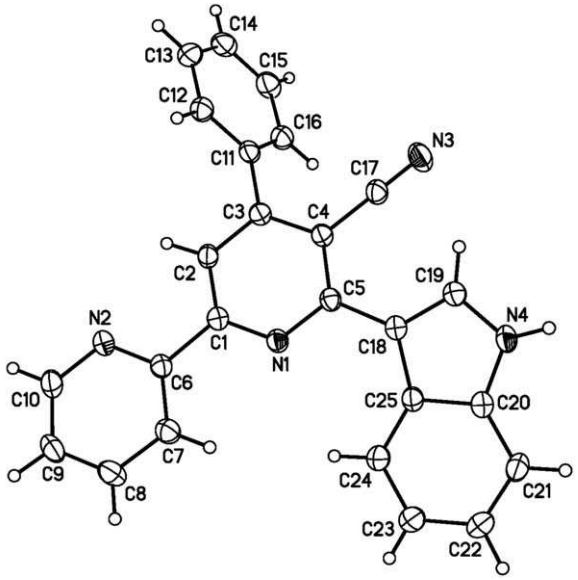


Figure 2 Crystal structure of **4f**

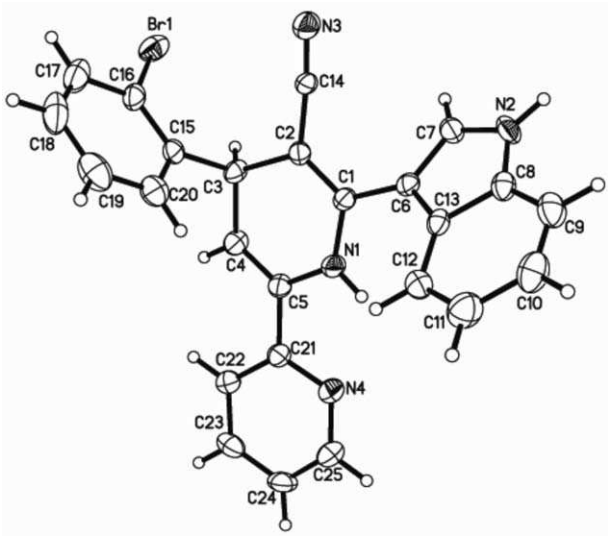


Figure 3 Crystal structure of **5b**

Melting points were recorded on an Electrothermal digital melting point apparatus and are uncorrected. IR spectra were recorded on a Varian FT-1000 spectrophotometer using KBr optics. ^{1}H NMR (400 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Varian Mercury MHz spectrometer using DMSO-d_6 (solvent) and TMS (internal standard). HRMS were obtained using a Micromass GCT-TOF instrument. X-ray diffraction data were recorded on a Rigaku Mercury CCD area detector with graphite monochromated Mo-Kα radiation.

4-Aryl-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitriles 4, 4-Aryl-6-(1*H*-indol-3-yl)-2,3′-bipyridine-5-carbonitriles 7, and 4-Aryl-2-(1*H*-indol-3-yl)-6-(2-thienyl)nicotinonitriles 9; General Procedure

A mixture of 3-(cyanoacetyl)indole **1** (1 mmol), aldehyde **2** (1 mmol), heterocyclic ketone **3**, **6**, or **8** (1 mmol), and NH_4OAc (3 mmol) in *n*-BuOH (3 mL) was stirred at 100 °C for several hours (see Tables 2– 4). When the starting materials had been consumed, a mixture of the non-aromatized 1,4-dihydropyridine derivative and the aromatized target product was obtained (TLC monitoring). The former was aromatized by the addition of DDQ (50 mol%) and the mixture was allowed to cool to r.t. The solid was filtered off and washed with cool anhyd EtOH (2 × 0.5 mL) to give **4**, **7**, and **9** as yellow powders (TLC pure) without further purification. Compounds for crystallographic analysis were recrystallized (anhyd EtOH and DMF).

4-Aryl-6-(1*H*-indol-3-yl)-1,4-dihydro-2,2′-bipyridine-5-carbonitriles 5a, 5b and 4-Aryl-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitriles 4q, 4r; General Procedure

A mixture of 3-(cyanoacetyl)indole **1** (1 mmol), 2-chloro- or 2-bromobenzaldehyde (1 mmol), 2-acetylpyridine (**3**, 1 mmol), and NH_4OAc (3 mmol) in *n*-BuOH (3 mL) was stirred at 100 °C for 3 h. When the starting materials had been consumed, the non-aromatized 1,4-dihydropyridine derivatives **5a** or **5b** deposited from the reaction system without the appearance of the aromatized products. The solid was filtered off and washed with cool anhyd EtOH (2 × 0.5 mL) to give **5a**,**b** as shiny yellow powders (TLC pure) without further purification. Compounds for crystallographic analysis were recrystallized (anhyd EtOH). The aromatized products **4q** and **4r** could be synthesized from **5a** and **5b**, respectively, by the addition of a stoichiometric amount of DDQ. The aromatized products were then filtered off and then washed with cool anhyd EtOH (2 × 0.5 mL) to give the pure products.

4-(4-Chlorophenyl)-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitrile (4a)

Yellow solid; mp >300 °C.

IR (KBr): 3351, 3057, 2221, 1575, 1538, 1492, 1368, 1213, 1016, 797, 744 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.85 (br s, 1 H, NH), 8.79 (d, *J* = 4.4 Hz, 1 H, ArH), 8.58 (d, *J* = 8.0 Hz, 1 H, ArH), 8.42–8.39 (m, 2 H, ArH), 8.30 (s, 1 H, ArH), 8.11 (dt, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.83 (d, *J* = 8.4 Hz, 2 H, ArH), 7.69 (d, *J* = 8.4 Hz, 2 H, ArH), 7.60–7.56 (m, 2 H, ArH), 7.29–7.24 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.29, 157.14, 153.79, 149.57, 137.69, 136.33, 135.56, 134.73, 130.50, 129.33, 128.80, 128.50, 125.93, 125.25, 122.37, 121.52, 121.15, 120.84, 118.48, 116.11, 112.68, 112.08, 102.70.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{25}H_{15}{}^{35}ClN_4$: 406.0985; found: 406.0991.

4-(4-Bromophenyl)-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitrile (4b)

Yellow solid; mp >300 °C.

IR (KBr): 3333, 3057, 2222, 1573, 1538, 1489, 1440, 1369, 1213, 1013, 744 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.88 (br s, 1 H, NH), 8.74 (d, *J* = 4.0 Hz, 1 H, ArH), 8.53 (d, *J* = 8.0 Hz, 1 H, ArH), 8.41–8.37 (m, 2 H, ArH), 8.22 (s, 1 H, ArH), 8.04 (t, *J* = 7.6 Hz, 1 H, ArH), 7.76 (d, *J* = 8.4 Hz, 2 H, ArH), 7.67 (d, *J* = 8.0 Hz, 2 H, ArH), 7.57 (d, *J* = 7.2 Hz, 1 H, ArH), 7.54–7.51 (m, 1 H, ArH), 7.29–7.23 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.23, 157.07, 153.71, 153.61, 149.41, 137.42, 136.36, 135.81, 131.59, 130.55, 128.71, 126.00, 125.05, 124.40, 122.35, 121.45, 121.28, 120.82, 118.48, 115.94, 112.73, 112.06, 102.31.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{25}H_{15}{}^{79}BrN_4$: 450.0480; found: 450.0467.

6-(1*H*-Indol-3-yl)-4-(4-nitrophenyl)-2,2′-bipyridine-5-carbonitrile (4c)

Yellow solid; mp >300 °C.

IR (KBr): 3401, 3059, 2217, 1565, 1539, 1431, 1347, 1237, 793, 753 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.93 (br s, 1 H, NH), 8.79 (d, *J* = 4.8 Hz, 1 H, ArH), 8.59 (d, *J* = 8.0 Hz, 1 H, ArH), 8.46–8.41 (m, 4 H, ArH), 8.33 (s, 1 H, ArH), 8.13 (dt, *J* = 8.0, 1.6 Hz, 1 H, ArH), 8.08 (d, *J* = 8.8 Hz, 2 H, ArH), 7.61–7.56 (m, 2 H, ArH), 7.30–7.25 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.37, 157.30, 153.68, 153.02, 149.67, 148.17, 143.06, 137.81, 136.35, 130.29, 128.92, 125.88, 125.42, 123.80, 122.44, 121.60, 121.11, 120.93, 118.21, 116.12, 112.59, 112.13, 102.65.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{25}H_{15}N_5O_2$: 417.1226; found: 417.1233.

6-(1*H*-Indol-3-yl)-4-(3-nitrophenyl)-2,2′-bipyridine-5-carbonitrile (4d)

Yellow solid; mp 272–273 °C.

IR (KBr): 3366, 3073, 2214, 1564, 1540, 1526, 1436, 1351, 741, 692 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.90 (br s, 1 H, NH), 8.79 (d, *J* = 4.0 Hz, 1 H, ArH), 8.64 (s, 1 H, ArH), 8.59 (d, *J* = 8.0 Hz, 1 H,

ArH), 8.45–8.43 (m, 3 H, ArH), 8.36 (s, 1 H, ArH), 8.26 (d, *J* = 7.6 Hz, 1 H, ArH), 8.12 (t, *J* = 7.6 Hz, 1 H, ArH), 7.91 (t, *J* = 8.0 Hz, 1 H, ArH), 7.60–7.56 (m, 2 H, ArH), 7.28–7.26 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.34, 157.31, 153.70, 152.65, 149.66, 147.82, 138.13, 137.78, 136.37, 135.32, 130.44, 128.98, 125.92, 125.40, 124.43, 123.56, 122.47, 121.60, 121.18, 120.97, 118.43, 116.28, 112.64, 112.17, 102.80.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{25}H_{15}N_5O_2$: 417.1226; found: 417.1224.

4-(2,4-Dichlorophenyl)-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitrile (4e)
Yellow solid; mp 275–277 °C.

IR (KBr): 3343, 3055, 2221, 1589, 1535, 1476, 1439, 1214, 820, 741 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.94 (br s, 1 H, NH), 8.77 (d, *J* = 4.8 Hz, 1 H, ArH), 8.60 (d, *J* = 7.6 Hz, 1 H, ArH), 8.47–8.44 (m, 1 H, ArH), 8.39 (d, *J* = 3.2 Hz, 1 H, ArH), 8.23 (s, 1 H, ArH), 8.13 (dt, *J* = 7.6, 1.2 Hz, 1 H, ArH), 7.94 (d, *J* = 2.0 Hz, 1 H, ArH), 7.74–7.67 (m, 2 H, ArH), 7.61–7.56 (m, 2 H, ArH), 7.30–7.27 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.41, 156.73, 153.67, 152.03, 149.68, 137.80, 136.41, 135.09, 134.67, 132.48, 132.13, 129.29, 128.70, 127.87, 125.79, 125.41, 122.51, 121.60, 121.19, 120.99, 117.58, 116.70, 112.47, 112.18, 103.90.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{25}H_{14}{}^{37}Cl_2N_4$: 444.0537; found: 444.0532.

6-(1*H*-Indol-3-yl)-4-phenyl-2,2′-bipyridine-5-carbonitrile (4f)
Yellow solid; mp 294–296 °C.

IR (KBr): 3337, 3050, 2218, 1573, 1535, 1438, 1214, 1145, 850, 745, 703 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.89 (br s, 1 H, NH), 8.78 (d, *J* = 4.4 Hz, 1 H, ArH), 8.58 (d, *J* = 8.0 Hz, 1 H, ArH), 8.41 (d, *J* = 5.2 Hz, 2 H, ArH), 8.31 (s, 1 H, ArH), 8.11 (dt, *J* = 8.0, 1.6 Hz, 1 H, ArH), 7.81–7.79 (m, 2 H, ArH), 7.66–7.56 (m, 5 H, ArH), 7.29–7.24 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.36, 157.09, 155.05, 153.91, 149.62, 137.68, 136.83, 136.39, 129.77, 128.82, 128.65, 126.04, 125.26, 122.42, 121.53, 121.25, 120.89, 118.74, 116.29, 112.78, 112.15, 102.78.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{25}H_{16}N_4$: 372.1375; found: 372.1371.

6-(1*H*-Indol-3-yl)-4-(4-tolyl)-2,2′-bipyridine-5-carbonitrile (4g)
Yellow solid; mp 288–290 °C.

IR (KBr): 3331, 3057, 2222, 1578, 1540, 1439, 1370, 1216, 1142, 743 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.89 (br s, 1 H, NH), 8.79 (d, *J* = 4.4 Hz, 1 H, ArH), 8.58 (d, *J* = 8.0 Hz, 1 H, ArH), 8.40–8.39 (m, 2 H, ArH), 8.30 (s, 1 H, ArH), 8.13 (dt, *J* = 8.0, 1.6 Hz, 1 H, ArH), 8.08 (d, *J* = 8.8 Hz, 2 H, ArH), 7.61–7.56 (m, 2 H, ArH), 7.43 (d, *J* = 8.0 Hz, 2 H, ArH), 7.27–7.25 (m, 2 H, ArH), 2.43 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.36, 156.99, 155.02, 153.93, 149.54, 139.51, 137.67, 136.32, 133.89, 129.33, 128.71, 128.50, 125.98, 125.17, 122.31, 121.49, 121.15, 120.77, 118.73, 116.13, 112.76, 112.04, 102.72, 20.82.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{26}H_{18}N_4$: 386.1531; found: 386.1541.

6-(1*H*-Indol-3-yl)-4-(4-methoxyphenyl)-2,2′-bipyridine-5-carbonitrile (4h)
Light yellow solid; mp 266–268 °C.

IR (KBr): 3373, 3058, 2213, 1609, 1577, 1529, 1513, 1427, 1254, 781, 765 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.86 (br s, 1 H, NH), 8.77 (d, *J* = 4.4 Hz, 1 H, ArH), 8.57 (d, *J* = 8.0 Hz, 1 H, ArH), 8.40–8.38 (m, 2 H, ArH), 8.29 (s, 1 H, ArH), 8.10 (dt, *J* = 8.0, 1.6 Hz, 1 H, ArH), 7.77 (d, *J* = 8.8 Hz, 2 H, ArH), 7.59–7.55 (m, 2 H, ArH), 7.29–7.23 (m, 2 H, ArH), 7.17 (d, *J* = 8.8 Hz, 2 H, ArH), 3.87 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 160.58, 157.48, 156.97, 154.71, 154.03, 149.67, 137.73, 136.39, 130.29, 128.90, 128.83, 126.08, 125.25, 122.42, 121.54, 121.26, 120.89, 119.08, 116.10, 114.30, 112.85, 112.16, 102.64, 55.38.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{26}H_{18}N_4O$: 402.1481; found: 402.1463.

6-(1*H*-Indol-3-yl)-4-(2-tolyl)-2,2′-bipyridine-5-carbonitrile (4i)
Yellow solid; mp 271–273 °C.

IR (KBr): 3331, 3057, 2219, 1581, 1535, 1438, 1366, 1147, 785, 743 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.91 (br s, 1 H, NH), 8.77 (d, *J* = 4.0 Hz, 1 H, ArH), 8.62 (d, *J* = 8.0 Hz, 1 H, ArH), 8.50–8.47 (m, 1 H, ArH), 8.42 (d, *J* = 2.8 Hz, 1 H, ArH), 8.18 (s, 1 H, ArH), 8.13 (t, *J* = 7.6 Hz, 1 H, ArH), 7.60–7.57 (m, 2 H, ArH), 7.47–7.38 (m, 4 H, ArH), 7.30–7.28 (m, 2 H, ArH), 2.27 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.12, 156.85, 155.81, 153.97, 149.75, 137.88, 136.93, 136.44, 134.87, 130.46, 129.35, 128.81, 126.15, 126.96, 125.40, 122.52, 121.63, 121.33, 121.00, 118.14, 116.74, 112.66, 112.22, 104.12, 19.45.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{26}H_{18}N_4$: 386.1531; found: 386.1531.

6-(1*H*-Indol-3-yl)-4-(2-methoxyphenyl)-2,2′-bipyridine-5-carbonitrile (4j)
Yellow solid; mp 283–285 °C.

IR (KBr): 3353, 3057, 2218, 1583, 1535, 1495, 1249, 1142, 756, 747 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.88 (br s, 1 H, NH), 8.75 (d, *J* = 4.8 Hz, 1 H, ArH), 8.58 (d, *J* = 8.0 Hz, 1 H, ArH), 8.43–8.41 (m, 1 H, ArH), 8.35 (d, *J* = 2.8 Hz, 1 H, ArH), 8.22 (s, 1 H, ArH), 8.10 (dt, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.58–7.53 (m, 3 H, ArH), 7.48 (dd, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.29–7.23 (m, 3 H, ArH), 7.15 (t, *J* = 7.6 Hz, 1 H, ArH), 3.84 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.08, 156.55, 156.04, 154.04, 153.04, 149.71, 137.82, 136.42, 131.39, 130.23, 128.52, 125.99, 125.73, 125.30, 122.47, 121.53, 121.21, 120.93, 120.84, 118.40, 117.36, 112.72, 112.20, 111.89, 104.88, 55.64.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{26}H_{18}N_4O$: 402.1481; found: 402.1481.

4-(1,3-Benzodioxol-5-yl)-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitrile (4k)
Brown solid; mp 258–260 °C.

IR (KBr): 3372, 3055, 2213, 1580, 1564, 1533, 1500, 1449, 1224, 1038, 766 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.86 (br s, 1 H, NH), 8.78 (d, *J* = 4.0 Hz, 1 H, ArH), 8.57 (d, *J* = 8.0 Hz, 1 H, ArH), 8.39 (d, *J* = 2.4 Hz, 2 H, ArH), 8.27 (s, 1 H, ArH), 8.10 (t, *J* = 7.6 Hz, 1 H, ArH), 7.59–7.56 (m, 2 H, ArH), 7.42 (s, 1 H, ArH), 7.30–7.25 (m, 3 H, ArH), 7.15 (d, *J* = 8.0 Hz, 1 H, ArH), 6.17 (s, 2 H, CH_2).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.38, 156.96, 154.65, 153.97, 149.62, 148.66, 147.63, 137.70, 136.35, 130.53, 128.83, 126.02, 125.22, 123.13, 122.37, 122.51, 121.20, 120.84, 118.89, 116.22, 112.80, 112.11, 109.00, 108.65, 102.83, 101.72.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{26}H_{16}N_4O_2$: 416.1273; found: 416.1256.

6-(1*H*-Indol-3-yl)-4-(2-thienyl)-2,2′-bipyridine-5-carbonitrile (4l)
Yellow solid; mp 275–277 °C.

IR (KBr): 3397, 3073, 2218, 1563, 1537, 1436, 1422, 1449, 1247, 1137, 1011, 796, 781, 749 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 11.91 (br s, 1 H, NH), 8.81 (d, *J* = 4.4 Hz, 1 H, ArH), 8.55 (d, *J* = 8.0 Hz, 1 H, ArH), 8.41–8.40 (d, *J* = 4.0 Hz, 2 H, ArH), 8.39–8.36 (m, 1 H, ArH), 8.09 (dt, *J* = 7.6, 2.0 Hz, 1 H, ArH), 7.99–7.97 (m, 2 H, ArH), 7.60–7.57 (m, 2 H, ArH), 7.38–7.35 (m, 1 H, ArH), 7.31–7.24 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 158.07, 157.18, 153.64, 149.62, 146.59, 137.67, 137.54, 136.35, 130.39, 129.86, 129.03, 128.75, 126.07, 125.35, 122.42, 121.50, 121.23, 120.90, 119.19, 115.03, 112.66, 112.15, 100.63.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{23}H_{14}N_4S$: 378.0939; found: 378.0940.

6-(1*H*-Indol-3-yl)-4-(3-thienyl)-2,2′-bipyridine-5-carbonitrile (4m)
Red solid; mp 253–255 °C.

IR (KBr): 3377, 3093, 2213, 1581, 1566, 1532, 1456, 1431, 1236, 1135, 772 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 11.87 (br s, 1 H, NH), 8.77 (d, *J* = 4.0 Hz, 1 H, ArH), 8.55 (d, *J* = 8.0 Hz, 1 H, ArH), 8.39 (d, *J* = 2.8 Hz, 2 H, ArH), 8.36 (s, 1 H, ArH), 8.25 (s, 1 H, ArH), 8.08 (t, *J* = 7.6 Hz, 1 H, ArH), 7.83–7.81 (m, 1 H, ArH), 7.67 (d, *J* = 4.8 Hz, 1 H, ArH), 7.58–7.55 (m, 2 H, ArH), 7.29–7.23 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.50, 157.14, 153.92, 149.48, 149.13, 137.51, 137.00, 136.32, 128.68, 127.57, 127.46, 127.43, 126.02, 125.09, 122.31, 121.44, 121.21, 120.76, 118.97, 115.66, 112.76, 112.03, 101.81.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{23}H_{14}N_4S$: 378.0939; found: 378.0928.

4-(2-Furyl)-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitrile (4n)
Yellow solid; mp 258–259 °C.

IR (KBr): 3402, 3310, 3118, 2219, 1589, 1550, 1485, 1432, 1247, 1029, 756 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 11.88 (br s, 1 H, NH), 8.81 (d, *J* = 4.4 Hz, 1 H, ArH), 8.66 (s, 1 H, ArH), 8.53 (d, *J* = 8.0 Hz, 1 H, ArH), 8.37 (d, *J* = 2.8 Hz, 1 H, ArH), 8.33 (d, *J* = 7.6 Hz, 1 H, ArH), 8.11–8.06 (m, 2 H, ArH), 7.67 (d, *J* = 3.6 Hz, 1 H, ArH), 7.60–7.55 (m, 2 H, ArH), 7.28–7.21 (m, 2 H, ArH), 6.86–6.85 (m, 1 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.92, 157.27, 153.79, 149.61, 148.00, 146.08, 141.46, 137.65, 136.33, 128.85, 126.07, 125.30, 122.40, 121.39, 121.23, 120.85, 119.19, 114.07, 113.05, 112.66, 112.11, 111.22, 97.20.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{23}H_{14}N_4O$: 362.1168; found: 362.1168.

6-(1*H*-Indol-3-yl)-4-(1-naphthyl)-2,2′-bipyridine-5-carbonitrile (4o)
Yellow solid; mp 270–271 °C.

IR (KBr): 3415, 3057, 2218, 1534, 1457, 1431, 1238, 805, 779, 747 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 11.88 (br s, 1 H, NH), 8.73 (d, *J* = 4.0 Hz, 1 H, ArH), 8.65 (d, *J* = 8.0 Hz, 1 H, ArH), 8.53–8.51 (m, 1 H, ArH), 8.40 (d, *J* = 2.4 Hz, 1 H, ArH), 8.30 (s, 1 H, ArH), 8.16–8.10 (m, 3 H, ArH), 7.73–7.55 (m, 7 H, ArH), 7.30–7.28 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.08, 156.98, 154.46, 153.96, 149.70, 137.85, 136.44, 134.60, 133.17, 130.16, 129.66, 128.80, 129.58, 127.26, 127.18, 126.49, 126.02, 125.43, 125.36, 124.72, 122.52, 121.67, 121.38, 121.00, 118.16, 117.63, 112.71, 112.21, 104.76.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{29}H_{18}N_4$: 422.1531; found: 422.1535.

6-(1*H*-Indol-3-yl)-4-(2-naphthyl)-2,2′-bipyridine-5-carbonitrile (4p)
Yellow solid; mp 262–264 °C.

IR (KBr): 3409, 3053, 2220, 1668, 1574, 1541, 1436, 784, 743 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 11.91 (br s, 1 H, NH), 8.78 (d, *J* = 4.0 Hz, 1 H, ArH), 8.59 (d, *J* = 8.0 Hz, 1 H, ArH), 8.44–8.40 (m, 3 H, ArH), 8.35 (s, 1 H, ArH), 8.14–8.03 (m, 4 H, ArH), 7.88 (d, *J* = 8.4 Hz, 1 H, ArH), 7.65–7.63 (m, 2 H, ArH), 7.58–7.55 (m, 2 H, ArH), 7.28–7.27 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 162.50, 157.47, 157.22, 155.10, 154.05, 149.66, 137.69, 136.50, 134.53, 134.32, 133.18, 132.65, 128.87, 128.54, 127.73, 127.44, 126.92, 126.15, 125.96, 125.30, 122.55, 121.67, 121.39, 121.01, 118.87, 116.59, 112.94, 112.22, 102.98.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{29}H_{18}N_4$: 422.1531; found: 422.1517.

4-(2-Chlorophenyl)-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitrile (4q)
Yellow solid; mp >300 °C.

IR (KBr): 3326, 3060, 2223, 1573, 1535, 1472, 1440, 1367, 1214, 1148, 742 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 11.91 (br s, 1 H, NH), 8.78 (d, *J* = 4.0 Hz, 1 H, ArH), 8.60 (d, *J* = 8.0 Hz, 1 H, ArH), 8.47–8.46 (m, 1 H, ArH), 8.39 (s, 1 H, ArH), 8.22 (s, 1 H, ArH), 8.13 (t, *J* = 7.6 Hz, 1 H, ArH), 7.73 (d, *J* = 7.2 Hz, 1 H, ArH), 7.67 (d, *J* = 7.2 Hz, 1 H, ArH), 7.61–7.57 (m, 4 H, ArH), 7.29–7.27 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.35, 156.78, 153.75, 153.16, 149.79, 137.94, 136.46, 135.76, 131.36, 131.29, 130.90, 129.81, 128.78, 127.74, 125.88, 125.52, 122.60, 121.67, 121.27, 121.09, 117.80, 116.83, 112.54, 112.27, 104.11.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{25}H_{15}{}^{35}ClN_4$: 406.0985; found: 406.0974.

4-(2-Bromophenyl)-6-(1*H*-indol-3-yl)-2,2′-bipyridine-5-carbonitrile (4r)
Yellow solid; mp >300 °C.

IR (KBr): 3322, 3056, 2222, 1593, 1571, 1532, 1472, 1439, 774, 743 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 11.92 (br s, 1 H, NH), 8.76 (d, *J* = 4.0 Hz, 1 H, ArH), 8.60 (d, *J* = 8.0 Hz, 1 H, ArH), 8.49–8.47 (m, 1 H, ArH), 8.40 (d, *J* = 2.4 Hz, 1 H, ArH), 8.19 (s, 1 H, ArH), 8.11 (t, *J* = 7.6 Hz, 1 H, ArH), 7.88 (d, *J* = 8.0 Hz, 1 H, ArH), 7.64–7.56 (m, 4 H, ArH), 7.51 (t, *J* = 7.6 Hz, 1 H, ArH), 7.29–7.27 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.33, 156.76, 154.80, 153.77, 149.79, 137.93, 137.86, 136.49, 132.92, 131.41, 130.71, 128.77, 128.20, 125.91, 125.51, 122.62, 121.67, 121.34, 121.11, 117.79, 116.76, 112.60, 112.30, 104.04.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{25}H_{15}{}^{79}BrN_4$: 450.0495; found: 450.0480.

6-(5-Methyl-1*H*-indol-3-yl)-4-phenyl-2,2′-bipyridine-5-carbonitrile (4s)
Yellow solid; mp 256–258 °C.

IR (KBr): 3319, 3055, 2915, 2223, 1573, 1527, 1370, 1217, 784, 762, 698 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.77 (br s, 1 H, NH), 8.80 (d, *J* = 4.0 Hz, 1 H, ArH), 8.60 (d, *J* = 8.0 Hz, 1 H, ArH), 8.36 (d, *J* = 2.8 Hz, 1 H, ArH), 8.30 (s, 1 H, ArH), 8.24 (s, 1 H, ArH), 8.13 (dt, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.81–7.79 (m, 2 H, ArH), 7.66–7.58 (m, 4 H, ArH), 7.45 (d, *J* = 8.0 Hz, 1 H, ArH), 7.11 (d, *J* = 8.4 Hz, 1 H, ArH), 2.49 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.55, 157.15, 155.21, 154.06, 149.81, 137.85, 136.92, 134.76, 129.90, 129.52, 128.94, 128.75, 126.32, 125.44, 124.05, 121.58, 121.04, 118.83, 116.21, 112.36, 111.87, 102.74, 21.68.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{26}H_{18}N_4$: 386.1531; found: 386.1532.

6–(6-Methyl-1*H*-indol-3-yl)-4-phenyl-2,2′-bipyridine-5-carbonitrile (4t)

Yellow solid; mp >300 °C.

IR (KBr): 3333, 3055, 2915, 2219, 1579, 1535, 1508, 1445, 1370, 1218, 1165, 811, 701 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.73 (br s, 1 H, NH), 8.77 (d, *J* = 4.8 Hz, 1 H, ArH), 8.56 (d, *J* = 8.0 Hz, 1 H, ArH), 8.32 (d, *J* = 2.8 Hz, 1 H, ArH), 8.29 (d, *J* = 8.0 Hz, 1 H, ArH), 8.27 (s, 1 H, ArH), 8.08 (t, *J* = 7.6 Hz, 1 H, ArH), 7.78–7.76 (m, 2 H, ArH), 7.61–7.55 (m, 4 H, ArH), 7.35 (s, 1 H, ArH), 7.08 (d, *J* = 8.0 Hz, 1 H, ArH), 2.46 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.41, 157.09, 155.10, 153.96, 149.67, 137.75, 136.88, 136.81, 131.64, 129.81, 128.86, 128.69, 128.25, 125.31, 123.96, 122.72, 121.56, 121.05, 118.80, 116.16, 112.73, 111.86, 102.57, 21.35.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{26}H_{18}N_4$: 386.1531; found: 386.1533.

6-(7-Methyl-1*H*-indol-3-yl)-4-phenyl-2,2′-bipyridine-5-carbonitrile (4u)

Yellow solid; mp 298–299 °C.

IR (KBr): 3334, 3053, 2220, 1566, 1533, 1449, 1372, 1219, 1174, 745, 702 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.84 (br s, 1 H, NH), 8.79 (d, *J* = 4.0 Hz, 1 H, ArH), 8.58 (d, *J* = 8.0 Hz, 1 H, ArH), 8.38 (d, *J* = 2.4 Hz, 1 H, ArH), 8.31 (s, 1 H, ArH), 8.24 (d, *J* = 8.0 Hz, 1 H, ArH), 8.11 (t, *J* = 7.6 Hz, 1 H, ArH), 7.81–7.79 (m, 2 H, ArH), 7.63–7.57 (m, 4 H, ArH), 7.17 (t, *J* = 7.6 Hz, 1 H, ArH), 7.07 (d, *J* = 7.2 Hz, 1 H, ArH), 2.56 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.51, 157.12, 155.11, 153.95, 149.72, 137.83, 136.88, 135.87, 129.86, 128.89, 128.73, 128.59, 125.78, 125.37, 122.93, 121.57, 121.31, 121.14, 118.84, 118.78, 116.30, 113.17, 103.02, 16.82.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{26}H_{18}N_4$: 386.1531; found: 386.1531.

6-(1-Methyl-1*H*-indol-3-yl)-4-phenyl-2,2′-bipyridine-5-carbonitrile (4v)

Yellow solid; mp 243–244 °C.

IR (KBr): 3053, 3008, 2934, 2216, 1575, 1564, 1539, 1471, 1363, 1242, 752 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.79 (d, *J* = 4.8 Hz, 1 H, ArH), 8.57 (d, *J* = 8.0 Hz, 1 H, ArH), 8.41 (d, *J* = 7.2 Hz, 1 H, ArH), 8.38 (s, 1 H, ArH), 8.31 (s, 1 H, ArH), 8.11 (dt, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.80–7.78 (m, 2 H, ArH), 7.63–7.57 (m, 5 H, ArH), 7.37–7.29 (m, 2 H, ArH), 3.96 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.19, 156.99, 155.20, 153.90, 149.74, 137.86, 136.94, 136.83, 132.54, 129.88, 128.91, 128.70, 126.37, 125.41, 122.53, 121.60, 121.39, 121.20, 118.58, 116.39, 111.87, 110.56, 102.84, 33.20.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{26}H_{18}N_4$: 386.1531; found: 386.1532.

6-(5-Bromo-1*H*-indol-3-yl)-4-phenyl-2,2′-bipyridine-5-carbonitrile (4w)

Yellow solid; mp >300 °C.

IR (KBr): 3343, 3059, 2218, 1577, 1547, 1531, 1447, 1369, 889, 760, 697 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.03 (br s, 1 H, NH), 8.80 (d, *J* = 4.0 Hz, 1 H, ArH), 8.61 (s, 1 H, ArH), 8.51 (d, *J* = 7.6 Hz, 1 H, ArH), 8.46 (s, 1 H, ArH), 8.31 (s, 1 H, ArH), 8.13–8.09 (m, 1 H, ArH), 7.79–7.78 (m, 2 H, ArH), 7.63–7.54 (m, 5 H, ArH), 7.41–7.39 (m, 1 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.08, 156.63, 155.09, 153.85, 149.73, 137.57, 136.66, 135.04, 130.01, 129.79, 128.80, 128.60, 127.73, 125.33, 124.89, 123.70, 121.24, 118.46, 116.59, 114.13, 113.48, 112.31, 102.84.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{25}H_{15}{}^{79}BrN_4$: 450.0480; found: 450.0482.

4-(2-Chlorophenyl)-6-(1*H*-indol-3-yl)-1,4-dihydro-2,2′-bipyridine-5-carbonitrile (5a)

Colorless solid; mp 246–248 °C.

IR (KBr): 3382, 3294, 3060, 2189, 1671, 1599, 1567, 1474, 1435, 765, 744 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.84 (br s, 1 H, NH), 8.66 (br s, 1 H, NH), 8.59 (d, *J* = 4.4 Hz, 1 H, ArH), 8.00 (d, *J* = 2.8 Hz, 1 H, ArH), 7.93 (d, *J* = 8.0 Hz, 1 H, ArH), 7.87–7.83 (m, 1 H, ArH), 7.76 (d, *J* = 8.0 Hz, 1 H, ArH), 7.61 (dd, *J* = 8.0, 1.6 Hz, 1 H, ArH), 7.55–7.50 (m, 2 H, ArH), 7.46–7.43 (m, 1 H, ArH), 7.41–7.38 (m, 1 H, ArH), 7.33 (dt, *J* = 8.0, 1.6 Hz, 1 H, ArH), 7.26–7.22 (m, 1 H, ArH), 7.20–7.17 (m, 1 H, ArH), 5.91 (dd, *J* = 5.2, 1.2 Hz, 1 H, CH), 5.11 (d, *J* = 5.2 Hz, 1 H, CH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 149.46, 148.34, 146.10, 142.47, 137.17, 136.16, 133.19, 131.08, 130.61, 129.46, 128.65, 128.09, 127.51, 124.61, 123.56, 122.13, 121.68, 120.34, 119.24, 119.15, 112.41, 107.95, 101.06, 74.90, 38.79.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{25}H_{17}{}^{35}ClN_4$: 408.1142; found: 408.1138.

4-(2-Bromophenyl)-6-(1*H*-indol-3-yl)-1,4-dihydro-2,2′-bipyridine-5-carbonitrile (5b)

Colorless solid; mp 262–264 °C.

IR (KBr): 3382, 3308, 3130, 2185, 1599, 1566, 1543, 1465, 1435, 764, 743 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.80 (br s, 1 H, NH), 8.62 (br s, 1 H, NH), 8.58 (d, *J* = 4.8 Hz, 1 H, ArH), 7.99 (d, *J* = 2.8 Hz, 1 H, ArH), 7.90 (d, *J* = 8.0 Hz, 1 H, ArH), 7.84 (dt, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.77 (d, *J* = 8.0 Hz, 1 H, ArH), 7.67 (d, *J* = 8.0, 1.6 Hz, 1 H, ArH), 7.62 (dd, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.55 (d, *J* = 8.0, 1.6 Hz, 1 H, ArH), 7.48 (t, *J* = 7.6 Hz, 1 H, ArH), 7.40–7.37 (m, 1 H, ArH), 7.26–7.17 (m, 3 H, ArH), 5.90 (dd, *J* = 4.8, 1.2 Hz, 1 H, CH), 5.10 (d, *J* = 5.2 Hz, 1 H, CH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 149.46, 148.37, 146.10, 144.23, 137.18, 136.18, 133.08, 132.72, 130.90, 129.03, 128.75, 127.58, 124.64, 123.59, 122.16, 121.71, 121.56, 120.37, 119.26, 119.21, 112.44, 107.94, 101.15, 75.15, 41.38.

HRMS: *m*/*z* [M]$^+$ calcd for $C_{25}H_{17}{}^{79}BrN_4$: 452.0637; found: 452.0625.

4-(4-Chlorophenyl)-6-(1*H*-indol-3-yl)-2,3′-bipyridine-5-carbonitrile (7a)

Yellow solid; mp 278–280 °C.

IR (KBr): 3369, 2217, 1594, 1575, 1533, 1493, 1447, 1360, 1089, 1015, 739 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.85 (br s, 1 H, NH), 9.50 (s, 1 H, ArH), 8.74 (d, J = 4.8 Hz, 1 H, ArH), 8.66 (dd, J = 8.0, 1.6 Hz, 1 H, ArH), 8.40–8.37 (m, 2 H, ArH), 8.05 (s, 1 H, ArH), 7.86 (d, J = 8.4 Hz, 2 H, ArH), 7.68 (d, J = 8.4 Hz, 2 H, ArH), 7.63–7.60 (m, 1 H, ArH), 7.56 (d, J = 8.0 Hz, 1 H, ArH), 7.30–7.22 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.53, 156.25, 154.03, 151.05, 148.65, 136.40, 135.44, 134.90, 133.05, 130.98, 129.01, 128.80, 125.97, 124.03, 122.50, 121.27, 120.93, 118.66, 116.75, 112.77, 112.21, 104.31, 101.98.

HRMS: m/z [M]$^+$ calcd for $C_{25}H_{15}{}^{35}ClN_4$: 406.0985; found: 406.0986.

6-(1*H*-Indol-3-yl)-4-(4-nitrophenyl)-2,3′-bipyridine-5-carbonitrile (7b)

Yellow solid; mp >300 °C.

IR (KBr): 3358, 2216, 1569, 1535, 1349, 853, 742, 700 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.93 (br s, 1 H, NH), 9.53 (d, J = 1.6 Hz, 1 H, ArH), 8.76–8.75 (m, 1 H, ArH), 8.70–8.68 (m, 1 H, ArH), 8.46 (d, J = 8.8 Hz, 2 H, ArH), 8.42–8.38 (m, 2 H, ArH), 8.16 (s, 1 H, ArH), 8.12 (d, J = 8.8 Hz, 2 H, ArH), 7.66–7.63 (m, 1 H, ArH), 7.58–7.56 (m, 1 H, ArH), 7.29–7.23 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.51, 156.43, 153.20, 151.21, 148.68, 148.24, 142.90, 136.44, 134.95, 132.92, 130.70, 129.12, 125.95, 124.10, 123.76, 122.61, 121.28, 121.06, 118.40, 116.73, 112.71, 112.27, 101.86.

HRMS: m/z [M]$^+$ calcd for $C_{25}H_{15}N_5O_2$: 417.1226; found: 417.1227.

6-(1*H*-Indol-3-yl)-4-phenyl-2,3′-bipyridine-5-carbonitrile (7c)

Yellow solid; mp 282–284 °C.

IR (KBr): 3205, 3104, 2223, 1582, 1567, 1533, 1447, 1218, 748, 701 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.90 (br s, 1 H, NH), 9.51 (d, J = 2.0 Hz, 1 H, ArH), 8.73 (d, J = 4.8 Hz, 1 H, ArH), 8.67 (d, J = 8.0 Hz, 1 H, ArH), 8.41 (d, J = 2.8 Hz, 1 H, ArH), 8.39–8.37 (m, 1 H, ArH), 8.06 (s, 1 H, ArH), 7.84–7.82 (m, 2 H, ArH), 7.63–7.60 (m, 4 H, ArH), 7.57–7.55 (m, 1 H, ArH), 7.28–7.22 (m, 2 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.49, 156.11, 155.24, 150.91, 148.58, 136.60, 136.34, 134.79, 133.06, 129.75, 128.93, 128.84, 128.66, 125.97, 123.89, 122.38, 121.24, 120.80, 118.67, 116.74, 112.78, 112.09, 101.99.

HRMS: m/z [M]$^+$ calcd for $C_{25}H_{16}N_4$: 372.1375; found: 372.1377.

6-(1*H*-Indol-3-yl)-4-(4-methoxyphenyl)-2,3′-bipyridine-5-carbonitrile (7d)

Yellow solid; mp 233–235 °C.

IR (KBr): 3216, 3163, 2962, 2213, 1607, 1581, 1536, 1514, 1260, 1186, 812, 751 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.83 (br s, 1 H, NH), 8.49 (s, 1 H, ArH), 8.73 (d, J = 4.4 Hz, 1 H, ArH), 8.65 (d, J = 8.0 Hz, 1 H, ArH), 8.40–8.36 (m, 2 H, ArH), 8.00 (s, 1 H, ArH), 7.80 (d, J = 8.4 Hz, 2 H, ArH), 7.62–7.59 (m, 1 H, ArH), 7.56 (d, J = 8.0 Hz, 1 H, ArH), 7.28–7.21 (m, 2 H, ArH), 7.16 (d, J = 8.0 Hz, 2 H, ArH), 3.87 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.68, 157.69, 156.02, 154.91, 150.95, 148.64, 136.43, 134.88, 133.23, 130.67, 128.95, 128.74, 126.10, 124.02, 122.49, 121.37, 120.92, 119.17, 116.60, 114.21, 112.93, 112.21, 101.83, 55.45.

HRMS: m/z [M]$^+$ calcd for $C_{26}H_{18}N_4O$: 402.1482; found: 402.1481.

4-(2-Furyl)-6-(1*H*-indol-3-yl)-2,3′-bipyridine-5-carbonitrile (7e)

Brown solid; mp 293–294 °C.

IR (KBr): 3137, 3102, 3045, 2214, 1591, 1534, 1487, 1446, 1233, 1031, 752, 740 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.84 (br s, 1 H, NH), 9.48 (s, 1 H, ArH), 8.74 (d, J = 4.4 Hz, 1 H, ArH), 8.64 (d, J = 7.6 Hz, 1 H, ArH), 8.39 (d, J = 2.4 Hz, 1 H, ArH), 8.31 (d, J = 7.2 Hz, 1 H, ArH), 8.25 (s, 1 H, ArH), 8.11 (s, 1 H, ArH), 7.72 (d, J = 3.6 Hz, 1 H, ArH), 7.64–7.61 (m, 1 H, ArH), 7.55 (d, J = 7.6 Hz, 1 H, ArH), 7.27–7.20 (m, 2 H, ArH), 6.86 (s, 1 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 158.19, 156.21, 150.93, 148.38, 148.13, 146.12, 141.72, 136.28, 134.65, 132.96, 128.94, 126.00, 123.90, 122.35, 121.21, 120.76, 118.92, 114.35, 112.98, 112.62, 112.05, 111.80, 96.60.

HRMS: m/z [M]$^+$ calcd for $C_{23}H_{14}N_4O$: 362.1168; found: 362.1169.

4-(4-Chlorophenyl)-2-(1*H*-indol-3-yl)-6-(2-thienyl)nicotinonitrile (9a)

Yellow solid; mp >300 °C.

IR (KBr): 3340, 3052, 2211, 1595, 1580, 1528, 1491, 1434, 1236, 1143, 835, 743 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.84 (br s, 1 H, NH), 8.55–8.53 (m, 1 H, ArH), 8.42 (d, J = 2.8 Hz, 1 H, ArH), 8.13 (d, J = 3.2 Hz, 1 H, ArH), 7.92 (s, 1 H, ArH), 7.85 (d, J = 4.8 Hz, 1 H, ArH), 7.79 (d, J = 8.4 Hz, 2 H, ArH), 7.67 (d, J = 8.4 Hz, 2 H, ArH), 7.57–7.54 (m, 1 H, ArH), 7.28–7.24 (m, 3 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.20, 153.79, 153.70, 143.59, 136.35, 135.56, 134.73, 131.28, 130.84, 129.04, 128.86, 128.77, 128.53, 126.05, 122.52, 121.78, 120.87, 118.90, 114.40, 112.41, 112.12, 100.17.

HRMS: m/z [M]$^+$ calcd for $C_{24}H_{14}{}^{35}ClN_3S$: 411.0597; found: 411.0598.

4-(4-Bromophenyl)-2-(1*H*-indol-3-yl)-6-(2-thienyl)nicotinonitrile (9b)

Yellow solid; mp >300 °C.

IR (KBr): 3332, 3049, 2213, 1572, 1526, 1433, 1237, 1143, 1010, 830, 742 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.84 (br s, 1 H, NH), 8.56–8.54 (m, 1 H, ArH), 8.42 (d, J = 2.8 Hz, 1 H, ArH), 8.12 (d, J = 3.2 Hz, 1 H, ArH), 7.91 (s, 1 H, ArH), 7.85 (d, J = 4.8 Hz, 1 H, ArH), 7.80 (d, J = 8.4 Hz, 2 H, ArH), 7.71 (d, J = 8.4 Hz, 2 H, ArH), 7.57–7.55 (m, 1 H, ArH), 7.28–7.23 (m, 3 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.14, 153.70, 153.64, 143.48, 136.28, 135.83, 131.57, 130.89, 128.85, 128.72, 128.35, 128.30, 125.99, 123.32, 122.39, 121.73, 120.74, 118.72, 114.24, 114.18, 112.38, 111.98, 99.98.

HRMS: m/z [M]$^+$ calcd for $C_{24}H_{14}{}^{79}BrN_3S$: 455.0092; found: 455.0091.

2-(1*H*-Indol-3-yl)-4-(4-nitrophenyl)-6-(2-thienyl)nicotinonitrile (9c)

Yellow solid; mp >300 °C.

IR (KBr): 3400, 2213, 1572, 1526, 1436, 1347, 1237, 854, 740 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.85 (br s, 1 H, NH), 8.57–8.54 (m, 1 H, ArH), 8.47–8.43 (m, 3 H, ArH), 8.14 (d, J = 3.2 Hz, 1 H, ArH), 8.05 (d, J = 8.4 Hz, 2 H, ArH), 7.99 (s, 1 H, ArH), 7.87 (d, J = 4.8 Hz, 1 H, ArH), 7.57–7.55 (m, 1 H, ArH), 7.29–7.25 (m, 3 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.17, 153.93, 152.85, 148.16, 143.46, 143.06, 136.37, 131.53, 130.56, 129.09, 128.96, 128.76, 126.01, 123.75, 122.59, 121.78, 120.95, 118.63, 114.39, 112.33, 112.17, 99.96.

HRMS: *m/z* [M]$^+$ calcd for $C_{24}H_{14}N_4O_2S$: 422.0837; found: 422.0838.

2-(1*H*-Indol-3-yl)-4-(3-nitrophenyl)-6-(2-thienyl)nicotinonitrile (9d)

Yellow solid; mp 285–286 °C.

IR (KBr): 3388, 2215, 1573, 1526, 1438, 1349, 1236, 740 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.90 (br s, 1 H, NH), 8.66–8.65 (m, 1 H, ArH), 8.56–8.54 (m, 1 H, ArH), 8.46–8.44 (m, 2 H, ArH), 8.26 (d, *J* = 8.0 Hz, 1 H, ArH), 8.18 (d, *J* = 4.0 Hz, 1 H, ArH), 8.08 (s, 1 H, ArH), 7.93 (d, *J* = 8.0 Hz, 1 H, ArH), 7.90–7.88 (m, 1 H, ArH), 7.57–7.55 (m, 1 H, ArH), 7.30–7.25 (m, 3 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.76, 157.22, 156.71, 154.71, 153.72, 150.39, 138.51, 137.08, 132.07, 130.90, 129.19, 126.65, 126.39, 125.99, 123.14, 122.21, 121.87, 121.60, 121.51, 119.06, 118.03, 113.38, 112.86, 112.57, 105.55.

HRMS: *m/z* [M]$^+$ calcd for $C_{24}H_{14}N_4O_2S$: 422.0837; found: 422.0852.

2-(1*H*-Indol-3-yl)-4-phenyl-6-(2-thienyl)nicotinonitrile (9e)

Yellow solid; mp 283–285 °C.

IR (KBr): 3307, 3062, 2220, 1573, 1539, 1526, 1431, 1238, 1140, 760, 695 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.88 (br s, 1 H, NH), 8.56–8.54 (m, 1 H, ArH), 8.43 (d, *J* = 2.8 Hz, 1 H, ArH), 8.16 (d, *J* = 3.6 Hz, 1 H, ArH), 7.95 (s, 1 H, ArH), 7.85 (d, *J* = 4.8 Hz, 1 H, ArH), 7.78–7.76 (m, 2 H, ArH), 7.61–7.55 (m, 4 H, ArH), 7.28–7.23 (m, 3 H, ArH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.27, 154.99, 153.74, 143.70, 136.79, 136.39, 131.16, 129.74, 129.03, 128.90, 128.85, 128.75, 128.42, 126.13, 122.54, 121.86, 120.88, 119.06, 114.49, 112.50, 112.13, 100.30.

HRMS: *m/z* [M]$^+$ calcd for $C_{24}H_{15}N_3S$: 377.0987; found: 377.0985.

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References

(1) Yates, F.; Courts, R. T.; Casy, A. F. *Pyridine and Its Derivatives: Supplement IV*; Abramovitch, R. A., Ed.; Wiley: New York, **1975**, 445.
(2) Yates, F. S. *Comprehensive Heterocyclic Chemistry*, Vol. 2; Katritzky, A. R.; Rees, C. W., Eds.; Pergamon: Oxford, **1984**, 511.
(3) (a) Dowell, R. I.; Hales, N. J.; Tucker, H. *Eur. J. Med. Chem.* **1993**, *28*, 513. (b) Zhou, X.-W.; Zhuang, Z.-L.; Chen, Q.-X. *J. Protein Chem.* **1999**, *18*, 735. (c) Zhang, B.; Breslow, R. *J. Am. Chem. Soc.* **1998**, *120*, 5854.
(4) (a) Constable, E. C. *Tetrahedron* **1992**, *48*, 10013. (b) Sauvage, J. P.; Collin, J. P.; Chambron, J. C.; Guillerez, S.; Coudret, C.; Balzani, V.; Barigelletti, F.; De Cola, L.; Flamigni, L. *Chem. Rev.* **1994**, *94*, 993. (c) Bernhard, S.; Barron, J. A.; Houston, P. L.; Abruna, H. D.; Ruglovksy, J. L.; Gao, X.; Malliaras, G. G. *J. Am. Chem. Soc.* **2002**, *124*, 13624. (d) Newkome, G. R.; Patri, A. K.; Holder, E.; Schubert, U. S. *Eur. J. Org. Chem.* **2004**, 235.
(5) (a) Namba, K.; Cui, S.; Wang, J.; Kishi, Y. *Org. Lett.* **2005**, *7*, 5417. (b) Namba, K.; Wang, J.; Cui, S.; Kishi, Y. *Org. Lett.* **2005**, *7*, 5421.
(6) (a) Juris, A.; Balzani, V.; Barigelletti, F.; Campagna, S.; Belser, A.; von Zelewsky, A. *Coord. Chem. Rev.* **1988**, *84*, 85. (b) Balzani, V.; Juris, A.; Venturi, M.; Campagna, S.; Serroni, S. *Chem. Rev.* **1996**, *96*, 759.
(7) Meyer, T. J. *Acc. Chem. Res.* **1989**, *22*, 163.
(8) (a) Dupray, L. M.; Devenney, M.; Striplin, D. R.; Meyer, T. J. *J. Am. Chem. Soc.* **1997**, *119*, 10243. (b) Newkome, G. R.; Patri, A. K.; Godinez, L. A. *Chem. Eur. J.* **1999**, *5*, 1445. (c) Constable, E. C.; Harverson, P.; Oberholzer, M. *Chem. Commun.* **1996**, 1821.
(9) (a) Schubert, U. S.; Eschbaumer, C.; Heller, M. *Org. Lett.* **2000**, *2*, 3373. (b) Tu, S.-J.; Jiang, B.; Yao, C.-S.; Jiang, H.; Zhang, J.-Y.; Jia, R.-H.; Zhang, Y. *Synthesis* **2007**, 1366. (c) Tu, S.-J.; Jiang, B.; Zhang, Y.; Zhang, J.-Y.; Jia, R.-H.; Yao, C.-S. *Chem. Lett.* **2006**, *35*, 1338.
(10) Houlihan, W. J.; Remers, W. A.; Brown, R. K. *Indoles: Part I*; Wiley: New York, **1992**.
(11) (a) Creed, D. *Photochem. Photobiol.* **1984**, *39*, 537. (b) Gupta, L.; Talwar, A.; Palne, N. S.; Gupta, S.; Chauhan, P. M. S. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 4075. (c) Jiang, B.; Xiong, X.; Yang, C. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 475. (d) Sakemi, S.; Sun, H. H. *J. Org. Chem.* **1991**, *56*, 4304.
(12) (a) Yan, C.-G.; Wang, Q.-F.; Song, X.-K.; Sun, J. *J. Org. Chem.* **2009**, *74*, 710. (b) Wang, S.-Y.; Ji, S.-J. *Synlett* **2007**, 2222. (c) Zhu, S.-L.; Ji, S.-J.; Zhang, Y. *Tetrahedron* **2007**, *63*, 9365. (d) Wang, S.-Y.; Ji, S.-J. *Tetrahedron* **2006**, *62*, 1527.
(13) (a) Lo, K. K.-W.; Tsang, K. H.-K.; Hui, W.-K.; Zhu, N. *Chem. Commun.* **2003**, *44*, 2704. (b) Lo, K. K.-W.; Tsang, K. H.-K.; Hui, W.-K.; Zhu, N. *Inorg. Chem.* **2005**, *44*, 6100. (c) Bowyer, P. K.; Black, D. St. C.; Craig, D. C.; Rae, A. D.; Willis, A. C. *J. Chem. Soc., Dalton Trans.* **2001**, 1948.
(14) (a) Kröehnke, F. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 380; *Angew. Chem.* **1963**, *75*, 317. (b) Kröehnke, F. *Synthesis* **1976**, 1.
(15) (a) Rode, T.; Breitmaier, E. *Synthesis* **1987**, 574. (b) Baxter, P. N. W.; Connor, J. A. *J. Organomet. Chem.* **1988**, *355*, 193. (c) Vögtle, F.; Hochberg, R.; Kochendoerfer, F.; Windscheif, P. M.; Volkmann, M.; Jansen, M. *Chem. Ber.* **1990**, *123*, 2181. (d) Percec, V.; Barboiu, B.; Kim, H.-J. *J. Am. Chem. Soc.* **1998**, 120, 305.
(16) (a) Uchida, Y.; Kajita, R.; Kawasaki, Y.; Oae, S. *Tetrahedron Lett.* **1995**, *36*, 4077. (b) Uchida, Y.; Kozawa, H. *Tetrahedron Lett.* **1989**, *30*, 6365. (c) Uchida, Y.; Onoue, K.; Tada, N.; Nagao, F. *Tetrahedron Lett.* **1989**, *30*, 567. (d) Newkome, G. R.; Hager, D. C. *J. Am. Chem. Soc.* **1978**, *100*, 5567.
(17) (a) Furukawa, N.; Shibutani, T.; Fujihara, H. *Tetrahedron Lett.* **1989**, *30*, 7091. (b) Oae, S.; Takeda, T.; Wakabayashi, S. *Tetrahedron Lett.* **1988**, *29*, 4445. (c) Kawai, T.; Furukawa, N. *Tetrahedron Lett.* **1984**, *25*, 2549.
(18) (a) Ishikura, M.; Kamada, M.; Terashima, M. *Synthesis* **1984**, 936. (b) Lehmann, U.; Henze, O.; Schlüter, D. *Chem. Eur. J.* **1999**, *5*, 854.

(19) Savage, S. A.; Smith, A. P.; Fraser, C. L. *J. Org. Chem.* **1998**, *63*, 10048.
(20) Zhu, S.-L.; Ji, S.-J.; Su, X.-M.; Sun, C.; Liu, Y. *Tetrahedron Lett.* **2008**, *49*, 1777.
(21) Kreher, R.; Wagner, P. H. *Chem. Ber.* **1980**, *113*, 3675.
(22) Slatt, J.; Romero, I.; Bergman, J. *Synthesis* **2004**, 2760.
(23) (a) Devi, I.; Kumarb, B. S. D.; Bhuyan, P. J. *Tetrahedron Lett.* **2003**, *44*, 8307. (b) Evdokimov, N. M.; Magedov, I. V.; Kireev, A. S.; Kornienko, A. *Org. Lett.* **2006**, *8*, 899.
(24) Structural parameters for **4f**: data collection: Rigaku Mercury CCD area detector; $C_{25}H_{16}N_4$, yellow solid, crystal dimension 0.55 × 0.35 × 0.30 mm, triclinic, space group $P\overline{1}$, a = 9.7744 (16) Å, b = 9.7927 (11) Å, c = 11.233 (2) Å, α = 73.121 (13)°, β = 86.008 (16)°, γ = 63.853 (10)°, V = 921.5 (2) Å^3, Mr = 372.42, Z = 2, Dc = 1.171 Mg/m^3, λ (Mo-Kα) = 0.71070 Å, μ = 0.082 mm^{-1}, F(000) = 388, 3.10° < θ < 25.34°, $R_{I>2\sigma(I)}$ = 0.0544, $wR_{I>2\sigma(I)}$ = 0.1159, largest diff. peak and hole: 0.158 and –0.205 e Å^{-3}. CCDC reference number 684602.
(25) Structural parameters for **5b**: data collection: Rigaku Mercury CCD area detector; $C_{25}H_{17}BrN_4$, colorless solid, crystal dimension 0.27 × 0.20 × 0.16 mm, triclinic, space group $P\overline{1}$, a = 11.286 (2) Å, b = 13.516 (2) Å, c = 14.423 (3) Å, α = 90.685 (2)°, β = 108.077 (3)°, γ = 102.674 (3)°, V = 2032.9 (6) Å^3, Mr = 452.33, Z = 4, Dc = 1.478 Mg/m^3, λ (Mo-Kα) = 0.71075 Å, μ = 2.042 mm^{-1}, F(000) = 916, 3.10° < θ < 25.50°, $R_{I>2\sigma(I)}$ = 0.0586, $wR_{I>2\sigma(I)}$ = 0.1540, largest diff. peak and hole: 2.424 and –0.662 e Å^{-3}. CCDC reference number 713488.