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Visible-Light Accelerated Pd-Catalyzed Cascade Addition/Cyclization of Aryl Boronic Acids to γ- and β-Ketodinitriles for the Construction of 3-Cyanopyridines and 3-Cyanopyrrole Analogues

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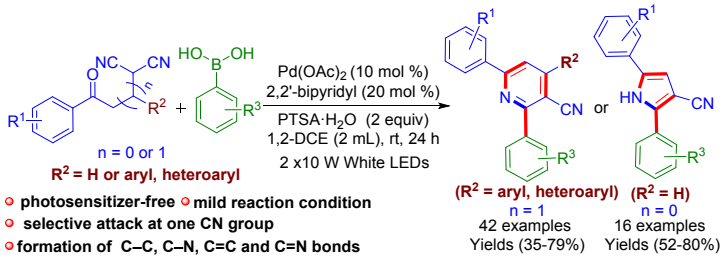


ABSTRACT

The one-pot synthetic strategies for 2,4,6-triarylnicotinonitriles and 2,5-diaryl-1*H*-pyrrole-3-carbonitriles have been accomplished *via* a Pd-catalyzed coupling of arylboronic acid with 2-(3-oxo-1,3-diarylpropyl)malononitrile and 2-(2-oxo-2-arylethyl)malononitrile, respectively under mild reaction conditions followed by intramolecular cyclization of an intermediate formed after the regeneration of catalyst under acidic rection conditions. The cascade reactions proceed in 1,2-dichloroethane solvent under visible-light irradiation, and the active catalyst is generated *in situ* in the presence of catalytic amounts of $Pd(OAc)_2$ and 2,2′-bipyridine. The active Pd-catalyst undergoes photoexcitation by the virtue of MLCT, and subsequent redox trans-metalation occurs with arylboronic acid, thus obviating the necessity of any exogenous photosensitizer. The targeted products, composed of a new C–C, a C–N, a C=N and two new C=C bonds, were isolated in good yields.

INTRODUCTION

Heteroaromatics are an essential class of molecules in the realm of organic chemistry, among which the nitrogen-heterocycles comprised of pyridine and pyrrole-frameworks have garnered the attention of chemists for several years. The widespread attention stems from the fact that substituted pyridine scaffolds constitute an essential structural feature in several natural products and other multipurpose molecules which find their applications in different fields of science ranging from biology to medicine to advanced materials.[1] Besides, pyridine-based structures also find utility in several other fields such as asymmetric catalysis,[2] supramolecular chemistry,[3] and cancer therapy.[4] Likewise, the pyrrole moiety has been identified in the structural frameworks of a wide array of natural products, unnatural products, and drug molecules.[5] The importance of pyrrole-based compounds can be substantiated by their diverse applications in the field of materials chemistry pertaining to the development of batteries, solar cells, and the exploration of diverse optoelectronic applications.[6] Interestingly, pyrrole and pyridine nuclei occur ubiquitously in a plethora of structurally diverse FDA approved pharmaceutical drugs, so much so that they are the most aromatic nuclei in these drugs (Figure 1 and 2).[7]

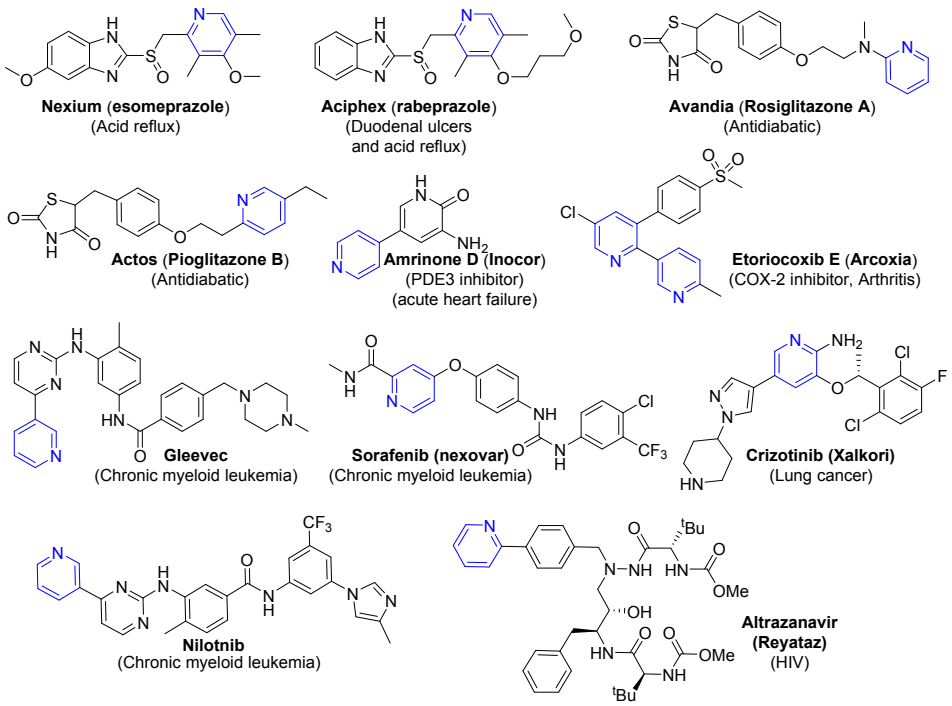


Figure 1. A few drugs bearing pyridine nucleus

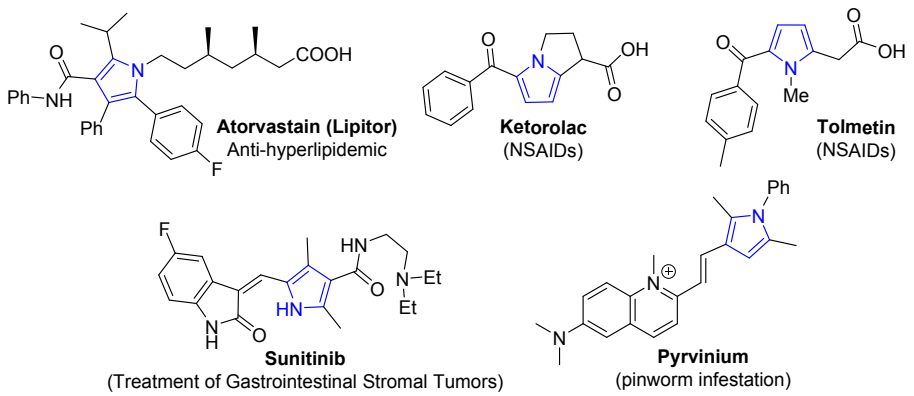


Figure 2. A few drugs bearing pyrrole nucleus

Some of these marketed drugs along with their targets are listed in Figure 1 and 2. Some renowned drugs bearing the pyridine moiety include nexium (esomeprazole) and aciphex (rabeprazole) for the treatment of acid reflux and duodenal ulcers (Figure 1);[7a,b] avandia (rosiglitazone A) and actos (pioglitazone B) as antidiabetic drugs;[7c,d] amrinone D (inocor) and etoriocoxib E (arcoxia) for treating patients with acute heart failure and arthritis.[7e,f] Moreover, some potent anticancer drugs such as gleevec,[7g] sorafenib (nexovar),[7h] crizotinib (xalkori),[7i] nilotnib,[7j] and the anti-HIV drug altrazanavir (reyataz)[7k] also contain the pyridine moiety (Figure 1). Similarly, few renowned drugs bearing the pyrrole moiety are atrovastatin, the best-selling cholesterol lowering drug which functions by inhibiting the HMG-CoA reductase enzyme;[8a] ketorolac and tolmetin are nonsteroidal anti-inflammatory drugs (NSAIDs) used for treating acute pain and inflammation;[8b-c] sunitinib is a multi-targeted tyrosine kinase inhibitor possessing antitumor and antiangiogenic activities, and pyrvinium is used for treating pinworm infestation.[8d-e]

On account of several multifaceted applications of substituted pyridines and pyrroles, synthetic chemists have long endeavoured the discovery of various pathways to achieve these important structural motifs. Several classical methods for the synthesis of pyridine are based upon the condensation of ammonia with a host of different carbonyl compounds.[1d,9] Few of these are the [5+1] condensation of 1,5-diketones with ammonia,[9b] the [2+2+1+1] Hantzsch pyridine synthesis,[9c] and the Kröhnke synthesis.[9d] Later on, several transition metal-mediated annulation protocols were explored which have been highlighted by Gulevich *et al.* in their review article, and the references cited therein.[10a] Few of these cascade catalytic strategies involve oxidative Michael condensation of oximes with α,β-unsaturated carbonyl compounds.[10b-c] Others exploit the transition metal-assisted coupling/condensation of diverse substrates to form the azatriene intermediates, which eventually follow the 6π-

electrocyclization route affording pyridines.[10a,d-f] These methods possess several advantages over the conventional condensation-based strategies, as highly substituted unsymmetrical pyridines can be prepared from eclectic starting materials with high regioselectivity. Nevertheless, many of these protocols suffer from disadvantages such as, the requirement of elevated temperatures and employ expensive metal catalysts. The past couple of decades have witnessed a surge in the thermal and transition metal-assisted [4+2] hetero Diels-Alder reaction involving 1-azadienes and alkynes,[11a-c] though inverse electron demand Diels-Alder strategies have also been explored.[11d-e] Earlier, researchers utilized the transition metals to catalyze the [2+2+2] cycloadditions of alkynes and nitriles,[11f-h] however, later on, they discovered that the annulation can also be achieved under metal-free condtions.[11i] Similarly, many other strategies follow greener protocols by employing other readily available catalytic systems in place of metal-based catalysts, or requiring solvent free conditions.[12] Researchers, have also managed to reap additional benefits by incorporating metal-free reaction conditions to multicomponent strategies for the synthesis of pyridines as delineated by Allais *et al.* in their review, and the references cited therein.[1b] Substituted pyridines synthesis have also been achieved under high stereo- and regioselectivity *via* direct C–H functionalization of the pyridine nucleus.[13] Advancements in synthetic strategies for achieving pyrrole motifs follow similar trends akin to the case of pyridines. Primeval strategies for the synthesis of pyrroles represent condensation-based protocols such as the Knorr, Paal–Knorr, and Hantzsch reactions that gained immense popularity. [14] Subsequently, the late 20th century marked an escalation in the transition metal-catalysed cyclizations, and multicomponent tandem coupling reactions.[15]

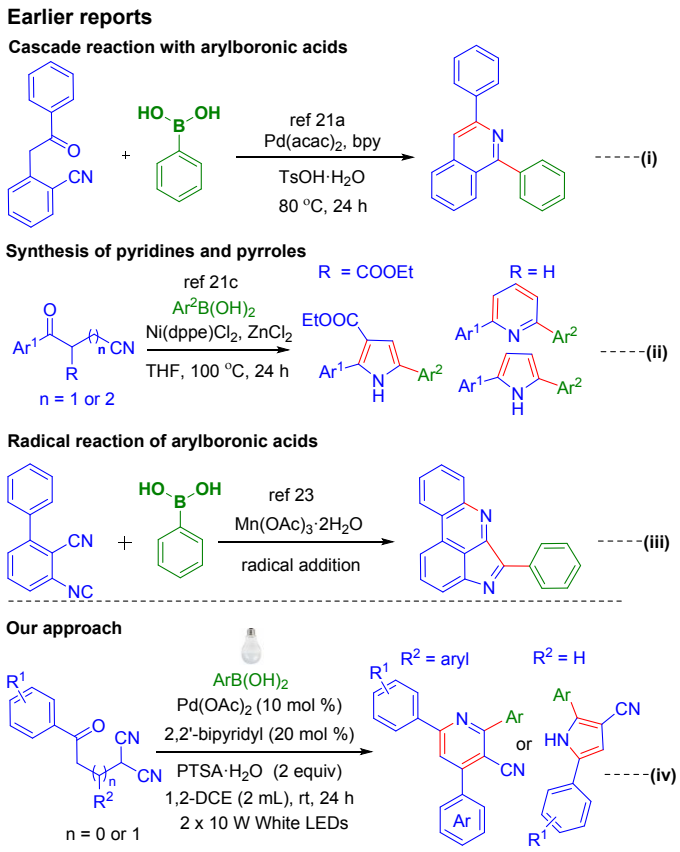
In the last couple of decades, visible light-mediated organic syntheses have gained immense popularity in the wake of several advantages associated with this regime. Several organic, as well as transition metal-based photocatalysts, have been developed to harness the energy of abundant visible light and transform it into chemical energy, thereby enabling the generation of carbon-centred radicals under mild catalytic conditions, and hence tap the novel reactivity of these intermediates.[16] Unprecedented Pd-catalyzed transformations have been achieved under visible-light irradiation, although an exogenous photo-catalyst may or may not be required.[17] In the case of latter, the Pd-catalyst plays a dual role[18a] in several elegant reactions, for instance, the C_{sp3}-C_{sp2} Heck coupling reaction,[18b-e] carbonylative cross coupling reactions,[18f-g] and others.[18h-j] The successful underpinnings of these strategies can be attributed to the fact that irradiation of Pd(0) catalyst induces a facile single electron transfer (SET) oxidative addition of unactivated alkyl halide, and the subsequent photoexcitation of Pd(II)-

alkyl complex restrains the undesired β-hydride elimination process, which otherwise plagues the traditional reactions.[18b]

Recently, our group developed a cascade [4+2] Ru-catalyzed annulation strategy for accessing fused isoquinolines, wherein, we noticed that one of the cyano groups, associated with malononitrile moiety, was selectively hydrolyzed.[19] We envisioned that the five-carbon core of the γ-ketomalononitrile (including this cyanide moiety) may act as a harbinger of pyridine nucleus, if cross coupled with a suitable partner via a cascade [5+1] annulation strategy. Thorough literature survey revealed that recently several protocols have been developed for the synthesis of 5- and 6- membered nitrogen heterocycles. These studies are an extension to the catalytic carbopalladation/carbonickelation of eclectic nitrile substrates with suitable coupling partners such as arylboronic acids and arylhydrazines to obtain ketones and imines,[20] followed by intramolecular cyclization to afford diverse *N*-heterocycles.[21] Few of these recent works are highlighted in Scheme 1. For instance, in 2017 Wu's group for the first time utilized the nitrile N atom via Pd-catalyzed nucleophilic addition of arylboronic acids with functionalized nitriles followed by an intramolecular cyclization to access biologically active isoquinolines and isoquinolones [Scheme 1 (i)].[21a] Chen *et al.* reported a Ni(II)-catalyzed cascade coupling of arylboronic acids to ketonitriles into substituted pyrroles and pyridines [Scheme 1 (ii)].[21c] A commonality that can be discerned from the mechanisms is that the initial step engages arylboronic acids in a traditional two-electron trans-metalation with electron-deficient Pd(II)-catalysts. The high activation energy barrier associated with this step predisposes the necessity of elevated temperatures.[22] Recently, Xu *et al.* discovered a Mn(III)-triggered radical pathway involving the cyclization of 3-isocyano-[1,1′-biphenyl]-2-carbonitriles with arylboronic acids to access pyrrolopyridine derivatives [Scheme 1 (iii)].[23] Keeping in mind the natural propensity of Pd-catalyzed reactions to follow a facile SET mechanistic pathway under visible-light irradiation, and arylboronic acids as readily available radical progenitors,[24] we envisaged the synthesis of 2,4,6-triaryl-3-cyanopyridines and 2,5-diaryl-3-cyanopyrrole derivatives [Scheme 1 (iv)]. In our strategy, the starting materials γ-ketomalononitriles and β-ketomalononitriles were readily prepared *via* the addition of malononitrile to various chalcones and α-bromoacetophenones. Further, most arylboronic acids are commercially available. This developed photocatalytic reaction proceeds at room temperature without the usage of exogenous photosensitizer. The constructed pyridine and pyrrole moiety having an inbuilt nitrile functionality can be further manipulated for various applications. Therefore, our protocol bypasses the toxic chemical maneuvers and harsh reaction

conditions generally associated with the introduction of a nitrile functionality in to aromatic rings, consequently endows synthetic benefits in the form of functional group transformations and derivatizations.

Scheme 1. Strategies for the Synthesis of Fused and Isolated Nitrogen-Heterocycles from Substrates Containing Functionalized or Activated Cyano Groups



RESULT AND DISCUSSION

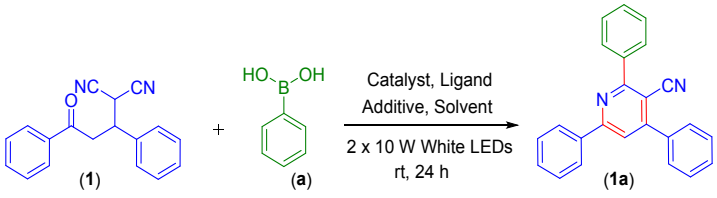
We embarked on our experimentation by selecting 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol) and phenylboronic acid (**a**) (1 equiv) as the rudimentary substrates; $Pd(OAc)_2$ (5 mol %) as the precatalyst, 2,2′-bipyridine (10 mol %) as the ligand, and PTSA·H_2O (1 equiv) as the additive. Toluene (2 mL) was employed as the solvent, and the reaction mixture was irradiated by 20 W (2 x 10 W) white LEDs at room temperature. The progress of the reaction was monitored via thin layer chromatography, which indicated the formation of some new species in the mixture, in the form of a new fluorescent blue spot in a 365 nm UV chamber. The new compound was isolated, characterized by standard spectroscopic techniques (IR, ^{1}H NMR, ^{13}C NMR, and HRMS). Delightfully, the analysis confirmed that the isolated compound was 2,4,6-triphenylnicotinonitrile (**1a**), and the yield was estimated to be 33%. Subsequently, single crystal X-ray diffraction studies were performed on

one of the derivatives (**1f**), which further validated the structure of the product (see the Supporting Information, Figure S1).[25] It is imperative to mention that the formation of 2,4,6-triphenylnicotinonitrile (**1a**) is associated with the genesis of a new C–C, a C–N, a C=N and two C=C bonds.

After successfully characterizing the desired product, further screening process was carried out to find the optimal reaction condition, for which 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol) was chosen as the model substrate and phenylboronic acid (**a)** (1 equiv) as the addition partner. Firstly, different solvents were screened by replacing toluene (33%) with *p*-xylene (35%), *m*-xylene (32%), cyclohexane (00%), 1,2-DCE (42%), MeOH (00%), CH_3CN (00%), DMF (00%) DMSO (00%), and H_2O (00%) (Table 1, entries 1–10). In conclusion, 1,2-DCE (42%), was found to be the most effective out of the lot (Table 1, entry 5). Next, the catalyst and ligands were screened by selecting alternatives to $Pd(OAc)_2$ and 2,2′-bipyridine. Although the replacement of $Pd(OAc)_2$ with $Pd(TFA)_2$ resulted in a relatively lower yield (38%; Table 1, entry 11), no product was isolated when the former was replaced with $PdCl_2$ as the catalyst (Table 1, entry 12). Moreover, the reaction completely failed in the absence of either $Pd(OAc)_2$, 2,2'-bipyridine or PTSA·H_2O (Table 1, entries 13–15). On the contrary, the yield of the isolated product enhanced to 56% when the loadings of $Pd(OAc)_2$, 2,2'-bipyridine and PTSA·H_2O were increased from that of the model reaction (Table 1, entry 16). Further increasing the amount of PTSA·H_2O from 2 to 5 equiv. did not significantly improve the isolated yield of the product (58%; Table 1, entries 16 and 17). After identifying $Pd(OAc)_2$ (10 mol%) and 1,2-DCE as the suitable catalyst and solvent, respectively, few ligands such as 1,10-phenanthroline (52%), L-proline (00%), PPh_3 (trace), XPhos (00%), 1,1'-bis-2-naphthol (00%) were also screened in lieu of 2,2′-bipyridine (Table 1, entries 18–22). Although the use of 1,10-phenanthroline as a ligand was able to produce the desired product in an appreciable yield (Table 1, entry 18), nevertheless it was unable to dethrone 2,2′-bipyridine as the favourable ligand, due to the higher yield of product in case of latter. Further, experiments were carried out by replacing the additive, PTSA·H_2O with other acids such as acetic acid and trifluoroacetic acid which produced (**1a**) in low yields (25% and 23%, respectively) (Table 1, entries 23–24). In contrast, the replacement of PTSA with benzoic acid or sulfuric acid turned out to be futile as almost no significant amount of the product obtained (Table 1, entries 25–26). Further fine-tuning of the reaction was achieved by increasing the amount of phenylboronic acid progressively from 1 to 5 equivalents. Adding 2 and 3 equivalents of phenylboronic acid resulted in escalated yields of (**1a**) to 66% and 72%,

respectively. Whereas, no further improvement was observed when 5 equiv. of the same were used (Table 1, entries 27–29). Reaction carried out in the presence of 2 x 5 W green LEDs light (42%) and 2 x 5 W blue LEDs light (51%) were also quite favorable to the product formation (Table 1, entries 30 and 31). The overall yield (42%) was decreased when the reaction stops after 12 h. (Table 1, entry 32). The reaction carried out in absence of LEDs is detrimental to product formation and and only 22% of the desired product was obtained (Table 1, entry 33). When the reaction was performed at a higher temperature (80 °C) in the absence of light the yield did not improve significantly. Further, the thermal reaction gave number of other side products causing difficulties during the separation. As measure the temperature in the vicinity of the reaction was near to the room temperature (27–30 °C) as it was performed in a well-ventilated room below a fan. Here, the white LEDs is accelerating the reaction by reducing Pd(II) to an active exited state Pd(0) in the presence of bipyridine ligand and enhance the subsequent formation of aryl palladium species (**I**) *via* redox trans-metalation. On the other hand in the absence of LEDs there might be competitive trans-metalation with Pd(II) species there by giving only 22% yield of the product at room temperature. After screening of various reaction parameters, the optimized standard conditions for this transformation were established to be the use of 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol), phenylboronic acid (**a**) (3 equiv), $Pd(OAc)_2$ (10 mol %), 2,2′-bipyridine (20 mol %) and PTSA·H_2O (2 equiv) in 1,2-DCE (2 mL) as the solvent under irradiation by 20 W (2 x 10 W) white LEDs at room temperature (Table 1, entry 28).

Table 1. Optimization of the Reaction Conditions[a-i]



entry	catalyst (mol %)	ligand (mol %)	additive (equiv)	solvent	yield (%)[b]
1	$Pd(OAc)_2$ (5)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	toluene	33
2	$Pd(OAc)_2$ (5)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	*p*-xylene	35
3	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	*m*-xylene	32
4	$Pd(OAc)_2$ (5)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	cyclohexane	00
5	$Pd(OAc)_2$ (5)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	1,2-DCE	42
6	$Pd(OAc)_2$ (5)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	MeOH	00
7	$Pd(OAc)_2$ (5)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	CH_3CN	00
8	$Pd(OAc)_2$ (5)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	DMF	00

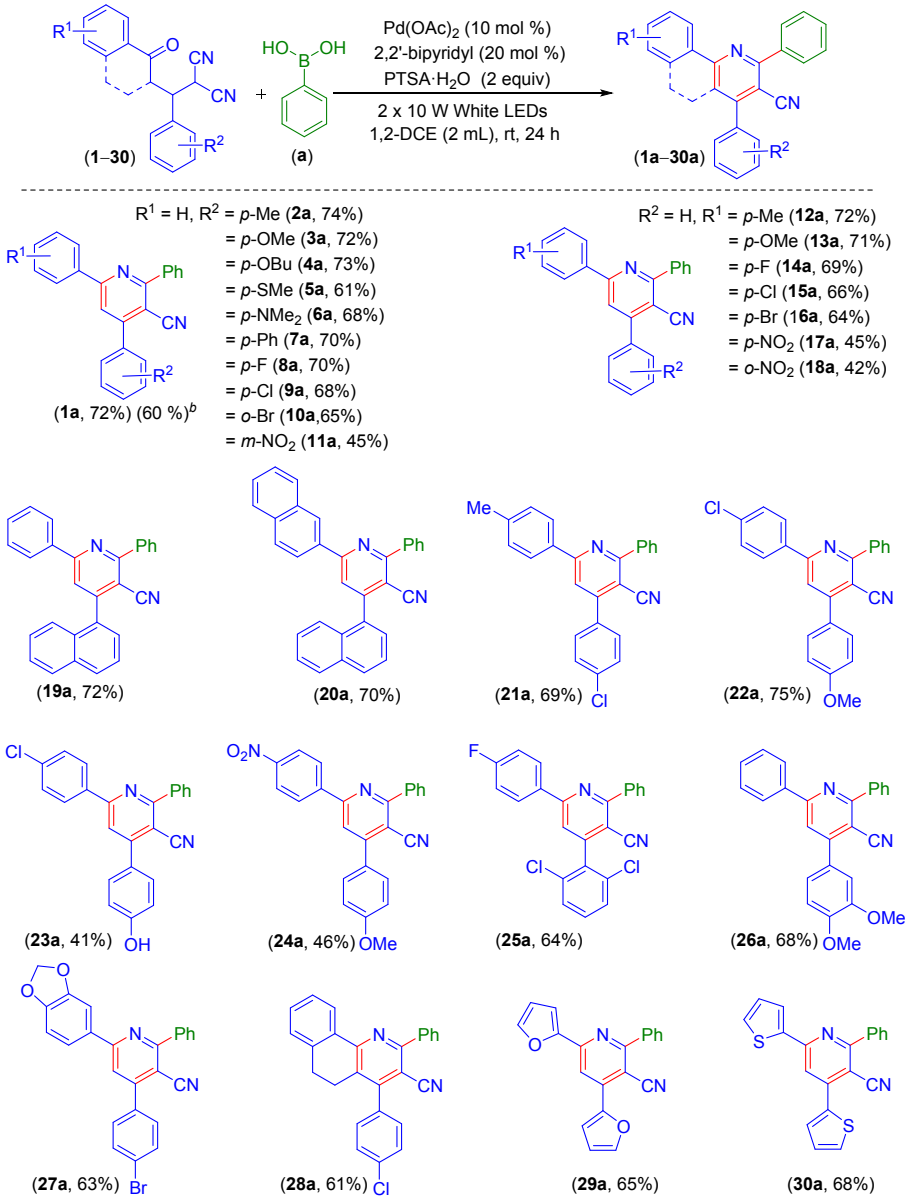
9	$Pd(OAc)_2$ (5)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	DMSO	00
10	$Pd(OAc)_2$ (5)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	H_2O	00
11	$Pd(TFA)_2$ (5)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	1,2-DCE	38
12	$PdCl_2$ (5)	2,2'-bipyridyl (10)	PTSA·H_2O (1)	1,2-DCE	00
13	---	2,2'-bipyridyl (10)	PTSA·H_2O (1)	1,2-DCE	00
14	$Pd(OAc)_2$ (5)	---	PTSA·H_2O (1)	1,2-DCE	00
15	$Pd(OAc)_2$ (5)	2,2'-bipyridyl (10)	---	1,2-DCE	00
16	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	PTSA·H_2O (2)	1,2-DCE	56
17	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	PTSA·H_2O (5)	1,2-DCE	58
18	$Pd(OAc)_2$ (10)	1,10-phen (20)	PTSA·H_2O (2)	1,2-DCE	52
19	$Pd(OAc)_2$ (10)	L-proline (20)	PTSA·H_2O (2)	1,2-DCE	00
20	$Pd(OAc)_2$ (10)	PPh_3 (20)	PTSA·H_2O (2)	1,2-DCE	trace
21	$Pd(OAc)_2$ (10)	XPhos (20)	PTSA·H_2O (2)	1,2-DCE	00
22	$Pd(OAc)_2$ (10)	1,1'-bi-2-naphthol (20)	PTSA·H_2O (2)	1,2-DCE	00
23	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	AcOH (2)	1,2-DCE	25
24	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	CF_3COOH (2)	1,2-DCE	23
25	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	$PhCO_2H$	1,2-DCE	trace
26	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	H_2SO_4	1,2-DCE	00
27	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	PTSA·H_2O (2)	1,2-DCE	66[c]
28	**$Pd(OAc)_2$ (10)**	**2,2'-bipyridyl (20)**	**PTSA·H_2O (2)**	**1,2-DCE**	**72[d]**
29	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	PTSA·H_2O (2)	1,2-DCE	73[e]
30	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	PTSA·H_2O (2)	1,2-DCE	42[f]
31	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	PTSA·H_2O (2)	1,2-DCE	51[g]
32	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	PTSA·H_2O (2)	1,2-DCE	42[h]
33	$Pd(OAc)_2$ (10)	2,2'-bipyridyl (20)	PTSA·H_2O (2)	1,2-DCE	22[i]

[a]Reaction condition: 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol), phenylboronic acid (**a**) (0.25 mmol), catalyst (mol %), ligand (mol %.), additive (equiv) at rt under 2 x 10 W white LEDs for 24 h. [b]Isolated yields. [c]2 equiv of (**a**) was used. [d]3 equiv of (**a**) was used. [e]5 equiv of (**a**) was used.[f]Reaction performed using 2 x 5 W green LEDs light. [g]Reaction performed using 2 x 5 W blue LEDs light. [h]Yield after 12 h. [i] in the absence of LEDs.

With the optimized reaction conditions in hand, this photoreaction was subjected to further studies for the elucidation of substrate scope. Firstly, various γ-keto-malononitriles bearing electron-donating (EDGs) and electron-withdrawing groups (EWGs) were taken alongside phenylboronic acid (**a**) in a series of different reactions to generate the corresponding triarylsubstituted cyanopyridines (Scheme 2). The unsubstituted γ-keto-malononitrile (**1**) coupled with phenylboronic acid (**a**), to yield 3-cyano-2,4,6-triphenylpyridine in (**1a**) in 72% yield (Scheme 2). Next, a series of γ-keto-malononitriles containing unsubstituted benzoyl ring alongside electron-rich phenyl ring bearing EDGs such as *p*-Me (**2**), *p*-OMe (**3**), *p*-OBu (**4**), *p*-SMe (**5**), *p*-NMe_2 (**6**), and *p*-Ph (**7**) were chosen to couple with the phenylboronic acid (**a**). The

corresponding products (**2a**, 74%), (**3a**, 72%), (**4a**, 73%), (**5a**, 61%), (**6a**, 68%), and (**7a**, 70%) were obtained in good yields (Scheme 2). Moreover, when the phenyl ring bore EWGs such as *p*-F (**8**), *p*-Cl (**9**), *o*-Br (**10**), and *m*-NO_2 (**11**), the corresponding products (**8a**, 70%), (**9a**, 68%), (**10a**, 65%), and (**11a**, 45%) were obtained in moderate to good yields (Scheme 2). Next, the effect of substitution on benzoyl ring was studied by choosing suitable γ-keto-malononitrile substrates bearing an unsubstituted phenyl ring, and subjecting them to the optimized reaction condition. Both the scenarios wherein the benzoyl ring possessed EDGs such as, *p*-Me (**12**) and *p*-OMe (**13**), and EWGs such as, *p*-F (**14**), *p*-Cl (**15**), *p*-Br (**16**), *p*-NO_2 (**17**), and *o*-NO_2 (**18**), resulted in the desired products (**12a**, 72%), (**13a**, 71%), (**14a**, 69%), (**15a**, 66%), (**16a**, 64%), (**17a**, 45%), and (**18a**, 42%) respectively (Scheme 2). It is interesting to note that akin to the previous set of experiments, the presence of an electron-deficient benzoyl ring abated the product formation. γ-Keto-malononitriles bearing the naphthyl moiety, (**19**) and (**20**), when chosen as substrates for the developed protocol, responded well to afford the respective products 3-cyano-4-(α-naphthyl)-2,6-diphenylpyridine (**19a**) and 3-cyano-4-(α-naphthyl)-6-(β-naphthyl)-2-phenylpyridine (**20a**) with 72% and 70% yields, respectively (Scheme 2). The protocol was also tested with γ-keto-malononitrile substrates bearing both substituted benzoyl/phenyl moieties simultaneously with groups such as EDG *p*-Me/EWG *p*-Cl (**21**), EWG *p*-Cl/EDG *p*-OMe (**22**), EWG *p*-Cl/EDG *p*-OH (**23**), and EWG *p*-NO_2/EDG *p*-OMe (**24**). All of these substrates coupled well with phenylboronic acid (**a**) to yield the respective substituted cyanopyridines (**21a**, 69%), (**22a**, 75%), (**23a**, 41%) and (**24a**, 46%), respectively. Further, substrates containing some di-substituted phenyl rings such as 2,6-dichlorophenyl (**25**), and the 3,4-dimethoxyphenyl (**26**), reacted efficiently to give the products (**25a**, 64%) and (**26a**, 68%), respectively, in good yields. The Michael adduct bearing 3,4-methylenedioxobenzoyl ring and *p*-bromophenyl ring (**27**) reacted under the standard conditions to afford the desired pyridine (**27a**, 63%). Besides, the cyclic γ-keto substrate (**28**) underwent efficient transformation to the product (**28a**) in 61% yield. Furthermore, Michael adducts bearing other aryl rings such as, furan (**29**) or a thiophene (**30**), were also compatible with the protocol and afforded the products (**29a**, 65%) and (**30a**, 68%), respectively, in good yields. To determine the efficiency of this photoinduced process and also to expand the scope of this method, 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (1.37 gm, 5 mmol), and phenylboronic acid (**a**) were reacted on a gram scale which provided 2,4,6-triphenylsubstituted nicotinonitrile (**1a**) in 60% yield (Scheme 2).

Scheme 2. Substrate Scope for the Synthesis of 2,4,6-Triarylsubstituted Nicotinonitrile [a,b]

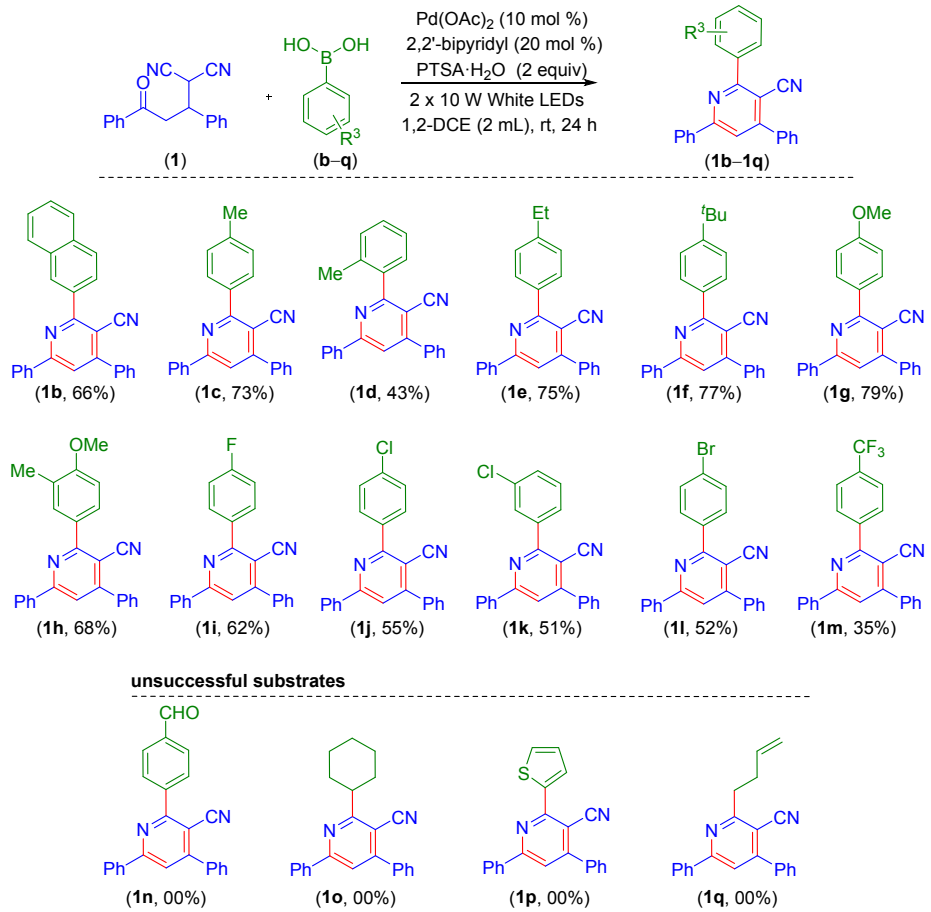


[a]Reaction conditions: (i) **1**–**30** (0.25 mmol), phenylboronic acid (**a**) (0.75 mmol), $Pd(OAc)_2$ (0.025 mmol), 2,2'-bipyridyl (0.05 mmol), PTSA·H_2O (0.5 mmol), and 1,2-DCE (2 mL) at rt for 24 h. under 2 x 10 W white LEDs. [b]Yield reported for 1 gm scale.

After successfully employing diverse γ-ketomalononitriles (**1-30**) to the developed strategy, the scope was further enhanced by reacting various arylboronic acids with 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) under standard conditions (Scheme 3). The reaction was successful with 2-napthylboronic acid (**b**), which had produced 2-(naphthalen-2-yl)-4,6-diphenylnicotinonitrile (**1b**) in 66% yield. Arylboronic acids possessing electron-donating groups such as *p*-Me (**c**), *o*-Me (**d**), *p*-Et (**e**), *p*-^{t}Bu (**f**), *p*-OMe (**g**) and 3-Me-4-OMe (**h**) also responded positively towards the protocol, and afforded the desired cyanopyridines (**1c**, 73%), (**1d**, 43%), (**1e**, 75%), (**1f**, 77%), (**1g**, 79%), and (**1h**, 68%), respectively, in good yields.

Arylboronic acids possessing electron-withdrawing groups such as *p*-F (**i**), *p*-Cl (**j**), *m*-Cl (**k**), *p*-Br (**l**) and *p*-CF_3 (**m**), also underwent efficient addition/cyclization with the γ-ketomalononitrile (**1**) to afford the desired cyanopyridines (**1i**, 62%), (**1j**, 55%), (**1k**, 51%), (**1l**, 52%), and (**1m**, 35%), respectively, albeit the yields were moderate to good in these cases. Unfortunately, the developed protocol turned out to be unsuccessful in case of few boronic acids such as *p*-CHO-phenylboronic acid (**n**), cyclohexylboronic acid (**o**), 2-thienylboronicacid (**p**), and allylboronic acid (**q**).

Scheme 3. Substrate Scope for Arylboronic Acids[a]



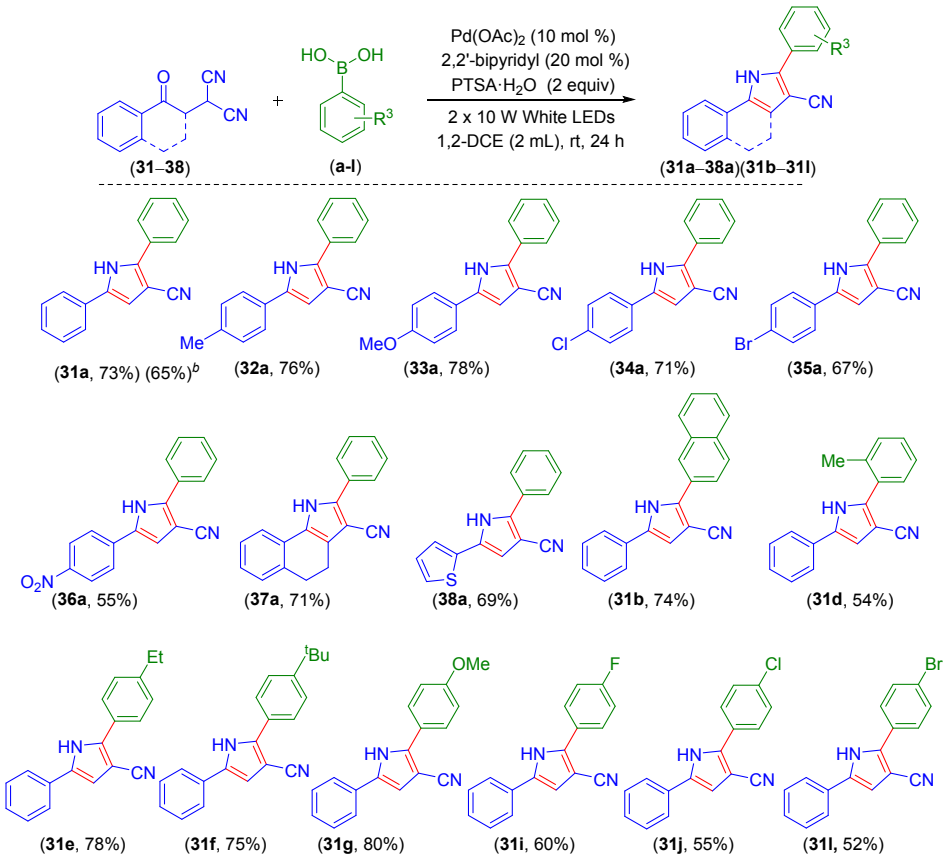
[a]Reaction conditions: (i) 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol), arylboronic acids (**b-q**) (0.75 mmol), $Pd(OAc)_2$ (0.025 mmol), 2,2'-bipyridyl (0.05 mmol), PTSA·H_2O (0.5 mmol), and 1,2-DCE (2 mL) at rt for 24 h. under 2 x 10 W white LEDs.

We speculate that the electron withdrawing substituents present in arylboronic acids may potentially impede the trans-metalation and the carbopalladation/migration of aryl group to the electrophilic carbon center of the nitrile moiety (Scheme 7). Perhaps, this might be the reason for the lower yields with electron withdrawing substituents. For an electron-deficient aryl moiety, *p*-CHO-phenylboronic acid (**n**), the carbopalladation does not occur efficiently

due to the poor migrating ability of such aryl moieties to electrophilic centres. The failure of boronic acids having a sp^3-C–B bond *viz.* cyclohexylboronic acid (**o**) and allylboronic acid (**q**) hints towards a putative two electron carbanion based-mechanism, wherein β-hydride elimination reaction may be occurring.[16f] For thiophene based boronic acid, the adjacent S atom may be depleting the electronic charge, built up at the C2-position by accepting electrons into its vacant d-orbitals, leading to an inefficient carbopalladation. Moreover, strongly coordinating sulfur atom in the thiophene ring is known to poison Pd(II) catalysts.

The synthetic utility of this photoreaction was further extended by investigating the addition/cyclization of phenylboronic acids to few β-ketomalononitriles under the optimized reaction conditions to yield the substituted pyrroles (Scheme 4). To our delight, the reaction of phenylboronic acid (**a**) with unsubstituted β-ketomalononitrile, 2-(2-oxo-2-phenylethyl)malononitrile (**31**) produced the five membered *N*-heterocycle, 2,5-diphenyl-1*H*-pyrrole-3-carbonitrile (**31a**) in 73% yield under the standard conditions. The formation of pyrrole skeleton was confirmed by the ^{1}H NMR, ^{13}C NMR and HRMS analysis. Later, β-ketomalononitriles bearing EDGs such as, *p*-Me (**32**) and *p*-OMe (**33**), and EWGs such as, *p*-Cl (**34**), *p*-Br (**35**), and *p*-NO_2 (**36**) were selected alongside the phenylboronic acid (**a**) to participate in our reaction strategy. Fortunately, the desired 2,5-diaryl-3-cyanopyrrol products– (**32a**, 76%), (**33a**, 78%), (**34a**, 71%), (**35a**, 67%), and (**36a**, 55%) were obtained in good to moderate yields. A bicyclic substrate, 2-(1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)malononitrile (**37**) and a β-ketomalononitrile containing thiophene moiety (**38**), also coupled successfully with phenylboronic acid (**a**), and subsequently cyclized to afford the corresponding pyrrole derivatives (**37a**, 71%) and (**38a**, 69%) in good yields. Naphthalen-2-ylboronic acid (**b**) reacted with 2-(2-oxo-2-phenylethyl)malononitrile (**31**) to yield 2-(β-naphthyl)-5-phenyl-1*H*-pyrrole-3-carbonitrile (**31b**) in 74% yield. Additionally, a host of phenylboronic acids possessing EDGs such as, *o*-Me (**d**), *p*-Et (**e**), *p*-^{t}Bu (**f**), and *p*-OMe (**g**), and EWGs such as, *p*-F (**i**), *p*-Cl (**j**), and *p*-Br (**l**) were reacted with 2-(2-oxo-2-phenylethyl)malononitrile (**31**) under standard conditions to afford the corresponding pyrroles– (**31d**, 54%), (**31e**, 78%), (**31f**, 75%), (**31g**, 80%), (**31i**, 60%), (**31j**, 55%), and (**31l**, 52%) in moderate to good yields.

Scheme 4. Substrate Scope for 2,5-Diarylsubstituted-3-cyano Pyrroles[a,b]

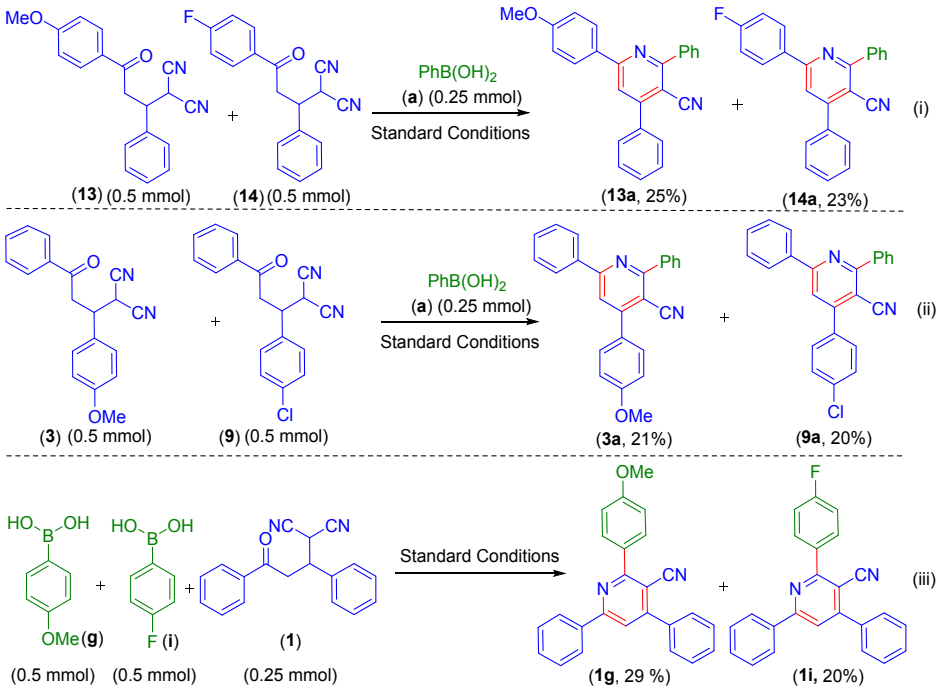


[a]Reaction conditions: (i) 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (0.25 mmol), arylboronic acids (**b-q**) (0.75 mmol), $Pd(OAc)_2$ (0.025 mmol), 2,2'-bipyridyl (0.05 mmol),PTSA·H_2O (0.5 mmol), and 1,2-DCE (2 mL) at rt for 24 h. under 2 x 10 W white LEDs. .[b]Yield reported for mmol scale.

Intermolecular competition reactions were performed in order to study the electronic influence of the substituents present on the aroyl/aryl moieties of γ-ketomalononitriles and arylboronic acids. In our first experiment, an equimolar mixture of substrates (**13**) and (**14**), composed of aroyl groups possessing an EDG, *p*-OMe and an EWG, *p*-F, respectively, were reacted with phenylboronic acid (**a**) [Scheme 5 (i)]. The yields of the corresponding products (**13a**, 25%) and (**14a**, 23%) were similar, which indicate that substrates possessing EDGs and EWGs in the aroyl moiety (R^1) show similar reactivity in our protocol. In the second experiment, two γ-ketomalononitrile substrates wherein the aryl moiety contains either an EDG *p*-OMe (**3**), or an EWG *p*-Cl (**9**) were chosen to react with the phenylboronic acid (**a**) under standard conditions. It was again observed that the electronic nature of the substituent R^2 present on the phenyl moiety had minimal effect on the outcome of reaction, as evident from the almost equal yields of products (**3a**, 21%) and (**9a**, 20%), respectively [Scheme 5 (ii)]. Finally, the effect of the electronic nature of substituents (R^3) present on the phenyl ring of the boronic acids were investigated. An equimolar mixture of electron-rich *p*-

methoxyphenylboronic acid (**g**), and a relatively electron-deficient *p*-fluorophenylboronic acid (**i**) was reacted with (**1**) to afford the respective cyanopyridines (**1g**, 29%) and (**1i**, 20%). This suggests that presence of an EDG on the phenyl ring of arylboronic acid renders higher compatibility with the protocol [Scheme 5 (iii)].

Scheme 5. **Intermolecular Competition Experiments**

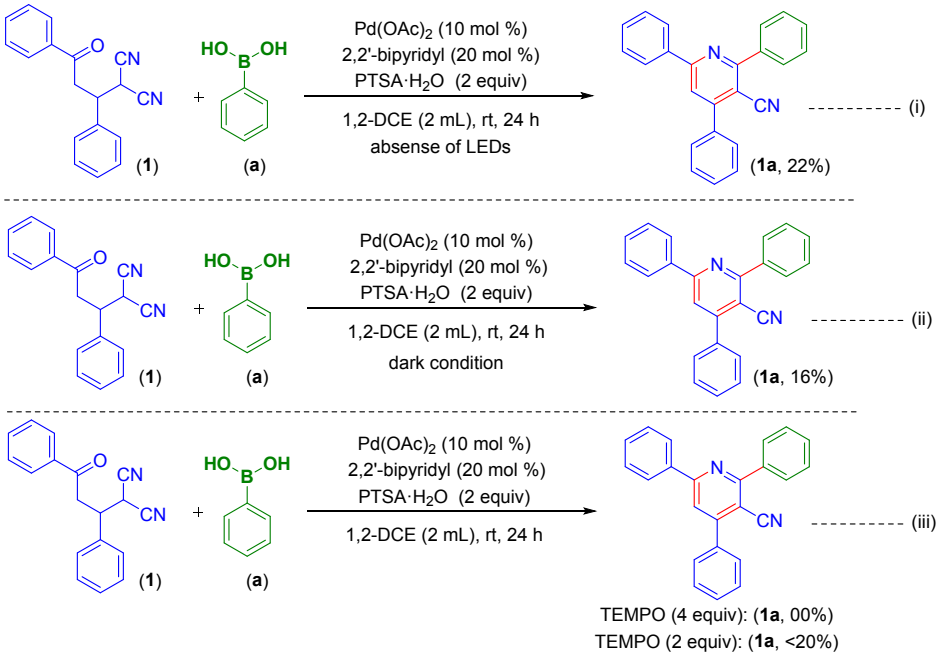


Mechanistic Pathway

To understand the mechanistic underpinnings of the photoreaction, few control experiments were performed as highlighted by Scheme 6. Our initial experiment was performed under normal laboratory conditions at room temperature. It was observed that the reaction proceeded slowly, and only 22% yield of the desired product was obtained after 24 h [Scheme 6 (i)]. In the next experiment, the reaction flask was wrapped carefully with an aluminium foil, and the reaction was carried out in complete dark conditions. This time, even less than 16% of the product was isolated [Scheme 6 (ii)]. Hence, it can be concluded that light does accelerate the desired reaction. Later, a radical scavenger 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) was added to the reaction mixture in varying quantities. Although the use of 2 equiv TEMPO resulted in poor yield (<20%), when 4 equiv TEMPO was added to the reaction mixture, no desired product was obtained [Scheme 6 (iii)]. These results indicate that a radical pathway may be operative. However, no TEMPO adducts were detected while performing the HRMS analysis of the reaction mixture. Moreover, the alkylboronic acids such

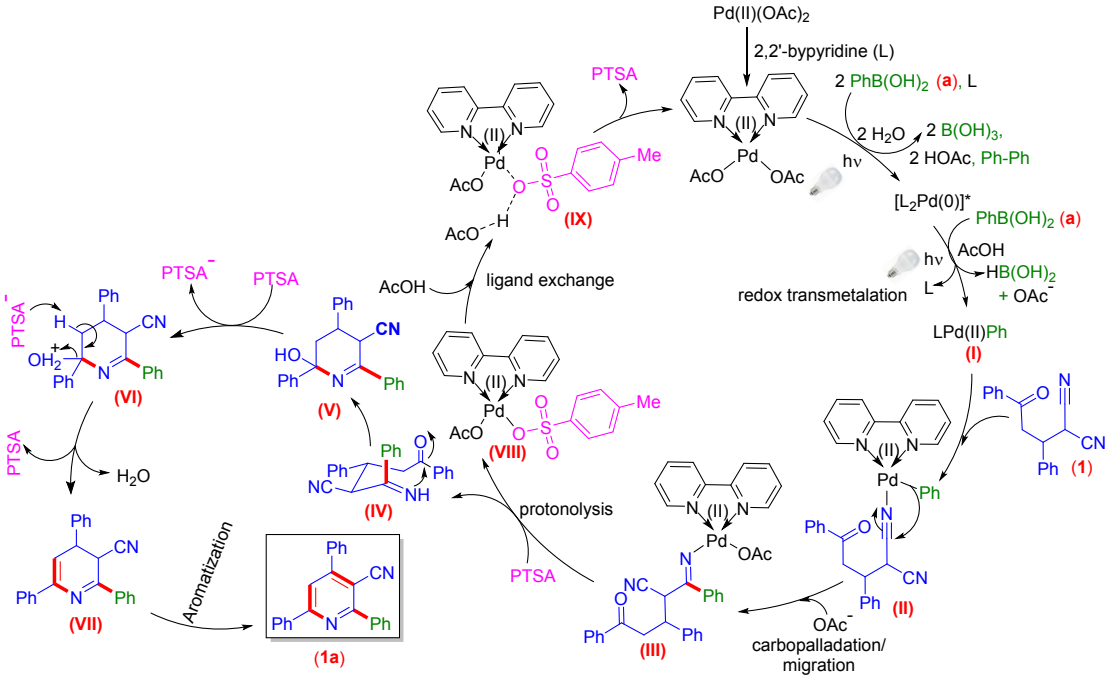
as cyclohexylboronic acid (**o**) and allylboronic acid (**q**) did not yield the desired products **1o** and **1q** when subjected to standard conditions (Scheme 3).[16f] Surprisingly, these observations refute the existence of a radical pathway. According to the literature reports, there is a possibility that TEMPO may oxidize Pd(0) to Pd(II), thereby inhibiting the reaction in the forward direction.[26]

Scheme 6. Control Experiments



Based on these facts, the likelihood of conventional SET mechanism involving organic radicals due to visible light irradiation is not obvious in our case, and a plausible reaction mechanism is outlined in Scheme 7. Initially, $Pd(OAc)_2$ combines with 2,2′-bipyridyl ligand (**L**) to form a complex $Pd(II)(bpy)(OAc)_2$ (detected by HRMS analysis of reaction mixture, Figure S2). The protocol requires 3 equivalents of arylboronic acid with respect to the reacting substrate. The requirement of excess boronic acid can be rationalized by the *in situ* generation of Pd(0) by the reduction of $Pd(II)(bpy)(OAc)_2$, which is also accelerated under visible irradiation.[27] Another 2,2′-bipyridine ligand (**L**) combines with the *in situ* generated Pd(0) species, which subsequently undergoes photoexcitation via MLCT to form an excited palladium complex, [$L_2Pd(0)^*$] (detected by HRMS analysis of reaction mixture, Figure S3). Although the next step, that is, transmetalation is not fully understood, we speculate that a redox reaction may be occurring, wherein the excited palladium complex, [$L_2Pd(0)^*$] reduces the phenylboronic acid (**a**).[28] Concomitantly, transfer of aryl group (of boronic acid), and an elimination of 2,2′-bipyridine ligand (**L**) occurs to give the intermediate (**I**) (detected by HRMS analysis of reaction mixture, Figure S2). The redox step may involve the M→Z σ-interaction

between the palladium centre and the boron centre of boronic acid.[29] The Pd(II) centre of intermediate (**I**) then cordinates with the γ-ketomalononitrile substrate (**1**) to give the intermediate (**II**) (detected by HRMS analysis of reaction mixture, Figure S4). Next, intramolecular carbopalladation of nitrile occurs *via* the insertion of the phenyl group to the nitrile moiety followed by insertion of an acetate anion to the palladium centre which results in the corresponding ketimine complex (**III**) (detected by HRMS analysis of reaction mixture, Figure S5). Later, PTSA·H_2O protonates this intermediate to release 2-(imino(phenyl)methyl)-5-oxo-3,5-diphenylpentanenitrile (**IV**) and coordination of PTSA to the Pd(II) centre forms the intermediate (**VIII**) (detected by HRMS analysis of reaction mixture, Figure S6). The intial Pd(II) species is regenerated via the intermidecy of (**IX**) (detected by HRMS analysis of reaction mixture, Figure S7) and continues the catalytic cycle. Finally, PTSA·H_2O triggers the intramolecular cyclization of **IV**, which is followed by dehydration to form the intermediate **VII** (detected by HRMS analysis of reaction mixture, Figure S8 and Figure S9). Finally, aromatization of the intermediate **VII** affords the desired product, 3-cyano-2,4,6-triphenylpyridine (**1a**).



Scheme 7. Proposed Mechanistic Pathway

CONCLUSION

In summary, we have devised an elegant strategy for the synthesis of 2,4,6-triarylnicotinonitriles and 2,5-diaryl-1*H*-pyrrole-3-carbonitriles at ambient temperature *via* a Pd-catalyzed reaction of arylboronic acid with γ- and β-ketodinitriles under visible-light

irradiation. The present one-pot synthetic protocol obviates the necessity of an external photosensitizer, and provides a convenient access to the desired products in moderate to good yields under mild reaction conditions. The desired products possess nitrile moiety which can be later functionalized to generate useful molecules for diverse applications.

EXPERIMENTAL SECTION

General information:

All the reagents were commercial grade and purified according to the established procedures. All the reactions were carried out in oven-dried glassware under a degassed atmosphere. Highest commercial quality reagents were purchased and were used without further purification unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) on a 0.25 mm silica gel plates ($60F_{254}$) visualized under UV illumination at 254 nm. Organic extracts were dried over anhydrous sodium sulfate (Na_2SO_4). Solvents were removed using a rotary evaporator under reduced pressure. Column chromatography was performed to purify the crude product on silica gel 60–120 mesh using a mixture of hexane and ethyl acetate as eluent. All the isolated compounds were characterized by ^1H, $^{13}C\{^1H\}$ NMR and IR spectroscopic (HRMS-spectrometric) techniques. NMR spectra for all the samples were recorded in deuterochloroform ($CDCl_3$) or deuterated dimethyl sulfoxide (DMSO-*d*6). ^1H, $^{13}C\{^1H\}$ were recorded in 600 (150) or 400 (100) MHz spectrometer and were calibrated using tetramethylsilane or residual undeuterated solvent for ^1H NMR, deuterochloroform for ^{13}C NMR as an internal reference {$Si(CH_3)_4$: 0.00 ppm or $CHCl_3$: 7.260 ppm for ^1H NMR, 77.230 ppm for ^{13}C NMR or $(CH_3)_2SO$: 2.50 ppm for ^1H NMR, 39.50 ppm for ^{13}C NMR}. ^{19}F NMR was calibrated using hexafluorobenzene as internal standard. The chemical shifts are quoted in δ units, parts per million (ppm). ^1H NMR data is represented as follows: Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentat, m = multiplet, br = broad, dd = doublet of doublet, tt = triplet of triplet), integration and coupling constant(s) *J* in hertz (Hz). High resolution mass spectra (HRMS) were recorded on a mass spectrometer using electrospray ionization-time of flight (ESI-TOF) reflection experiments. FT-IR spectra were recorded in KBr or neat and reported in frequency of absorption (cm^{-1}).

General Procedure for the Synthesis of 2-(3-Oxo-1,3-diarylpropyl)malononitriles (1–30).

Compounds **(1–30)** were synthesized by slightly modification of the literature procedure.[30]

To an oven-dried 50 mL round bottom flask was added chalcone, 1,3-diphenyl-2-propen-1-one (1.04 g, 5.0 mmol.), malononitrile (0.66 g, 10.0 mmol), K_2CO_3 (1.38 g, 10.0 mmol) and DCE (10 mL). The reaction mixture was stirred at room temperature for 12 h. Then the reaction mixture was admixed with ethyl acetate (50 mL) and the organic layer was washed with water (2 x 10 mL). The organic layer was dried over anhydrous Na_2SO_4, and solvent was evaporated under reduced pressure. The crude product so obtained was purified over a column of silica gel (hexane / ethyl acetate, 9:1) to give pure 2-(3-oxo-1,3-diaryllpropyl)malononitriles (**1**) (1.30 g, 95%).

General Procedure for the Synthesis of 2-(2-oxo-2-arylylethyl)malononitriles (31–38).

Compounds (**31**–**38**) were synthesized by slightly modification of the literature procedures.[31a,b]

To an oven-dried 100 mL round bottom flask was added α-bromoacetophenone (1.97 g, 10.0 mmol) and malononitrile (0.66 g, 10.0 mmol) were dissolved in EtOH (20 mL) and cooled in an ice bath. On the other hand, NaOH (0.4 g, 10.0 mmol) was dissolved in H_2O (20 mL), cooled in an ice bath and added to the above reaction mixture over a period of 5 min. After letting the reaction mixture stir for 30 min at 0 ^oC, H_2O (20 mL) was added from which colorless residue appeared which was filtered off and dried under a constant stream of air. Recrystallization from EtOH to give 2-(2-oxo-2-arylylethyl)malononitriles (**31**) as a white solid (1.39 g, yield 76%).

General Procedure for the Synthesis of 2,4,6-Triarylnicotinonitriles (1a–30a) from 2-(3-Oxo-1,3-diarylpropyl)malononitriles (1–30) and Phenylboronic acid (a).

To an oven-dried 10 mL round bottom flask was added 2-(3-oxo-1,3-diphenylpropyl)malononitrile (**1**) (68.5 mg, 0.25 mmol), phenylboronic acid (**a**) (90.6 mg, 0.75 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), 2,2′-bipyridyl (7.8 mg, 0.05 mmol), PTSA·H_2O (95 mg, 0.5 mmol) and 1,2-DCE (2 mL). The reaction mixture was stirred at room temperature for 24 h, maintaining an approximate distance of ~6-8 cm from two 10W white LED bulbs (Flux 46 mw/cm2). After completion of the reaction (monitored by TLC analysis), the reaction mixture was admixed with ethyl acetate (25 mL) and the organic layer was washed with saturated sodium bicarbonate solution (1 x 5 mL). The organic layer was dried over anhydrous Na_2SO_4, and solvent was evaporated under reduced pressure. The crude product so obtained was purified over a column of silica gel using 2% ethyl acetate in hexane to give pure 2,4,6-

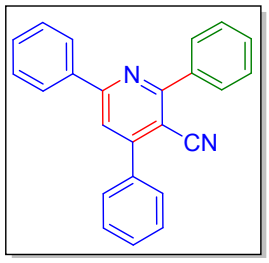
triarylnicotinonitrile (**1a**) (60 mg, yield 72%). The identity and purity of the product was confirmed by spectroscopic analysis.

General Procedure for the Synthesis of 2,5-diaryl-1*H*-pyrrole-3-carbonitriles (31a–38a) from 2-(2-oxo-2-arylethyl)malononitriles (31–38) and Phenylboronic acid (a)

To an oven-dried 10 mL round bottom flask was added 2-(2-oxo-2-phenylethyl)malononitrile (**31**) (46 mg, 0.25 mmol), phenylboronic acid (**a**) (90.6 mg, 0.75 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), 2,2′-bipyridyl (7.8 mg, 0.05 mmol), PTSA·H_2O (95 mg, 0.5 mmol) and 1,2-DCE (2 mL). The reaction mixture was stirred at room temperature for 24 h, maintaining an approximate distance of ~6-8 cm from two 10W white LED bulbs (Flux 46 mw/cm^2). After completion of the reaction (monitored by TLC analysis), the reaction mixture was admixed with ethyl acetate (25 mL) and the organic layer was washed with saturated sodium bicarbonate solution (1 x 5 mL). The organic layer was dried over anhydrous Na_2SO_4 and solvent was evaporated under reduced pressure. The crude product so obtained was purified over a column of silica gel using 5% ethyl acetate in hexane to give pure 2,5-diaryl-1*H*-pyrrole-3-carbonitriles (**31a**) (45 mg, yield 73%). The identity and purity of the product was confirmed by spectroscopic analysis.

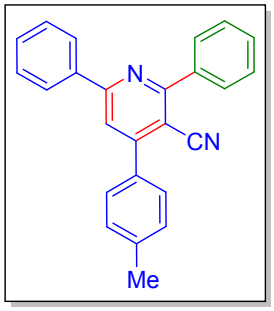
Spectral Data

2,4,6-Triphenylnicotinonitrile (**1a**):[32]



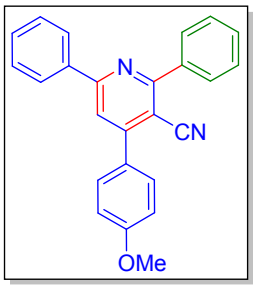
As a white solid (60 mg, 72% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19 (d, 2H, J = 7.6 Hz), 8.06 (d, 2H, J = 7.8 Hz), 7.83 (s, 1H), 7.70 (d, 2H, J = 7.6 Hz), 7.60–7.55 (m, 6H), 7.53–7.48 (m, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.6, 159.3, 155.6, 138.2, 137.7, 136.9, 130.7, 130.2, 130.1, 129.6, 129.17, 129.16, 128.9, 128.7, 127.8, 118.8, 117.9, 104.5; IR (KBr, cm^{-1}): 2924, 2858, 2215, 1727, 1571, 1530, 1488, 1372, 1276, 1171, 1073, 1025, 873, 748, 688, 616, 568, 485; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{17}N_2$ $[M + H]^+$ 333.1386; found 333.1391.

2,6-Diphenyl-4-(p-tolyl)nicotinonitrile (**2a**):



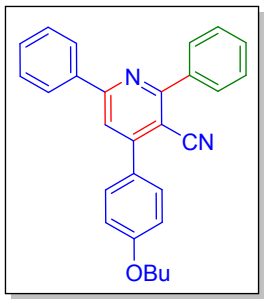
As a white solid (64 mg, 74% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19 (d, 2H, J = 7.8 Hz), 8.07 (d, 2H, J = 7.8 Hz), 7.82 (s, 1H), 7.62–7.52 (m, 8H), 7.39 (d, 2H, J = 8.0 Hz), 2.48 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.5, 159.2, 155.6, 140.3, 138.2, 137.8, 134.0, 130.6, 130.2, 129.9, 129.6, 129.1, 128.8, 128.6, 127.7, 118.7, 118.1, 104.4, 21.6; IR (KBr, cm^{-1}): 2925, 2862, 2214, 1578, 1511, 1377, 1290, 1247, 1170, 1072, 1024, 971, 875, 828, 762, 693, 609, 572, 520; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{19}N_2$ $[M + H]^+$ 347.1543; found 347.1558.

4-(4-Methoxyphenyl)-2,6-diphenylnicotinonitrile (**3a**):[32,33]



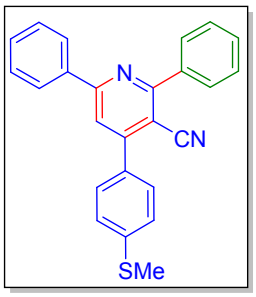
As a white solid (65 mg, 72% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.18 (d, 2H, J = 7.8 Hz), 8.05 (d, 2H, J = 6.6 Hz), 7.80 (s, 1H), 7.67 (d, 2H, J = 8.4 Hz), 7.59–7.49 (m, 6H), 7.09 (d, 2H, J = 8.8 Hz), 3.90 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.7, 161.2, 159.2, 155.2, 138.3, 137.8, 130.6, 130.4, 130.2, 129.2, 129.1, 128.6, 127.7, 118.6, 118.3, 114.6, 114.3, 104.3, 55.6; IR (KBr, cm^{-1}): 2924, 2861, 2218, 1669, 1582, 1514, 1459, 1373, 1253, 1175, 1027, 819, 758, 690, 563; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{19}N_2O$ $[M + H]^+$ 363.1492; found 363.1497.

4-(4-Butoxyphenyl)-2,6-diphenylnicotinonitrile (**4a**):



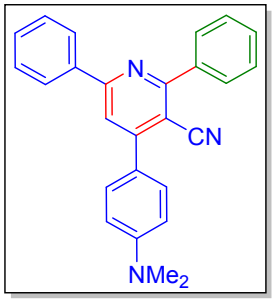
As a white solid (73 mg, 73% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.18 (d, 2H, J = 7.8 Hz), 8.05 (d, 2H, J = 7.6 Hz), 7.80 (s, 1H), 7.66 (d, 2H, J = 8.8 Hz), 7.59–7.49 (m, 6H), 7.08 (d, 2H, J = 8.4 Hz), 4.06 (t, 2H, J = 6.4 Hz), 1.87–1.80 (m, 2H), 1.59–1.50 (m, 2H), 1.02 (t, 3H, J = 7.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): 162.7, 160.8, 159.2, 155.3, 138.3, 137.9, 130.6, 130.3, 130.2, 129.6, 129.1, 128.9, 128.6, 127.7, 118.5, 118.3, 115.1, 104.2, 68.1, 31.4, 19.4, 14.0; IR (KBr, cm^{-1}): 2919, 2857, 2213, 1660, 1574, 1529, 1455, 1373, 1237, 1179, 1074, 1024, 880, 816, 754, 684, 588, 546, 494; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{28}H_{25}N_2O$ $[M + H]^+$ 405.1961; found 405.1976.

4-(4-(Methylthio)phenyl)-2,6-diphenylnicotinonitrile (**5a**):



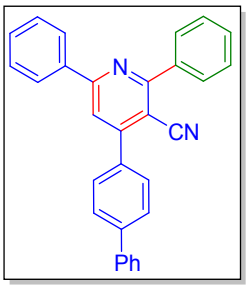
As a white solid (57 mg, 61% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.18 (d, 2H, J = 7.4 Hz), 8.04 (d, 2H, J = 7.6 Hz), 7.80 (s, 1H), 7.63 (d, 2H, J = 8.4 Hz), 7.58–7.50 (m, 6H), 7.42 (d, 2H, J = 8.4 Hz), 2.56 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.7, 159.4, 154.9, 141.9, 138.2, 137.8, 133.2, 130.7, 130.3, 129.6, 129.23, 129.17, 128.7, 127.8, 126.4, 118.5, 118.0, 104.3, 15.4; IR (KBr, cm^{-1}): 2923, 2855, 2217, 1674, 1571, 1372, 1264, 1188, 1028, 812, 758, 690, 577, 497; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{19}N_2S$ $[M + H]^+$ 379.1263; found 379.1265.

4-(4-(Dimethylamino)phenyl)-2,6-diphenylnicotinonitrile (**6a**):[34]



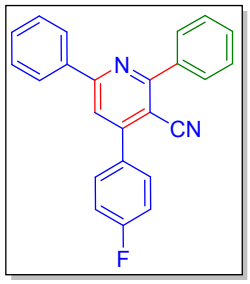
As a white solid (63 mg, 68% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.17 (d, 2H, J = 7.2 Hz), 8.03 (d, 2H, J = 7.4 Hz), 7.80 (s, 1H), 7.66 (d, 2H, J = 8.8 Hz), 7.58–7.48 (m, 6H), 6.85 (d, 2H, J = 8.8 Hz), 3.07 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.9, 158.9, 155.6, 151.6, 138.6, 138.2, 130.4, 130.1, 130.0, 129.6, 129.1, 128.6, 127.7, 123.9, 118.8, 118.2, 103.8, 40.4; IR (KBr, cm^{-1}): 2922, 2854, 2216, 1677, 1615, 1573, 1453, 1369, 1523, 1200, 1026, 815, 757, 692; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{26}H_{22}N_3$ $[M + H]^+$ 376.1808; found 376.1820.

4-([1,1'-Biphenyl]-4-yl)-2,6-diphenylnicotinonitrile (**7a**):



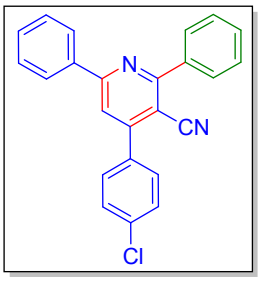
As a white solid (71 mg, 70% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.20 (d, 2H, J = 7.8 Hz), 8.06 (d, 2H, J = 7.8 Hz), 7.88 (s, 1H), 7.79 (s, 4H), 7.68 (d, 2H, J = 7.2 Hz), 7.58–7.48 (m, 8H), 7.41 (t, 1H, J = 7.2 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.7, 159.4, 155.2, 143.0, 140.3, 138.2, 137.8, 135.8, 130.8, 130.3, 129.6, 129.4, 129.20, 129.16, 128.7, 128.1, 127.9, 127.8, 127.4, 118.8, 118.1, 104.4,; IR (KBr, cm^{-1}): 2923, 2857, 2215, 1573, 1527, 1456, 1372, 1266, 1074, 1024, 838, 754, 689, 575; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{30}H_{21}N_2$ $[M + H]^+$ 409.1699; found 409.1698.

4-(4-Fluorophenyl)-2,6-diphenylnicotinonitrile (**8a**):



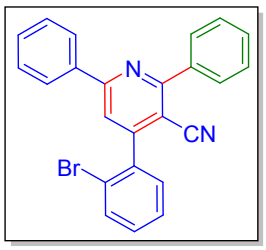
As a white solid (61 mg, 70% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.11–8.09 (m, 2H), 797–7.95 (m, 2H), 7.71 (s, 1H), 7.62–7.59 (m, 2H), 7.49–7.43 (m, 6H), 7.21–7.17 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 163.9 (d, J = 249.1 Hz), 162.7, 159.5, 154.6, 138.1, 137.6, 133.0 (d, J = 3.4 Hz), 130.9, 130.8 (d, J = 3.7 Hz), 130.4, 129.6, 129.2, 128.7, 127.8, 118.7, 117.8, 116.4 (d, J = 21.8 Hz), 104.5; ^{19}F NMR ($CDCl_3$ + hexafluorobenzene): δ –113.8 (s); IR (KBr, cm^{-1}): 2923, 2855, 2212, 1644, 1576, 1504, 1454, 1377, 1226, 1164, 1097, 1022, 876, 836, 751, 688, 548; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}FN_2$ $[M + H]^+$ 351.1292; found 351.1304.

4-(4-Chlorophenyl)-2,6-diphenylnicotinonitrile (**9a**):



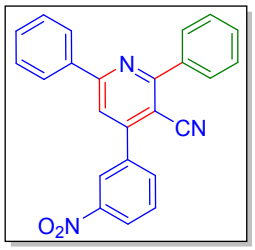
As a white solid (62 mg, 68% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19–8.16 (m, 2H), 8.05–8.03 (m, 2H), 7.79 (s, 1H), 7.63 (d, 2H, J = 8.8 Hz), 7.56–7.51 (m, 8H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.7, 159.6, 154.4, 138.0, 137.6, 136.6, 135.4, 130.9, 130.4, 130.2, 129.6, 129.5, 129.2, 128.8, 127.8, 118.6, 117.8, 104.3; IR (KBr, cm^{-1}): 2923, 2858, 2216, 1677, 1573, 1529, 1485, 1370, 1263, 1172, 1089, 1015, 822, 752, 688, 492; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}ClN2$ $[M + H]^+$ 367.0997; found 367.0999.

4-(2-Bromophenyl)-2,6-diphenylnicotinonitrile (**10a**):



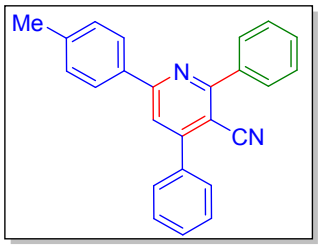
As a white solid (66 mg, 65% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.20 (d, 2H, J = 7.2 Hz), 8.10 (d, 2H, J = 7.6 Hz), 7.79 (s, 2H), 7.59–7.48 (m, 7H), 7.45–7.44 (m, 1H), 7.41–7.37 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.7, 159.2, 154.9, 137.98, 137.92, 137.6, 133.6, 131.2, 130.8, 130.6, 130.4, 129.5, 129.2, 128.8, 127.9, 127.8, 122.3, 119.4, 117.0, 105.9; IR (KBr, cm^{-1}): 2923, 2855, 2219, 1572, 1532, 1470, 1404, 1262, 1078, 1374, 1024, 887, 755, 693; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}BrN_2$ $[M + H]^+$ 411.0491; found 411.0474.

4-(3-Nitrophenyl)-2,6-diphenylnicotinonitrile (**11a**):



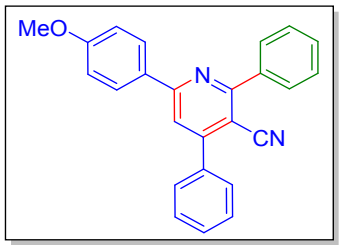
As a white solid (42 mg, 45% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.53 (s, 1H), 8.43–8.41 (m, 1H), 8.21–8.19 (m, 2H), 8.08–8.04 (m, 3H), 7.84 (s, 1H), 7.78 (t, 1H, J = 8.0 Hz), 7.58–7.53 (m, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.8, 159.9, 153.0, 148.8, 138.5, 137.8, 137.3, 134.9, 131.2, 130.6, 130.4, 129.6, 129.3, 128.8, 127.8, 124.8, 124.0, 118.5, 104.3; IR (KBr, cm^{-1}): 2924, 2857, 2218, 1713, 1576, 1528, 1460, 1350, 1263, 1178, 1082, 1031, 882, 805, 693, 521; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}N_3O_2$ $[M + H]^+$ 378.1237; found 378.1248.

2,4-Diphenyl-6-(p-tolyl)nicotinonitriletrile (**12a**):[35]



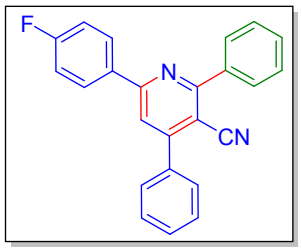
As a white solid (62 mg, 72% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.11–8.06 (m, 4H), 7.80 (s, 1H), 7.71–7.68 (m, 2H), 7.60–7.53 (m, 6H), 7.33 (d, 2H, J = 8.4 Hz), 2.44 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.5, 159.3, 155.4, 141.1, 138.3, 137.1, 134.9, 130.2, 129.99, 129.87, 129.6, 129.1, 128.8, 128.6, 127.6, 118.4, 117.9, 104.1, 21.6; IR (KBr, cm^{-1}): 2923, 2856, 2215, 1575, 1532, 1494, 1451, 1404, 1373, 1261, 1157, 1079, 1026, 881, 818, 766, 701, 620, 530; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{19}N_2$ $[M + H]^+$ 347.1543; found 347.1560.

6-(4-Methoxyphenyl)-2,4-diphenylnicotinonitrile (**13a**):



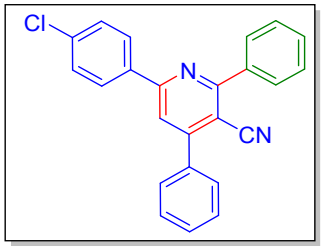
As a white solid (64 mg, 71% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.16 (d, 2H, J = 8.8 Hz), 8.04 (d, 2H, J = 7.6 Hz), 7.75 (s, 1H), 7.68 (d, 2H, J = 7.6 Hz), 7.58–7.53 (m, 6H), 7.02 (d, 2H, J = 8.8 Hz), 3.89 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.5, 161.9, 158.9, 155.4, 138.4, 137.2, 130.3, 130.2, 130.0, 129.6, 129.3, 129.2, 128.9, 128.7, 118.1, 117.9, 114.6, 103.6, 55.6; IR (KBr, cm^{-1}): 2923, 2856, 2211, 1575, 522, 1457, 1372, 1251, 1167, 1025, 879, 829, 761, 696, 542; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{19}N_2O$ $[M + H]^+$ 363.1492; found 363.1500.

6-(4-Fluorophenyl)-2,4-diphenylnicotinonitrile (**14a**):



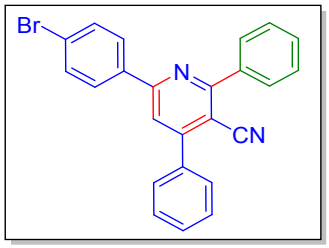
As a white solid (60 mg, 69% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.22–8.18 (m, 2H), 8.06–8.04 (m, 2H), 7.77 (s, 1H), 7.70–7.68 (m, 2H), 7.59–7.55 (m, 6H), 7.20 (t, 2H, J = 8.6 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 164.6 (d, J = 249.7 Hz), 162.6, 158.2, 155.7, 138.1, 136.9, 133.9 (d, J = 3.0 Hz), 130.3, 130.1, 129.8 (d, J = 8.6 Hz), 129.5, 129.2, 128.8, 128.7, 118.4, 117.8, 116.2 (d, J = 21.7 Hz), 104.5; ^{19}F NMR ($CDCl_3$ + hexafluorobenzene): δ –113.8 (s); IR (KBr, cm^{-1}): 2923, 2862, 2216, 1683, 1574, 1525, 1370, 1227, 1151, 1091, 1024, 830, 752, 690, 618, 527; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}FN_2$ $[M + H]^+$ 351.1292; found 351.1298.

6-(4-Chlorophenyl)-2,4-diphenylnicotinonitrile (**15a**):



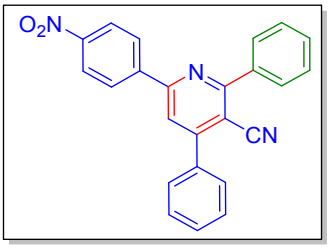
As a white solid (60 mg, 66% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.14 (d, 2H, J = 8.8 Hz), 8.04–8.02 (m, 2H), 7.79 (s, 1H), 7.69–7.67 (m, 2H), 7.59–7.55 (m, 6H), 7.49 (d, 2H, J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.7, 158.4, 155.8, 138.0, 137.0, 136.8, 136.1, 130.4, 130.2, 129.5, 129.4, 129.2, 129.0, 128.85, 128.75, 118.6, 117.8, 104.8; IR (KBr, cm^{-1}): 2923, 2862, 2217, 1652, 1573, 1528, 1489, 1369, 1260, 1172, 1091, 1018, 824, 753, 690, 492; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}ClN_2$ $[M + H]^+$ 367.0997; found 367.0998.

6-(4-Bromophenyl)-2,4-diphenylnicotinonitrile (**16a**):



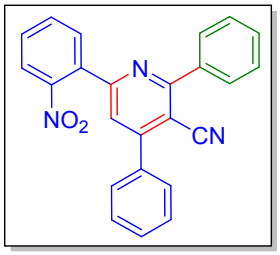
As a white solid (65 mg, 64% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.07–8.02 (m, 4H), 7.79 (s, 1H), 7.69–7.63 (m, 4H), 7.59–7.55 (m, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.7, 158.1, 155.9, 138.0, 136.8, 136.6, 132.4, 130.4, 130.2, 129.5, 129.24, 129.22, 128.8, 128.7, 125.5, 118.5, 117.7, 104.9; IR (KBr, cm^{-1}): 2922, 2862, 2218, 1681, 1573, 1528, 1486, 1367, 1272, 1169, 1071, 1004, 821, 753, 689, 622, 487; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}BrN_2$ $[M + H]^+$ 411.0491; found 411.0499.

6-(4-Nitrophenyl)-2,4-diphenylnicotinonitrile (**17a**):



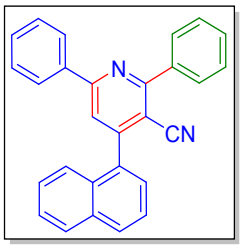
As a white solid (42 mg, 45% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.36 (s, 4H), 8.05–8.03 (m, 2H), 7.89 (s, 1H), 7.71–7.68 (m, 2H), 7.59–7.57 (m, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.9, 156.7, 156.4, 149.2, 143.5, 137.7, 136.5, 130.6, 130.5, 129.6, 129.4, 128.9, 128.6, 124.4, 119.6, 117.4, 106.1; IR (KBr, cm^{-1}): 2923, 2862, 2220, 1607, 1453, 1406, 1272, 1094, 1039, 807, 692; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}N_3O_2$ $[M + H]^+$ 378.1237; found 378.1245.

6-(2-Nitrophenyl)-2,4-diphenylnicotinonitrile (**18a**):



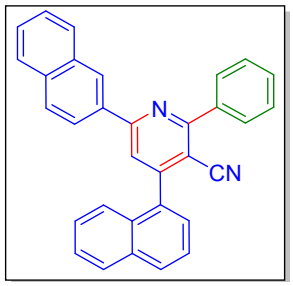
As a white solid (39 mg, 42% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.96 (d, 1H, J = 7.8 Hz), 7.93 (d, 2H, J = 7.5 Hz), 7.72–7.68 (m, 4H), 7.62–7.59 (m, 2H), 7.57–7.55 (m, 3H), 7.54–7.51 (m, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 162.4, 157.8, 155.9, 149.5, 137.4, 136.2, 134.0, 132.8, 131.2, 130.5, 130.44, 130.35, 129.5, 129.2, 128.9, 128.7, 124.9, 121.1, 117.4, 105.5; IR (KBr, cm^{-1}): 2922, 2856, 2216, 1694, 1567, 1522, 1453, 1340, 1235, 1159, 1076, 1028, 901, 850, 751, 695, 616, 483; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}N_3O_2$ $[M + H]^+$ 378.1237; found 378.1254.

4-(Naphthalen-1-yl)-2,6-diphenylnicotinonitrile (**19a**):



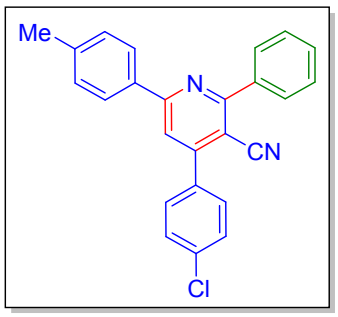
As a white solid (68 mg, 72% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.21–8.19 (m, 2H), 8.12 (d, 2H, J = 8.0 Hz), 8.03 (d, 1H, J = 8.0 Hz), 7.99 (d, 1H, J = 8.0 Hz), 7.89 (s, 1H), 7.68 (d, 1H, J = 8.4 Hz), 7.64 (d, 1H, J = 8.0 Hz), 7.61–7.56 (m, 5H), 7.54–7.51 (m, 4H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.1, 158.9, 155.1, 138.0, 137.6, 134.6, 133.9, 130.9, 130.8, 130.4, 130.2, 129.6, 129.2, 128.9, 128.8, 127.8, 127.44, 127.35, 126.7, 125.5, 125.0, 120.3, 117.3, 106.6; IR (KBr, cm^{-1}): 2921, 2853, 2215, 1732, 1656, 1569, 1528, 1446, 1374, 1262, 1073, 1025, 906, 771, 692, 616, 533; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{28}H_{19}N_2$ $[M + H]^+$ 383.1543; found 383.1548.

4-(Naphthalen-1-yl)-6-(naphthalen-2-yl)-2-phenylnicotinonitrile (**20a**):



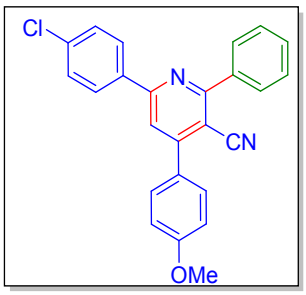
As a white solid (75 mg, 70% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.69 (s, 1H), 8.33 (d, 1H, J = 8.8 Hz), 8.16 (d, 2H, J = 7.8 Hz), 8.05–7.94 (m, 6H), 7.89 (d, 1H, J = 7.8 Hz), 7.72 (d, 1H, J = 8.0 Hz), 7.68–7.52 (m, 8H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.1, 158.8, 155.0, 138.1, 134.9, 134.7, 134.6, 133.9, 133.5, 130.4, 130.2, 129.6, 129.2, 128.9, 128.8, 127.89, 127.92, 127.6, 127.4, 127.3, 126.8, 126.7, 125.4, 125.0, 124.6, 120.4, 117.3, 106.6; IR (KBr, cm^{-1}): 2921, 2850, 2218, 1679, 1564, 1529, 1385, 1336, 1233, 1168, 1026, 862, 763, 696, 628; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{32}H_{21}N_2$ $[M + H]^+$ 433.1699; found 433.1730.

4-(4-Chlorophenyl)-2-phenyl-6-(p-tolyl)nicotinonitrile (**21a**):



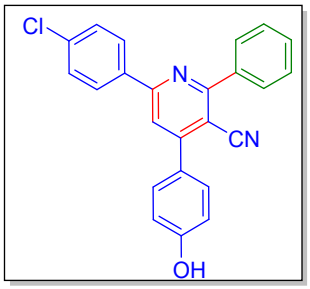
As a white solid (65 mg, 69% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.08 (d, 2H, J = 8.0 Hz), 8.04–8.02 (m, 2H), 7.75 (s, 1H), 7.62 (d, 2H, J = 8.4 Hz), 7.57–7.53 (m, 5H), 7.32 (d, 2H, J = 8.0 Hz), 2.44 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.6, 159.5, 154.2, 141.3, 138.1, 136.5, 135.5, 134.8, 130.3, 130.2, 129.9, 129.6, 129.5, 128.7, 127.7, 118.2, 117.9, 103.9, 21.6; IR (KBr, cm^{-1}): 2923, 2860, 2212, 1658, 1575, 1531, 1486, 1455, 1370, 1266, 1174, 1089, 1016, 815, 753, 688, 628, 540, 495; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{18}ClN_2$ $[M + H]^+$ 381.1153; found 381.1170.

6-(4-Chlorophenyl)-4-(4-methoxyphenyl)-2-phenylnicotinonitrile (**22a**):



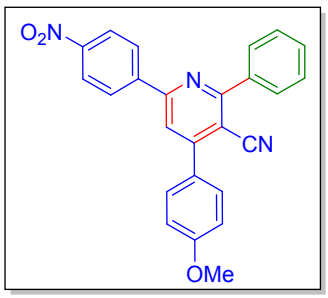
As a white solid (74 mg, 75% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05 (d, 2H, J = 8.8 Hz), 7.96–7.93 (m, 2H), 7.68 (s, 1H), 7.58 (d, 2H, J = 8.8 Hz), 7.49–7.47 (m, 3H), 7.40 (d, 2H, J = 8.4 Hz), 7.01 (d, 2H, J = 8.8 Hz), 3.82 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.7, 161.3, 157.9, 155.4, 138.1, 136.9, 136.2, 130.4, 130.3, 129.5, 129.3, 128.9, 128.7, 128.5, 118.3, 118.1, 114.7, 104.5, 55.6; IR (KBr, cm^{-1}): 2923, 2856, 2216, 1727, 1574, 1514, 1459, 1373, 1177, 1259, 1089, 1025, 820, 689, 568, 514; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{18}ClN_2O$ $[M + H]^+$ 397.1102; found 397.1106.

6-(4-Chlorophenyl)-4-(4-hydroxyphenyl)-2-phenylnicotinonitrile (**23a**):



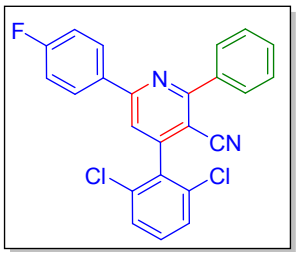
As a white solid (39 mg, 41% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6 + $CDCl_3$, 400 MHz): δ 10.07 (s, 1H), 8.30 (d, 2H, J = 8.4 Hz), 8.07 (s, 1H), 7.96–7.94 (m, 2H), 7.67 (d, 2H, J = 8.4 Hz), 7.57–7.54 (m, 5H), 6.96 (d, 2H, J = 8.8 Hz); ^{13}C{^{1}H} NMR (DMSO-d^6 + $CDCl_3$, 100 MHz): δ 161.7, 159.3, 156.8, 154.9, 137.9, 135.8, 135.5, 130.6, 129.9, 129.3, 129.2, 128.9, 128.3, 126.7, 118.3, 117.9, 115.6, 103.9; IR (KBr, cm^{-1}): 3415, 2955, 2922, 2853, 2215, 1667, 1594, 1565, 1491, 1462, 1387, 1308, 1262, 1219, 1090, 1017, 807, 702; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}ClN_2O$ [M + H]$^+$ 383.0946; found 383.0949.

4-(4-Methoxyphenyl)-6-(4-nitrophenyl)-2-phenylnicotinonitrile (**24a**):



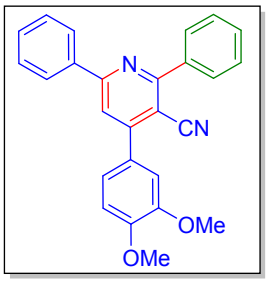
As a white solid (46 mg, 46% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.35 (s, 4H), 8.03–8.01 (m, 2H), 7.86 (s, 1H), 7.67 (d, 2H, J = 8.8 Hz), 7.58–7.56 (m, 3H), 7.10 (d, 2H, J = 8.8 Hz), 3.91 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 163.1, 161.6, 156.6, 155.9, 149.4, 149.2, 143.6, 137.8, 130.6, 130.4, 129.6, 128.8, 128.6, 124.3, 119.4, 117.8, 114.8, 105.8, 55.7; IR (KBr, cm^{-1}): 2923, 2854, 2218, 1727, 1602, 1568, 1513, 1352, 1296, 1260, 1180, 1111, 1023, 825, 757, 691, 568, 511; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{18}N_3O_3$ [M + H]$^+$ 408.1343; found 408.1347.

4-(2,6-Dichlorophenyl)-6-(4-fluorophenyl)-2-phenylnicotinonitrile (**25a**):



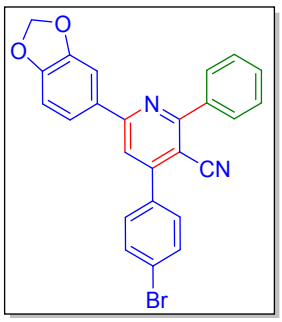
As a white solid (66 mg, 64% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.24–8.20 (m, 2H), 8.13–8.10 (m, 2H), 7.69 (s, 1H), 7.59–7.57 (m, 3H), 7.54–7.52 (m, 2H), 7.43–7.39 (m, 1H), 7.22 (t, 2H, J = 8.8 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 164.7 (d, J = 250.1 Hz), 161.8, 158.6, 151.4, 137.6, 134.8, 134.3, 133.6 (d, J = 3.1 Hz), 131.4, 130.5, 129.9 (d, J = 8.6 Hz), 129.4, 128.8 (d, J = 8.3 Hz), 118.9, 116.4, 116.2 (d, J = 21.6 Hz), 106.1; ^{19}F NMR ($CDCl_3$ + hexafluorobenzene): δ –112.9 (s); IR (KBr, cm^{-1}): 2922, 2855, 2217, 1660, 1589, 1535, 1406, 1369, 1230, 1151, 1094, 1013, 840, 778, 689, 512; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{14}Cl_2FN_2$ [M + H]$^+$ 419.0513; found 419.0514.

4-(3,4-Dimethoxyphenyl)-2,6-diphenylnicotinonitrile (**26a**):



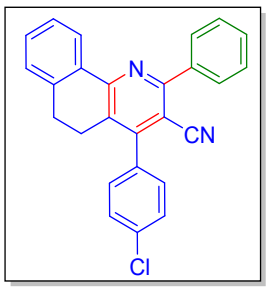
As a white solid (66 mg, 68% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.21 (d, 2H, J = 7.8 Hz), 8.06 (d, 2H, J = 7.4 Hz), 7.85 (s, 1H), 7.59–7.54 (m, 6H), 7.33–7.26 (m, 2H), 7.07 (d, 1H, J = 8.4 Hz), 4.02 (s, 3H), 3.99 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.7, 159.2, 155.3, 150.8, 149.3, 138.3, 137.8, 130.6, 130.2, 129.6, 129.4, 129.2, 128.7, 127.7, 121.9, 118.6, 118.3, 112.0, 111.6, 104.3, 56.4, 56.2; IR (KBr, cm^{-1}): 2927, 2840, 2213, 1665, 1571, 1515, 1452, 1376, 1321, 1256, 1180, 1140, 1077, 1020, 920, 858, 803, 756, 691, 594; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{26}H_{21}N_2O_2$ $[M + H]^+$ 393.1598; found 393.1598.

6-(Benzo[d][1,3]dioxol-5-yl)-4-(4-bromophenyl)-2-phenylnicotinonitrile (**27a**):



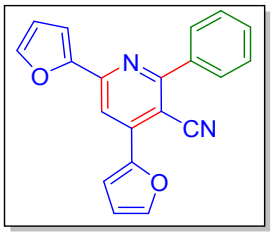
As a white solid (71 mg, 63% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02–8.00 (m, 2H), 7.72–7.69 (m, 4H), 7.66 (s, 1H), 7.56–7.53 (m, 5H), 6.93 (d, 1H, J = 8.0 Hz), 6.05 (s, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.5, 158.8, 154.2, 150.2, 148.8, 138.0, 135.9, 132.4, 131.9, 130.42, 130.37, 129.5, 128.7, 124.8, 122.4, 117.84, 117.75, 108.8, 107.9, 103.6, 101.9; IR (KBr, cm^{-1}): 2923, 2859, 2214, 1650, 1591, 1484, 1446, 1319, 1255, 1106, 1039, 935, 810, 690, 488; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{16}BrN_2O_2$ $[M + H]^+$ 455.0390; found 455.0417.

4-(4-Chlorophenyl)-2-phenyl-5,6-dihydrobenzo[h]quinoline-3-carbonitrile (**28a**):



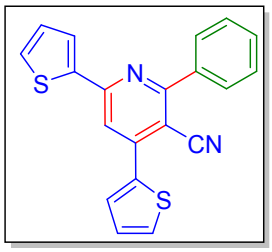
As a white solid (59 mg, 61% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.51–8.49 (m, 1H), 8.03 (d, 2H, J = 7.8 Hz), 7.57–7.51 (m, 5H), 7.42–7.38 (m, 2H), 7.33 (d, 2H, J = 8.4 Hz), 7.26 (s, 1H), 2.91–2.87 (m, 2H), 2.79–2.76 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 159.6, 155.4, 152.3, 138.9, 138.1, 135.7, 134.2, 133.7, 131.1, 130.3, 130.1, 129.5, 129.4, 128.7, 128.4, 128.0, 127.6, 126.9, 117.7, 105.9, 27.7, 25.5; IR (KBr, cm^{-1}): 2924, 2854, 2221, 1598, 1544, 1489, 1391, 1240, 1177, 1086, 1018, 836, 757, 699, 589, 485; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{26}H_{18}ClN_2$ $[M + H]^+$ 393.1153; found 393.1139.

4,6-Di(furan-2-yl)-2-phenylnicotinonitrile (**29a**):



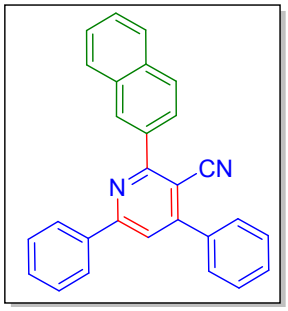
As a white solid (50 mg, 65% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.14 (s, 1H), 7.93–7.91 (m, 2H), 7.71 (d, 1H, J = 3.6 Hz), 7.68 (s, 1H), 7.63 (s, 1H), 7.54–7.53 (m, 3H), 7.31 (d, 1H, J = 3.6 Hz), 6.66–6.64 (m, 1H), 6.60–6.59 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 163.5, 152.9, 151.2, 148.4, 145.13, 145.07, 141.9, 138.0, 130.3, 129.5, 128.6, 118.6, 114.7, 113.1, 112.9, 112.6, 111.7, 98.5; IR (KBr, cm^{-1}): 2923, 2853, 2214, 1639, 1510, 1465, 1372, 1261, 1028, 812, 756, 705; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{20}H_{13}N_2O_2$ $[M + H]^+$ 313.0972; found 313.0991.

2-Phenyl-4,6-di(thiophen-2-yl)nicotinonitrile (**30a**):



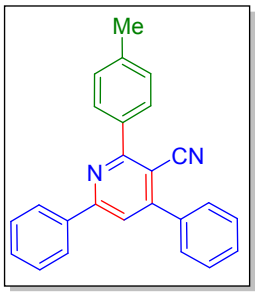
As a white solid (58 mg, 68% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02–7.99 (m, 2H), 7.92 (d, 1H, J = 4.0 Hz), 7.78 (d, 1H, J = 3.6 Hz), 7.74 (s, 1H), 7.58–7.52 (m, 5H), 7.24 (t, 1H, J = 4.4 Hz), 7.16 (t, 1H, J = 4.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 163.3, 154.6, 146.9, 143.4, 137.69, 137.66, 130.6, 130.4, 129.9, 129.6, 129.3, 128.9, 128.65, 128.60, 127.4, 118.4, 115.9, 101.9; IR (KBr, cm^{-1}): 2921, 2852, 2215, 1639, 1591, 1552, 1513, 1495, 1462, 1377, 1289, 1266, 1111, 1069, 1012, 885, 798, 748, 723, 699; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{20}H_{13}N_2S_2$ $[M + H]^+$ 345.0515; found 345.0522.

2-(Naphthalen-2-yl)-4,6-diphenylnicotinonitrile (**1b**):



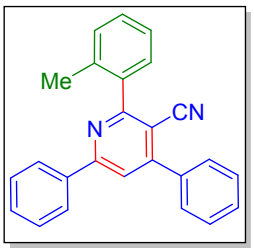
As a white solid (63 mg, 66% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.59 (s, 1H), 8.24–8.22 (m, 2H), 8.19–8.16 (m, 1H), 8.05–8.02 (m, 2H), 7.95–7.93 (m, 1H), 7.86 (s, 1H), 7.75–7.72 (m, 2H), 7.59–7.53 (m, 8H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.5, 159.4, 155.7, 137.7, 136.9, 135.5, 134.1, 133.1, 130.7, 130.1, 129.7, 129.2, 129.1, 128.9, 128.5, 127.9, 127.8, 127.4, 126.7, 126.6, 118.8, 118.0, 104.7; IR (KBr, cm^{-1}): 2924, 2851, 2216, 1657, 1572, 1500, 1468, 1401, 1371, 1322, 1262, 1226, 1153, 1091, 1023, 873, 827, 761, 728, 701; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{28}H_{19}N_2$ $[M + H]^+$ 383.1543; found 383.1548.

4,6-Diphenyl-2-(p-tolyl)nicotinonitrile (**1c**):[36]



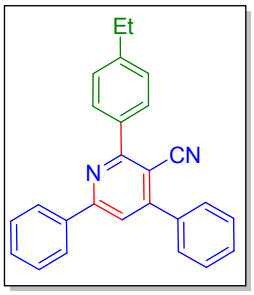
As a white solid (63 mg, 73% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19 (d, 2H, J = 7.6 Hz), 7.97 (d, 2H, J = 8.0 Hz), 7.80 (s, 1H), 7.69 (d, 2H, J = 7.8 Hz), 7.58–7.51 (m, 6H), 7.37 (d, 2H, J = 8.0 Hz), 2.46 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.6, 159.2, 155.6, 140.5, 137.8, 137.1, 135.4, 130.6, 130.0, 129.5, 129.4, 129.2, 129.1, 128.9, 127.7, 118.6, 118.1, 104.3, 21.6; IR (KBr, cm^{-1}): 2922, 2856, 2213, 1570, 1527, 1449, 1375, 1231, 1176, 1084, 1024, 874, 820, 755, 691, 490; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{19}N_2$ [M + H]$^+$ 347.1543; found 347.1545.

4,6-Diphenyl-2-(o-tolyl)nicotinonitrile (**1d**):



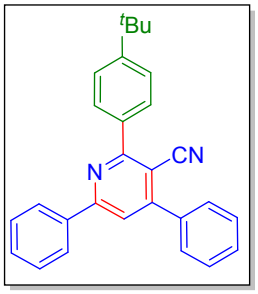
As a white solid (37 mg, 43% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.16–8.14 (m, 2H), 7.86 (s, 1H), 7.72 (d, 2H, J = 7.8 Hz), 7.59–7.55 (m, 3H), 7.52–7.49 (m, 4H), 7.44–7.34 (m, 3H), 2.41 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 164.5, 159.2, 154.6, 138.2, 137.8, 136.8, 136.4, 130.9, 130.7, 130.2, 129.73, 129.70, 129.24, 129.16, 128.8, 127.8, 126.1, 118.8, 117.1, 106.6, 20.1; IR (KBr, cm^{-1}): 2922, 2856, 2215, 1570, 1529, 1488, 1455, 1372, 1260, 1166, 1072, 1029, 875, 747, 690, 620, 576, 453; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{19}N_2$ [M + H]$^+$ 347.1543; found 347.1528.

2-(4-Ethylphenyl)-4,6-diphenylnicotinonitrile (**1e**):



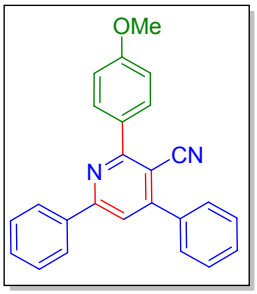
As a white solid (67 mg, 75% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19 (d, 2H, J = 7.8 Hz), 8.00 (d, 2H, J = 8.0 Hz), 7.80 (s, 1H), 7.70 (d, 2H, J = 7.6 Hz), 7.59–7.51 (m, 6H), 7.40 (d, 2H, J = 8.0 Hz), 2.77 (q, 2H, J = 7.6 Hz), 1.32 (t, 3H, J = 7.6 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.6, 159.2, 155.6, 146.7, 137.8, 137.1, 135.6, 130.6, 130.0, 129.6, 129.14, 129.12, 128.9, 128.2, 127.7, 118.5, 118.1, 104.3, 29.0, 15.6; IR (KBr, cm^{-1}): 2923, 2864, 2214, 1572, 1529, 1448, 1374, 1261, 1184, 1075, 1024, 874, 832, 754, 693, 564, 488; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{26}H_{21}N_2$ [M + H]$^+$ 361.1699; found 361.1712.

2-(4-(tert-Butyl)phenyl)-4,6-diphenylnicotinonitrile (**1f**):



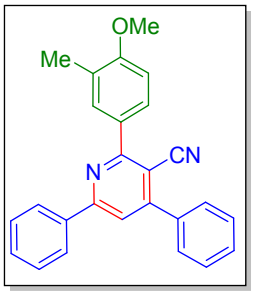
As a white solid (74 mg, 77% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19 (d, 2H, J = 7.6 Hz), 8.03 (d, 2H, J = 8.4 Hz), 7.81 (s, 1H), 7.69 (d, 2H, J = 7.8 Hz), 7.60–7.56 (m, 5H), 7.53–7.51 (m, 3H), 1.41 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 162.4, 159.2, 155.6, 153.6, 137.8, 137.1, 135.4, 130.6, 130.0, 129.3, 129.2, 129.1, 128.9, 127.7, 125.7, 118.6, 118.1, 104.2, 35.1, 31.5; IR (KBr, cm^{-1}): 2924, 2857, 2222, 1576, 1531, 1456, 1379, 1262, 1102, 1024, 804, 766, 696, 555; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{28}H_{25}N_2$ $[M + H]^+$ 389.2012; found 389.2041.

2-(4-Methoxyphenyl)-4,6-diphenylnicotinonitrile (**1g**):[36]



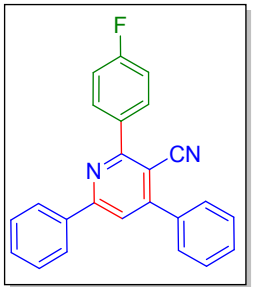
As a white solid (71 mg, 79% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.18 (d, 2H, J = 7.8 Hz), 8.06 (d, 2H, J = 8.4 Hz), 7.77 (s, 1H), 7.68 (d, 2H, J = 7.2 Hz), 7.58–7.51 (m, 6H), 7.08 (d, 2H, J = 8.4 Hz), 3.90 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 162.0, 161.4, 159.2, 155.7, 137.8, 137.1, 131.2, 130.7, 130.6, 130.0, 129.2, 128.9, 127.7, 118.3, 114.1, 103.8, 55.6; IR (KBr, cm^{-1}): 2922, 2860, 2214, 1665, 1581, 1512, 1455, 1374, 1253, 1175, 1017, 819, 758, 691, 562; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{19}N_2O$ $[M + H]^+$ 363.1492; found 363.1514.

2-(4-Methoxy-3-methylphenyl)-4,6-diphenylnicotinonitrile (**1h**):



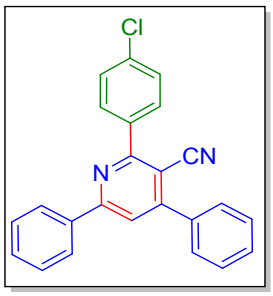
As a white solid (64 mg, 68% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.18 (d, 2H, J = 7.2 Hz), 7.92 (d, 1H, J = 8.4 Hz), 7.86 (s, 1H), 7.76 (s, 1H), 7.68 (d, 2H, J = 7.7 Hz), 7.57–7.51 (m, 6H), 6.98 (d, 1H, J = 8.4 Hz), 3.92 (s, 3H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 162.4, 159.6, 159.2, 155.6, 137.9, 137.2, 131.9, 130.6, 130.2, 130.0, 129.1, 128.9, 128.6, 127.8, 127.1, 118.4, 118.2, 109.7, 103.9, 55.7, 16.6; IR (KBr, cm^{-1}): 2923, 2856, 2213, 1574, 1532, 1496, 1453, 1373, 1247, 1173, 1131, 1027, 879, 811, 759, 690, 578; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{26}H_{21}N_2O$ $[M + H]^+$ 377.1648; found 377.1655.

2-(4-Fluorophenyl)-4,6-diphenylnicotinonitrile (**1i**):



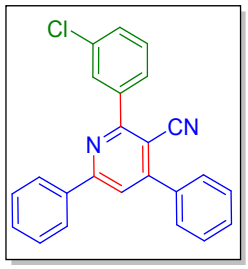
As a white solid (54 mg, 62% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.22–8.19 (m, 2H), 8.12–8.08 (m, 2H), 7.86 (s, 1H), 7.73–7.71 (m, 2H), 7.63–7.55 (m, 6H), 7.30–7.28 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 164.2 (d, J = 249.0 Hz), 161.4, 159.4, 155.7, 137.6, 136.9, 134.3 (d, J = 3.2 Hz), 131.7 (d, J = 8.6 Hz), 130.8, 130.2, 129.2, 128.8, 127.7, 118.9, 117.9, 115.8 (d, J = 21.7 Hz), 104.4; ^{19}F NMR ($CDCl_3$ + hexafluorobenzene): δ –113.8 (s); IR (KBr, cm^{-1}): 2923, 2858, 2214, 1662, 1594, 1543, 1480, 1369, 1261, 1153, 1078, 1017, 879, 811, 748, 686, 587; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}FN_2$ $[M + H]^+$ 351.1292; found 351.1292.

2-(4-Chlorophenyl)-4,6-diphenylnicotinonitrile (**1j**):



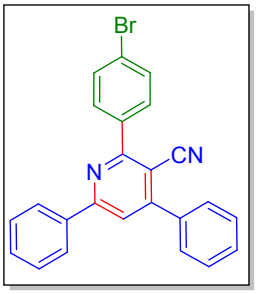
As a white solid (50 mg, 55% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.18–8.16 (m, 2H), 8.01 (d, 2H, J = 8.4 Hz), 7.84 (s, 1H), 7.69–7.67 (m, 2H), 7.58–7.52 (m, 8H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.3, 159.5, 155.8, 137.6, 136.8, 136.62, 136.59, 135.4, 130.95, 130.87, 130.2, 129.2, 129.0, 128.9, 127.8, 119.0, 117.8, 104.4; IR (KBr, cm^{-1}): 2923, 2856, 2216, 1578, 1529, 1454, 1381, 1262, 1091, 1028, 804, 757, 693; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}ClN_2$ $[M + H]^+$ 367.0997; found 367.1006.

2-(3-Chlorophenyl)-4,6-diphenylnicotinonitrile (**1k**):



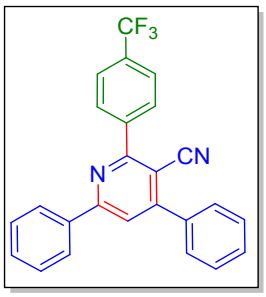
As a white solid (46 mg, 51% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.17 (d, 2H, J = 7.6 Hz), 8.02 (s, 1H), 7.94 (d, 1H, J = 6.8 Hz), 7.85 (s, 1H), 7.69–7.68 (m, 2H), 7.58–7.57 (m, 3H), 7.54–7.49 (m, 5H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.1, 159.5, 155.7, 139.9, 137.5, 136.8, 134.8, 130.9, 130.3, 130.2, 129.9, 129.8, 129.2, 128.9, 127.8, 127.6, 119.3, 117.6, 104.6; IR (KBr, cm^{-1}): 2923, 2857, 2214, 1662, 1571, 1529, 1457, 1375, 1262, 1168, 1083, 1030, 876, 801, 755, 688, 579; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}ClN_2$ $[M + H]^+$ 367.0997; found 367.1003.

2-(4-Bromophenyl)-4,6-diphenylnicotinonitrile (**1l**):[36]



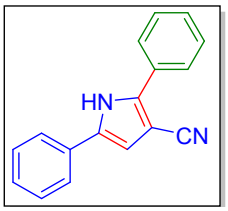
As a white solid (53 mg, 52% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.17 (d, 2H, J = 7.2 Hz), 7.94 (d, 2H, J = 8.4 Hz), 7.84 (s, 1H), 7.71–7.67 (m, 4H), 7.58–7.56 (m, 3H), 7.53–7.51 (m, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.4, 159.5, 155.8, 137.5, 137.0, 136.8, 131.9, 131.2, 130.9, 130.2, 129.2, 128.8, 127.8, 125.0, 119.1, 117.8, 104.4; IR (KBr, cm^{-1}): 2923, 2855, 2214, 1732, 1571, 1530, 1485, 1459, 1378, 1266, 1174, 1073, 1016, 825, 755, 692, 491; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{24}H_{16}BrN_2$ $[M + H]^+$ 411.0491; found 411.0497.

4,6-Diphenyl-2-(4-(trifluoromethyl)phenyl)nicotinonitrile (**1m**):



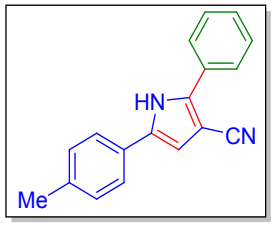
As a white solid (35 mg, 35% yield); Purified over a column of silica gel (2% EtOAc in hexane). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19–8.15 (m, 4H), 7.89 (s, 1H), 7.83 (d, 2H, J = 8.0 Hz), 7.71–7.68 (m, 2H), 7.59–7.57 (m, 3H), 7.55–7.52 (m, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 161.1, 159.6, 155.8, 137.4, 136.7, 130.9, 130.3, 130.0, 129.29, 129.27, 128.8, 128.4, 128.2, 128.0, 127.8, 125.7 (q, J = 3.8 Hz), 119.5, 117.8, 104.8; IR (KBr, cm^{-1}): 2923, 2855, 2216, 1675, 1571, 1534, 1492, 1450, 1392, 1262, 1165, 1109, 1068, 1021, 807, 761, 692, 597, 495; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{25}H_{16}F_3N_2$ $[M + H]^+$ 401.1260; found 401.1266.

2,5-Diphenyl-1H-pyrrole-3-carbonitrile (**31a**):[37]



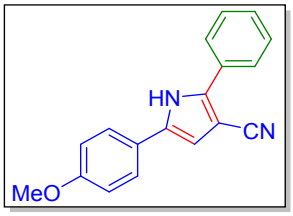
As a white solid (44 mg, 73% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 600 MHz): δ 12.20 (s, 1H), 7.85 (d, 2H, J = 7.8 Hz), 7.81 (d, 2H, J = 7.8 Hz), 7.55 (t, 2H, J = 7.8 Hz), 7.45–7.42 (m, 3H), 7.30 (t, 1H, J = 7.2 Hz), 7.07 (s, 1H); ^{13}C{^{1}H} NMR (DMSO-d^6, 150 MHz): δ 139.6, 133.8, 130.7, 129.7, 128.9, 128.8, 128.6, 127.3, 126.5, 124.8, 117.6, 110.2, 90.2; IR (KBr, cm^{-1}): 3224, 3034, 2756, 2219, 1597, 1465, 1296, 1184, 1071, 1027, 908, 808, 760, 688, 595, 535, 490; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{17}H_{13}N_2$ $[M + H]^+$ 245.1073; found 245.1077.

2-Phenyl-5-(p-tolyl)-1H-pyrrole-3-carbonitrile (**32a**):



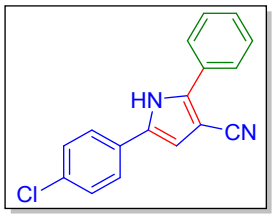
As a white solid (49 mg, 76% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 600 MHz): δ 12.14 (s, 1H), 7.83 (d, 2H, J = 7.8 Hz), 7.69 (d, 2H, J = 8.4 Hz), 7.54 (t, 2H, J = 7.8 Hz), 7.43 (t, 1H, J = 7.5 Hz), 7.24 (d, 2H, J = 7.8 Hz), 7.00 (s, 1H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d^6, 150 MHz): δ 139.4, 136.8, 134.0, 129.8, 129.4, 129.0, 128.6, 128.0, 126.5, 124.8, 117.8, 109.6, 90.1, 20.8; IR (KBr, cm^{-1}): 3258, 2905, 2864, 2218, 1601, 1455, 1263, 1075, 1036, 803, 755, 692, 430; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{18}H_{15}N_2$ $[M + H]^+$ 259.1230; found 259.1241.

5-(4-Methoxyphenyl)-2-phenyl-1H-pyrrole-3-carbonitrile (**33a**):



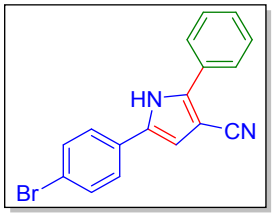
As a white solid (53 mg, 78% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 400 MHz): δ 12.07 (s, 1H), 7.83 (d, 2H, J = 7.6 Hz), 7.73 (d, 2H, J = 8.8 Hz), 7.53 (t, 2H, J = 7.8 Hz), 7.42 (t, 1H, J = 7.4 Hz), 7.00 (d, 2H, J = 8.8 Hz), 6.92 (s, 1H), 3.78 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d^6, 100 MHz): δ 158.7, 139.0, 133.9, 129.8, 128.9, 128.4, 126.4, 126.3, 123.5, 117.8, 114.2, 108.9, 89.9, 55.2; IR (KBr, cm^{-1}): 3221, 2922, 2835, 2219, 1606, 1527, 1461, 1295, 1266, 1156, 1126, 1043, 939, 830, 805, 761, 692, 573, 515 HRMS (ESI/Q-TOF) (m/z) calcd for $C_{18}H_{15}N_2O$ $[M + H]^+$ 275.1179; found 275.1187.

5-(4-Chlorophenyl)-2-phenyl-1H-pyrrole-3-carbonitrile (**34a**):



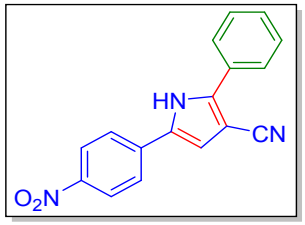
As a white solid (49 mg, 71% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 400 MHz): δ 12.24 (s, 1H), 7.84–7.81 (m, 4H), 7.54 (t, 2H, J = 7.6 Hz), 7.48 (d, 2H, J = 8.4 Hz), 7.44 (t, 1H, J = 7.4 Hz), 7.09 (s, 1H); ^{13}C{^{1}H} NMR (DMSO-d^6, 100 MHz): δ 140.0, 132.6, 131.8, 129.7, 129.6, 129.0, 128.84, 128.78, 126.6, 126.5, 117.6, 110.8, 90.4; IR (KBr, cm^{-1}): 3226, 2928, 2853, 2221, 1599, 1473, 1299, 1263, 1171, 1092, 1024, 832, 805, 762, 687, 603, 495; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{17}H_{12}ClN_2$ $[M + H]^+$ 279.0684; found 279.0697.

5-(4-Bromophenyl)-2-phenyl-1H-pyrrole-3-carbonitrile (**35a**):



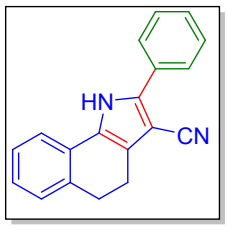
As a white solid (54 mg, 67% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 400 MHz): δ 12.24 (s, 1H), 7.83 (d, 2H, J = 7.2 Hz), 7.76 (d, 2H, J = 8.8 Hz), 7.61 (d, 2H, J = 8.8 Hz), 7.54 (t, 2H, J = 7.6 Hz), 7.44 (t, 1H, J = 7.4 Hz), 7.10 (s, 1H); ^{13}C{^{1}H} NMR (DMSO-d^6, 100 MHz): δ 140.0, 132.6, 131.7, 129.9, 129.6, 128.9, 128.8, 126.7, 126.6, 120.3, 117.5, 110.8, 90.4; IR (KBr, cm^{-1}): 3225, 2921, 2856, 2223, 1600, 1471, 1384, 1303, 1264, 1174, 1076, 1022, 807, 751, 692, 491; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{17}H_{12}BrN_2$ [M + H]$^+$ 323.0178; found 323.0181.

5-(4-Nitrophenyl)-2-phenyl-1H-pyrrole-3-carbonitrile (**36a**):



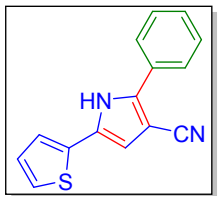
As a white solid (40 mg, 55% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 400 MHz): δ 12.51 (s, 1H), 8.28 (d, 2H, J = 9.2 Hz), 8.07 (d, 2H, J = 8.8 Hz), 7.85 (d, 2H, J = 7.2 Hz), 7.57 (t, 2H, J = 7.6 Hz), 7.48 (t, 1H, J = 7.4 Hz), 7.41 (s, 1H); ^{13}C{^{1}H} NMR (DMSO-d^6, 100 MHz): δ 145.7, 141.5, 136.9, 131.5, 129.2, 129.0, 126.8, 125.1, 124.3, 117.1, 113.81, 113.78, 91.2; IR (KBr, cm^{-1}): 3224, 2926, 2746, 2219, 1595, 1464, 1298, 1183, 1072, 1027, 908, 805, 763, 687, 595, 535, 494; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{17}H_{12}N_3O_2$ [M + H]$^+$ 290.0924; found 290.0947.

2-Phenyl-4,5-dihydro-1H-benzo[g]indole-3-carbonitrile (**37a**):



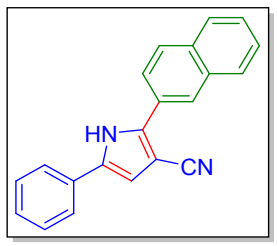
As a white solid (48 mg, 71% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 400 MHz): δ 12.26 (s, 1H), 7.85 (d, 2H, J = 7.2 Hz), 7.75 (d, 1H, J = 7.6 Hz), 7.54 (t, 2H, J = 7.8 Hz), 7.42 (t, 1H, J = 7.4 Hz), 7.28–7.23 (m, 2H), 7.12 (t, 1H, J = 7.4 Hz), 2.93 (t, 2H, J = 7.6 Hz), 2.74 (t, 2H, J = 7.6 Hz); ^{13}C{^{1}H} NMR (DMSO-d^6, 100 MHz): δ 138.5, 134.4, 129.9, 129.3, 129.0, 128.4, 128.3, 127.7, 127.4, 126.7, 126.4, 126.0, 123.3, 120.6, 117.0, 88.7, 28.5, 19.9; IR (KBr, cm^{-1}): 3228, 3033, 2765, 2221, 1599, 1455, 1286, 1187, 1080, 1026, 918, 801, 765, 678, 585, 532, 498; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{19}H_{15}N_2$ [M + H]$^+$ 271.1230; found 271.1238.

2-Phenyl-5-(thiophen-2-yl)-1H-pyrrole-3-carbonitrile (**38a**):



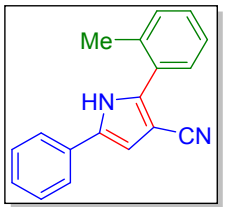
As a white solid (43 mg, 69% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^{6}, 400 MHz): δ 12.36 (s, 1H), 7.83 (d, 2H, J = 7.6 Hz), 7.56–7.49 (m, 4H), 7.44 (t, 1H, J = 7.4 Hz), 7.12 (t, 1H, J = 4.4 Hz), 7.12 (t, 1H, J = 7.4 Hz), 6.84 (s, 1H); ^{13}C{^{1}H} NMR (DMSO-d^{6}, 100 MHz): δ 139.3, 133.4, 129.5, 129.0, 128.7, 128.4, 127.9, 126.5, 125.0, 123.9, 117.4, 110.1, 90.0; IR (KBr, cm^{-1}): 3225, 2998, 2753, 2219, 1598, 1455, 1297, 1186, 1101, 1028, 918, 828, 762, 686, 594, 537, 490; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{15}H_{11}N_2S$ $[M + H]^+$ 251.0637; found 251.0642.

2-(Naphthalen-2-yl)-5-phenyl-1H-pyrrole-3-carbonitrile (**31b**):



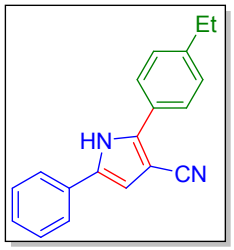
As a white solid (54 mg, 74% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^{6}, 600 MHz): δ 12.37 (s, 1H), 8.39 (s, 1H), 8.08 (d, 1H, J = 9.0 Hz), 7.98 (t, 3H, J = 8.4 Hz), 7.85 (d, 2H, J = 7.2 Hz), 7.61–7.56 (m, 2H), 7.45 (t, 2H, J = 7.8 Hz), 7.31 (t, 1H, J = 7.5 Hz), 7.13 (s, 1H); ^{13}C{^{1}H} NMR (DMSO-d^{6}, 150 MHz): δ 139.5, 134.1, 132.8, 132.6, 130.8, 128.9, 128.6, 128.2, 127.8, 127.4, 127.2, 127.0, 126.9, 125.5, 124.9, 124.3, 117.8, 110.5, 90.7; IR (KBr, cm^{-1}): 3225, 2924, 2855, 2224, 1582, 1459, 1377, 1263, 1178, 1100, 1026, 808, 753, 694; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{21}H_{15}N_2$ $[M + H]^+$ 295.1230; found 295.1234.

5-Phenyl-2-(o-tolyl)-1H-pyrrole-3-carbonitrile (**31d**):



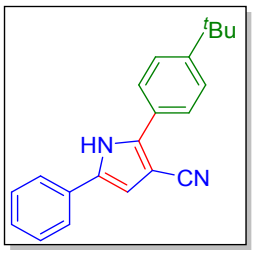
As a white solid (35 mg, 54% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^{6}, 600 MHz): δ 12.25 (s, 1H), 7.75 (d, 2H, J = 7.8 Hz), 7.42–7.39 (m, 5H), 7.35–7.34 (m, 1H), 7.27 (t, 1H, J = 7.2 Hz), 7.07 (s, 1H), 2.34 (s, 1H); ^{13}C{^{1}H} NMR (DMSO-d^{6}, 150 MHz): δ 140.3, 136.8, 132.9, 130.9, 130.6, 130.5, 129.8, 129.3, 127.1, 125.9, 124.3, 117.2, 108.6, 92.3, 19.8; IR (KBr, cm^{-1}): 3259, 2924, 2862, 2218, 1601, 1456, 1265, 1175, 1036, 806, 756, 692, 446; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{18}H_{15}N_2$ $[M + H]^+$ 259.1230; found 259.1234.

2-(4-Ethylphenyl)-5-phenyl-1H-pyrrole-3-carbonitrile (**31e**):



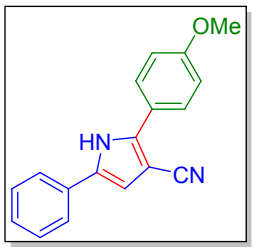
As a white solid (53 mg, 78% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 600 MHz): δ 12.14 (s, 1H), 7.80 (d, 2H, J = 7.8 Hz), 7.76 (d, 2H, J = 8.4 Hz), 7.42 (t, 2H, J = 7.5 Hz), 7.38 (d, 2H, J = 8.4 Hz), 7.29 (t, 1H, J = 7.5 Hz), 7.05 (s, 1H), 2.66 (q, 2H, J = 7.6 Hz), 1.21 (t, 3H, J = 7.8 Hz); ^{13}C{^{1}H} NMR (DMSO-d^6, 150 MHz): δ 144.6, 139.9, 133.5, 130.8, 128.8, 128.4, 127.3, 127.2, 126.6, 124.8, 117.8, 110.1, 89.8, 28.0, 15.6; IR (KBr, cm^{-1}): 3227, 2960, 2923, 2866, 2223, 1602, 1500, 1459, 1301, 1183, 1122, 1001, 833, 805, 759, 690, 512; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{19}H_{17}N_2$ [M + H]$^+$ 273.1386; found 273.1387.

2-(4-(tert-Butyl)phenyl)-5-phenyl-1H-pyrrole-3-carbonitrile (**31f**):



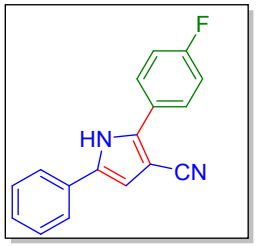
As a white solid (56 mg, 75% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 600 MHz): δ 12.14 (s, 1H), 7.80 (d, 2H, J = 7.8 Hz), 7.77 (d, 2H, J = 8.4 Hz), 7.56 (d, 2H, J = 8.4 Hz), 7.43 (t, 2H, J = 7.5 Hz), 7.29 (t, 1H, J = 7.5 Hz), 7.05 (s, 1H), 1.32 (s, 9H); ^{13}C{^{1}H} NMR (DMSO-d^6, 150 MHz): δ 151.3, 139.9, 133.5, 130.8, 128.8, 127.2, 126.9, 126.4, 125.7, 124.7, 117.8, 110.0, 89.8, 34.5, 31.0; IR (KBr, cm^{-1}): 3247, 2924, 2860, 2219, 1602, 1537, 1383, 1264, 1457, 1183, 1104, 1022, 834, 807, 755, 690, 526; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{21}H_{21}N_2$ [M + H]$^+$ 301.1699; found 301.1697.

2-(4-Methoxyphenyl)-5-phenyl-1H-pyrrole-3-carbonitrile (**31g**):[38]



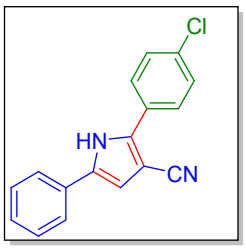
As a white solid (55 mg, 80% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 400 MHz): δ 12.05 (s, 1H), 7.80 (d, 4H, J = 7.6 Hz), 7.42 (t, 2H, J = 7.6 Hz), 7.28 (t, 1H, J = 7.4 Hz), 7.11 (d, 2H, J = 8.8 Hz), 7.01 (s, 1H), 3.83 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d^6, 100 MHz): δ 159.5, 139.9, 133.1, 130.8, 128.7, 128.0, 127.1, 124.6, 122.3, 117.9, 114.4, 109.8, 89.2, 55.3; IR (KBr, cm^{-1}): 3217, 2921, 2839, 2223, 1606, 1528, 1463, 1291, 1246, 1176, 1116, 1033, 937, 830, 806, 760, 690, 574, 516; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{18}H_{15}N_2O$ [M + H]$^+$ 275.1179; found 275.1179.

2-(4-Fluorophenyl)-5-phenyl-1H-pyrrole-3-carbonitrile (**31i**):



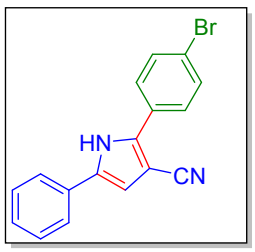
As a white solid (39 mg, 60% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 400 MHz): δ 12.19 (s, 1H), 7.89–7.86 (m, 2H), 7.80 (d, 2H, J = 7.8 Hz), 7.45–7.38 (m, 4H), 7.30 (t, 1H, J = 7.4 Hz), 7.05 (s, 1H); ^{13}C{^{1}H} NMR (DMSO-d^6, 100 MHz): δ 162.1 (d, J = 245.0 Hz), 138.6, 133.7, 130.7, 128.8, 128.77, 128.74, 127.3, 126.2 (d, J = 3.2 Hz), 124.8, 117.5, 115.9 (d, J = 21.8 Hz), 90.2; IR (KBr, cm^{-1}): 3228, 2923, 2855, 2220, 1603, 1529, 1494, 1458, 1247, 1182, 1100, 1024, 835, 807, 756, 689, 511; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{17}H_{12}FN_2$ [M + H]$^+$ 263.0979; found 263.0974.

2-(4-Chlorophenyl)-5-phenyl-1H-pyrrole-3-carbonitrile (**31j**):[38]



As a white solid (38 mg, 55% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 600 MHz): δ 12.26 (s, 1H), 7.86 (d, 2H, J = 8.4 Hz), 7.80 (d, 2H, J = 7.8 Hz), 7.63 (d, 2H, J = 8.4 Hz), 7.44 (t, 2H, J = 7.5 Hz), 7.31 (t, 1H, J = 7.5 Hz), 7.09 (s, 1H); ^{13}C{^{1}H} NMR (DMSO-d^6, 150 MHz): δ 138.2, 134.2, 133.2, 130.6, 129.1, 128.8, 128.5, 128.2, 127.5, 124.9, 117.5, 110.4, 90.6; IR (KBr, cm^{-1}): 3226, 2923, 2854, 2223, 1597, 1463, 1299, 1268, 1181, 1092, 1014, 830, 809, 760, 689, 604, 495; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{17}H_{12}ClN_2$ [M + H]$^+$ 279.0684; found 279.0692.

2-(4-Bromophenyl)-5-phenyl-1H-pyrrole-3-carbonitrile (**31l**):



As a white solid (42 mg, 52% yield); Purified over a column of silica gel (5% EtOAc in hexane). ^{1}H NMR (DMSO-d^6, 600 MHz): δ 12.26 (s, 1H), 7.80 (d, 4H, J = 8.4 Hz), 7.76 (d, 2H, J = 9.0 Hz), 7.44 (t, 2H, J = 7.8 Hz), 7.31 (t, 1H, J = 7.5 Hz), 7.09 (s, 1H); ^{13}C{^{1}H} NMR (DMSO-d^6, 150 MHz): δ 138.2, 134.2, 131.9, 130.6, 128.8, 128.4, 127.5, 124.93, 124.87, 121.8, 117.5, 110.5, 90.6; IR (KBr, cm^{-1}): 3227, 2923, 2855, 2223, 1600, 1461, 1387, 1301, 1262, 1184, 1074, 1022, 807, 761, 690, 492; HRMS (ESI/Q-TOF) (m/z) calcd for $C_{17}H_{12}BrN_2$ [M + H]$^+$ 323.0178; found 323.0171.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org.

X-ray data's for **1f** (CIF), light information, crystallographic description, mechanestic investigations, control experiments, competitive experiments, ^{1}H and ^{13}C spectras of all compounds (PDF).

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Notes

The authors declare no competing financial interest.

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