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PAPER

Divergent Synthesis of 4, 6-Diarylated Pyridin-2(1*H*)-ones from Chalcones: Novel Access to 2, 4, 6-Triaryl Pyridines

Cite this: DOI: 10.1039/x0xx00000x

Received 00th 2015
Accepted 00th 2015

DOI: 10.1039/x0xx00000x

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A wide range of 4,6-diarylated/heterylated pyridin-2(1*H*)-one derivatives were synthesized in good to excellent yields from 1,3-diarylated/heterylated-2-propen-1-ones (chalcones) in one pot under metal and base-free conditions. This domino reaction suggests a novel mechanism comprising of Michael addition followed by amination, subsequent intramolecular amidation and finally dehydronitrosation. The usefulness of the designed 4,6-diarylated/heterylated pyridin-2(1*H*)-one derivatives has further been demonstrated by synthesizing medicinally important 2,4,6-triaryl/heteryl pyridines *via* Pd-catalyzed cross-coupling reaction.

Introduction

The pyridin-2(1*H*)-one unit is a previleged heterocyclic motif, widely distributed in natural products and several biologically active synthetic compounds (Fig. 1).[1] Pyridin-2(1*H*)-one and its derivatives serve as ligands in co-ordination chemistry usually as 1,3 bridging ligand akin to carboxylate.[2] Apart from enjoying importance as bioactive molecules, substituted pyridin-2(1*H*)-ones *viz* 4,6-diarylated/heterylated pyridin-2(1*H*)-ones can be conceived as useful precursors for the synthesis of 2,4,6-triaryl/heteryl pyridines. The 2,4,6-triaryl pyridines serve as synthons in biologically active compounds (Fig. 1).[3] Further, due to their π-stacking ability, the importance of 2,4,6-triaryl pyridines in supramolecular chemistry is also well documented.[4]

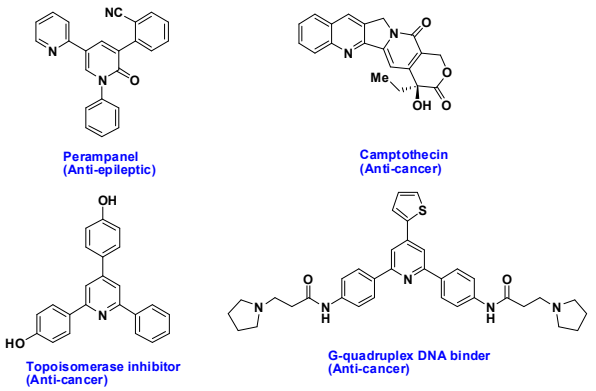

Fig. 1 Biologically active pyridin-2(1*H*)-ones and triaryl pyridines

In our pursuit to synthesize 4,6-disubstituted-3-nitropyridin-2(1*H*)-ones, we got encouraged by the work reported by Manna *et al.,* for the synthesis of 4,6-disubstituted-3-cyanopyridin-2(1*H*)-ones from chalcones, ammonium acetate and ethyl 2-cyanoacetate.[5] Therefore, we envisaged the replacement of ethyl 2-cyanoacetate by ethyl 2-nitroacetate for the synthesis of 4,6-disubstituted-3-nitropyridin-2(1*H*)-one but to our surprise 4,6-disubstituted pyridin-2(1*H*)-one was obtained which lacked nitro group at 3-position. Thus, we became curious to probe the mechanism and scope of this reaction for the synthesis of 4,6-diarylated/heterylated pyridin-2(1*H*)-ones in the light of their significance in medicinal/material chemistry, as well as precursor for 2,4,6-triarylpyridines. Literature survey revealed that there are several methods known for the synthesis of functionalized pyridin-2(1*H*)-ones[6] but a very few methods are available for the exclusive synthesis of 4,6-diarylated pyridin-2(1*H*)-ones.[7] Most of these methods[7a-c] rely on the Michael addition of 2-substituted acetamides to 1,3-diarylated-2-propen-1-ones followed by intramolecular cyclization and elimination to yield 4,6-diarylated pyridin-2(1*H*)-ones (Scheme 1). Pertinent to mention here is the substitution of acetamide at 2-position, which leads to double bond while the amino group of acetamide serves as a 'nitrogen' source for the pyridin-2(1*H*)-one ring in the final product. These methods suffer from one or more of the drawbacks such as limited accessibility of starting materials, usage of strong base, column chromatography for separation and purification of final products, harsh reaction conditions and non-eco friendly solvents.

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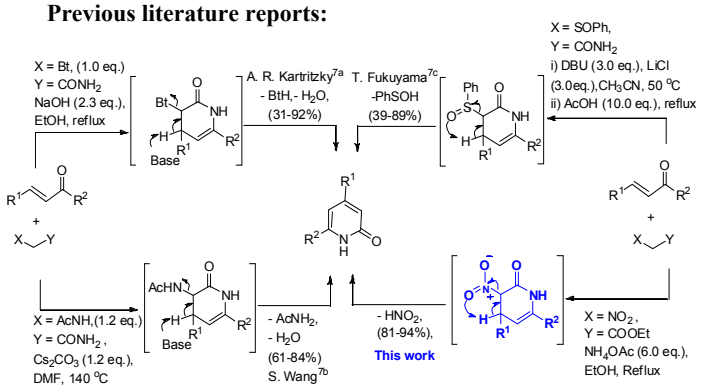
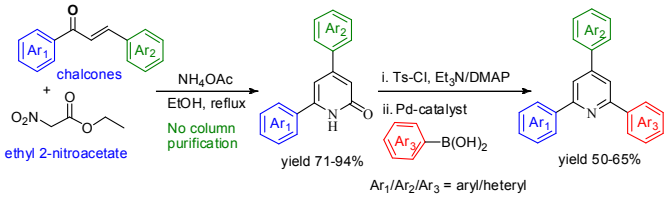
Previous literature reports:



Scheme 1 Synthesis of 4,6-diarylated pyridin-2(1*H*)-ones

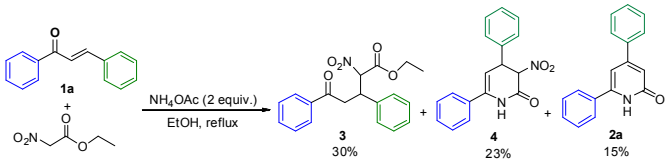
Hence, we envisaged a one-pot reaction of 1,3-diarylated/heterylated-2-propen-1-ones using ethyl 2-nitroacetate (NO_2 group for the installation of double bond) and ammonium acetate as a nitrogen source in the product. The aim of the present work was to develop an efficient divergent route to 4,6-diarylated/heterylated pyridin-2(1*H*)-one framework from 1,3-diarylated/heterylated -2-propen-1-ones and ethyl 2-nitroacetate, and subsequent conversion to 2,4,6-triaryl/heteryl pyridines *via* Suzuki coupling (Scheme 2).



Scheme 2 Synthesis of 4,6-diarylated/heterylated pyridin-2(1*H*)-ones and 2,4,6-triaryl/heteryl pyridines

Results and discussion

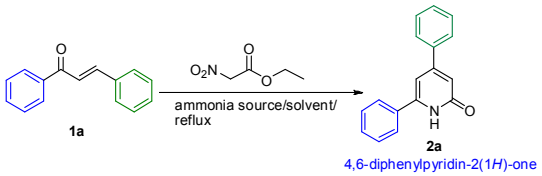
In our earlier successful attempts[8] towards the synthesis of useful heterocyclic systems using 1,3-diarylated-2-propen-1-ones as significant precursors, we now contemplated their use for the synthesis of 2,4,6-triaryl/heteryl pyridines *via* 4,6-diarylated/heterylated pyridin-2(1*H*)-ones (Scheme 2). Recently, we have reported the reductive cyclization of the Michael adduct ethyl 2-nitro-5-oxo-3,5-diarylated/heterylated pentanoates (γ-nitroketones) to ethyl 3,5-diarylated/heterylated-1*H*-pyrrole-2-carboxylates under microwave conditions.[9] Inspired by these findings, we envisaged a domino three-component reaction of 1,3-diarylated/heterylated-2-propen-1-ones, ethyl 2-nitroacetate and ammonium acetate for the synthesis of 4,6-diarylated/heterylated pyridin-2(1*H*)-ones. Refluxing a mixture of 1,3-diphenyl-2-propen-1-one **1a** (1.0 equiv.), ethyl 2-nitroacetate (1.0 equiv.) and NH_4OAc (2.0 equiv.) in ethanol (5.0 mL) for 3 h led to the formation of three products, which were separated by successive crystallization and characterized as ethyl 2-nitro-5-oxo-3,5-diphenylpentanoate[10] **3** (30%), 3,4-dihydro-3-nitro-4,6-diphenylpyridin-2(1*H*)-one **4** (23%) and 4,6-diphenylpyridin-2(1*H*)-one[7c] **2a** (15%) (Scheme 3).



Scheme 3 Outcome of reaction between 1,3-diphenyl-2-propen-1-one **1a** and ethyl 2-nitroacetate with NH_4OAc.

Further to optimize the reaction conditions, a mixture of 1, 3-diphenyl-2-propen-1-one **1a** (1 equiv.) and ethyl 2-nitroacetate (1 equiv.) was refluxed in ethanol using 4 to 6 equiv. of NH_4OAc. To our delight, exclusive formation of **2a** was noticed with 6 equiv. of NH_4OAc. The above experiment was also carried out by using various ammonia sources such as NH_4OH, NH_4NO_3, $(NH_4)_2SO_4$, NH_4Cl, NH_4HCO_3, $NH_4H_2PO_4$, $(NH_4OOCH)_2$ and $NH_4(OOCH)$, and the results are depicted in Table 1. Best result was obtained with NH_4OAc as ammonia source (84%, entry 9, Table 1) while NH_4OH, NH_4NO_3, $(NH_4)_2SO_4$, NH_4Cl and NH_4HCO_3 (6 equiv. each) proved ineffective and the starting material was recovered intact (entries 1-5, Table 1). $NH_4H_2PO_4$, $(NH_4OOCH)_2$ and $NH_4(OOCH)$ were less effective as the desired product **2a** was isolated in poor yields (entries 6-8, Table 1). To further improve upon the yield of the product **2a**, ethanol was replaced with various solvents such as MeOH, EtOH, *i*PrOH, *n*BuOH, $CHCl_3$, CH_3CN, 1:1 DMF:H_2O, 1:1 EtOH:H_2O, diglyme, 1,4-dioxane and toluene (entries 9-19, Table 1) but EtOH remained the most suitable solvent for this transformation.

Table 1 Optimization of reaction conditions[a]



entry	ammonia source	solvent	yield (%)[b]
1	NH_4OH	EtOH	n.r.
2	NH_4NO_3	EtOH	n.r.
3	$(NH_4)_2SO_4$	EtOH	n.r.
4	NH_4Cl	EtOH	n.r.
5	NH_4HCO_3	EtOH	n.r.
6	$NH_4H_2PO_4$	EtOH	25
7	$(NH_4OOCH)_2$	EtOH	20
8	HCO_2NH_4	EtOH	40
9	**NH_4OAc**	**EtOH**	**84**
10	NH_4OAc	MeOH	n.r.
11	NH_4OAc	*i*PrOH	45
12	NH_4OAc	*n*BuOH	62
13	NH_4OAc	$CHCl_3$	n.r.
14	NH_4OAc	CH_3CN	n.r.
15	NH_4OAc	1:1 DMF:H_2O	n.r.
16	NH_4OAc	1:1 EtOH:H_2O	n.r.
17	NH_4OAc	diglyme	n.r.
18	NH_4OAc	1,4-dioxane	15
19	NH_4OAc	toluene	20

[a]Reaction conditions: **1a** (1.0 mmol), ethyl 2-nitroacetate (1.0 mmol), NH_3 source (6.0 mmol), solvent (5.0 mL), 4 h; [b] isolated yields; n.r. = no reaction.

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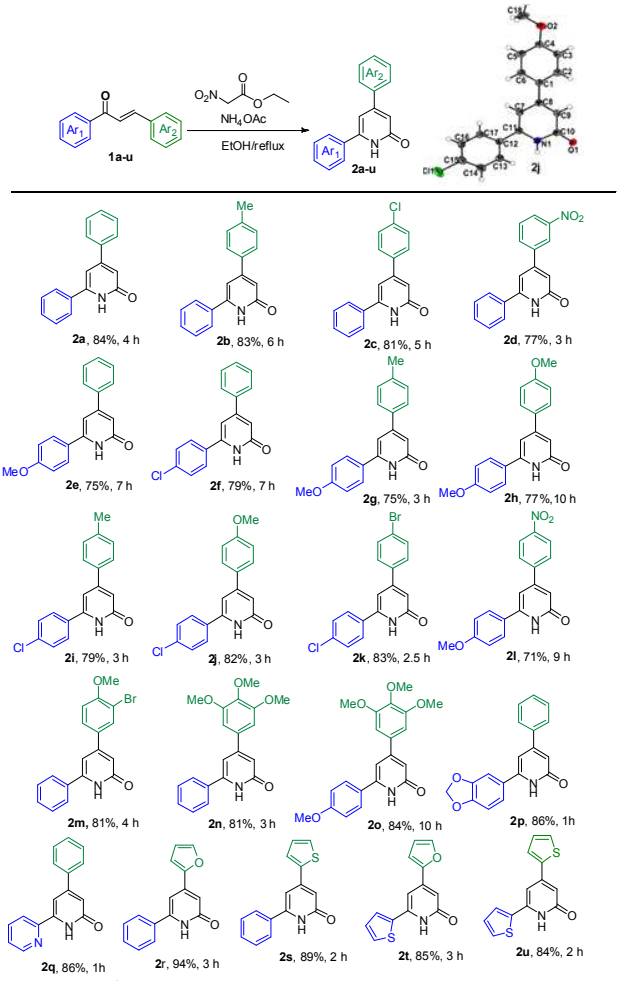
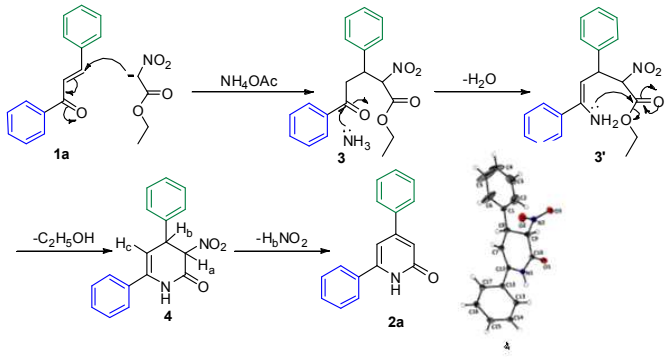
Under the optimized conditions, diversely substituted 1,3-diarylated/heterylated-2-propen-1-ones (**1a-u**) were investigated (Table 2). 1,3-Diarylated-2-propen-1-ones bearing electron donating (Me, OMe) or electron withdrawing groups (Br, Cl, NO_2) in both the phenyl rings (para or meta positions) were converted into their corresponding 4,6-diarylated pyridin-2(1*H*)-ones (**2a-l**) efficiently (71-84 % yields). It is notable that bromo-containing substrates react to yield the corresponding pyridin-2(1*H*)-ones (**2k** and **2m**) which along with other chloro derivatives (**2c**, **2f** and **2i-j**) can serve as suitable substrates for further modification of the pyridin-2(1*H*)-one moiety. The 1,3-diarylated-2-propen-1-ones bearing di- or tri-substitutions on the phenyl ring gave the desired product (**2m-o**) in excellent yields. Further, to enhance the generality of this reaction, various arylated/heterylated combinations were investigated under these optimized conditions. Interestingly, the corresponding arylated/heterylated (**2q-s**) and heterylated/heteroarylated (**2t-u**) pyridin-2(1*H*)-ones were isolated in excellent yields (84-94%). The construction of pyridin-2(1*H*)-ones bearing aryl and bi-cyclic substitutions (**2p**) was also achieved under these optimized conditions. Further the structure of the pyridin-2(1*H*)-ones bearing different aryl rings have been confirmed by X-ray analysis (**2a**, **2c**, **2e**, **2j**) (for details see the supporting information).

Table 2 Substrate scope of the 4,6-diarylated/heterylated pyridin-2(1*H*)-ones synthesis[a]



[a]Reaction conditions: **1** (1.0 mmol), ethyl 2-nitroacetate (1.0 mmol), NH_4OAc (6.0 mmol), EtOH (5.0 mL),reflux

In order to have an insight into the mechanism of the reaction, Michael product **3** was refluxed in ethanol for 1 h with 2 equiv. of NH_4OAc. The formation of **4** and **2a** in the ratio 3:2 was noticed. Interestingly, in **4**, H_b and NO_2 are syn to each other as revealed by the J values ($^3J_{HaHb}$ = 13.2 Hz) and further corroboration by its X-ray data. Further, **4** also produced **2a** upon refluxing in ethanol with 2 equiv. of NH_4OAc. Finally to our delight, 4,6-diphenylpyridin-2(1*H*)-one **2a** was the only product obtained from refluxing a mixture of 1,3-diphenyl-2-propen-1-one **1a** (1.0 equiv.) and ethyl 2-nitroacetate (1.0 equiv.) with 6.0 equiv. of NH_4OAc in ethanol for 4 h. In the light of these observations, following mechanism is proposed (Scheme 4). 1,3-diphenyl-2-propen-1-one **1a** undergo NH_4OAc catalyzed Michael addition with ethyl 2-nitroacetate to give adduct **3**, which upon base-promoted cyclization results in 3,4-dihydro-3-nitro-4,6-diphenyl pyridin-2(1*H*)-one **4** followed by loss of H_2O, EtOH and aromatization of **4** (*syn elimination* of H_bNO_2) to yield the corresponding 4,6-diphenyl pyridin-2(1*H*)-one **2a**. To the best of our knowledge, this is *hitherto* the first report of Michael reaction of 1,3-diarylated/heterylated-2-propen-1-ones with ethyl 2-nitroacetate in presence of NH_4OAc.



Scheme 4 Plausible reaction mechanism for the formation of **2a**

After successful synthesis of 4,6-diarylated/heterylated pyridin-2(1*H*)-ones in one-pot, we focused on exploring conditions that would enable us to obtain 2,4,6-triaryl/heteryl pyridines. There are reports available for cross-coupling reactions at the C-2 position of pyridine.[11] However to the best of our knowledge, C-2 arylation has rarely been explored in the presence of the 4,6-diarylated pyridine system.[12] Therefore, finding the generalised cross-coupling conditions for C-2 arylation would be useful from a synthetic standpoint. Traditionally, organohalides were widely studied and broadly used as the electrophile, in Suzuki-Miyaura cross-coupling reactions in synthesizing heteroaromatic compounds.[13] Development of new electrophiles particularly C−O based electrophiles as cross-coupling partner in Suzuki-Miyaura coupling reaction has attracted interest from various research groups.[14] The advantage of using phenol derivatives as aryl electrophiles is apparent, as they are often readily available and inexpensive. Initial reports toward achieving this goal employed aryl triflates as electrophiles.[15] The present use of tosylates as cross-coupling partner would constitute a more robust methodology because these sulfonates are easy to handle and are generally stable to hydrolysis.[16] Therefore, we prepared O-tosyl derivatives of 4,6-

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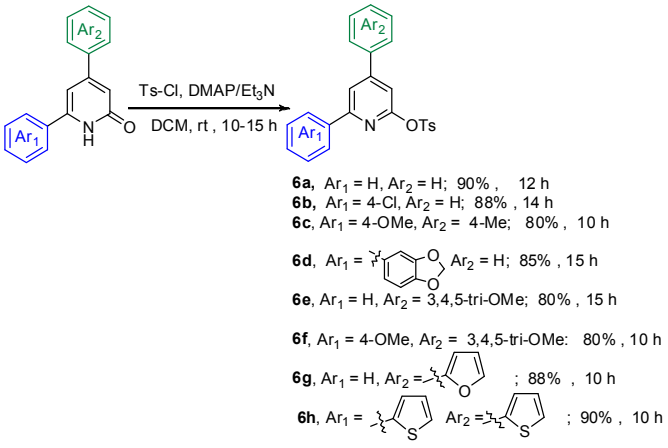
disubstituted pyridin-2(1*H*)-ones, and the corresponding tosylated compounds were isolated in high yields (80-90%) (Scheme 5). [17]

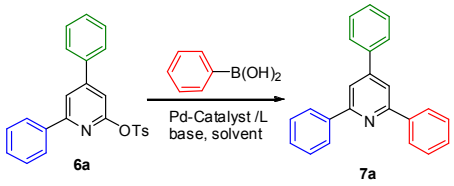


Scheme 5 Tosylation of pyridin-2(1*H*)-ones

Initial optimization studies were performed with 4,6-diphenyl pyridin-2-yl 4-methylbenzenesulfonate **6a** and phenylboronic acid as a cross-coupling partner in the presence of $Pd(PPh_3)_4$ (10 mol %), and Na_2CO_3 as a base in 1,4-dioxane at 100 ^oC, and 7**a** was isolated in only 10% yield (entry 1, Table 3). When we performed the reaction in combination with PPh_3 (10 mol %) as a ligand, and Na_2CO_3 as a base in 1,4-dioxane/H_2O at 100 ^oC, formation of desired product was not observed even after 24 h (entry 2, Table 3). Several ligands and bases were examined with variation in time and temperature (entries 3-12, Table 3). As depicted in Table 2, when NaOH was used in combination with $Pd(OAC)_2$ and XPhos at 100 ^oC in *n*BuOH/ EtOH/H_2O (6:1:1), the isolated yield was 65% (entry 8, Table 3). Further screening of different ligands systems such as PPh_3, dppf, JPhos, PCy_3 (entries 3-5 and 12, Table 3) and bases such as KOH, KF, K_3PO_4 (entries 9-12, Table 2) respectively remained less effective. Further use of different Pd-catalysts (entries 12-13, Table 3) resulted in lower yield. Lower yields were also obtained when we changed the solvent system to *t*AmOH /EtOH/H_2O (6/1/1) (entry 9, Table 3).

With the optimized protocol in hand, the scope of the cross-coupling reactions was explored using various aryl/heterylboronic acids with differently substituted 4,6-diphenylpyridin-2-yl 4-methylbenzenesulfonate (Table 4). For example, electron-donating (**7b-c**,**7g**) and electron-withdrawing phenylboronic acids (**7h**) all afforded C-2 arylated derivatives in good yields. In addition to substituted phenylboronic acids, benzo[*d*][1,3]dioxol-5-ylboronic acid (**7d**, **7f**) and heterocyclic boronic acid (**7i**) were also investigated under these conditions. This route thus offers significant flexibility to access these important heteroaromatic frameworks with unexplored and/or otherwise challenging substitution patterns. As an example, structurally diverse 2,4,6-triarylpyridine **7f**, an important structural motif in designed compounds with interesting biological properties[18] synthesized in good yield (50%). In this context, X-ray crystal structure analysis of 2,6-diphenyl-4-(3,4,5-trimethoxyphenyl) pyridine **7e** was studied (see the Supporting information).

Table 3 Optimization studies for C-2 arylation[a]



entry	cat (10 mol%)	L	base	solvent	yield (%)
1	$Pd(PPh_3)_4$	....	Na_2CO_3	1,4-Dioxane	10
2	$Pd(PPh_3)_4$	PPh_3	Na_2CO_3	1,4-Dioxane /H_2O(7/3)	n.r
3	$Pd(OAc)_2$	PPh_3	K_3PO_4	1,4-Dioxane	10
4	$Pd(OAc)_2$	Dppf	K_3PO_4	*t*AmOH	15
5	$Pd(OAc)_2$	Jphos	K_3PO_4	*t*AmOH	10
6	$Pd(OAc)_2$	Xphos	K_3PO_4	*t*AmOH	40.
7	$Pd(OAc)_2$	Xphos	NaOH	*t*AmOH / H_2O (4/1)	42
8	**$Pd(OAc)_2$**	**Xphos**	**NaOH**	***n*BuOH/EtOH /H_2O(6/1/1)**	**70 (65)[b]**
9	$Pd(OAc)_2$	Xphos	NaOH	*t*AmOH /EtOH /H_2O(6/1/1)	40
10	$Pd(OAc)_2$	Xphos	KOH	*n*BuOH/EtOH /H_2O(6/1/1)	35
11	$Pd(OAc)_2$	Xphos	KF	*n*BuOH/EtOH /H_2O(6/1/1)	40
12	Pd(dppf) Cl_2	Xphos	K_3PO_4	*n*BuOH/EtOH /H_2O(6/1/1)	trace
13	$Pd_2(dba)_3$	PCy_3	K_3PO_4	*n*BuOH/EtOH /H_2O(6/1/1)	10

[a]Reaction conditions: **6a** (1.0 equiv), phenylboronic acid (1.2 equiv), cat. Pd (10 mol %), L (10 mol %), base (2.equiv), solvent (1.0 mL), [b]isolated yield, reaction performed under N_2 atmosphere, n.r. = no reaction

Conclusion

In summary, we have developed metal/base-free synthesis of 4,6-diarylated/heterylated pyridin-2(1*H*)-ones from 1,3-diarylated/heterylated-2-propen-1-ones. This protocol is general and efficient with respect to diverse substrates. The successful implementation of this synthetic strategy would imply developing a new route that by passes the difficulties associated with previous methods, providing an alternative protocol to 4,6-diarylated pyridin-2(1*H*)-ones. This paper further reports the synthesis of 2, 4, 6-triaryl pyridines. This Pd-catalyzed strategy based on C-O activation of tosylates affords a complementary way to obtain aryl/heteryl functionalized molecules, known to be of great interest for their biological/material properties. Finally, these two new protocols and their mechanistic understanding will definitely make an avenue in synthesizing triaryl/heteryl structural motif in a programmed manner.

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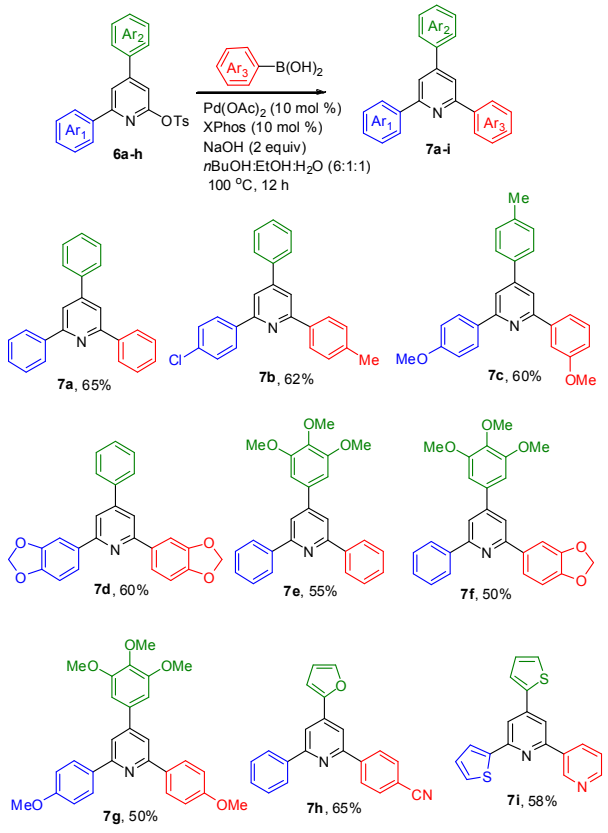
Table 4 Pd-Catalysed C-2 arylation of 4,6-diphenylpyridin-2-yl 4-methylbenzene sulfonate[a]



[a]Reaction conditions: **6a** (1.0 equiv), phenylboronic acid (1.2 equiv), $Pd(OAc)_2$ (10 mol %), X-Phos (10 mol %), NaOH (2.equiv), *n*BuOH/EtOH/H_2O (6:1:1, 1.0 mL)

Experimental

General Information

Melting points were uncorrected. ^1H and ^{13}C NMR spectra in $CDCl_3$ and DMSO–d_6 were recorded on Bruker Avance III-400 MHz, using $(CH_3)_4Si$ as an internal standard. Chemical shifts (δ) are expressed in parts per million referenced to the residual solvent (i.e., ^1H 7.24 ppm, ^{13}C 77.1 ppm for $CDCl_3$; ^1H 2.50 ppm, ^{13}C 39.5 ppm for DMSO–d_6). Signal multiplicity is expressed as follows: s (singlet),br s (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet). J values are given in hertz (Hz). For the HRMS measurement, Q-TOF was used. All reactions and purity of the synthesized compounds were monitored by TLC using silica gel 60 F254 aluminium plates. Visualization was accomplished by UV light, exposure to iodine vapours and by treating the plates with dragendorff reagent followed by heating. Crystals suitable for X-ray single crystal analyses were obtained by EtOH. X-ray data were collected on a Bruker Kappa Apex-II diffractometer at RT with Mo-Kα radiation (λ = 0.71073 Å) at Department of Chemistry, Center for Advanced Studies, Guru Nanak Dev University, Amritsar. These were reduced applying Lorentz and polarization corrections as well as an absorption correction. A multi-scan structures were solved by direct methods (SIR-92)[19] and refined by full-matrix least squares on F^2 (SHELX 97).[20] All the non-H atoms were treated anisotropically and all H atoms were attached geometrically. Materials unless otherwise indicated, materials and solvents were purchased and used without further purification. 1,3-Diarylated/heterylated-2-propen-1-ones **1a-u** were prepared according to the reported procedure.[21]

General procedures

Synthesis of 4,6-diarylated/heterylated pyridin-2(1*H*)-one derivatives 2a-u (General Procedure A):
A mixture of 1,3-diarylated/heterylated-2-propen-1-one (**1a-u**) (1.0 mmol), ethyl 2-nitroacetate (1.0 mmol) and ammonium acetate (6.0 mmol) in ethanol (5.0 mL) was refluxed for the appropriate time (Table 2). The reaction mixture was cooled to room temperature and the solid obtained was filtered, washed with ethanol, dried and recrystallized from ethanol to obtain the pure product (**2a-u**).

4,6-Diphenylpyridin-2(1*H*)-one (2a): The title compound **2a** was obtained from (2E)-1,3-diphenyl-2-propen-1-one **1a** (1.0 mmol) as a brown solid (0.207 g, 84% yield); mp 206–207 °C (lit.[7c] 203–204 °C); ^1H NMR (400 MHz, DMSO-d_6) δ 11.77 (br s, 1H, exchangeable with D_2O), 7.89 (dd, *J* = 7.5, 1.9 Hz, 2H), 7.81 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.53–7.48 (m, 6H), 6.99 (s, 1H), 6.67 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 152.3, 148.7, 137.8, 134.8, 130.1, 129.9, 129.4, 129.2, 127.0, 127.3, 113.1, 104.9; IR (KBr): 3440.28, 1642.58 cm^{-1}; HRMS (ESI): calcd. for $C_{17}H_{14}NO$ $[M+H]^+$, 248.1070; found: 248.1058.

4-(4-Methylphenyl)-6-phenylpyridin-2(1*H*)-one (2b): The title compound **2b** was obtained from (E)-1-phenyl-3-(4-methylphenyl)-2-propen-1-one **1b** (1.0 mmol) as a shiny green solid (0.217 g, 83% yield); mp 233–234 °C (lit.[7b] 238–240 °C); ^1H NMR (400 MHz, DMSO-d_6) δ 11.68 (br s, 1H, exchangeable with D_2O), 7.89 (d, *J* = 6.3 Hz, 2H), 7.72 (d, *J* = 7.9 Hz, 2H), 7.50 (d, *J* = 6.2 Hz, 3H), 7.32 (d, *J* = 7.9 Hz, 2H), 6.97 (s, 1H), 6.64 (s, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 152.1, 139.5, 134.9, 130.0, 129.1, 127.4, 127.2, 112.5, 104.8, 21.2; IR (KBr): 3235.62, 1613.47 cm^{-1}; HRMS (ESI): calcd. for $C_{18}H_{16}NO$ $[M+H]^+$, 262.1226; found: 262.1228.

4-(4-Chlorophenyl)-6-phenylpyridin-2(1*H*)-one (2c): The title compound **2c** was obtained from (E)-3-(4-chlorophenyl)-1-phenyl-2-propen-1-one **1c** (1.0 mmol) as a pale-yellow solid (0.242 g, 81% yield); mp 232–234 °C (lit.[7a] 237–238 °C); ^1H NMR (400 MHz, DMSO-d_6) δ 11.78 (br s, 1H, exchangeable with D_2O), 7.91–7.85 (m, 4H), 7.57–7.49 (m, 5H), 7.01 (s, 1H), 6.68 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) 164.1, 150.9, 136.6, 134.7, 130.1, 129.4, 129.2, 129.2, 127.5, 113.0, 104.8; IR (KBr): 3441.15, 1644.48 cm^{-1}; HRMS (ESI): calcd. for $C_{17}H_{13}ClNO$ $[M+H]^+$, 282.0680; found: 282.0680.

4-(3-Nitrophenyl)-6-phenylpyridin-2(1*H*)-one (2d): The title compound **2d** was obtained from (E)-3-(3-nitrophenyl)-1-phenyl-2-propen-1-one **1d** (1.0 mmol) as a brown solid (0.225 g, 77% yield); mp 247–249 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.83 (br s, 1H,

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exchangeable with D_2O), 8.57 (s, 1H), 8.33–8.26 (m, 2H), 7.95–7.91 (m, 2H), 7.80 (t, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 5.9 Hz, 3H), 7.13 (s, 1H), 6.79 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.1, 150.1, 148.8, 139.6, 134.9, 134.0, 131.0, 130.2, 129.1, 127.5, 124.4, 122.1, 113.6, 105.1; IR (KBr): 3442.95, 1651.33 cm^{-1}; HRMS (ESI): calcd. for $C_{17}H_{13}N_2O_3$ $[M+H]^+$, 293.0921; found: 293.0919.

6-(4-Methoxyphenyl)-4-phenylpyridin-2(1*H*)-one (2e): The title compound **2e** was obtained from (E)-1-(4-methoxyphenyl)-3-phenyl-2-propen-1-one **1e** (1.0 mmol) as a pale-yellow solid (0.208 g, 75% yield); mp 248–250 °C (lit.[7c] 247–251 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.76 (br s, 1H, exchangeable with D_2O), 7.83 (dd, *J* = 24.5, 8.0 Hz, 4H), 7.50 (d, *J* = 5.1 Hz, 3H), 7.05 (d, *J* = 7.8 Hz, 2H), 6.90 (s, 1H), 6.59 (s, 1H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 160.9, 152.3, 138.0, 129.8, 129.4, 128.9, 127.3, 114.6, 103.8, 55.8; IR (KBr): 3442.45, 1643.38 cm^{-1}; HRMS (ESI): calcd. for $C_{18}H_{16}NO_2$ $[M+H]^+$, 278.1176; found: 278.1186.

6-(4-Chlorophenyl)-4-phenylpyridin-2(1*H*)-one (2f): The title compound **2f** was obtained from (E)-1-(4-chlorophenyl)-3-phenyl-2-propen-1-one **1f** (1.0 mmol) as a grey solid (0.222 g, 79% yield); mp 260 °C (lit.[7b] 262–264 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.70 (br s, 1H, exchangeable with D_2O), 7.97 (d, *J* = 8.5 Hz, 2H), 7.85–7.80 (m, 2H), 7.54 (dd, *J* = 24.0, 8.1 Hz, 5H), 7.13 (s, 1H), 6.72 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 152.2, 137.8, 134.7, 129.9, 129.4, 129.3, 129.1, 127.4, 112.4, 106.0; IR (KBr): 3441.68, 1645.48 cm^{-1}; HRMS (ESI): calcd. for $C_{17}H_{13}ClNO$ $[M+H]^+$, 282.0680; found: 282.0731.

6-(4-Methoxyphenyl)-4-(4-methylphenyl)pyridin-2(1*H*)-one (2g): The title compound **2g** was obtained from (E)-1-(4-methoxyphenyl) -3-(4-methyl)-2-propen-1-one **1g** (1.0 mmol) as a shiny brown solid (0.218 g, 75% yield); mp 254–256 °C (lit.[7a] 258–260 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.74 (br s, 1H, exchangeable with D_2O), 7.85 (d, *J* = 8.7 Hz, 2H), 7.70 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.88 (s, 1H), 6.56 (s, 1H), 3.82 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 160.9, 152.2, 139.5, 135.0, 130.1, 130.0, 129.7, 128.9, 127.5, 127.2, 114.5, 103.5, 55.7, 21.2; IR (KBr): 3083.71, 1632.46 cm^{-1}; HRMS (ESI): calcd. for $C_{19}H_{18}NO_2$ $[M+H]^+$, 292.1332; found: 292.1323.

4,6-Bis(4-methoxyphenyl)pyridin-2(1*H*)-one (2h): The title compound **2h** was obtained from (E)-1,3-bis(4-methoxyphenyl)-2-propen-1-one **1h** (1.0 mmol) as a black solid (0.236 g, 77% yield); mp 280–281 °C; ^{1}H NMR (400 MHz, DMSO-d_6)12.00 (br s, 1H, exchangeable with D_2O), 7.77 (d, *J* = 8.7 Hz, 2H), 7.66 (d, *J* = 8.7 Hz, 1H), 7.39 (d, *J* = 8.7 Hz, 1H), 7.00 (t, *J* = 7.0 Hz, 4H), 6.72 (s, 1H), 6.50 (d, *J* = 10.4 Hz, 1H), 3.80 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 160.9, 152.2, 148.1, 139.5, 135.0, 130.0, 128.9, 127.2, 127.0, 114.6, 112.0, 103.5, 55.8; IR (KBr): 3437.23, 1639.30 cm^{-1}; HRMS (ESI): calcd. for $C_{19}H_{18}NO_3$ $[M+H]^+$, 308.1281; found: 308.1281.

6-(4-Chlorophenyl)-4-(4-methyl)pyridin-2(1*H*)-one (2i): The title compound **2i** was obtained from (E)-1-(4-chlorophenyl)-3-(4-methyl)-2-propen-1-one **1i** (1.0 mmol) as a brown solid (0.233 g, 79% yield); mp 258–259 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.84 (br s, 1H, exchangeable with D_2O), 7.82 (dd, *J* = 26.9, 8.2 Hz, 4H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 6.94 (s, 1H), 6.63 (s, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.1, 150.9, 141.5, 139.9, 136.7, 134.7, 129.9, 129.7, 129.6, 129.4, 129.2, 128.1, 127.3, 112.9, 104.1, 21.2; IR (KBr): 3401.12, 1689.24 cm^{-1}; HRMS (ESI): calcd. for $C_{18}H_{15}ClNO$ $[M+H]^+$, 296.0837; found: 296.0841.

6-(4-Chlorophenyl)-4-(4-methoxyphenyl)pyridin-2(1*H*)-one (2j): The title compound **2j** was obtained from (E)-1-(4-chlorophenyl)-3-(4-methoxyphenyl)-2-propen-1-one **1j** (1.0 mmol) as a reddish-brown solid (0.255 g, 82% yield); mp 294–295 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.60 (br s, 1H, exchangeable with D_2O), 7.95 (d, *J* = 8.6 Hz, 2H), 7.80 (d, *J* = 8.9 Hz, 2H), 7.56 (d, *J* = 8.7 Hz, 2H), 7.08 (s, 1H), 7.05 (d, *J* = 8.9 Hz, 2H), 6.66 (s, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 160.8, 151.6, 148.2, 134.7, 134.4, 129.8, 129.2, 129.1, 128.7, 114.8, 111.4, 105.5, 55.7; IR (KBr): 3442.18, 1658.53 cm^{-1}; HRMS (ESI): calcd. for $C_{18}H_{15}ClNO_2$ $[M+H]^+$, 312.0786; found: 312.0785.

4-(4-Bromophenyl)-6-(4-chlorophenyl)pyridin-2(1*H*)-one (2k): The title compound **2k** was obtained from (E)-3-(4-bromophenyl)-1-(4-chlorophenyl)-2-propen-1-one **1k** (1.0 mmol) as a grey solid (0.298 g, 83% yield); mp 326–327 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.70 (br s, 1H, exchangeable with D_2O), 7.97 (d, *J* = 8.3 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.14 (s, 1H), 6.73 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 150.9, 136.9, 134.8, 134.2, 132.3, 129.5, 129.3, 129.1, 123.4, 112.1, 105.9; IR (KBr): 3437.44, 1658.80 cm^{-1}; HRMS (ESI): calcd. for $C_{17}H_{12}BrClNO$ $[M+H]^+$, 359.9785; found: 359.9771.

6-(4-Methoxyphenyl)-4-(4-nitrophenyl)pyridin-2(1*H*)-one (2l): The title compound **2l** was obtained from (E)-1-(4-methoxyphenyl)-3-(4-nitrophenyl)-2-propen-1-one **1l** (1.0 mmol) as a yellow solid (0.229 g, 71% yield); mp 297–299 °C ; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.81 (br s, 1H, exchangeable with D_2O), 8.31 (d, *J* = 7.7 Hz, 2H), 8.08 (d, *J* = 7.8 Hz, 2H), 7.87 (d, *J* = 7.9 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.99 (s, 1H), 6.69 (s, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.0, 161.0, 150.1, 148.2, 144.4, 131.6, 130.2, 129.0, 128.8, 124.4, 114.5, 113.4, 103.8, 55.8; IR (KBr): 3439.82, 1658.82 cm^{-1}; HRMS (ESI): calcd. for $C_{18}H_{15}N_2O_4$ $[M+H]^+$, 323.1026; found: 323.1006.

4-(3-Bromo-4-methoxyphenyl)-6-phenylpyridin-2(1*H*)-one (2m): The title compound **2m** was obtained from (E)-3-(3-bromo-4-methoxyphenyl)-1-phenyl-2-propen-1-one **1m** (1.0 mmol) as a brown solid (0.288 g, 81% yield); mp 258–259 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.72 (br s, 1H, exchangeable with D_2O), 8.11 (s, 1H), 7.94–7.85 (m, 3H), 7.51 (s, 3H), 7.23 (d, *J* = 8.5 Hz, 1H), 7.02 (s, 1H), 6.67 (s, 1H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.1, 156.8, 150.4, 148.7, 134.9, 131.7, 131.4, 130.1, 129.1, 128.2, 127.5, 113.3, 112.4, 111.8, 104.5, 56.9; IR (KBr): 3436.86, 1643.80 cm^{-1}; HRMS (ESI): calcd. for $C_{18}H_{15}BrNO_2$ $[M+H]^+$, 356.0281; found: 356.0273.

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4-(3,4,5-Trimethoxyphenyl)-6-phenylpyridin-2(1*H*)-one (2n): The title compound **2n** was obtained from (E)-1-phenyl-3-(3,4,5-trimethoxyphenyl)-2-propen-1-one **1n** (1.0 mmol) as a shiny brown solid (0.273 g, 81% yield); mp 288 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.76 (br s, 1H, exchangeable with D_2O), 7.89 (d, *J* = 5.3 Hz, 2H), 7.51 (s, 3H), 7.05 (s, 2H), 6.99 (s, 1H), 6.71 (s, 1H), 3.90 (s, 6H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 153.6, 152.6, 148.3, 139.0, 134.7, 133.6, 130.1, 129.2, 127.5, 113.4, 104.8, 60.5, 56.5; IR (KBr): 3439.30, 1643.32 cm^{-1}; HRMS (ESI): calcd. for $C_{20}H_{20}NO_4$ $[M+H]^+$, 338.1387; found: 338.1383.

6-(4-Methoxyphenyl)-4-(3,4,5-trimethoxyphenyl)pyridin-2(1*H*)-one (2o): The title compound **2o** was obtained from (E)-1-(4-methoxyphenyl)-3-(3,4,5-trimethoxyphenyl)-2-propen-1-one **1o** (1.0 mmol) as a shiny green solid (0.308 g, 84% yield); mp 279–281 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.70 (br s, 1H, exchangeable with D_2O), 7.84 (d, *J* = 8.7 Hz, 2H), 7.07–7.01 (m, 4H), 6.89 (s, 1H), 6.62 (s, 1H), 3.88 (s, 6H), 3.82 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 160.9, 153.6, 152.6, 147.9, 138.9, 133.7, 129.0, 126.9, 114.5, 112.7, 104.8, 103.9, 60.5, 56.5, 55.7; IR (KBr): 3265.89, 1640.63 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{22}NO_5$ $[M+H]^+$, 368.1492; found: 368.1476.

6-(Benzo[*d*][1,3]dioxol-5-yl)-4-phenylpyridin-2(1*H*)-one (2p): The title compound **2p** was obtained from (E)-1-(benzo[*d*][1,3]dioxo-5-yl)-3-phenyl-2-propen-1-one **1p** (1.0 mmol) as a pale yellow solid (0.250 g, 86% yield); mp 326–327 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.66 (br s, 1H, exchangeable with D_2O), 7.81 (d, *J* = 6.7 Hz, 2H), 7.52–7.44 (m, 5H), 7.04 (d, *J* = 8.2 Hz, 1H), 6.95 (s, 1H), 6.61 (s, 1H), 6.11 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.1, 152.3, 149.0, 148.2, 137.9, 129.8, 129.4, 127.3, 121.8, 108.9, 107.7, 102.0; IR (KBr): 3441.95, 1627.33 cm^{-1}; HRMS (ESI): calcd. for $C_{18}H_{14}NO_3$ $[M+H]^+$, 292.0968; found: 292.0964.

4-Phenyl-6-(2-pyridyl)pyridin-2(1*H*)-one (2q): The title compound **2q** was obtained from (E)-3-phenyl-1-(pyridin-2-yl)-2-propen-1-one **1q** (1.0 mmol) as a brown solid (0.213 g, 86% yield); mp 210–212 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.15 (br s, 1H, exchangeable with D_2O), 8.72 (s, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 8.00 (t, *J* = 7.4 Hz, 1H), 7.84 (d, *J* = 7.0 Hz, 2H), 7.59–7.52 (m, 5H), 6.81 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.2, 152.3, 149.7, 138.1, 137.5, 130.0, 129.5, 127.3, 125.2, 121.4, 115.0, 105.1; IR (KBr): 3440.82, 1650.92 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{13}N_2O$ $[M+H]^+$, 249.1022; found: 249.1013.

4-(Furan-2-yl)-6-phenylpyridin-2(1H)-one (2r): The title compound **2r** was obtained from (E)-3-(furan-2-yl)-1-phenyl-2-propen-1-one **1r** (1.0 mmol) as a light brown solid (0.223 g, 94% yield); mp 217–218 °C (lit.[7b] 212–214 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.67 (br s, 1H, exchangeable with D_2O), 7.91–7.83 (m, 3H), 7.53–7.48 (m, 3H), 7.37 (d, *J* = 3.4 Hz, 1H), 7.00 (s, 1H), 6.70 (dd, *J* = 3.3, 1.7 Hz, 1H), 6.62 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.0, 150.8, 145.6, 141.3, 134.5, 130.2, 129.2, 127.4, 113.0, 111.6, 108.8, 101.3; IR (KBr): 3437.54, 1641.40 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{12}NO_2$ $[M+H]^+$, 238.0863; found: 238.0858.

6-Phenyl-4-(thiophen-2-yl)pyridin-2(1*H*)-one (2s): The title compound **2s** was obtained from (E)-1-phenyl-3-(thiophen-2-yl)-2-propen-1-one **1s** (1.0 mmol) as a shiny brown solid (0.225 g, 89% yield); mp 206–207 °C (lit.[7b] 202–204 °C); ^{1}H NMR (400 MHz, DMSO-d_6)) δ 11.70 (br s, 1H, exchangeable with D_2O), 7.88 (d, *J* = 3.4 Hz, 3H), 7.76 (d, *J* = 5.0 Hz, 1H), 7.53 (d, *J* = 5.3 Hz, 3H), 7.25–7.23 (t, *J* = 4.2 Hz, 1H), 7.00 (s, 1H), 6.61 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.0, 148.8, 145.4, 140.6, 134.5, 130.2, 129.2, 129.0, 127.8, 127.4, 111.0, 103.3; IR (KBr): 3449.97, 1623.04 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{12}NOS$ $[M+H]^+$, 254.0634; found: 254.0635.

4-(Furan-2-yl)-6-(thiophen-2-yl)pyridin-2(1*H*)-one (2t): The title compound **2t** was obtained from (E)-3-(furan-2-yl)-1-(thiophen-2-yl) -2-propen-1-one **1t** (1.0 mmol) as a brown solid (0.207 g, 85% yield); mp 241–243 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.40 (br s, 1H, exchangeable with D_2O), 7.88–7.86 (m, 2H), 7.68 (d, *J* = 4.9 Hz, 1H), 7.34–7.17 (m, 3H), 6.68 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.0, 150.8, 145.3, 141.2, 128.8, 126.8, 113.0, 111.0, 105.1, 102.5; IR (KBr): 3442.62, 1650.48 cm^{-1}; HRMS (ESI): calcd. for $C_{13}H_{10}NO_2S$ $[M+H]^+$, 244.0427; found: 244.0415.

4,6-Di(thiophen-2-yl)pyridin-2(1*H*)-one (2u): The title compound **2u** was obtained from (E)-1,3-di(thiophen-2-yl)-2-propen-1-one **1u** (1.0 mmol) as a shiny brown solid (0.218 g, 84% yield); mp 244–247 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.39 (br s, 1H, exchangeable with D_2O), 7.87 (dd, *J* = 18.5, 3.1 Hz, 2H), 7.71 (dd, *J* = 21.8, 4.9 Hz, 2H), 7.29 (s, 1H), 7.23–7.17 (m, 2H), 6.65 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.1, 145.2, 140.6, 129.2, 128.9, 128.8, 127.4, 126.8; IR (KBr): 3448.61, 1637.58 cm^{-1}; HRMS (ESI): calcd. for $C_{13}H_{10}NOS_2$ $[M+H]^+$, 260.0198; found: 260.0217.

Ethyl 2-nitro-5-oxo-3,5-diphenylpentanoate (3): White solid (30% yield); mp 114–116 °C (lit.[10] 116–117 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92–7.81 (m, 2H), 7.56–7.49 (m, 1H), 7.43–7.38 (m, 2H), 7.29–7.20 (m, 5H), 5.55 (d, *J* = 8.0 Hz, 1H), 4.53–4.46 (m, 1H), 4.24–4.03 (m, 2H), 3.74–3.51 (m, 2H), 1.09 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 163.2, 136.9, 136.3, 133.4, 128.9, 128.7, 128.4, 128.3, 128.1, 128.0, 91.6, 63.0, 41.8, 40.4, 13.6; MS (ESI): m/z = 342 $(M+H)^+$.

3,4-Dihydro-3-nitro-4,6-diphenylpyridin-2(1*H*)-one (4): Shiny yellow solid (23% yield); mp 244–245 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.58 (br s, 1H, exchangeable with D_2O), 7.85–7.56 (m, 3H), 7.41–7.36 (m, 7H), 6.27 (d, *J* = 12 Hz, 1H), 5.46 (s, 1H), 4.67 (d, *J* = 16 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.3, 138.3, 136.7, 133.19, 128.9, 128.8, 128.4, 127.83, 126.7, 125.6, 105.0, 89.6, 43.2; MS (ESI): m/z = 295 $(M+H)^+$.

Synthesis of 4,6-diarylated/heterylated pyridin-2-yl sulfonates 6a-h (General Procedure B):
4,6-Disubstituted pyridin-2(1*H*)-ones (100 mg, 0.404 mmol), *p*-toluenesulfonyl chloride (92.3 mg, 0.485 mmol), triethylamine (112.2 µL, 0.809 mmol) and 4-(N,N-dimethylamino) pyridine (1.3 mg, 0.012 mmol) were added into a 25 mL round-bottom flask containing 1 mL of analytical-grade CH_2Cl_2. After stirring at 25 °C

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for 10-15 h, the reaction mixture was diluted with water (50 mL) and extracted with Et_2O (50 mL X 2). The organic extracts were dried over Na_2SO_4 and then concentrated on a rotary evaporator. The resulting residue was purified by silica gel flash chromatography (ethyl acetate/hexane 1:5 to 1:3) to afford the titled compound (80–90%) (**6a-h**).

4,6-Diphenylpyridin-2-yl 4-methylbenzenesulfonate (6a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.2 Hz, 2H), 7.83 (s, 1H), 7.76 (dd, *J* = 6.5, 2.9 Hz, 2H), 7.65 (d, *J* = 6.4 Hz, 2H), 7.50 (m, 3H), 7.42–7.39 (m, 3H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.25 (s, 1H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 156.5, 153.8, 145.0, 137.5, 137.4, 134.4, 129.6, 129.6, 129.2, 128.8, 128.6, 127.1, 127.0, 117.0, 111.6, 21.7; MS (ESI): m/z = 401.2

6-(4-Chlorophenyl)-4-phenylpyridin-2-yl 4-methyl benzene sulfonate (6b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.3 Hz, 2H), 7.71 (s, 1H), 7.67 (dd, *J* = 6.6, 2.9 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.37–7.28 (m, 5H), 7.16 (s, 1H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.7, 155.7, 151.4, 144.1, 136.3, 134.9, 134.7, 133.3, 128.7, 128.5, 128.4, 127.8, 127.6, 127.3, 125.9, 115.7, 110.4, 20.7; MS (ESI): m/z = 436.1

6-(4-Methoxyphenyl)-4-(4-methylphenyl)pyridin-2-yl 4-methyl benzenesulfonate (6c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.3 Hz, 2H), 7.74 (d, *J* = 1.1 Hz, 1H), 7.71 (d, *J* = 8.9 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.16 (d, *J* = 1.0 Hz, 1H), 6.91 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H), 2.48 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8, 157.6, 156.1, 153.6, 144.9, 139.8, 134.6, 134.5, 130.3, 129.9, 129.5, 128.8, 128.3, 126.9, 115.9, 113.9, 110.5, 55.4, 21.7, 21.3; MS (ESI): m/z = 445.3

6-(Benzo[d][1,3]dioxol-5-yl)-4-phenylpyridin-2-yl 4-methyl benzenesulfonate (6d): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.72 (s, 1H), 7.64 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.50 (d, *J* = 7.6 Hz, 3H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.31 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.20 (s, 1H), 7.11 (d, *J* = 1.6 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.02 (s, 2H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 154.9, 152.7, 147.8, 147.1, 144.1, 136.3, 133.4, 130.9, 128.6, 128.1, 127.7, 126.0, 120.0, 115.3, 110.1, 107.1, 106.3, 100.3, 20.6; MS (ESI): m/z = 445.1

6-Phenyl-4-(3,4,5-trimethoxyphenyl)pyridin-2-yl 4-methyl benzenesulfonate (6e): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.2 Hz, 2H), 7.77 (s, 1H), 7.76–7.72 (m, 2H), 7.43–7.40 (m, 3H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.21 (s, 1H), 6.83 (s, 2H), 3.96 (s, 6H), 3.92 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 156.4, 153.8, 153.7, 145.1, 139.3, 137.4, 134.4, 133.0, 129.6, 128.8, 128.6, 127.0, 116.9, 111.5, 104.3, 60.9, 56.3, 21.7; MS (ESI): m/z = 491.4

6-(4-Methoxyphenyl)-4-(3,4,5-trimethoxyphenyl)pyridin-2-yl 4-methylbenzenesulfonate (6f): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.3 Hz, 2H), 7.59 (s, 1H), 7.57 (d, *J* = 1.9 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 6.97 (d, *J* = 1.0 Hz, 1H), 6.77 (d, *J* = 8.9 Hz, 2H), 6.69 (s, 2H), 3.81 (s, 6H), 3.79 (s, 3H), 3.70 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.9, 157.5, 156.2, 153.7, 145.0, 139.3, 134.5, 133.1, 130.0, 129.6, 128.7, 128.3, 115.9, 113.9, 110.6, 104.4, 60.9, 56.3, 55.3, 21.7; MS (ESI): m/z = 521.2

4-(Furan-2-yl)-6-phenylpyridin-2-yl 4-methylbenzenesulfonate (6g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.87 (s, 1H), 7.73 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.58 (d, *J* = 1.2 Hz, 1H), 7.42–7.39 (m, 3H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.32–7.21 (m, 1H), 6.95 (d, *J* = 3.4 Hz, 1H), 6.56 (dd, *J* = 3.4, 1.8 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 156.6, 150.5, 145.0, 144.3, 142.3, 137.4, 134.3, 129.6, 129.6, 128.8, 128.6, 126.9, 112.9, 112.3, 109.9, 107.7, 21; MS (ESI): m/z = 391.3

4,6-Di(thiophen-2-yl)pyridin-2-yl 4-methylbenzenesulfonate (6h) : ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.3 Hz, 2H), 7.66 (d, *J* = 1.0 Hz, 1H), 7.56–7.50 (m, 2H), 7.49–7.44 (m, 1H), 7.39 (dd, *J* = 8.1, 4.3 Hz, 3H), 7.18–7.14 (m, 1H), 7.14 (d, *J* = 1.0 Hz, 1H), 7.08 (dd, *J* = 4.9, 3.8 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 152.0, 146.4, 145.1, 142.9, 139.9, 134.1, 129.6, 128.9, 128.6, 128.44, 128.0, 126.3, 125.8, 113.6, 109.3, 21.7; MS (ESI): m/z = 413.12

Synthesis of 2,4,6-triaryl/heteryl pyridine derivatives 7a-i (General Procedure C):

A sealed tube (50.0 mL), fitted with a septum, containing $Pd(OAc)_2$ (7.2 mg, 0.1 mmol) and XPhos (15.5 mg, 0.1 mmol) was evacuated and purged with nitrogen. 2,4-diarylated pyridine-2-yl sulfonate (1.0 mmol), arylboronic acid (1.2 mmol), NaOH (2.0 equiv.), and *n*BuOH/EtOH/H_2O (6/1/1, 1.0 mL), were added to the system and the reaction mixture was stirred at 100 °C for 12 h. Upon completion of the reaction, the mixture was cooled to room temp, extracted with ethyl acetate (25 mLx 2), and washed with water**.** The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 98:2) to provide the desired products (**7a-i).**

2,4,6-Triphenylpyridine (7a): The title compound **7a** was obtained from 4,6-diphenylpyridin-2-yl 4-methylbenzenesulfonate **6a** (1.0 mmol) as a white solid (49.8 mg, 65% yield); mp 130–132 °C (lit.[22] 134–135 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 1.4 Hz, 2H), 8.20 (d, *J* = 5.0 Hz, 2H), 7.89 (s, 1H), 7.76 (d, *J* = 1.5 Hz, 1H), 7.74 (s, 1H), 7.56–7.52 (m, 5H), 7.49 (d, *J* = 4.0 Hz, 2H), 7.47–7.41 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 150.2, 139.6, 139.1, 129.1, 129.1, 129.0, 128.7, 127.2, 127.2, 117.1; HRMS (ESI): calcd. for $C_{23}H_{18}N$ $[M+H]^+$, 308.1434; found: 308.1436.

2-(4-Chlorophenyl)-4-phenyl-6-(4-methylphenyl)pyridine (7b): The title compound **7b** was obtained from 6-(4-chlorophenyl)-4-phenylpyridin-2-yl 4-methylbenzenesulfonate **6b** (1.0 mmol) as a white solid (40.5 mg, 62% yield); mp 164–167 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.5 Hz, 2H), 8.08 (d, *J* = 8.1 Hz, 2H), 7.86 (s, 1H), 7.82 (s, 1H), 7.73 (d, *J* = 7.0 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 2H), 7.48 (dd, *J* = 7.6, 3.9 Hz, 3H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 156.1, 150.3, 139.2, 139, 138.1, 136.6, 135.1, 129.5, 129.4, 129.1, 129, 128.8,

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128.8, 128.4, 127.1, 126.1, 117, 116.5, 21.3; HRMS (ESI): calcd. for $C_{24}H_{19}ClN$ $[M+H]^+$, 356.1201; found: 356.1197.

2-(3-Methoxyphenyl)-6-(4-methoxyphenyl)-4-(4-methylphenyl) pyridine (7c): The title compound **7c** was obtained from 6-(4-methoxyphenyl)-4-(4-methylphenyl)pyridin-2-yl 4-methylbenzene sulfonate **6c** (1.0 mmol) as a white solid (0.210 g, 60% yield); mp 144–148 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.3 Hz, 2H), 7.70 (s, 3H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 7.9 Hz, 2H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.21 (d, *J* = 7.8 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.2 Hz, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.50, 159.00, 156.00, 155.97, 148.89, 140.30, 137.94, 135.15, 131.23, 128.75, 128.58, 127.35, 125.94, 118.50, 115.34, 115.18, 113.48, 113.01, 111.71, 54.34, 54.30, 20.19; HRMS (ESI): calcd. for $C_{26}H_{24}NO_2$ $[M+H]^+$, 382.1802; found: 382.1799.

2,6-Bis(benzo[*d*][1,3]dioxol-5-yl)-4-phenylpyridine (7d): The title compound **7d** was obtained from 6-(benzo[*d*][1,3]dioxol-5-yl)-4-phenylpyridin-2-yl 4-methylbenzenesulfonate **6d** (1.0 mmol) as a white solid (79.9 mg, 60% yield); mp 142–146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (m, 4H), 7.73 (d, *J* = 1.5 Hz, 1H), 7.71–7.69 (m, 2H), 7.67 (d, *J* = 1.7 Hz, 1H), 7.54–7.52 (m, 2H), 7.49–7.46 (m, 1H), 6.93 (d, *J* = 8.1 Hz, 2H), 6.04 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.7, 150.1, 148.5, 148.2, 139.1, 134.0, 129.1, 128.9, 127.1, 121.0, 116.1, 108.3, 107.6, 101.3; HRMS (ESI): calcd. for $C_{25}H_{18}NO_4$ $[M+H]^+$, 396.1231; found: 396.1230.

2,6-Diphenyl-4-(3,4,5-trimethoxyphenyl)pyridine (7e): The title compound **7e** was obtained from 6-phenyl-4-(3,4,5-trimethoxyphenyl)pyridin-2-yl 4-methylbenzenesulfonate **6e** (1.0 mmol) as a white solid (53.5 mg, 55% yield); mp 108–109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 1.4 Hz, 2H), 8.11 (d, *J* = 1.3 Hz, 2H), 7.74 (s, 2H), 7.48–7.41 (m, 4H), 7.39 (m, 1H), 7.36 (d, *J* = 7.3 Hz, 1H), 6.83 (s, 2H), 3.89 (s, 6H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 152.7, 149.4, 138.5, 138.0, 133.9, 128.0, 127.6, 126.1, 116.0, 103.6, 59.9, 55.3; HRMS (ESI): calcd. for $C_{27}H_{24}NO_3$ $[M+H]^+$, 398.1751; found: 398.1751.

2-(Benzo[d][1,3]dioxol-5-yl)-6-phenyl-4-(3,4,5-trimethoxy phenyl)pyridine (7f): The title compound **7f** was obtained from 6-(4-methoxyphenyl)-4-(3,4,5-trimethoxyphenyl)pyridin-2-yl 4-methyl benzenesulfonate **6e** (1.0 mmol) as a white solid (45.1 mg, 50% yield); mp 149–151 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.2 Hz, 2H), 7.68 (s, 2H), 7.63 (s, 1H), 7.60 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.42 (m, 2H), 7.36 (d, *J* = 7.9 Hz, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 6.80 (s, 2H), 5.94 (s, 2H), 3.87 (s, 6H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 156.9, 153.8, 150.4, 148.5, 148.2, 139.5, 135.0, 134.0, 129.0, 128.7, 127.1, 121.1, 116.7, 116.4, 108.3, 107.6, 104.6, 101.3, 61.0, 56.4; HRMS (ESI): calcd. for $C_{27}H_{24}NO_5$ $[M+H]^+$, 442.1649; found: 442.1651.

2,6-Bis(4-methoxyphenyl)-4-(3,4,5-trimethoxyphenyl)pyridine (7g): The title compound **7g** was obtained from 6-(4-methoxyphenyl)-4-(3,4,5-trimethoxyphenyl)pyridin-2-yl 4-methyl benzenesulfonate **6f** (1.0 mmol) as a liquid (23.7 mg, 50% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.8 Hz, 4H), 7.61 (s, 2H), 6.94 (d, *J* = 8.8 Hz, 4H), 6.80 (s, 2H), 3.87 (s, 6H), 3.84 (s, 3H), 3.78 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 155.9, 152.7, 149.3, 137.9, 134.2, 131.1, 127.4, 114.7, 113.0, 103.5, 59.9, 55.3, 54.3; HRMS (ESI): calcd. for $C_{28}H_{28}NO_5$ $[M+H]^+$, 458.1962; found: 458.1959.

4-(4-(Furan-2-yl)-6-phenylpyridin-2-yl)benzonitrile (7h): The title compound **7h** was obtained from 4-(furan-2-yl)-6-phenylpyridin-2-yl 4-methylbenzenesulfonate **6g** (1.0 mmol) as a white solid (48.2 mg, 65% yield); mp 154–156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.4 Hz, 2H), 8.04 (d, *J* = 7.0 Hz, 2H), 7.83 (d, *J* = 0.9 Hz, 1H), 7.78 (d, *J* = 0.9 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 1.2 Hz, 1H), 7.42–7.37 (m, 3H), 6.87 (d, *J* = 3.3 Hz, 1H), 6.48 (dd, *J* = 3.4, 1.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8, 155.1, 151.4, 143.9, 143.4, 139.3, 138.8, 132.4, 129.4, 128.8, 127.5, 127.0, 118.9, 113.9, 113.3, 112.4, 112.3, 109.0; HRMS (ESI): calcd. for $C_{22}H_{15}N_2O$ $[M+H]^+$, 323.1179; found: 323.1175.

4,6-Di(thiophen-2-yl)-2,3'-bipyridine (7i): The title compound **7i** was obtained from 4,6-di(thiophen-2-yl)pyridin-2-yl 4-methyl benzenesulfonate **6h** (1.0 mmol) as a white solid (31.5 mg, 58% yield); mp 164–167 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.34 (s, 1H), 8.69 (d, *J* = 3.6 Hz, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 7.81 (s, 1H), 7.80 (d, *J* = 1.2 Hz, 1H), 7.73 (d, *J* = 4.5 Hz, 1H), 7.62 (s, 1H), 7.46 (dd, *J* = 8.7, 6.0 Hz, 2H), 7.21–7.10 (m, 2H), 6.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 153.3, 150.0, 148.2, 145.7, 144.7, 143.3, 134.5, 128.5, 128.1, 128.0, 127.3, 125.6, 125.0, 123.6, 120.2, 114.9, 114.1; HRMS (ESI): calcd. for $C_{18}H_{13}N_2S_2$ $[M+H]^+$, 321.0515; found: 321.0512.

Acknowledgements

R. K., P. K., A. G., G. R. and A. K. J. thank to UGC, CSIR, DST - New Delhi, India for their research fellowships.

Notes and references

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†Electronic Supplementary Information (ESI) available: spectroscopic data ^{1}H and ^{13}C NMR spectra for all compounds and X-ray data of compounds *viz.* **2a**, **2c**, **2e**, **2j**, **4** and **7e**. See DOI: 10.1039/c000000x/

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