JOC The Journal of Organic Chemistry

Article

A Metal-and Solvent-Free Approach to Diversely Substituted Picolinates via Domino Reaction of Cyclic Sulfamidate Imines with #,#-Unsaturated #-Ketocarbonyls

Soumen Biswas, Debashis Majee, Soumitra Guin, and Sampak Samanta

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b01792 • Publication Date (Web): 21 Sep 2017

Just Accepted

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

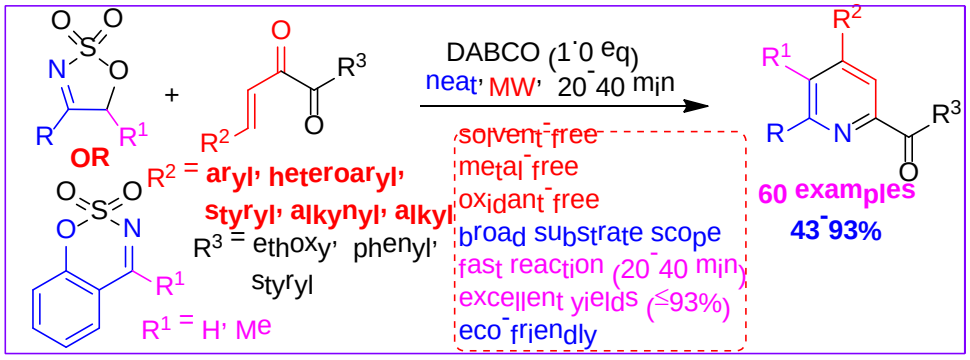
A Metal-and Solvent-Free Approach to Diversely Substituted Picolinates via Domino Reaction of Cyclic Sulfamidate Imines with β,γ-Unsaturated α-Ketocarbonyls

*Soumen Biswas, Debashis Majee, Soumitra Guin and Sampak Samanta**

Discipline of Chemistry, Indian Institute of Technology Indore, Simrol, Indore, 453552, Madhya Pradesh, India.

*Corresponding author. Tel +91-731-2438753

Email: sampaks@iiti.ac.in



ABSTRACT: An efficient, solvent-free and eco-friendly domino reaction of 5/6-membered cyclic sulfamidate imines with a variety of β,γ-unsaturated α-ketocarbonyls in a neat condition under MW irradiation promoted by DABCO as a solid organobase has been developed for the rapid construction of a novel class of densely functionalized picolinates. This interesting metal-solvent-free tactic allows allows a wide range of useful functionalities on the aryl rings and delivers good to excellent yields of the aforesaid aza-heterocycles within short span of times (20-

40 min). A biologically promising imidazo[1,2-*a*]pyridine was successfully synthesized through our unique procedure.

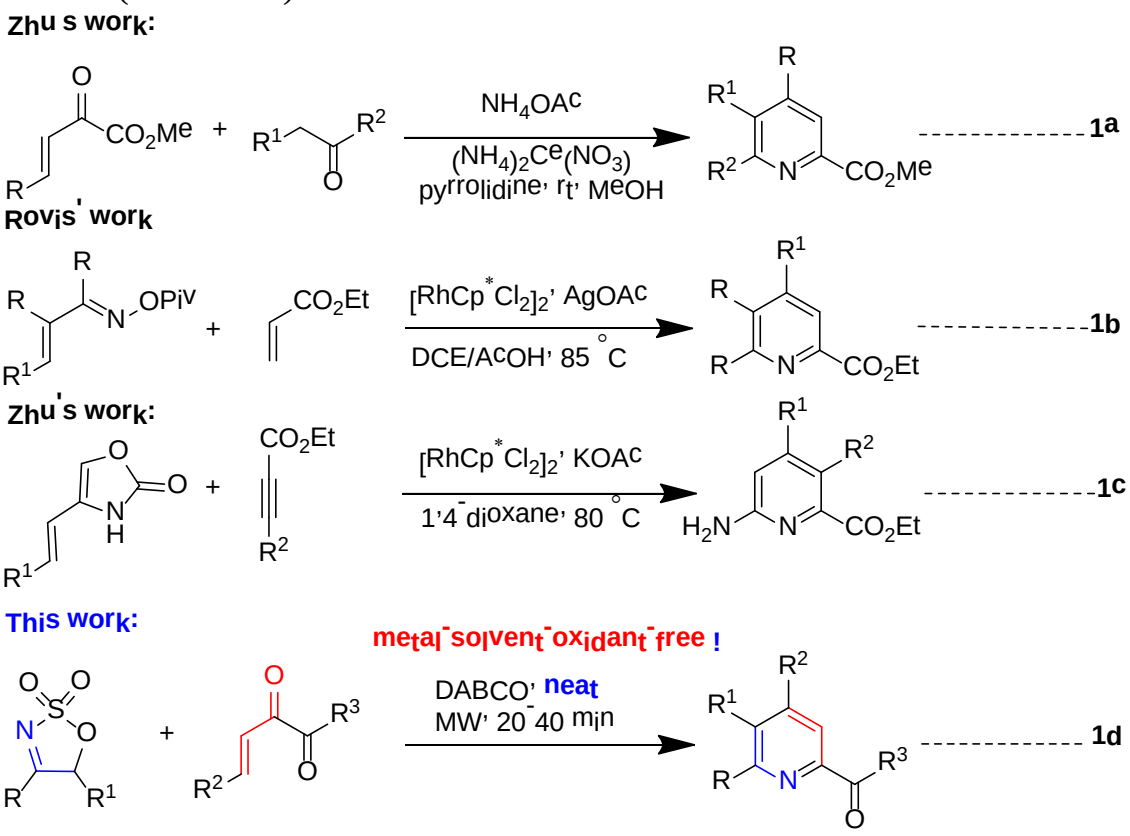
KEYWORDS: Cyclic sulfamidate imine, β,γ-unsaturated α-ketocarbonyl, functionalized pyridines, microwave-assisted synthesis, neat condition, metal-free, green method.

The pyridine rings represent one of the most fascinating classes of aza-heterocyclic molecules which are commonly encountered in numerous biologically active natural products[1], top-selling marketable drugs[2,] active pharmaceuticals,[3] advanced functional materials,[4] agrochemicals,[5] metal complexes[6] and catalysts[7]. Furthermore, this most studied aza-heterocyclic ring is also an essential subunit of vitamins[8] (B_6 and B_3) and enzymes[9] in our body which regulates many therapeutic responses. Therefore, the design and development of a new, efficient, green and metal-free based new protocol for the synthesis of interesting functionalized pyridines remains a pivotal research area in synthetic and medicinal chemistry. In this context, several traditional and modern protocols have been documented for the access to functionalized pyridine scaffolds since the inception of pyridine synthesis which include condensation reaction involving ammonia/amines and 1,5-dicarbonyls/alkylaldehydes (Chichibabin method),[10] tandem reaction of enamines (in situ generated enamines) with enones/ynones (Tsuda/Bohlmann–Rahtz methods),[11] pseudo four-component reaction between aldehydes and β-keto esters in the presence ammonia (Hantzsch pyridine synthesis)[12], multicomponent reaction,[13] 6π-aza-electrocylization[14] etc. Lately, transition-metal catalyzed [4+2][15]/[2+2+2][16] cycloaddition reactions of α,β-unsaturated oximes/nitriles/enamides with alkynes have emerged as powerful methods for the construction of unsymmetrical pyridine scaffolds.

Very recently, an alternative, atom-economical route to direct functionalization on pyridine ring has also been developed through a C-H bond activation catalyzed by several transition-metal-salts[17]. In spite of remarkable development in the synthesis of pyridines, the efficient metal-free access to versatile substituted picolinates has been underdeveloped[18] even though they have proven biological and pharmaceutical significance.[1a-c] Towards the synthesis of picolinates, Zhu's research group has nicely documented a three-component approach to picolinate derivatives from β,γ-unsaturated α-ketoesters, enolizable ketones and ammonium acetate promoted by CAN/pyrrolidine (Scheme **1a**)[18a]. Moreover, Rovis and his coworkers have discovered an elegant method for the regioselective synthesis of picolinates through a [4+2] cycloaddition reaction of α,β-unsaturated oxime esters with acrylates at 85 °C in the presence of Rh-salt/AgOAc as combined catalytic system (Scheme **1b**)[18b]. Furthermore, Rh-(III)-catalyzed oxadiazolone-directed alkenyl C-H coupling with β-alkynyl esters was reported by Zhu et al. (Scheme **1c**).[18d] Nevertheless, the above procedures are associated with certain drawbacks like poor yields due to multiple side products, drastic reaction conditions, use of expensive and precious metal-salts, limited substrate scope etc. On the other hand, our group also disclosed a DABCO-promoted one-pot synthesis of 2,6-diarylpicolinates in THF involving cyclic sulfamidate imines as important synthetic precursors.[19] However, this method shows varying degrees of achievements as well as limitations such as prolonged reaction times, use of a toxic and hazardous organic solvent (THF) as well as excess amount of a base, applicable for only aryl-substituents. Thus, an alternative, general, solvent-free and environmentally sustainable procedure is urgently required for

the quick synthesis of picolinate derivatives with multiple substitutions including alkyl group on the pyridine rings.

As part of our ongoing research in the development of metal-free based new synthetic techniques for the construction of pyridine derivatives,[20] here in, we further report a unique, green method for the straightforward access to diversely functionalized pyridine derivatives through a domino Michael-elimination-cyclization reaction between several 5/6-membered cyclic sulfamidate imines and a variety of γ-substituted-β,γ-unsaturated α-ketocarbonyls in a neat condition irradiated by microwave using 1.0 equiv. of DABCO as an organic base (Scheme **1d**).



Scheme 1: Different protocols for the synthesis of picolinates

By taking 4-phenyl-5*H*-1,2,3-oxathiazole-2,2-dioxide (**1a**) as a suitable nucleophile[21] and (*E*)-ethyl 2-oxo-4-phenylbut-3-enoate (**2a**) as model reactants, the initial reaction was

performed in THF at room temperature in the presence of DABCO (0.5 equiv, entry 1, Table 1). Interestingly, after 24h, 32% yield of expected 4,6-diphenylpicolinate (**3aa**) was isolated in a pure form. This fascinating result motivated us to examine this domino reaction in detail. Upon increasing the reaction temperature to 70 °C, after 5h, the compound **3aa** was afforded 59% yield (entry 2). Furthermore, by using 1.0 equiv of

Table 1. Optimization Reaction Conditions.[a]

entry	base	solvent	temp (°C)	time	yield (%)[b]
1[c]	DABCO	THF	rt	24h	36
2[c]	DABCO	THF	70	5h	59
3[d]	DABCO	THF	70	5h	81
4[e]	DABCO	THF	70	5h	83
5	DABCO	neat	70	2h	85
6	DABCO	neat	MW	20 min	91
7	DBU	neat	MW	20 min	32
8	DIPEA	neat	MW	20 min	28
9	DMAP	neat	MW	20 min	55
10	Et_3N	neat	MW	20 min	36

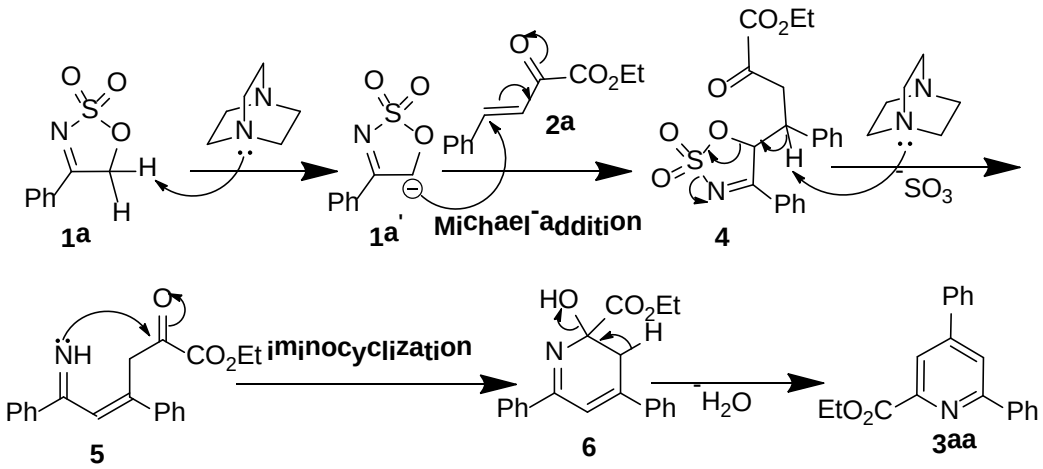
[a]Unless otherwise noted, all of the reactions were performed with **1a** (0.2 mmol), **2a** (0.22 mmol), and DABCO (0.2 mmol, 1.0 equiv) in a neat condition under microwave (MW)

irradiation at 70 °C in an open atmosphere. [b] Isolated yield after column chromatography. [c] 0.5 equiv DABCO was used in THF (0.5 mL). [d]1.0 equivalent of DABCO. [e]2.0 equivalent of DABCO.

DABCO at 70 °C, the yield of **3aa** was dramatically improved from 59% to 81% after 5h (entry 3). However, no noticeable enhancement of yield (83%) of **3aa** was observed when the loading of DABCO was increased from 1.0 equiv. to 2.0 equiv. In order to make this procedure more economical, practical and eco-friendly, we performed this domino reaction in a neat condition under Microwave irradiation at 70 °C. Intriguingly, excellent results were obtained in terms of yield 91% (**3aa**) and reaction time (20 min). Whereas, by conventional heating at 70 °C, this domino reaction furnished a little lower yield (85%) of **3aa** with longer reaction time (2h, entry 5) in comparison to MW irradiation. Moreover, the role of other organic bases like DBU, DIPEA, DMAP and triethylamine on this domino reaction was also examined under MW irradiation. But all the bases were appeared to be less effective as compared to DABCO, providing yields within the range of 28 % to 55% (entries 7-10).

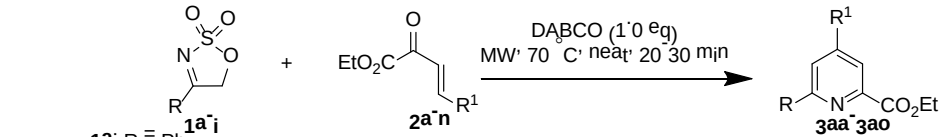
In keeping view of the above results, a reasonable reaction mechanism has been proposed for the formation of **3aa** as depicted in Scheme 2. At the onset, DABCO may abstract a methylene proton of cyclic sulfamidate imine to form a carbanion intermediate **1a'**. Afterwards, the Michael addition reaction takes place between carbanion intermediate **1a'** and β,γ-unsaturated α-ketoester (**2a**) to generate the Michael adduct **4** which is subsequently underwent elimination of SO_3 under the influence of base, leading to a very reactive intermediate **5.** The latter in turn converts into intermediate **6** via an iminocyclization, followed by dehydration which leads to the final product **3aa**.

Scheme 2. Probable Mechanism for the Formation of Picolinate 3aa



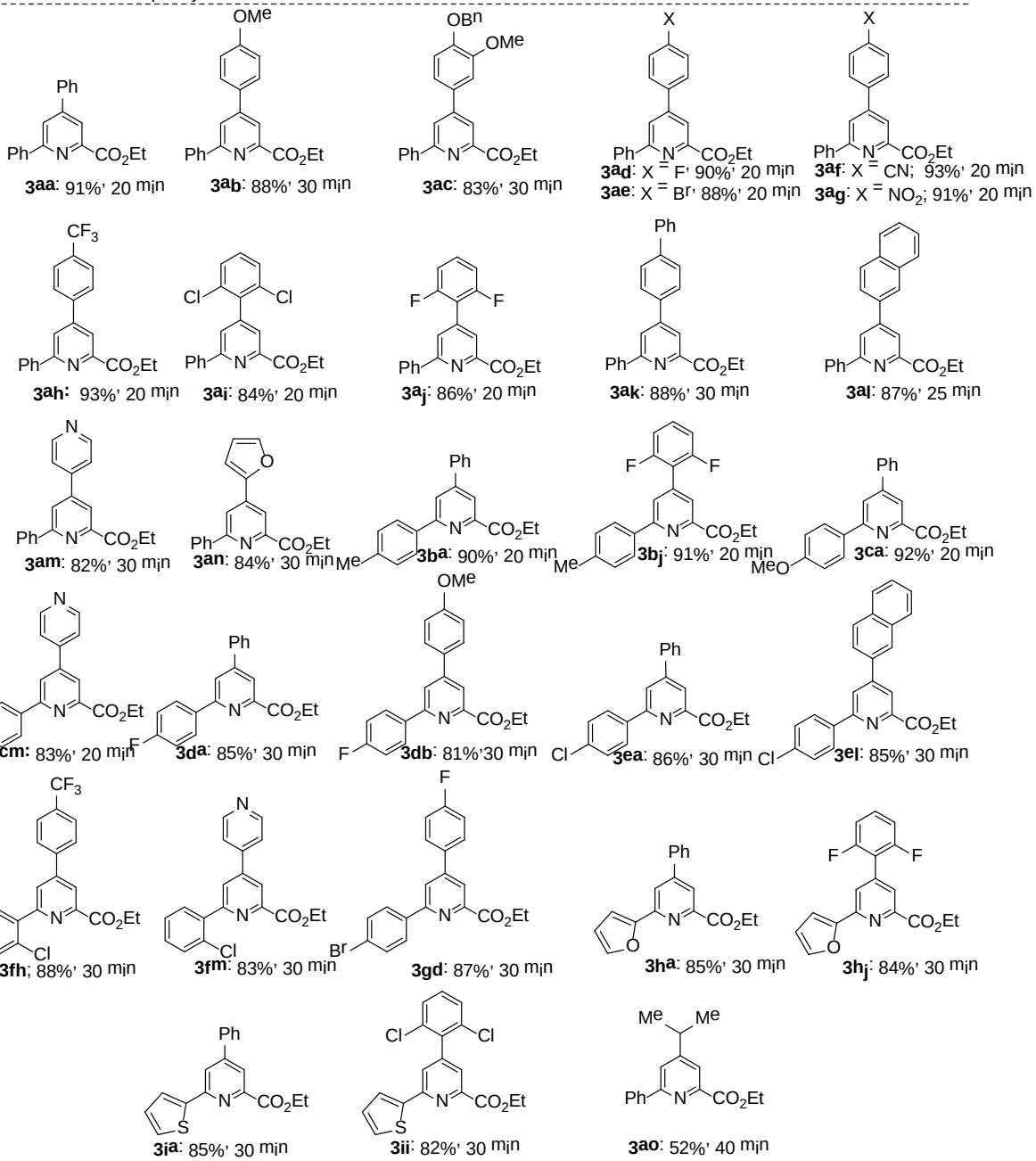
Having optimal reaction parameters in hand, we explored the generality and scope of this solvent-free microwave-assisted domino reaction by involving numerous 4-aryl/heteroaryl-substituted cyclic sulfamidate imines and γ-aryl/heteroaryl/alkyl-substituted β,γ-unsaturated α-ketoesters in our optimal conditions to access a wide range of substituted picolinate derivatives. The obtained results are systematically arranged in Table 2. Not only phenyl but also aryl-substituted-β,γ-unsaturated α-ketoesters (**2b**-**2h**) bearing either electron-donating (OMe, OBn) or electron-withdrawing (F, Cl, Br, CF_3, CN, NO_2) substituents on the aryl rings underwent a clean reaction with **1a** under the present conditions to provide corresponding 4,6-diarylpicolinates (**3ab**-**3ah**) in high to excellent yields (83-93%) within 20-30 min. Pleasantly, attaching with bulky aryl-substituents such as 2,6-dichlorophenyl (**2i**), 2,6-difluorophenyl (**2j**), biphenyl **(2k**) and 2-naphthyl (**2l**) at the γ-position of β,γ-unsaturated α-ketoesters did not make any difficulty in the reaction with cyclic imine **1a** to afford very high yields (84-88%) of the corresponding picolinates (**3ai**-**3al**). Moreover, by using heteroaryl-substituted

Table 2. Substrate Scope of 4,6-Disubstitutedpicolinate Synthesis (3aa-3ao)



1a: R = Ph
1b: R = 4-MeC$_6$H$_4$
1c: R = 4-MeOC$_6$H$_4$
1d: R = 4-FC$_6$H$_4$
1e: R = 4-ClC$_6$H$_4$
1f: R = 2-ClC$_6$H$_4$
1g: R = 4-BrC$_6$H$_4$
1h: R = 2-furyl
1i: R = 2-thiophenyl

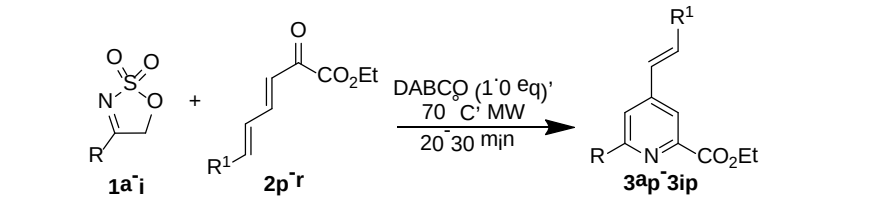
2a: R^1 = Ph, **2b**: R^1 = 4-MeOC$_6$H$_4$
2c: R^1 = 3-MeO-4-BnOC$_6$H$_3$, **2d**: R^1 = 4-FC$_6$H$_4$
2e: R^1 = 4-BrC$_6$H$_4$, **2f**: R^1 = 4-NCC$_6$H$_4$
2g: R^1 = R^1 = 4-O$_2$NC$_6$H$_4$, **2h**: R^1 = 4-CF$_3$C$_6$H$_4$
2i: R^1 = 2,6-Cl$_2$C$_6$H$_3$, **2j**: 2,6-F$_2$C$_6$H$_3$, **2k**: R^1 = 4-Ph-C$_6$H$_4$,
2l: R^1 = 2-naphthyl, **2m**: R^1 = 4-pyridyl, **2n**: R^1 = 2-furyl
2o: R^1 = (Me)$_2$CH

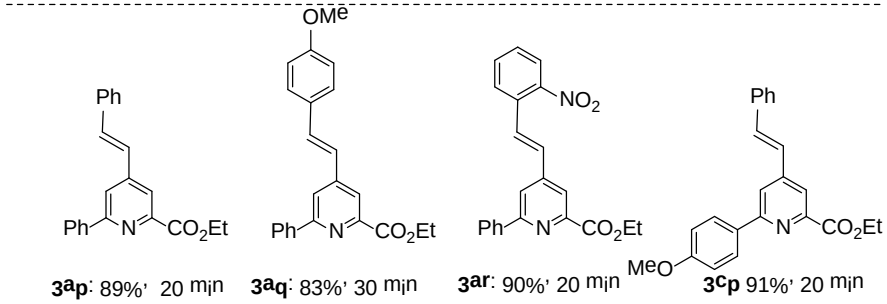


(pyridyl and furyl) β,γ-unsaturated α-ketoesters (**2m-2n**), the domino reaction responded elegantly in this imposed conditions and resulted in 82% yield of bipyridyl derivative **3am** and 84% yield of 4-furylpicolinate **3an**. Next, the effect of substitutions on the aryl rings of cyclic sulfamidate imines was also taken under investigation. For instance, cyclic sulfamidate imines (**1d-1g**) having halide atoms (F, Cl, Br) on the aryl rings slightly diminished their reactivities towards β,γ-unsaturated α-ketoesters as compared to cyclic sulfamidate imines (**1b-c**) bearing electron donating ones (Me, MeO). However, all the cases led to high yields (81-92%) of the corresponding products (**3ba-3gd**). Gratifyingly, heteroaryl-substituted cyclic imines **1h** and **1i** also afforded the corresponding products **3ha, 3hj, 3ia,** and **3ii** in 85%, 84%, 85%, and 82% chemical yields respectively. Interestingly, by this procedure, γ-alkyl-substituted-βγ-unsaturated α-ketoester (**2o**) also reacted with **1a** to afford 4-alkylatedpicolinate **3ao** in 52% yield after 40 min. Importantly, a range of functionalities such as MeO, OBn, F, Cl, Br, CN, NO_2, CF_3, CO_2Et, furan, thiophene, pyridine etc. have been retained under this MW irradiation conditions.

In order to further investigate the possible substrate scope, the chemically challenging Michael acceptors like γ-styryl-substituted α-ketoesters (**2p-2r**) were subjected to the coupling reaction with several 4-aryl/hetero-substituted cyclic imines (**1a-i**). Gratifyingly, under the MW irradiation, cyclic amines attacked only at the γ-position of β,γ-unsaturated α-ketoesters. Consequently, all of the cyclization reactions delivered consistently high to excellent yields (83-91%) of the corresponding 4-(*E*)-styryl-substituted picolinates (**3ap-3ip**) after 20-30 min (Table 3).

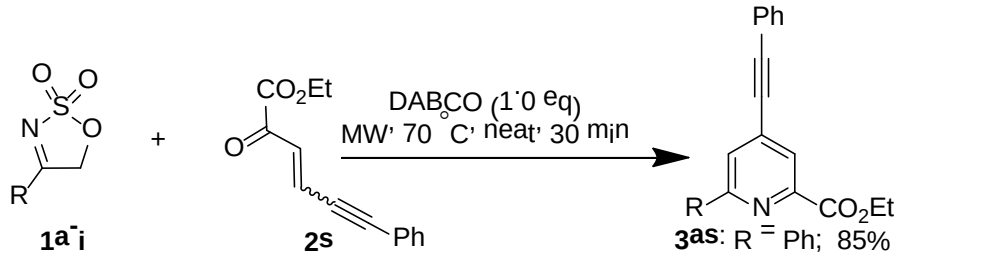
Table 3. Synthesis of (*E*)-6-Aryl-4-Styryl-Substituted Picolinates (3ap-3ip)





After successfully synthesizing styryl-substituted picolinate derivatives, we envisioned that the synthesis of alkynyl-substituted picolinates under metal-free conditions may be achieved by using γ-alkynyl α-ketoester as an appropriate Michael acceptor which is traditionally followed through the Sonagashira cross-coupling reaction.[22] In this line,

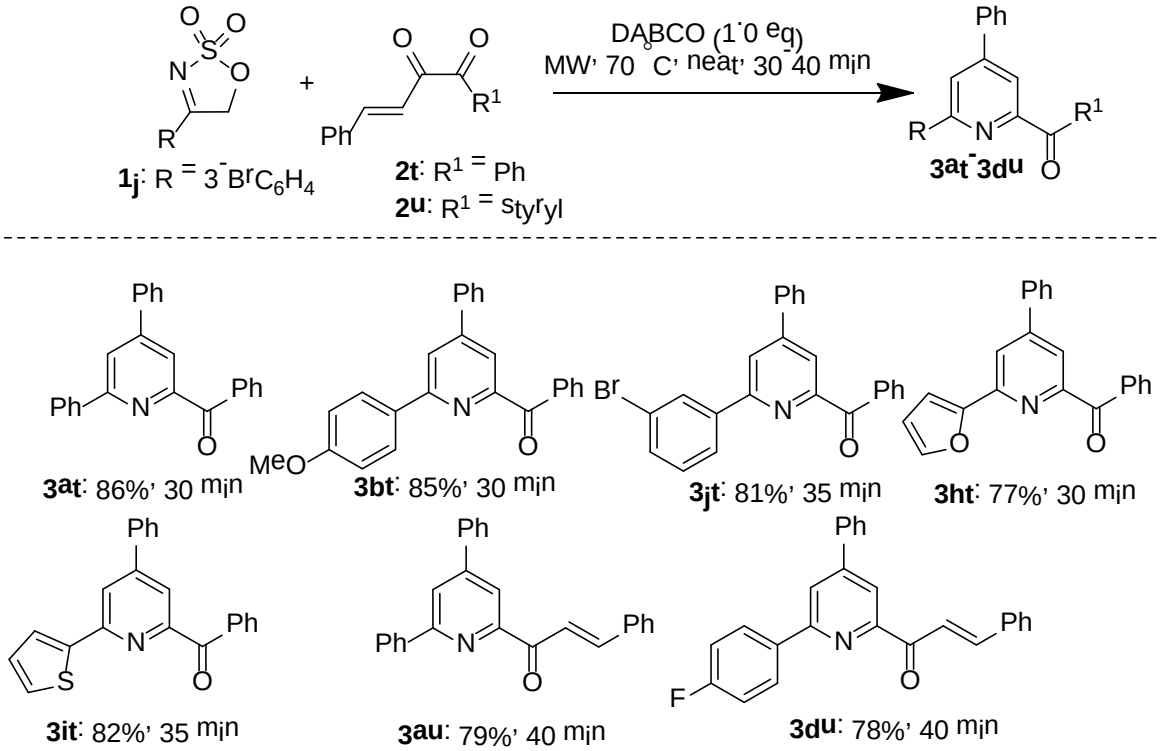
Scheme 3. Synthesis of 4-Phenylacetylenyl Picolinate Derivatives (3as-3is)



γ-phenylacetylenyl-β,γ-unsaturated α-ketoester (**2s**) as was allowed to react with several 4-aryl/heteroaryl-substituted cyclic imines (**1a-b, 1e,** and **1h-i**) under MW irradiation in the presence of DABCO. Notably, all of the domino reactions took place exclusively at the γ-position of β,γ-unsaturated α-ketoesters by this method which led to a range of anticipated 6-aryl/furyl/thiophenyl-4-phenylacetylenylpicolinates (**3as**-**3is**) in high yields (80-86%, Scheme 3).

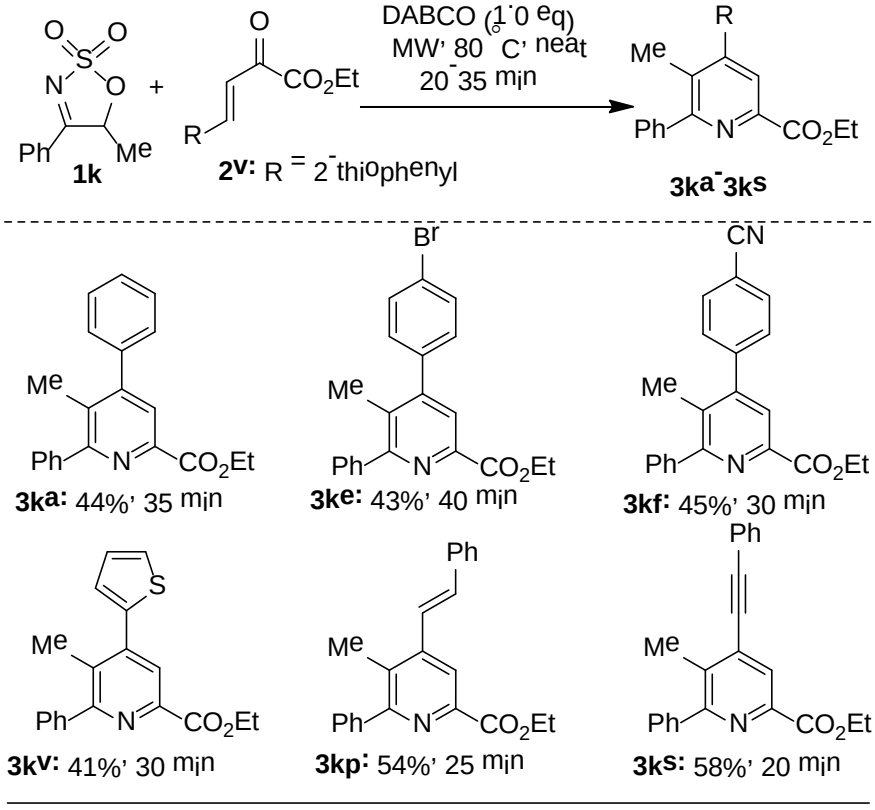
Furthermore, replacing β,γ-unsaturated α-ketoesters by other interesting Michael acceptors namely β,γ-unsaturated α-ketobenzoyl (**2t**) and cinnamil (**2u**), they participated efficiently in the reaction with several 4-aryl/heteroaryl-substituted cyclic imines by our metal-free conditions. To our great pleasure, after 30-40 min, an interesting class of trisubstituted pyridines (**3at**-**3du**) having a benzoyl or cinnamoyl group at C-2 position were obtained in promising yields 77-86% as shown in Table 4.

Table 4. Synthesis of 4,6-Diaryl-2-Benzoyl/Cinnamoylpyridine Scaffolds (3at-3du)



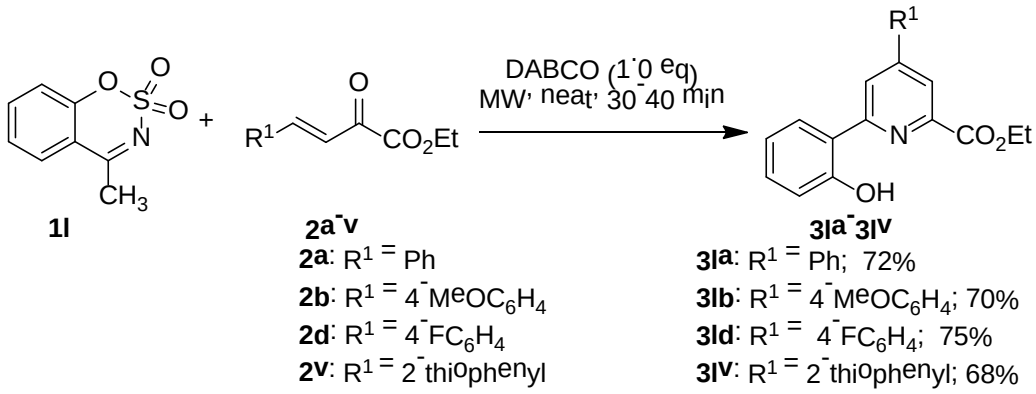
Next, our motivation towards the metal-free access to synthetically challenging alkyl-substituted picolinate derivatives has been successfully addressed by performing the reaction of 5-methyl-4-phenyl cyclic sulfamidate imine (**1k**) with several aryl/hetero-aryl/alkyenyl/alkynyl-substituted α-ketoesters (**1a** and **1b**), furnishing acceptable yields (41-58%, Table 5) of the corresponding tetrasubstituted pyridines having alkyl, alkenyl and alkynyl groups on the pyridine rings. Therefore, the current methodology was not restricted only for the synthesis of aryl-substituted pyridines but it could be also fairly applicable for the access to non-arylated pyridine derivatives.

Table 5. Synthesis of 5-Methyl-4,6-Disubstituted Picolinates (3ka-3ks)



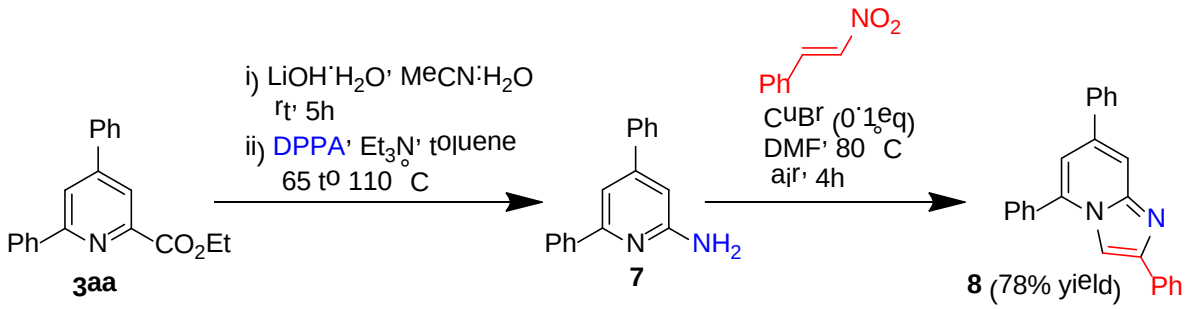
For the further exploration of the designed methodology, we inspired to use a 4-alkyl-benzo[*e*][1,2,3]oxathiazine 2,2-dioxide (**1l**) instead of a 5-membered cyclic imine as a nucleophile for the first time, while reacting with a number of β,γ-unsaturated α-ketoesters (**2a-v**) under MW irradiation at 80 °C. To our immense surprise, after 30-40 min, all of the reactions produced a fascinating class of several 6-(2-hydroxyphenyl)-4-arylpicolinates **3la, 3lb, 3ld,** and **3lv** in 72%, 70%, 75% and 68% yields respectively (Scheme 4).

Scheme 4. Synthesis of 2-Hydroxyphenyl Substituted Picolinates (3la-3lv)



Next, we have demonstrated the potential synthetic utility of synthesized picolinate derivative, the picolinate **3aa** was successfully converted into a synthetically useful 4,6-diphenyl-2-aminopyridine in 72% yield by two-step procedures. After that, the resultant

Scheme 5. Synthesis of Imidazo[1,2-*a*]pyridine Derivative (8)



2-aminopyridine derivative was subjected to the annulation reaction with β-nitrostyrene in the presence of 10 mol% of CuBr in DMF at 80 °C for 4h to provide a biologically as well as synthetically useful imidazo[1,2-*a*]pyridine derivative in 78% yield (Scheme 5).[23]

CONCLUSION

In this manuscript, we have developed first time a fast, general, expedient, environment-friendly and MW-assisted domino reaction of different types of 5/6-membered cyclic sulfamidate imines as useful Michael donors with a range of γ-aryl/heteroaryl/alkenyl/alkynyl/alkyl-substituted-β,γ-unsaturated α-ketocarbonyls in a neat condition promoted by DABCO. This unique Michael-elimination-cyclization (C-C and C-N bonds formation) process furnishes a series of pharmaceutically relevant tri-and tetra-substituted pyridines possessing a carboxylate, benzoyl or cinnamoyl group at C-2 position in high to excellent yields under metal-free conditions. Moreover, our present method excludes the use of volatile organic solvents, expensive and toxic metal-salts, strong acids, large excess of additional oxidants, multistep etc. In addition, the operational simplicity, wider substrate scope, high to excellent yields, short reaction time, compatibility with a variety of functional groups on aryl rings and environment-friendly nature make this procedure a good alternative to the reported methods. Further efforts towards more substrates as well as their applications in medicinal chemistry are under progress which will be published in due course of time.

EXPERIMENTAL SECTION

General Information: All the cyclic sulfamidate imines (**1a-j**,[24a] **1k** [24b] and **1l** [24c])[24] and β, γ-unsaturated α-ketocarbonyls/cinnamil (**2a-v)**[25] were synthesized by known literature procedures.

All the catalysts were purchased from commercial sources. All the reactions were carried out either under air and monitored by TLC using Merck 60 F_{254} pre coated silica gel plates and the products were visualized by UV detection. Flash chromatography was carried out using silica gel (200-300 mesh). FT-IR spectra were recorded on a KBr plate. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer. Data for ^{1}H NMR are reported as a chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant *J* (Hz), integration, and assignment, data for ^{13}C are reported as a chemical shift. High resolutions mass spectral analyses (HRMS) were carried out using ESI-TOF-MS. Melting points were recorded on an Electro thermal melting points apparatus and are uncorrected. All the microwave irradiation reactions were carried out in a MILESTONE microwave oven apparatus (microwave labstation, power 1150W) under open atmosphere.

Representative Procedure for the Synthesis of Ethyl 4,6-Diphenylpicolinate (3aa):

A mixture of compound **1a** (39.4 mg, 0.2 mmol), **2a** (44.9 mg, 0.22 mmol) and DABCO (22.4 mg, 0.2 mmol) in a 5 mL round bottom flask was placed inside the micro oven under stirring (teflon-coated magnetic stir bar) condition. The reaction mixture was exposed to microwave irradiation (1150 W) in an open atmosphere at 70 °C (temperature was monitored at the external surface vessel using an in-built infrared sensor system) for 30 min. Upon completion of the reaction, the crude mass was directly purified without any workup by column chromatography over silica-gel using a mixture of EtOAc/hexane (1:4, v/v) to afford the desired product 4,6-diphenylpicolinate (**3aa**) as a white solid (91%, 55.0 mg).

All the synthesized products in Table 2- 5 and Scheme 3-4 were followed the above procedure. All the new products were characterized by their corresponding spectroscopic data (IR, ^{1}H, ^{13}C NMR and HRMS).

Ethyl 4,6-diphenylpicolinate (3aa):[19] yield 92% (55.0 mg).

Ethyl 4-(4-methoxyphenyl)-6-phenylpicolinate (3ab):[19] yield 88% (58.6 mg).

Ethyl 4-(4-(benzyloxy)-3-methoxyphenyl)-6-phenylpicolinate (3ac):[19] yield 83% (72.9 mg).

Ethyl 4-(4-fluorophenyl)-6-phenylpicolinate (3ad): [19] yield 90% (57.8 mg).

Ethyl 4-(4-bromophenyl)-6-phenylpicolinate (3ae): white solid; yield 88% (67.2 mg); mp 106-108 °C; R_f = 0.75 (EtOAc:hexane = 1:4); IR (KBr) ν 1715, 1605, 1545, 1493, 1434, 1372 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.10 (d, J = 6.8 Hz, 2H), 8.04 (s, 1H), 7.60-7.67 (m, 4H), 7.45-7.52 (m, 3H), 4.52 (q, J = 7.2 Hz, 2H), 1.48 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 158.5, 149.1, 149.0, 138.4, 136.6, 132.4, 129.5, 128.8, 128.6, 127.3 (2C), 121.1, 121.0, 62.0, 14.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{16}{}^{79}BrNO_2Na$ 404.0257; Found 404.0256; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{16}{}^{81}BrNO_2Na$ 406.0237; Found 406.0242.

Ethyl 4-(4-cyanophenyl)-6-phenylpicolinate (3af):[19] yield 93% (61.0 mg).

Ethyl 4-(4-nitrophenyl)-6-phenylpicolinate (3ag): light yellowish solid; yield 91% (63.4 mg); mp 114-116 °C; R_f = 0.50 (EtOAc:hexane = 1:4); IR (KBr) ν 1733, 1592, 1551, 1513, 1430, 1346 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 8.8 Hz, 2H), 8.28 (s, 1H), 8.09-8.13 (m, 3H), 7.90 (d, J = 8.8 Hz, 2H), 7.46-7.54 (m, 3H), 4.53 (q, J = 7.2 Hz, 2H), 1.49 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 158.7, 149.3, 148.3, 147.9, 143.9, 138.0, 129.8, 128.9, 128.2, 127.3, 124.4, 121.4, 121.3, 62.1, 14.3; HRMS (ESI-TOF) m/z: $C_{21}H_{16}N_2O_4[M+H]^+$ Calcd for 349.1183; Found 349.1181.

Ethyl 6-phenyl-4-(4-trifluoromethylpheny)picolinate (3ah): white solid; yield 93 % (69.0 mg); mp 93-95 °C; R_f = 0.68 (EtOAc:hexane = 1:4); IR (KBr) ν 1735, 1596, 1550, 1463, 1429,

1387 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 8.12 (d, J = 7.0 Hz, 2H), 8.08 (s, 1H), 7.78-7.86 (m, 4H), 7.47-7.53 (m, 3H), 4.53 (d, J = 7.2 Hz, 2H), 1.49 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 158.6, 149.2, 148.9, 141.3, 138.3, 131.4 (q, J_{C-F} = 32 Hz), 129.7, 128.9, 127.6, 127.3, 126.1 (q, J_{C-F} = 4.0 Hz), 125.2 (q, J_{C-F} = 270 Hz), 121.4 (2C), 62.0, 14.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{16}F_3NO_2Na$ 394.1025; Found 394.1028.

Ethyl 4-(2,6-dichlorophenyl)-6-phenylpicolinate (3ai): pale yellow solid; yield 84% (62.4 mg); mp 102-104 °C; R_f = 0.77 (EtOAc:hexane = 1:4); IR (KBr) ν 1735, 1600, 1551, 1463, 1427 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 7.6 Hz, 2H), 7.97 (s, 1H), 7.82 (s, 1H), 7.42-7.51 (m, 5H), 7.30-7.34 (m, 1H), 4.51 (q, J = 7.2 Hz, 2H), 1.47 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 158.0, 148.6, 146.6, 138.3, 136.5, 134.2, 130.2, 129.5, 128.8, 128.3, 127.3, 124.5, 124.4, 61.9, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{16}Cl_2NO_2$ 372.0553; Found 372.0543.

Ethyl 4-(2,6-difluorophenyl)-6-phenylpicolinate (3aj): white solid; yield 86% (58.3 mg); mp 90-92 °C; R_f = 0.78 (EtOAc:hexane = 1:4); IR (KBr) ν 1739, 1626, 1597, 1546, 1469, 1423 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.09 (d, J = 7.6 Hz, 2H), 7.99 (s, 1H), 7.38-7.52 (m, 4H), 7.05-7.09 (m, 2H), 4.51 (q, J = 7.2 Hz, 2H), 1.47 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 159.9 (d, J_{C-F} = 250 Hz), 157.9, 148.5, 130.7 (t, J_{C-F} = 10.0 Hz), 129.5, 128.8 , 127.3, 124.7 (d, J_{C-F} = 22.0 Hz), 115.5 (t, J_{C-F} = 18.0 Hz), 112.0, 111.9, 111.8, 61.9, 14.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{15}F_2O_2NNa$ 362.0962; Found 362.0963.

Ethyl 4-[4-(1,1'-biphenyl)]-6-phenylpicolinate (3ak): light yellowish solid; yield 88% (66.6 mg); mp 110-112 °C; R_f = 0.78 (EtOAc:hexane = 1:4); IR (KBr) ν 1712, 1600, 1537, 1431, 1372 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.13-8.15 (m, 3H), 7.83-7.85 (m, 2H), 7.75-7.77 (m, 2H), 7.66 (d, J = 7.6 Hz, 2H), 7.38-7.54 (m, 6H), 4.53 (q, J = 6.8 Hz, 2H), 1.50 (t, J =

6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 158.3, 149.8, 149.0, 142.3, 140.0, 138.6, 136.4, 129.4, 128.9, 128.8, 127.8 (2C), 127.5, 127.3, 127.0, 121.2, 121.1, 61.9, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{26}H_{22}NO_2$ 380.1645; Found 380.1652.

Ethyl 4-(2-naphthyl)-6-phenylpicolinate (3al): pale yellow solid; yield 87% (61.4 mg); mp 86-88 °C; R_f = 0.76 (EtOAc:hexane = 1:4); IR (KBr) ν 1708, 1598, 1546, 1429, 1375 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.23 (d, *J* = 6.0 Hz, 2H), 8.16 (d, *J* = 7.6 Hz, 2H), 7.84-8.01 (m, 4H), 7.45-7.58 (m, 5H), 4.54 (q, *J* = 7.2 Hz, 2H), 1.50 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 158.3, 150.2, 149.0, 138.6, 134.9, 133.5, 133.4, 129.4, 129.0, 128.8, 128.5, 127.7, 127.3, 127.0, 126.8, 126.7, 124.4, 121.6 (2C), 61.9, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{20}NO_2$ 354.1489; Found 354.1486.

Ethyl 4-(4-pyridyl)-6-phenylpicoline (3am): white solid; yield 82% (49.8 mg); mp 88-90 °C; R_f = 0.24 (EtOAc:hexane = 1:4); IR (KBr) ν 1719, 1594, 1537, 1457, 1427, 1372 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.82 (br s, 2H), 8.28 (s, 1H), 8.10-8.14 (m, 3H), 7.67 (br s, 2H), 7.47-54 (m, 3H), 4.53 (q, *J* = 6.8 Hz, 2H), 1.49 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 158.8, 149.4, 147.6, 145.2, 138.1, 129.8 , 128.9 (2C), 127.3 (2C), 121.2 (2C), 62.1, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{17}N_2O_2$ 305.1285; Found 305.1288.

Ethyl 4-(2-furyl)-6-phenylpicolinate (3an):[19] yield 84% (49.2 mg).

Ethyl 4-phenyl-6-(4-methylphenyl)picolinate (3ba):[19] yield 90% (57.1 mg).

Ethyl 4-(2,6-difluorophenyl)-6-(4-methylphenyl)picolinate (**3bj**): light yellow solid; yield 91% (64.3 mg); mp 93-95 °C; R_f = 0.78 (EtOAc:hexane = 1:4); IR (KBr) ν 1738, 1622, 1602, 1544, 1469, 1414, 1367 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.92 (d, *J* = 8.0 Hz, 2H), 7.89 (s, 1H), 7.30-7.35 (m, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.96-7.00 (m, 2H), 4.43 (q, *J* = 7.2 Hz, 2H), 2.34 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 159.9 (d, *J*

= 250 Hz), 157.9, 148.4, 139,6, 139.2, 135.5, 130.6 (t, J_{C-F} = 10 Hz), 129.5, 127.2, 124,5, 124.3, 115.6 (t, J_{C-F} = 19 Hz), 112.0 (dd, J_{12} = 6 Hz, J_{13} = 20 Hz), 61.8, 21.2, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{18}F_2O_2N$ 354.1300; Found 354.1308.

Ethyl 6-(4-methoxyphenyl)-4-phenylpicolinate (3ca): [19] yield 92% (61.3 mg).

Ethyl 4-(4-pyridyl)-6-(4-methoxyphenyl)picolinate (3cm): white solid; yield 83% (55.5 mg); mp 100-102 °C; R_f = 0.20 (EtOAc:hexane = 1:4); IR (KBr) ν 1714, 1590, 1535, 1479, 1431, 1374 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, J = 3.2 Hz, 2H), 8.21 (s, 1H), 8.09 (d, J = 8.4 Hz, 2H), 8.03 (s, 1H), 7.62 (d, J = 3.3 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 4.52 (q, J = 7.6 Hz, 2H), 3.88 (s, 3H), 1.48 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 161.1, 158.3, 150.7, 149.2, 147.4, 145.3, 130.6, 128.6, 121.5, 120.4, 120.3, 114.2 (2C), 62.0, 55.3, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{19}N_2O_3$ 335.1390; Found 335.1378.

Ethyl 6-(4-fluorophenyl)-4-phenylpicolinate (3da):[19] yield 85% (54.5 mg).

Ethyl 6-(4-fluorophenyl)-4-(4-methoxyphenyl)picolinate (3db): white solid; yield 81% (54.8 mg); mp 94-96 °C; R_f = 0.55 (EtOAc:hexane = 1:4); IR (KBr) ν 1712, 1604, 1546, 1511, 1433, 1369 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.08-8.12 (m, 2H), 7.99 (s, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.16-7.20 (t, J = 8.4 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 4.51 (q, J = 7.2 Hz, 2H), 3.88 (s, 3H), 1.48 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 163.8 (d, J_{C-F} = 252 Hz), 160.9, 157.2, 149.9, 148.9, 135.0, 129.8, 129.2, 129.1, 128.3, 120.6 (d, J_{C-F} = 46 Hz) 115.7 (d, J_{C-F} = 21 Hz), 114.7, 61.9, 55.4, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{19}FO_3N$ 352.1343; Found 352.1343.

Ethyl 6-(4-chlorophenyl)-4-phenylpicolinate (3ea): [19] yield 86% (58.0 mg).

Ethyl 6-(4-chlorophenyl)-4-(2-naphthyl)picolinate (3el): white solid; yield 85% (65.9 mg); mp 104-106 °C; R_f = 0.72 (EtOAc:hexane = 1:4); IR (KBr) ν 1708, 1598, 1546, 1493, 1438 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.22 (s, 1H), 8.18 (s, 1H), 8.11 (d, *J* = 8.8 2H), 7.90-8.01 (m, 3H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.56-7.58 (m, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 4.54 (q, *J* = 7.2 Hz, 2H), 1.50 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 157.0, 150.3, 149.0, 137.0, 135.6, 134.6, 133.5, 133.3, 129.1, 128.9, 128.5, 128.4, 127.7, 127.0, 126.8, 126.7, 124.3, 121.8, 121.2, 62.0, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{19}ClNO_2$ 388.1099; Found 388.1099.

Ethyl 6-(2-chlorophenyl)-4-(4-trifluoromethylphenyl)picolinate (3fh): [19] yield 88% (71.3 mg).

Ethyl 4-(4-pyridyl)-6-(2-chlorophenyl)picolinate (3fm): white solid; yield 83% (56.2 mg); mp 104-106 °C; R_f = 0.24 (EtOAc:hexane = 1:4); IR (KBr) ν 1714, 1589, 1535, 1479, 1431, 1373 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 2.0 Hz, 2H), 8.36 (s, 1H), 8.09 (s, 1H), 7.73 (d, *J* = 6.8 Hz, 1H), 7.63 (d, *J* = 2.4 Hz, 2H), 7.49-7.51 (m, 1H), 7.37-7.42 (m, 2 H), 4.53 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 157.9, 150.8, 149.4, 146.5, 144.7, 138.0, 132.1, 131.9, 130.2, 130.0, 127.2, 125.7, 121.4 (2 C), 62.1, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{16}ClN_2O_2$ 339.0895; Found 339.0878.

Ethyl 6-(4-bromophenyl)-4-(4-fluorophenyl)picolinate (3gd):[19] yield 87% (69.5 mg).

Ethyl 6-(2-furyl)-4-phenylpicolinate (3ha): light yellow solid; yield 85% (49.8 mg); mp 78-80 °C; R_f = 0.68 (EtOAc:hexane = 1:4); IR (KBr) ν 1706, 1609, 1547, 1493, 1446, 1407, 1382 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 8.07 (s, 1H), 7.75 (d, *J* = 7.2 Hz, 2H), 7.48-7.57 (m, 4H), 7.26 (s, 1H), 6.57 (s, 1H), 4.51 (q, *J* = 6.8 Hz, 2H), 1.47 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 165.3, 152.9, 150.2, 150.1, 148.9, 143.7, 137.3, 129.5, 129.1, 127.0, 121.0, 119.1, 112.2, 110.1, 61.9, 14.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{16}NO_3$ 294.1125; Found 294.1129.

Ethyl 4-(2,6-difluorophenyl)-6-(2-furyl)picolinate (3hj): light yellow solid; yield 84% (55.3 mg); mp 81-83 °C; R_f = 0.70 (EtOAc:hexane = 1:4); IR (KBr) ν 1740, 1622, 1468, 1367 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.96 (s, 1H), 7.56 (s, 1H), 7.37-7.44 (m, 1H), 7.27 (s, 1H), 7.04-7.09 (m, 2H), 6.57 (s, 1H), 4.50 (q, J = 6.8 Hz, 2H), 1.46 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 159.9 (d, J_{C-F} = 250.0 Hz), 152.6, 149.8, 148.5, 143.8, 139.3, 130.8 (t, J_{C-F} = 10.0 Hz), 124.3, 122.7, 115.3 (t, J_{C-F} = 20 Hz), 112.2, 112.0 (dd, J_1 = 6.0 Hz, J_2 = 19.0 Hz), 110.3, 61.9, 14.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{14}F_2NO_3$ 330.0936; Found 330.0933.

Ethyl 6-(2-thiophenyl)-4-phenylpicolinate (3ia): white solid; yield 85% (52.5 mg); mp 74-76 °C; R_f = 0.70 (EtOAc:hexane = 1:4); IR (KBr) ν 1709, 1597, 1544, 1443, 1371 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.97 (s, 1H), 7.71-7.75 (m, 3H), 7.44-7.55 (m, 4H), 7.13-7.15 (m, 1H), 4.50 (q, J = 7.2 Hz, 2H), 1.48 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 153.4, 150.4, 148.8, 143.9, 137.5, 129.5, 129.2, 128.3, 128.0, 127.0, 125.6, 121.3, 119.7, 61.9, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{16}O_2NS$ 310.0896; Found 310.0898.

Ethyl 4-(2,6-dichlorophenyl)-6-(2-thiophenyl)picolinate (3ii): white solid; yield 83% (61.8 mg); mp 82-84 °C; R_f = 0.70 (EtOAc:hexane = 1:4); IR (KBr) ν 1739, 1600, 1548, 1435 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.61-7.62 (m, 2H), 7.37-7.40 (m, 2H), 7.23-7.27 (m, 1H), 7.18 (s, 1H), 7.04-7.07 (m, 1H), 4.41 (q, J = 7.2 Hz, 2H), 1.39 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 153.2, 148.5, 146.6, 143.7, 136.3, 134.1, 130.3, 128.5, 128.3, 128.1,

125.9, 124.1, 122.8, 61.9, 14.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{14}Cl_2NO_2S$ 378.0117; Found 378.0108.

(*E*)-Ethyl 4-isopropyl-6-phenylpicolinate (3ao): gummy liquid; yield 52% (28.0 mg), R_f = 0.78 (EtOAc:hexane = 1:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 2H), 7.92 (s, 1H), 7.73 (s, 1H), 7.42-7.49 (m, 3H), 4.48 (q, J = 7.2 Hz, 2H), 3.00-3.07 (m, 1H), 1.46 (t, J = 7.2 Hz, 3H), 1.33 (d, J = 3.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 159.5, 157.8, 148.4, 138.9, 129.2, 128.7, 127.3, 121.9, 121.8, 61.8, 33.9, 23.1, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{20}NO_2$: 270.1489; Found 270.1485.

(*E*)-Ethyl 6-phenyl-4-styrylpicolinate (3ap):[19] Yield 89% (58.6 mg).

(*E*)-Ethyl 4-(4-methoxystyryl)-6-phenylpicolinate (3aq): light yellow solid; yield 83% (59.6 mg); mp 70-72 °C; R_f = 0.52 (EtOAc:hexane = 1:4); IR (KBr) ν 1723, 1676, 1608, 1514, 1456, 1375 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 8.09 (d, J = 7.2 Hz, 2H), 7.88 (s, 1H), 7.38-7.53 (m, 6H), 7.00 (d, J = 16.4 Hz, 1H), 6.94 (d, J = 8.0 Hz, 2H), 4.51 (q, J = 7.2 Hz, 2H), 3.85 (s, 3H), 1.48 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 160.4, 158.2, 148.7, 147.0, 138.8, 133.7, 129.3, 128.8, 128.7, 128.5, 127.3, 123.2, 120.6, 120.1, 114.3, 61.9, 55.4, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{22}NO_3$ 360.1594; Found 360.1609.

(*E*)-Ethyl 4-(2-nitrostyryl)-6-phenylpicolinate (3ar): white solid; yield 90% (67.3 mg); mp 76-78 °C; R_f = 0.50 (EtOAc:hexane = 1:4); IR (KBr) ν 1711, 1600, 1515, 1435, 1345 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.04-8.11 (m, 3H), 7.91-7.76 (m, 2H), 7.76-7.79 (m, 1H), 7.66-7.69 (m, 1H), 7.45-7.51 (m, 4H), 7.09 (d, 16.0 Hz, 1H), 4.52 (q, J = 7.2 Hz, 2H), 1.48 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 158.4, 149.0, 148.0, 145.6, 138.3, 133.5,

131.9, 130.5, 129.5, 129.3, 129.2, 128.8, 128.7, 127.2, 124.9, 120.8, 61.9, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{19}N_2O_4$ 375.1339; Found 375.1344.

(*E*)-Ethyl 6-(4-methoxyphenyl)-4-styrylpicolinate (3cp): white solid; yield 91% (65.4 mg); mp 78-80 °C; R_f = 0.53 (EtOAc:hexane = 1:4); IR (KBr) ν 1710, 1601, 1546, 1429, 1375 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05-8.01 (m, 3H), 7.84 (s, 1H), 7.56-7.58 (m, 2H), 7.34-7.45 (m, 4H), 7.12 (d, *J* = 16.4 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 2H), 4.50 (q, *J* = 6.4 Hz, 2H), 3.87 (s, 3H), 1.48 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 160.8, 157.9, 148.6, 146.2, 135.9, 133.9, 131.2, 128.9, 1288, 128.5, 127.1, 125.6, 120.1, 119.6, 114.1, 61.8, 55.3, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{22}NO_3$ 360.1594; Found 360.1594.

(*E*)-Ethyl 6-(4-fluorophenyl)-4-styrylpicolinate (3dp): light yellow solid; yield 83% (57.6 mg); mp 91-93 °C; R_f = 0.75 (EtOAc:hexane = 1:4); IR (KBr) ν 1714, 1601, 1549, 1510, 1437, 1370 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.09-8.11 (m, 2H), 7.86 (s, 1H), 7.58 (d, *J* = 7.0 Hz, 2H), 7.35-7.43 (m, 4H), 7.12-7.20 (m, 3H), 4.51 (q, *J* = 6.8 Hz, 2H), 1.48 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 163.8 (d, J_{C-F} = 250.0 Hz), 157.2, 148.8, 146.7, 135.8, 134.8, 134.2, 129.1, 129.0, 128.9, 127.1, 125.3, 120.4 (d, J_{C-F} = 46.0 Hz), 115.8, 115.6, 61.9, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{19}NO_2F$ 348.1394; Found 348.1391.

(*E*)-Ethyl 6-(4-bromophenyl)-4-styrylpicolinate (3gp):[19] yield 85% (69.4 mg).

(*E*)-Ethyl 6-(2-furyl)-4-styrylpicolinate (3hp): gummy liquid; yield 84% (53.6 mg); R_f = 0.67 (EtOAc:hexane = 1:4); IR (KBr) ν 1714, 1608, 1546, 1493, 1370 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.89 (s, 1H), 7.54-7.58 (m, 3H), 7.34-7.45 (m, 4H), 7.22 (s, 1H), 7.09 (d, *J* = 16.4 Hz, 1H), 6.55 (s, 1H), 4.50 (q, *J* = 6.8 Hz, 2H), 1.47 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 152.9, 150.1, 148.7, 146.5, 143.6, 135.8, 134.2, 129.0, 128.9, 127.1,

125.2, 120.0, 118.5, 112.2, 109.9, 62.0, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{18}NO_3$ 320.1281; Found 320.1276.

(*E*)-Ethyl 6-(2-thiophenyl)-4-styrylpicolinate (3ip): gummy liquid; yield 85% (57.0 mg); R_f = 0.70 (EtOAc:hexane = 1:4); IR (KBr) ν 1737, 1713, 1635, 1593, 1544, 1494, 1443, 1369 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.79 (s, 1H), 7.72 (d, *J* = 2.4 Hz, 1H), 7.57 (d, *J* = 7.2 Hz, 2H), 7.33-7.44 (m, 5H), 7.07-7.14 (m, 2H), 4.49 (q, *J* = 7.2 Hz, 2H), 1.48 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 153.3, 148.6, 146.5, 143.9, 135.8, 134.2, 129.0, 128.8, 128.1, 128.0, 127.1, 125.5, 125.1, 119.9, 119.2, 61.9, 14.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{17}NO_2SNa$ 358.0872; Found 358.0877.

Ethyl 6-phenyl-4-(phenylethynyl)picolinate (3as): white solid; yield 85% (55.6 mg); mp 98-100 °C; R_f = 0.75 (EtOAc:hexane = 1:4); IR (KBr) ν 1721, 1596, 1540, 1455, 1426, 1372 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01-8.05 (m, 3H), 7.91 (s, 1H), 7.50-7.52 (m, 2H), 7.38-7.44 (m, 3H), 7.32-7.36 (m, 3H), 4.43 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 157.9, 148.5, 137.9, 133.3, 131.9, 129.6, 129.4, 128.8, 128.5, 127.2, 125.1 (2C), 121.9, 94.7, 86.4, 61.9, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{18}NO_2$ 328.1332; Found 328.1334.

Ethyl 6-(4-methoxyphenyl)-4-(phenylethynyl)picolinate (3bs): light yellow solid; yield 80% (57.1 mg); mp 108-110 °C; R_f = 0.53 (EtOAc:hexane = 1:4); IR (KBr) ν 1736, 1599, 1513, 1370 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05-8.07 (m, 3H), 7.92 (s, 1H), 7.57-7.59 (m, 2H), 7.39-7.42 (m, 3H), 7.01 (d, *J* = 8.0 Hz, 2H), 4.49 (q, *J* = 7.2 Hz, 2H), 3.87 (s, 3H), 1.47 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 161.0, 157.4, 148.3, 133.0, 131.9, 130.5, 129.3,

128.5 (2C), 124.3, 124.2, 121.9, 114.1, 94.4, 86.5, 61.8, 55.3, 14.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{19}NO_3Na$ 380.1257; Found 380.1258.

Ethyl 6-(4-chlorophenyl)-4-(phenylethynyl)picolinate (3es): white solid; yield 86% (62.2 mg); mp 102-104 °C; R_f = 0.77 (EtOAc:hexane = 1:4); IR (KBr) ν 1714, 1595, 1534, 1490, 1419 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 8.02 (d, J = 8.0 Hz, 2H), 7.93 (s, 1H), 7.57-7.59 (m, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.37-7.41 (m, 3H), 4.48 (d, J = 6.8 Hz, 2H), 1.46 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 156.6, 148.6, 136.3, 135.9, 133.5, 131.9, 129.5, 129.0, 128.6, 128.5, 125.3, 124.8, 121.7, 95.0, 86.2, 62.0, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{17}ClNO_2$ 362.0942; Found 362.0966.

Ethyl 6-(2-furyl)-4-(phenylethynyl)picolinate (3hs): white solid; yield 82% (52.0 mg); mp 83-85 °C; R_f = 0.65 (EtOAc:hexane = 1:4); IR (KBr) ν 1712, 1606, 1542, 1511, 1435 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.93 (s, 1H), 7.55-7.58 (m, 3H), 7.40-7.43 (m, 3H), 7.23 (s, 1H), 6.56 (s, 1H), 4.48 (q, J = 7.2 Hz, 2H), 1.46 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 152.4, 149.8, 148.5, 143.9, 133.3, 131.9, 129.4, 128.5, 124.7, 123.0, 121.8, 112.2, 110.5, 94.9, 86.2, 62.0, 14.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{15}NO_3Na$ 340.0944; Found 340.0925.

Ethyl 6-(2-thiophenyl)-4-(phenylethynyl)picolinate (3is): white solid; yield 83% (55.3 mg); mp 90-92 °C; R_f = 0.72 (EtOAc:hexane = 1:4); IR (KBr) ν 1709, 1594, 1534, 1441, 1373 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.86 (s, 1H), 7.70 (s, 1H), 7.58-7.60 (m, 2H), 7.41-7.46 (m, 4H), 7.14 (s, 1H), 4.48 (q, J = 6.8 Hz, 2H), 1.47 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 153.0, 148.4, 143.3, 133.3, 132.0, 129.4, 128.6, 128.5, 128.1, 125.9,

124.8, 123.4, 121.7, 94.9, 86.2, 62.0, 14.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{15}NO_2SNa$ 356.0716; Found 356.0719.

2-Benzoyl-4,6-diphenylpyridine (3at): white solid; yield 86% (57.6 mg); mp 76-78 °C; R_f = 0.75 (EtOAc:hexane = 1:4); IR (KBr): ν 1663, 1591, 1538, 1494, 1445 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23-8.27 (m, 3H), 8.15 (s, 1H), 8.10 (d, J = 7.6 Hz, 2H), 7.78 (d, J = 7.6 Hz, 2H), 7.61-7.64 (m, 1H), 7.45-7.56 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 156.7, 155.4, 150.5, 138.6, 138.0, 136.5, 132.8, 131.3, 129.4 (2C), 129.2, 128.8, 128.0, 127.2, 127.0, 121.0, 120.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{18}NO$ 336.1383; Found 336.1387.

2-Benzoyl-4-phenyl-6-(4-methoxyphenyl)pyridine (3bt): light yellow solid; yield 85% (62.0 mg); mp 84-86 °C; R_f = 0.55 (EtOAc:hexane = 1:4); IR (KBr) ν 1658, 1593, 1541, 1507, 1453, 1418 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 7.6 Hz, 2H), 8.16 (s, 1H), 8.05-8.08 (m, 3H), 7.77 (d, J = 7.2 Hz, 2H), 7.60-7.64 (m, 1H), 7.47-7.56 (m, 5H), 7.00 (d, J = 8.4 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 160.8, 156.3, 155.3, 150.4, 138.1, 136.6, 132.8, 131.3, 131.2, 129.3, 129.2, 128.4, 128.0, 127.2, 120.3, 119.7, 114.2, 55.4; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{19}NO_2Na$ 388.1308; Found 388.1311.

2-Benzoyl-4-phenyl-6-(3-bromophenyl)pyridine (3jt): white solid; yield 81% (66.9 mg); mp 94-96 °C; R_f = 0.76 (EtOAc:hexane = 1:4); IR (KBr) ν 1658, 1590, 1537, 1484, 1445, 1415 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (m, 3H), 8.1 (s, 1H), 8.02 (d, J = 7.6 Hz, 2H), 7.77 (d, J = 7.2 Hz, 2H), 7.62-7.66 (m, 1H), 7.52-7.56 (m, 6H), 7.34-7.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.5, 155.4, 155.0, 150.8, 140.6, 137.7, 136.3, 132.9, 132.3, 131.3, 130.4, 130.2, 129.6, 129.3, 128.0, 127.2, 125.6, 123.1, 121.4, 120.5; HRMS (ESI-TOF) m/z: Calcd for

$C_{24}H_{17}{}^{79}BrNO[M+H]^+$ 414.0489; Found 414.0501. HRMS (ESI-TOF) m/z: Calcd for $C_{24}H_{17}{}^{81}BrNO[M+H]^+$ 416.0468; Found 416.0517.

2-Benzoyl-4-phenyl-6-(2-furyl)pyridine (3ht): white solid; yield 77% (50.1 mg); mp 72-74 °C; R_f = 0.66 (EtOAc:hexane = 1:4); IR (KBr) ν 1660, 1606, 1541, 1492, 1446 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 7.6 Hz, 2H), 8.13 (s, 1H), 8.10 (s, 1H), 7.78 (d, J = 7.2 Hz, 2H), 7.74-7.63 (m, 7H), 7.09 (d, J = 3.0 Hz, 1H), 6.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.3, 155.3, 153.3, 150.3, 148.8, 143.6, 137.6, 136.3, 132.9, 131.4, 129.5, 129.2, 128.0, 127.1, 120.4, 118.2, 112.2, 109.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{16}NO_2$ 326.1176; Found 326.1176.

2-Benzoyl-4-phenyl-6-(2-thiophenyl)pyridine (3it): light green solid; yield 82% (55.9 mg); mp 78-80 °C, R_f = 0.72 (EtOAc:hexane = 1:4); IR (KBr) ν 1654, 1587, 1541, 1500, 1438, 1359 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 7.2 Hz, 2H), 8.17 (s, 1H), 8.01 (s, 1H), 7.71-7.77 (m, 3H), 7.61-7.65 (m, 1H), 7.51-7.54 (m, 5H), 7.42 (d, J = 4.0 Hz, 1H), 7.14 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.9, 155.0, 151.9, 150.5, 144.4, 137.7, 136.2, 132.8, 131.5, 129.5, 129.2, 128.3, 128.2, 127.9, 127.1, 125.2, 120.7, 118.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{16}NOS$ 342.0947; Found 342.0942.

2-Cinnamoyl-4,6-diphenylpyridine (3au): white solid; yield 79% (57.0 mg); mp 108-110 °C; R_f = 0.77 (EtOAc:hexane = 1:4); IR (KBr) ν 1677, 1596, 1543, 1496, 1452 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, J = 16.0 Hz, 1H), 8.38 (s, 1H), 8.20 (d, J = 7.6 Hz, 2H), 8.15 (s, 1H), 8.03 (d, J = 16.0 Hz, 1H), 7.76-7.80 (m, 4H), 7.44-7.59 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.7, 157.2, 154.6, 150.5, 144.6, 138.8, 137.9, 135.3, 130.5, 129.5, 129.4, 129.2, 128.9 (2C),

128.8, 127.2, 127.1, 121.4, 121.2, 119.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{26}H_{20}NO$ 362.1539; Found 362.1543.

2-Cinnamoyl-4-phenyl-6-(4-fluorophenyl)pyridine (3du): white solid; yield 78% (59.1 mg); mp 114-116 °C; R_f = 0.78 (EtOAc:hexane = 1:4); IR (KBr) ν 1672, 1600, 1509, 1449, 1414 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, J = 16.0 Hz, 1H), 8.37 (s, 1H), 8.18-8.21 (m, 2H), 8.09 (s, 1H), 8.01 (d, J = 16.0 Hz, 1H), 7.75-7.79 (m, 4H), 7.45-7.56 (m, 6H), 7.23-7.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.6, 163.9 (d, J_{C-F} = 250 Hz), 150.6, 144.8, 137.9, 135.3, 134.9 (2 C), 130.6, 129.4, 129.2, 129.0, 128.9, 128.8, 127.2, 121.2, 121.1, 121.0, 119.3, 115.9 (d, J_{C-F} = 19 Hz); HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{26}H_{19}NOF$ 380.1445; Found 380.1443.

Ethyl 5-methyl-4,6-diphenylpicolinate (3ka): white solid; yield 44% (27.9 mg); mp 86-88 °C; R_f = 0.65 (EtOAc:hexane = 1:4); IR (KBr) ν 1712, 1580, 1545, 1499, 1448, 1384 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.57 (d, J = 7.2 Hz, 2H), 7.37-7.50 (m, 8H), 4.46 (q, J = 7.2 Hz, 2H), 2.25 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 160.3, 151.6, 145.3, 140.4, 139.2, 132.6, 129.4, 128.7, 128.5, 128.2, 128.1 (2 C), 124.5, 61.7, 18.5, 14.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{19}NO_2Na$ 340.1308; Found 340.1309.

Ethyl 4-(4-bromophenyl)-5-methyl-6-phenylpicolinate (3ke): light yellow solid; yield 43% (34.0 mg); mp 108-110 °C; R_f = 0.66 (EtOAc:hexane = 1:4); IR (KBr) ν 1714, 1594, 1542, 1488, 1448 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.62 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 6.8 Hz, 2H), 7.40-7.47 (m, 3H), 7.26 (d, J = 8.0 Hz, 2H), 4.46 (q, J = 6.8 Hz, 2H), 2.24 (s, 3H), 1.41 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 160.4, 150.4, 145.5, 140.1, 138.0, 132.4, 131.8, 130.4, 129.3, 128.3, 128.2, 124.2, 122.6, 61.8, 18.5, 14.3; HRMS (ESI-TOF) m/z:

$[M+H]^+$ Calcd for $C_{21}H_{19}{}^{79}BrNO_2$ 396.0594; Found 396.0585. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{19}{}^{81}BrNO_2$ 398.0574; Found 398.0568.

Ethyl 4-(4-cyanophenyl)-5-methyl-6-phenylpicolinate (3kf): white solid, yield 45% (30.8 mg); mp 100-102 °C; R_f = 0.53 (EtOAc:hexane = 1:4); IR (KBr) ν 1711, 1636, 1578, 1543, 1502, 1449 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.79 (d, J = 8.4 2H), 7.42-7.57 (m, 7H), 4.47 (q, J = 6.8 Hz, 2H), 2.23 (s, 3H), 1.41 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 160.6, 149.6, 145.7, 143.8, 139.9, 132.4, 132.1, 129.6, 129.3, 128.5, 128.3, 123.9, 118.3, 112.4, 61.9, 18.4, 14.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{18}N_2O_2Na$ 365.1260; Found 365.1269.

Ethyl 4-(2-thiophenyl)-5-methyl-6-phenylpicolinate (3kv): light green solid; yield 41% (26.5 mg); mp 92-94 °C; R_f = 0.62 (EtOAc:hexane = 1:4); IR (KBr) ν 1709, 1578, 1542, 1443, 1372 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.55 (d, J = 6.8 Hz, 2H), 7.39-7.48 (m, 4H), 7.26-7.27 (m, 1H), 7.15-7.17 (m, 1H), 4.46 (q, J = 6.8 Hz, 2H), 2.43 (s, 3H), 1.41 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 160.7, 145.5, 144.0, 140.3, 139.8, 132.6, 129.4, 128.4, 128.3, 128.2, 127.6, 127.3, 124.5, 61.8, 19.1, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{18}NO_2S$ 324.1053; Found 324.1056.

(*E*)-Ethyl 5-methyl-6-phenyl-4-styrylpicolinate (3kp): white solid; yield 54% (37.0 mg); mp 102-104 °C; R_f = 0.65 (EtOAc:hexane = 1:4); IR (KBr) ν 1712, 1627, 1576, 1540, 1446, 1392 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.59 (d, J = 7.6 Hz, 2H), 7.51-7.54 (m, 2H), 7.33-7.47 (m, 5H), 7.35 (d, J = 7.2 Hz, 1H), 7.31-7.33 (m, 2H), 4.48 (q, J = 7.2 Hz, 2H), 2.42 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 160.2, 145.8, 145.5, 140.3,

136.3, 135.0, 131.8, 129.3, 128.8 (2C), 128.1 (2C), 127.0, 123.8, 119.7, 61.7, 16.9, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{22}NO_2$ 344.1645; Found 344.1645.

Ethyl 5-methyl-6-phenyl-4-(phenylethynyl)picolinate (3ks): light yellow solid; yield 58% (39.6 mg); mp 108-110 °C; R_f = 0.65 (EtOAc:hexane = 1:4); IR (KBr) ν 1734, 1572, 1535, 1493, 1445 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (s, 1H), 7.53-7.59 (m, 4H), 7.38-7.48 (m, 6H), 4.47 (q, *J* = 6.8 Hz, 2H), 2.55 (s, 3H), 1.43 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 159.6, 145.4, 139.8, 135.9, 133.4, 131.8, 129.3, 129.2, 128.5, 128.3, 128.2, 125.7, 122.1, 98.5, 85.8, 61.8, 18.6, 14.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{19}NO_2Na$ 364.1308; Found 364.1303.

Ethyl 6-(2-hydroxyphenyl)-4-phenylpicolinate (3la): white solid; yield 72% (45.9 mg); mp 112-114 °C; R_f = 0.70 (EtOAc:hexane = 1:4); IR (KBr) ν 3429, 1719, 1609, 1546, 1498, 1474, 1411 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 14.19 (s, 1H), 8.26 (d, *J* = 2.0 Hz, 2H), 7.92 (d, *J* = 6.8 Hz, 1H), 7.74 (d, *J* = 6.8 Hz, 2H), 7.51-7.58 (m, 3H), 7.34-7.38 (m, 1H), 7.09 (d, *J* = 7.6 Hz, 1H), 6.93-6.97 (m, 1H), 4.51 (q, *J* = 7.2 Hz, 2H), 1.49 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 160.3, 158.0, 151.4, 145.1, 137.4, 132.1, 129.8, 129.4, 127.2, 126.3, 120.9, 119.8, 119.0, 118.9, 118.4, 62.2, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{18}NO_3$ 320.1281; Found 320.1288.

Ethyl 4-(4-methoxyphenyl)-6-(2-hydroxyphenyl)picolinate (3lb): light green solid; yield (48.9 mg); mp 98-100 °C; R_f = 0.53 (EtOAc:hexane = 1:4); IR (KBr) ν 3422 1720, 1606, 1549, 1500, 1461, 1418 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 14.25 (s, 1H), 8.22 (d, *J* = 5.6 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.8 Hz, 2H), 7.33-7.37 (m, 1H), 7.05-7.09 (m, 3H), 6.92-6.96 (m, 1H), 4.50 (q, *J* = 7.2 Hz, 2H), 3.89 (s, 3H), 1.49 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 164.3, 161.2, 160.3, 157.9, 150.8, 145.0, 132.0, 129.6, 128.5, 126.3, 120.3, 119.0 (2C), 118.9, 118.4, 114.8, 62.2, 55.5, 14.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{19}NO_4Na$ 372.1206; Found 372.1206.

Ethyl 4-(4-fluorophenyl)-6-(2-hydroxyphenyl)picolinate (3ld): light yellow solid; yield 75% (59.7 mg); mp 107-109 °C; R_f = 0.69 (EtOAc:hexane = 1:4); IR (KBr) ν 3427, 1725, 1609, 1551, 1510, 1474, 1419 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 14.12 (s, 1H), 8.20 (d, J = 3.2 Hz, 1H), 7.89-7.91 (m, 1H), 7.71-7.74 (m, 2H), 7.33-7.38 (m, 1H), 7.22-7.27 (m, 2H), 7.08 (d, J = 7.6 Hz, 1H), 6.93-6.96 (m, 1H), 4.50 (q, J = 6.8 Hz, 2H), 1.49 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 163.9 (d, J_{C-F} = 248 Hz), 160.2, 158.1, 150.3, 145.2, 133.3 (d, J_{C-F} = 3.0 Hz), 132.2, 129.2, 129.0, 126.2, 120.6, 119.0, 119.0 (d, J_{C-F} = 2.0Hz), 118.2, 116.4 (d, J_{C-F} = 20.0 Hz), 62.2, 14.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{16}NO_3FNa$ 360.1006; Found 360.1007.

Ethyl 6-(2-hydroxyphenyl)-4-(thiophen-2-yl)picolinate (3lv): white solid; yield 68% (44.2 mg); mp 94-96 °C; R_f = 0.70 (EtOAc:hexane = 1:4); IR (KBr) ν 3422, 1719, 1605, 1548, 1525, 1499, 1473, 1441, 1405 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 14.10 (s, 1H), 8.22 (s, 1H), 8.20 (s, 1H), 7.88 (d, J = 7.2 Hz, 1H), 7.67 (d, J = 3.2 Hz, 1H), 7.51 (d, J = 4.8 Hz, 1H)7.34-7.38 (m, 1H), 7.19-7.21 (m, 1H), 7.08 (d, J = 8.4 Hz, 1H), 6.96 (t, J = 7.2 Hz, 1H), 4.50 (q, J = 6.8 Hz, 2H), 1.49 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 160.4, 158.3, 145.4, 144.4, 140.4, 132.3, 128.9, 128.5, 126.8, 126.4, 119.1, 118.3, 117.7, 62.4, 14.4; HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{15}NO_3SNa$ 348.0665; Found 348.0685

Synthesis of 2-amino-4,6-diphenylpyridine (7)[19]. $LiOH.H_2O$ (210 mg, 5.0 mmol) was added to a stirred solution of ethyl 4,6-diphenylpicolinate (**3aa**, 303.3 mg, 1.0 mmol) in $MeCN/H_2O$ (5.0

mL, 4:1) at room temperature. Then the reaction mixture was allowed to stir for 5 h (monitored by TLC). After completion of the reaction, organic solvent was removed by rotary evaporator and acidified by 1M acetic acid. Then water layer was extracted with ethyl acetate (5 × 10 mL), washed with brine solution and dried over Na_2SO_4. Evaporation of the solvent left the crude 4,6-diphenylpicolinic acid which was reasonable pure and directly used for the next step without further purification.

A mixture of resultant 4,6-diphenylpicolinic acid, DPPA (385.0 mg, 1.4 mmol), and triethylamine (405.0 mg, 4.0 mmol) in toluene (2.0 mL) was heated at 65 °C for 2 h and then 100 °C for 6 h. After completion of the reaction (monitored by TLC), the reaction mixture was extracted with ethyl acetate (3 × 10 mL) before being quenched with water. The combined organic layer was washed with brine solution and dried over Na_2SO_4. Afterwards, the organic phase was concentrated under reduced pressure to furnish the crude product. It was purified by flash chromatography over silica gel using EtOAc/hexane (2:3 v/v) as the eluent to give 2-amino-4,6-diphenylpyridine (**7**) in 76% yield (187.0 mg, overall).

Synthesis of compound 2,5,7-Triphenylimidazo[1,2-*a*]pyridine (8)[26]: 2-Amino-4,6-diphenylpyridine (0.20 mmol, 52.8 mg), β-nitrostyrene (0.24 mmol, 35.7 mg), and CuBr (0.02 mmol, 2.9 mg) were taken in round bottom flask followed by the addition of 1.5 mL of DMF. Then the reaction mixture was allowed to stir at 80 °C under open air for 4 h. After completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and 10 mL of ethyl acetate was added. The organic layer was separated after washing with of brine (2 × 5 mL). The organic layer was dried over anhydrous Na_2SO_4, followed by evaporation of organic solvent to give the crude mass. The crude product was purified by column chromatography using EtOAc/hexane (2:3 v/v) as the eluent to afford title compound **8** in 78% yield.

2,5,7-Triphenylimidazo[1,2-*a*]pyridine (8): light yellow solid; yield 78% (54.0 mg); mp 143-145 °C; R_f = 0.35 (EtOAc:hexane = 1:4); IR (KBr) ν 1636, 1600, 1525, 1480, 1445, 1343 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88-7.94 (m, 4H), 7.69-7.73 (m, 4H), 7.57-7.60 (m, 3H), 7.48 (t, J = 7.2 Hz, 2H), 7.39-7.42 (m, 3H), 7.29-7.32 (m, 1H), 7.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 146.3, 138.8, 138.1 (2C), 134.5, 133.7, 129.9, 129.3, 129.1, 128.7, 128.4, 128.3, 128.0, 126.8, 126.1, 113.0, 112.8, 106.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{19}N_2$ 347.1543; Found 347.1548.

ASSOCIATED CONTENT

Supporting information

"This material is available free of charge via the Internet at http://pubs.acs.org." copies of ^1H and ^{13} NMR spectra for the products are available in ESI.

ORCID[id]

Sampak Samanta**:** 0000-0002-9659-8216

NOTES

The authors declare no competing financial interest.

ACKNOWLEDGEMENTS

The authors thank CSIR (Project No. 02(0273)/16/EMR-II) research grant, Govt. of India for generous financial support and SIC facility, IIT Indore. The authors wish to thank UGC for the fellowship of S. Biswas.

REFERENCES

(1) (a) Fu, P.; Wang, S. X.; Hong, K.; Li, X.; Liu, P. P.; Wang, Y.; Zhu, W. M. *J. Nat. Prod.* **2011**, *74*, 1751. (b) Donohoe, T. J.; Jones, C. R.; Kornahrens, A. F.; Barbosa, L. C. A.;

Walport, L. J.; Tatton, M. R.; O'Hagan, M.; Rathi, A. H.; Baker, D. B. *J. Org. Chem.* **2013**, *78*, 12338. (c) Grant, R. S.; Coggan, S. E.; Smythe, G. A. Int. J. Tryptophan Res. **2009**, *2*, 71. (d) Hopper, D. W.; Kuterer, K. M. K.; Crombie, A. L.; Clemens, J. J. In *Progress In Heterocyclic Chemistry*; Gribble, G. W.; Joule, J. A., Eds.; Elsevier: Amsterdam, **2009**, *20*, 289. (e) Hill, M. D. *Chem. Eur. J.* **2010**, *16*, 12052. (f) Fraser, H. L.; Hopper, D. W.; Kutterer, K. M. K.; Crombie, A. L. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Joule, J. A., Eds.; Elsevier: Amsterdam, **2008**, Vol. 19, pp 314.

(2) (a) Baumann, M.; Baxendale, I. R. *Beilstein J. Org. Chem.* **2013**, *9*, 2265. (b) Deininger, M. W. N.; Druker, B. *J. Pharmacol. Rev.* **2003**, *55*, 401. (c) Longstreet, A. R.; Opalka, S. M.; Campbell, B. S.; Gupton, B. F.; McQuade, D. T. *Beilstin J. Org. Chem.* **2013**, *9*, 2570. (d) Harrison, S. T.; Scott, L. J. *Drugs* **2005**, *65*, 2309.

(3) (a) Trist, I. M. L.; Nannetti, G.; Tintori, C.; Fallacara, A. L.; Deodato, D.; Mercorelli, B.; Palu, G.; Wijtmans, M. I.; Gospodova, T.; Edink, E.; Verheij, M.; Esch, I. D.; Viteva, L.; Loregian, A.; Botta, M. *J. Med. Chem.* **2016**, *59*, 2688. (b) Roughley, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54*, 3451. (c) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* **2006**, *4*, 2337. (d) Chen, Y. L.; Braselton, J.; Forman, J.; Gallaschun, R. J.; Mansbach, R.; Schmidt, A. W.; Seeger, T. F.; Sprouse, J. S.; Tingley, F. D., III; Winston, E.; Schulz, D. W. *J. Med. Chem.* **2008**, *51*, 1377. (e) Roth, H. J.; Kleemann, A. *Drug Synthesis in Pharmaceutical Chemistry*; John Wiley and Sons: New York, **1988**; Vol. 1.

(4) (a) Sasabe, H.; Kido, J. *Chem. Mater.* **2011**, *23*, 621. (b) Liu, W.; Zheng, C.-J.; Wang, K.; Chen, Z.; Chen, D.-Y.; Li, F.; Ou, X.-M.; Dong, Y.-P.; Zhang, X.-H. *ACS Appl. Mater. Interfaces* **2015**, *7*, 18930. (c) Sun, Y.; Duan, L.; Zhang, D.; Qiao, J.; Dong, G.; Wang, L.;

Qiu, Y. *Adv. Funct. Mater.* **2011**, *21*, 1881. (d) Müller, T. J. J., Bunz, U. H. F., Eds.; Wiley-VCH: Weinheim, 2007.

(5) (a) Hamaker, J. W.; Johnston, H.; Martin, R. T.; Redemann, C. T. *Science* **1963**, *141*, 363. (b) Guan, A.-Y.; Liu, C.-L.; Sun, X.-F.; Xie, Y.; Wang, M.-A. *Bioorg. Med. Chem.* **2016**, *24*, 342. (c) Masters, R. A.; Lo, W. C.; Gast, R. E. Aminopyralid. In *Modern Crop Protection Compounds*, 2nd ed.; Kraemer, W., Ed.; Wiley- VCH: Weinheim, **2012**, 287.

(6) (a) Sumby, C. J. *Coord. Chem. Rev.* **2011**, *255*, 1937. (b) Kiss, E.; Garribba, E.; Micera, G.; Kiss, T.; Sakurai, H. *J. Inorg. Biochem.* **2000**, *78*, 97. (c) Ross, A.; Moretti, J.; Du, B. D.; Stack, T. D. P. *Org. Lett.* **2016**, *18*, 2528. (d) Dasgupta, M.; Tadesse, H.; Blake, A. J.; Bhattacharya, S. *J. Organomet. Chem.* **2008**, *693*, 3281. (e) Liu, Z.; Habtemariam, A.; Pizarro, A. M.; Fletcher, S. A.; Kisova, A.; Vrana, O.; Salassa, L.; Bruijnincx, P. C.; Clarkson, G. J.; Brabec, V.; Sadler, P. J. *J. Med. Chem.* **2011**, *54*, 3011. (f) Chan, Y.-T.; Moorefield, C. N.; Soler, M.; Newkome, G. R. *Chem. Eur. J.* **2010**, *16*, 1768.

(7) (a) Shibatomi, K.; Muto, T.; Sumikawa, Y.; Narayama, A.; Iwasa, S. *Synlett* **2009**, *19*, 241. (b) De, R. N.; Couty, F.; David, O. R. P. *Chem. Eur. J.* **2011**, *17*, 12852. (c) Murugan, R.; Scriven, E. F. V. *Aldrichimica Acta* **2003**, *36*, 21.

(8) (a) Dewick, P. M. *Medicinal Natural Products A Biosynthetic Approach*, 2nd ed., Wiley, New York, **2002**, 311. (b) Jones, R.G. *J. Am. Chem. Soc.* **1951**, *73*, 5244. (c) Tracy, A. H.; Elderfield, R. C. *J. Org. Chem.* **1941**, *6*, 54.

(9) (a) Ramsay, R. R.; Salach, J. I.; Dadgar, J.; Singer, T. P.; *Biochem. Biophys. Res. Communs*. **1986**, *135*, 269. (b) Tanouchi, T.; Kawamura, M.; Ohyama, I.; Kajiwara, I.; Iguchi, Y.; Takanori Okada, T.; Miyamoto, T.; Taniguchi, K.; Hayashi, M. *J. Med. Chem.* **1981**, *24*,

1149. (c) Wo, J.; Kong, D.; Brock, N. L.; Xu, F.; Zhou, X.; Deng, Z.; Lin, S. *ACS Catal.* **2016**, *6*, 2831.

(10) (a) Kharchenko, V. G.; Markova, L. I.; Fedotova, O. V.; Pchelintseva, N. V. *Chem. Heterocycl. Compd.* **2003**, *39*, 1121. (b) Sausins, A.; Duburs, G. *Heterocycles* **1988**, *27*, 269. (c) Eliel, E. L.; McBride, R. T.; Kaufmann, S. *J. Am. Chem. Soc*. **1953**, *75*, 4291. (d) Chichibabin, A. E. *J. Russ Phys. Chem. Soc*. **1906**, *37*, 1229. (e) Li, Z.; Huang, X.; Chen, F.; Zhang, C.; Wang, X.; Jiao, N. *Org. Lett*. **2015**, *17*, 584.

(11) (a) Bohlmann, F.; Rahtz, D. *Chem. Ber*. **1957**, *90*, 2265. (b) Bagley, M. C.; Glover, C.; Merritt, E. A. *Synlett* **2007**, *16*, 2459. (c) Bagley, M. C.; Dale, J. W.; Bower, J. *Chem. Commun*. **2002**, 1682. (d) Tsuda, K.; Satch, Y.; Ikekawa, N.; Mishima, H. *J. Org. Chem*. **1956**, *21*, 800. (e) Gade, N. R.; Devendram, V.; Pal, M.; Iqbal, J. *Chem. Commun.* **2013**, *49*, 7926.

(12) A. Hantzsch, *Ber. Dtsch. Chem. Ges*. **1881**, *14*, 1637.

(13) (a) Allais, C.; Constantieux, T.; Rodriguez, J. *Chem. Eur. J.* **2009**, *15*, 12945. (b) Allais, C.; Grassot, J.-M.; Rodriguez, J.; Constantieux, T. *Chem. Rev*. **2014**, *114*, 10829. (c) Allais, C.; Lieby-Muller, F.; Rodriguez, J.; Constantieux, T. *Eur. J. Org. Chem*. **2013**, 4131. (d) Sasada, T.; Sakai, N.; Konakahara, T. *J. Org. Chem.* **2008**, *73*, 6905. (e) Song, Z.; Huang, Z.; Yi, W.; Zhang, W. *Org. Lett*. **2016**, *18*, 5640. (f) Jiang, H.; Yang, J.; Tang, X.; Li, J.; Wu, W. *J. Org. Chem.* **2015**, *80*, 8763. (g) Wu, Q.; Zhang, Y.; Cui, S. *Org. Lett.* **2014,** *16*, 1350. (h) He, Z.; Dobrovolsky, D.; Trinchera, P.; Yudin, A. K. *Org. Lett.* **2013**, *15*, 334. (i) Song, Z.; Huang, X.; Yi, W.; Zhang, W. *Org. Lett*. **2016**, *18*, 5640.

(14) (a) Jiang, Y.; Park, C.-M.; Loh, T.-P. *Org. Lett.* **2014**, *16*, 3432. (b) Nakamura, I.; Oyama, Y.; Zhang, D.; Terada, M. *Org. Chem. Front*. **2017**, *4*, 1034. (c) Wei, H.; Li, Y.;

Xiao, K.; Cheng, B.; Wang, H.; Hu, L.; Zhai, H. *Org. Lett.* **2015**, *17*, 5974. (d) Chen, Z. B.; Hong, D.; Wang, Y. G. *J. Org. Chem*. **2009**, *74*, 903.

(15) Selected examples of transition metal-catalyzed [4+2]cycloaddition for the synthesis of pyridines: (a) Parthasarathy, K.; Jeganmohan, M.; Cheng, C.-H. *Org. Lett.* **2008**, *10*, 325. (b) Zhang, X.; Chen, D.; Zhao, M.; Zhao, J.; Jia, A.; Li, X. *Adv. Synth. Catal.* **2011**, *353*, 719. (c) Chen, S.; Bergman, R. G.; Ellman, J. A. *Org. Lett*. **2015**, *17*, 2567. (d) Zhang, Q.-R.; Huang, J.-R.; Zhang, W.; Dong, L. *Org. Lett*. **2014**, *16*, 1684. (e) Too, P. C.; Chua, S. H.; Wong, S. H.; Chiba, S. *J. Org. Chem*. **2011**, *76*, 6159. (f) Wu, J.; Xu, W.; Yu, Z.-X.; Wang, J. *J. Am. Chem. Soc*. **2015**, *137*, 9489. (g) Neely, J. M.; Rovis, T. *Org. Chem. Front*. **2014**, *1*, 1010. (h) Martin, R. M.; Bergman, R. G.; Ellman, J. A. *J. Org. Chem*. **2012**, *77*, 2501. (i) Jiang, Y.; Park, C.-M. *Chem. Sci.* **2014**, *5*, 2347.

(16) Examples of transition metal-catalyzed [2+2 +2]cycloaddition for the synthesis of pyridines : (a) Heller, B.; Hapke, M. *Chem. Soc. Rev*. **2007**, *36*, 1085. (b) Tanaka, R.; Yuza, A.; Watai, Y.; Suzuki, D.; Takayama, Y.; Sato, F.; Urabe, H. *J. Am. Chem. Soc*. **2005**, *127*, 7774. (c) Hapke, M.; Kral, K.; Fischer, C.; Spannenberg, A.; Gutnov, A.; Redkin, D.; Heller, B. *J. Org. Chem.* **2010**, *75*, 3993. (d) Komine, Y.; Tanaka, K. *Org. Lett*. **2010**, *12*, 1312. (e) Kumar, P.; Prescher, S.; Louie, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 10694. (f) Wang, C.; Li, X.; Wu, F.; Wan, B. *Angew. Chem., Int. Ed*. **2011**, *50*, 7162. (g) Onodera, G.; Shimizu, Y.; Kimura, J.; Kobayashi, J.; Ebihara, Y.; Kondo, K.; Sakata, K.; Takeuchi, R. *J. Am. Chem. Soc*. **2012**, *134*, 10515.

(17) C-H functionalization of pyridines: (a) Mai, D.N.; Baxter, R. D. *Org. Lett*. **2016**, *18*, 3738. (b) Do, H.-Q.; Khan, R. M. K.; Daugulis, O. *J. Am. Chem. Soc*. **2008**, *130*, 15185. (c) Berman, A. M.; Lewis, J. C.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc*. **2008**, *130*,

14926. (d) Engle, K. M.; Yu, J.-Q. *J. Org. Chem*. **2013**, *78*, 8927. (e) Billingsley, K. L.; Buchwald, S. L. *Angew. Chem., Int. Ed*. **2008**, *47*, 4695.

(18) Synthesis of picolinates, see: (a) Zhu, C.; Bi, B.; Ding, Y.; Zhang, T.; Chen, Q.-Y. *Org. Biomol. Chem.* **2015**, *13*, 6278. (b) Neely, J. M.; Rovis, T. *J. Am. Chem. Soc*. **2013**, *135*, 66. (c) Yu, J.; Kim, K. H.; Lee, H. J.; Kim, J. N. *Bull. Korean Chem. Soc*. **2013**, *34*, 3027. (d) Yu, X.; Chen, K.; Wang, Q.; Guo, S.; Zha, S.; Zhu, J. *Angew. Chem., Int. Ed*. **2017**, *56*, 5222. (e) Bremer, P. T.; Xue, S.; Janda, K. D. *Chem. Commun.* **2016**, *52*, 12521. (f) Lu, J.-Y.; Arndt, H.-D. *J. Org. Chem*. **2007**, *72*, 4205. (g) Johnson, P. L.; Renga, J. M.; Galliford, C. V.; Whiteker, G. T.; Giampietro, N. C. *Org. Lett*. **2015**, *17*, 2905. (h) Zhu, X.; Wang, Y.-F.; Zhang, F.-L.; Chiba, S. *Chem. Asian J*. **2014**, *9*, 2458.

(19) Majee, D.; Biswas, S.; Mobin, S. M.; Samanta, S. *J. Org. Chem.* **2016**, *81*, 4378.

(20) (a) Majee, D.; Biswas, S.; Mobin, S. M.; Samanta, S. *Org. Biomol. Chem.* **2017**, *15*, 3286. (b) Dagar, A.; Biswas, S.; Samanta, S. *RSC Adv.* **2015**, *5*, 52497. (c) Biswas, S.; Jaiswal, P. K.; Singh, S.; Mobin, S. M.; Samanta, S. *Org. Biomol. Chem.* **2013**, *11*, 7084. (d) Majee, D.; Guin, S.; Biswas, D.; S. Samanta, *ChemSelect* **2017**, *2*, 3423.

(21) (a) Majee, D.; Srivastava, A.; Mobin, S. M.; Samanta, S. *RSC Adv*. **2013**, *3*, 11502. (b) Majee, D.; S. Biswas, S. M. Mobin and S. Samanta, *Tetrahedron Lett.* **2014**, *55*, 4553.

(22) (a) Zhou, J.; Ding, C.; Cunningham, K. A. *U.S. Pat. Appl. Publ.* **2014**, US 20140336375 A1 20141113. (b) Storm, O.; Lüning, U. *Eur. J. Org. Chem.* **2003**, 3109.

(23) (a) Bagdi, A. K.; Santra, S.; Monir, K.; Hajra, A. *Chem. Commun*. **2015**, *51*, 1555. (b) Mondal, S.; Samanta, S.; Jana, S.; Hajra, A. J. *Org. Chem.* **2017**, *82*, 4504. (c) Sun, P.; Jiang, P.; Wei, W.; Li, W.; Yang, D.; Wang, H. *J. Org. Chem.* **2017**, *82*, 2906.

(24) (a) Wang, Y.-Q.; Yu, C.-B.; Wang, D.-W.; Wang, X.-B.; Zhou, Y.-G. *Org. Lett*. **2008**, *10*, 2071. (b) Kang, S.; Han, J.; Lee, E. S.; Choi, E. B.; Lee, H.-K. *Org. Lett*. **2010**, *12*, 4184. (c) Osborne, C. A.; Endean, T. B. D.; Jarvo, E. R. *Org. Lett*. **2015**, *17*, 5340.

(25) (a) Meng, Q.; Zhu, L.; Zhang, Z. *J. Org. Chem.* **2008**, *73*, 7209. (b) Belmessieri, D.; Morrill, L. C.; Simal, C.; Slawin, A. M. Z.; Smith, A. D. *J. Am. Chem. Soc.* **2011**, *133*, 2714. (c) Meng, Q.; Zhu, L.; Zhang, Z. *J. Org. Chem*. **2008**, *73*, 7209. (d) Sinu, C. R.; Suresh, E.; Nair, V.; *Org. Lett*. **2013**, *15*, 6230. (e) Shi, S.; Wang, T.; Weingand, V.; Rudolph, M.; Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2014**, *53*, 1148. (f) Juste-Navarro, V.; Marqués-López, E.; Herrera, R. P. *Asian J. Org. Chem.* **2015**, *4*, 884.

(26) Yan, R.-L.; Yan, H.; Ma, C.; Ren, Z.-Y.; Gao, X.-A.; Huang, G.-S.; Liang, Y.-M. *J. Org. Chem.* **2012**, *77*, 2024.