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ARTICLE

Domino reaction of cyclic sulfamidate imines with Morita-Baylis-Hillman acetates promoted by DABCO: a metal-free approach to functionalized nicotinic acid derivatives

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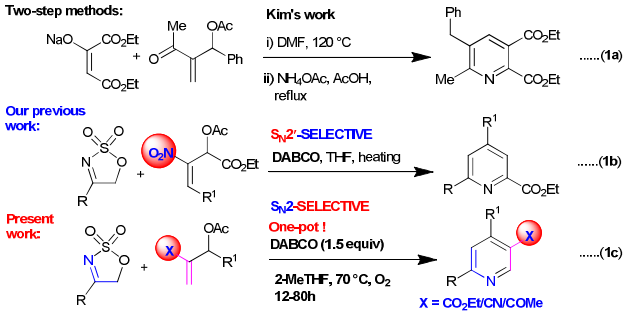
Debashis Majee, Soumen Biswas, Shaikh M. Mobin and Sampak Samanta*

A facile, green, metal-free based new one-pot synthetic strategy has been developed for the easy access to a wide array of medicinally promising functionalized pyridines having an ester, nitrile or acetyl group at the C-3 position in good to excellent yields via a domino S_N2/elimination/6π-aza-electrocyclization/aromatization reaction of several 4-aryl/hetero-aryl-substituted 5-membered cyclic sulfamidate imines with a broad range of MBH acetates of acrylate/acrylonitrile/MVK in 2-MeTHF promoted by DABCO as an organobase under O_2 atmosphere. Moreover, a biologically interesting triazolopyridine derivative was achieved through a unique procedure.

Introduction

Efficient construction of poly-functionalized pyridine containing an ester, nitrile or acetyl group at C-3 position (as surrogate of nicotinic acid or niacin or vitamin B_3) is a key research topic in chemical science.[1] Importantly, this evergreen aza-heterocycle as well as its nicotinic acid frameworks constitute several marketable drugs,[1b,e] biologically active natural products,[1c-e] pharmaceuticals,[2] agrochemicals,[3] functional materials,[4] and ligands for catalysis.[5] Owing to their vast applications including the treatment of human health, several chemists have been devoted towards the efficient preparation of nicotinic acid derivatives by adopting several modern techniques.[1, 6-7] For example, Bohlman–Rahtz,[6a] Bagley and other groups [6b-e] have independently developed general and powerful synthetic strategies for the access to nicotinic acid derivatives by involving the β-enaminoesters (or in situ generated β-enaminoesters from β-ketoesters and ammonium acetate) and alkynones catalysed by several Brønsted and Lewis acids, or assisted by microwave irradiation. Alternatively, the acid catalyzed complete regioselective multicomponent reaction for the one-pot synthesis of poly-substituted nicotinates from simple 1,3-dicarbonyl compounds, β,γ-unsaturated-α-keto esters and ammonium acetate was realized by the Rodriguez group.[7a-c] Furthermore, Kim *et al*. also developed the two-step synthetic methods for the preparation of nicotinate derivatives using Morita-Baylis-Hillman (MBH) acetates of methyl vinyl ketone (MVK) as bielectrophiles (Scheme **1a**).[7o] Despite spectacular advances on the synthesis of nicotinic acid derivatives, use of expensive metal-salts and strong acids, lack of generality, poor chemical yields with multiple by-products, harsh reaction conditions, multi-steps etc are major drawbacks of the aforesaid protocols. To bypass the above difficulties, the development of a simple, efficient, more flexible (structural diversity), metal-free based new synthetic technique for the construction of an interesting functionalized nicotinic acid derivatives from simple substances remains an industrial as well as an academic challenge.

On the other hand, we also reported a novel one-pot protocol for the synthesis of 4,6-diarylpicolinates via a domino S_N2' addition-elimination sequence reaction of cyclic sulfamidate imines as nucleophiles with MBH acetates of nitroolefins using DABCO as an organobase (Scheme **1b**).[8] With this background, it is quite reasonable to envisage that in order to access a similar kind of pyridine derivative, well known nucleophilic acceptor like β-unsubstituted MBH acetate of acrylate [9] may be employed instead of β-substituted MBH acetate of nitroolefin in the domino reaction with cyclic sulfamidate imine which may proceed via a S_N2 manner, leading to the nicotinic acid derivative.



Scheme 1. Various synthetic approaches for pyridine synthesis using MBH acetate adducts.

[a] Discipline of Chemistry, Indian Institute of Technology Indore, Simrol, 453552, Indore, India
[b] Email: sampaks@iiti.ac.in; Phone: 91-731-2438753

† Footnotes relating to the title and/or authors should appear here.
Electronic Supplementary Information (ESI) available: [copies of ^1H and ^{13}C NMR, ORTEP data of **3ai** are available in ESI]. See DOI: 10.1039/x0xx00000x

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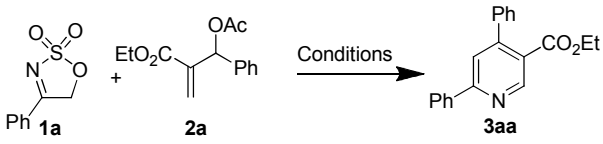
As a part of our continued research interest involving cyclic sulfamidate imine as a nucleophile for various transformations,[10] herein we are pleased to report an interesting domino reaction of several cyclic sulfamidate imines with different types of aryl-substituted MBH acetates bearing ester/nitrile/acetyl groups in 2-MeTHF as an eco-friendly solvent promoted by DABCO to afford a novel series of 4,6-diarylnicotinates/nicotinonitriles/3-acetylpyridines (Scheme **1c**).

Results and Discussion

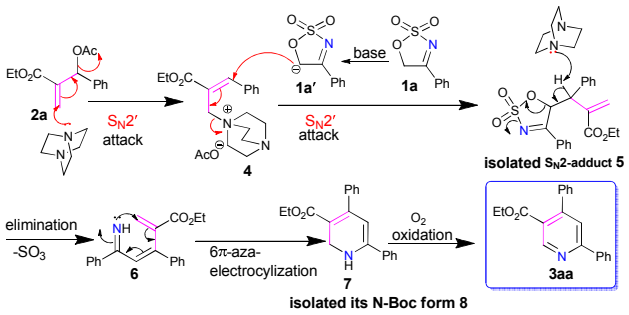
Table 1. Optimization of reaction conditions.[a]



Entry	Ease	Solvent	Temp (°C)	Time(h)	Yield (%)[b]
1	DABCO	2-MeTHF	rt	60	10
2	DABCO	2-MeTHF	45	60	52
3	DABCO	2-MeTHF	70	48	82
4[c]	DABCO	2-MeTHF	70	48	83
5[d]	DABCO	2-MeTHF	70	48	56
6	DABCO	THF	70	48	79
7	DABCO	toluene	70	48	74
8	DABCO	EtOAc	70	48	59
9	DABCO	DMSO	70	48	33
10	DABCO	DMF	70	48	27
11	DABCO	EtOH	70	48	21
12	DBU	2-MeTHF	70	60	5
13	DIPEA	2-MeTHF	70	60	<8
14	DMAP	2-MeTHF	70	60	41
15	Et_3N	2-MeTHF	70	60	32
16	Quinine	2-MeTHF	70	60	52

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.22 mmol), base (0.3 mmol) in solvent (1.0 mL) were heated at specified temperature under O_2 atmosphere. [b]Isolated yield. [c]DABCO (2.5 equiv.). [d]Open air.

By using 4-phenyl-5*H*-1,2,3-oxathiazole-2,2-dioxide (**1a**) and MBH acetate of acrylate (**2a**) as the test substrates, the reaction was carried out in 2-MeTHF as a green solvent at room temperature in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO, 1.5 equiv) as an organobase under O_2 atmosphere. Interestingly, after 60h, we were able to isolate a trace amount of an important class of 4,6-diarylnicotinate (**3aa**) in 10% yield (entry 1, Table 1). Gratifyingly, on increasing the reaction temperature from 45 °C to 70 °C, significant yield of **3aa** was enhanced from 52% to 82% after 48h (entries 2-3). This breakthrough result promoted us to investigate the above unprecedented domino reaction in various common organic solvents. Results clearly indicated that the polar solvents namely DMSO, DMF and EtOH led to poor yields (21-33% , entries 9-11) of **3aa** as compared to the non-polar ones (59-79%, entries 6-8). Considering the yield (82%, entry 3) and environment benign nature of 2-MeTHF, it was chosen as the best solvent for this conversion. It should be noted that a mediocre yield (56%, entry 5) of **3aa** was obtained when the same reaction was carried out under open atmosphere instead of O_2 balloon. Next, several common organic bases namely DBU, DMAP, DIPEA, Et_3N and quinine were tested for this domino reaction at 70 °C for 60 h. Surprisingly, all these bases led to unsatisfactory results (5-52% yields of **3aa**, entries 12-16) as compared to DABCO (82%, 48h, entry 3).



Scheme 2. Possible mechanism of this domino reaction.

According to the above reaction results, a reasonable mechanism of this domino reaction has been presented in Scheme 2. At first, DABCO may attack at the β-position of MBH acetate **2a** in a S_N2' manner to form a reactive allylammonium salt **4**.[9] The latter is nucleophilically (S_N2') attacked by carbanion intermediate **1a'** (generated from **1a** under basic conditions) to give an isolable S_N2 adduct **5** in a non-separable mixture of diastereomer (dr = 3:1). The latter undergoes elimination of SO_3 under the influence of base to form an aza-triene intermediate **6** which in turn converts to 1,2-dihydropyridine **7** (isolated in its N-Boc protected form **8**, see experimental section) through a 6π-aza-electrocyclization process.[7j-m] Finally, the product **3aa** is generated from **7** through aromatization under O_2 atmosphere.

Under the above optimal reaction conditions, several 4-aryl/heteroaryl-substituted cyclic sulfamidate imines (**1a-i**) have been used as nucleophiles in the one-pot reaction with a diverse range of aryl/styryl-substituted MBH acetates of acrylate (**2a-k**) to evaluate the scope and generality of this reaction. As shown in Table 2, incorporation of the electron donating (Me, OMe, OBn) groups on the aryl rings of MBH acetates (**2b-c**) lowered their reactivities towards **1a** (48-72h vs 36-40h) as compared to the electron withdrawing ones such as F, Cl, Br, CF_3, CN and NO_2. However, all of the reactions afforded typically high yields (77-87%) of 4,6-diarylnicotinates (**3ab-3aj**, ORTEP data of **3ai**, ESI). Moreover, the cyclic sulfamidate imines (**1b-h**) possessing both electron rich (Me, OMe) and electron poor (F, Cl, Br) functionalities on the aryl nuclei attacked MBH acetates (**2a-j**) in a S_N2 manner, resulting in good to high yields (74-86%) of the corresponding nicotinates (**3ba-3hg**). It is noted that electron withdrawing functionalities (e.g. F, Cl, Br) reduce the nucleophilicities of cyclic sulfamidate imines, thus slowing the rates of the reactions (48-60h). Pleasantly, the cyclic imines having

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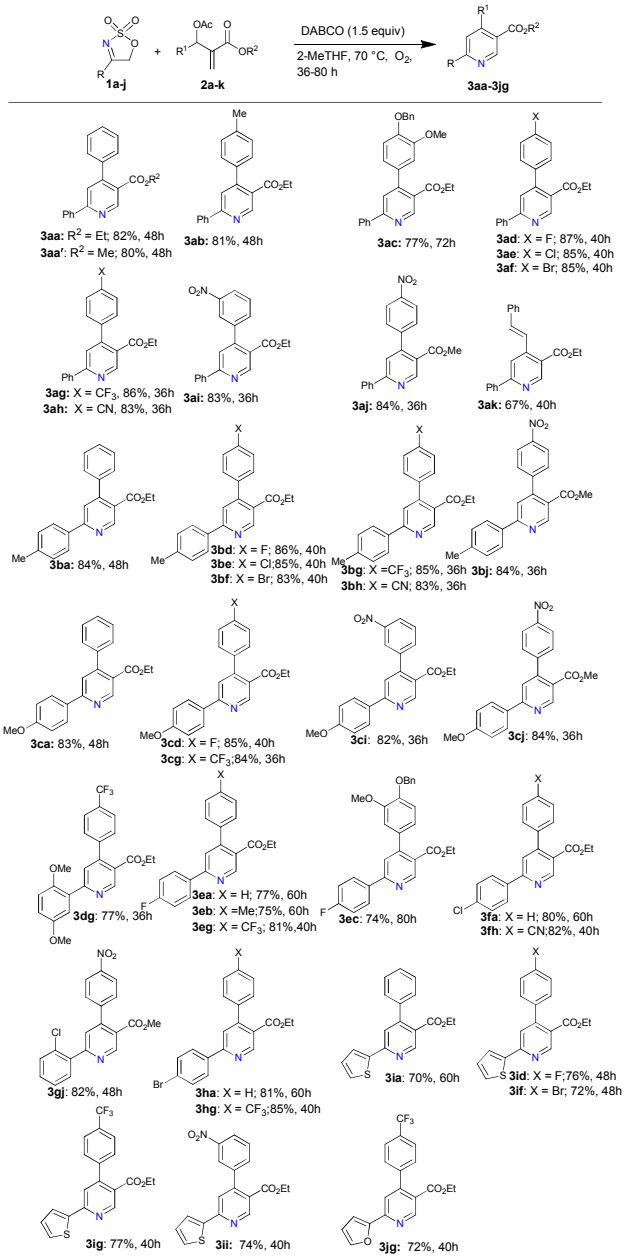
heteroaryl-substituents (**1i-g**) such as thiophene (**1i**)/furan (**1g**) also proceeded very well with a variety of MBH acetates under the present conditions which led to satisfactory chemical yields (70-77%) of 6-heteroaryl-substituted nicotinates (**3ia-3jg**). Notably, chemically challenging alkenyl MBH acetate **2k** was also found to be suitable substrate for the domino reaction with **1a**, leading to good yield (67%) of 4-styryl-6-phenylnicotinate (**3ak).** Moreover, several synthetically useful functionalities such as Me, OMe, OBn, F, Cl, Br, CF_3, NO_2, CN, CO_2Et, CO_2Me,

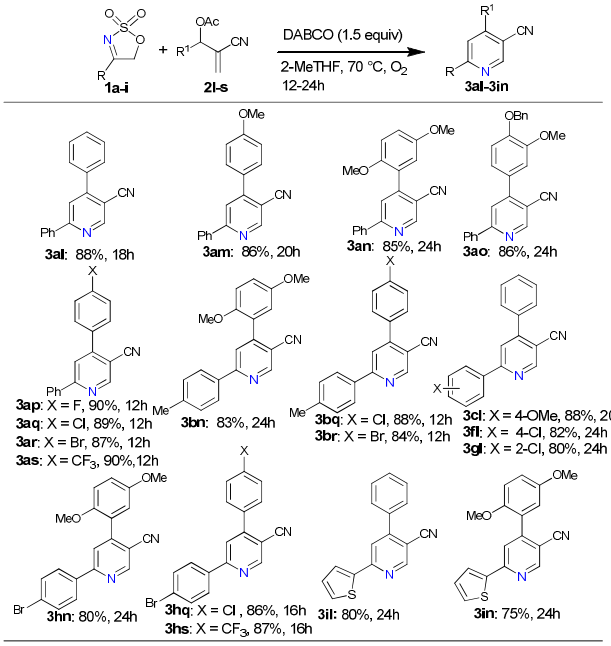
Table 2. Substrate scope of 4,6-diarylnicotinates synthesis.



thiophene, furan etc. were unaltered in the present mild conditions. Furthermore, this protocol offers an easy entry to unsymmetrically substituted nicotinates, in contrast to the traditional Hantzsch pyridine synthesis which affords substituted symmetrical pyridines.[11]

After successfully developing a simple metal-free based one-pot synthesis of 4,6-diarylnicotinates, we then applied the same procedure for the preparation of synthetically challenging[12] 4,6-diarylnicotinonitriles by involving the aryl-substituted MBH acetates derived from an acrylonitrile as reactive electrophiles. The obtained results in Table 3 demonstrated that regardless of the nature of the substituents (Me, OMe, OBn, F, Cl, Br, CF_3) and their positions on the aryl-rings of MBH adducts (**2l-s**), they underwent spotless reactions with a diverse range of aryl-substituted cyclic imines (**1a-h**) under established conditions, providing consistently high to excellent yields (80-90%) of the corresponding 4,6-diarylnicotinonitriles (**3al-3hs**, surrogates of nicotinic acid) after 12-24h. Moreover, this one–pot operation was not limited only for aryl-substituted cyclic imines **1a-h**, but it could be also equally applicable for heteroaryl-substituted cyclic imine. For instance, good yields (75-80%) of 6-thiophenyl-2-arylnicotinonitriles (**3il-3in**) were obtained after 24h when a 4-thiophenyl cyclic sulfamidate imine **1i** was used for this reaction**.**

Table 3. Synthesis of 4,6-diarylnicotonitriles.



In order to further expand the possible substrate scope, we were inspired to use aryl-substituted MBH acetates of MVK (**2t-2u**) as chemically challenging acceptors for this domino reaction. Gratifyingly, by using the cyclic imines (**1a-i**), all of the transformations were found reasonably clean and furnished 74-

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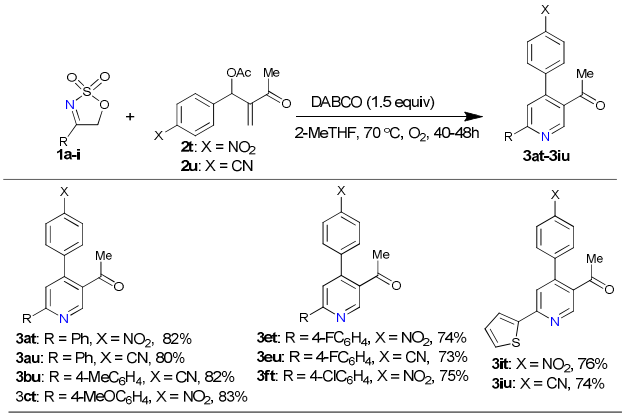
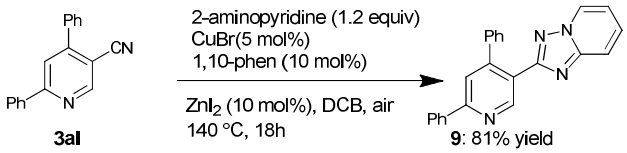
83% yields of 3-acetylpyridines (**3at-3iu**) after 40-48h (Table 4). Usually, they are very difficult to prepare through the conventional methods.[13]

Table 4. Substrate scope of MBH acetates of MVK.



Finally, to demonstrate the potential utility of prepared compound, **3al** was further converted into a potential PDE10A inhibitor[14] triazolopyridine derivative **9** in 81% yield using a reported method[15] (Scheme 6).



Scheme 3. Synthesis of the triazolopyridine derivative **9**

Conclusions

In the current manuscript, we have established a general, expedient, metal-free based novel domino reaction of several aryl/heteroaryl-substituted cyclic sulfamidate imines as suitable nucleophiles with a broad range of MBH acetates bearing ester/cyano/acetyl groups in the presence of DABCO as a base under O_2 atmosphere at 70 °C. This unprecedented tactic delivers a series of pharmacologically valuable 3-carboxylate/cyano/acetyl-4,6-diarylpyridine derivatives in high to excellent yields. Moreover, this smart pot-economy approach eliminates the use of highly expensive and toxic metal-salts, strong acids, large excess of external oxidants, multistep etc. In addition, the operational simplicity, broad substrate generality, compatibility with a variety of functional groups on the aryl rings and high to excellent yields make this procedure more powerful alternative to the established methods. Additional efforts towards the application of this method to generate therapeutically active pyridine derivatives are under progress.

Experimental Section

General information:

All the 4-aryl/heteroaryl-*5H*-1,2,3-oxathiazole-2,2-dioxides (**1a-j**)[16] and Morita-Baylis-Hillman acetates (**2a-2l**)[17] were synthesized by literature known procedures. All the bases were purchased from commercial sources (Sigma-Aldrich). All the reactions were carried out under O_2 atmosphere and monitored by TLC using Merck 60 F_{254} pre coated silica gel plates (0.25 mm thickness) and the products were visualized by UV detection. Flash chromatography was carried out with silica gel (200-300 mesh). FT-IR spectra were recorded on a BrukerTensor-27 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance (III) 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.

Representative one-pot procedure for the synthesis of ethyl 4,6-diphenylnicotinate (3aa):

To a stirred solution of compound **1a** (39.4 mg, 0.2 mmol) and **2a** (54.6 mg, 0.22 mmol) in 2-MeTHF (1.0 mL) was added DABCO (33.6 mg, 0.3 mmol) at room temperature. Then the reaction mixture was heated at 70 °C for 48h under O_2 atmosphere (monitored by TLC). Upon completion of the reaction, the reaction mixture was extracted with ethyl acetate (3 × 10 mL), washed with water and brine respectively, dried over Na_2SO_4. The combined organic phases were evaporated under reduced pressure to afford the crude product. Finally it was obtained in a pure form (49.7 mg, 82%) through column chromatography over silica-gel using a mixture of EtOAc/hexane (1:4, v/v) as the eluent. The product was fully characterized by its spectroscopic data (IR, ^{1}HNMR, ^{13}C NMR and HRMS).

All the products (**3ab-3jg**) in Table 2, **3al-3in** in Table 3 and **3at-3iu** in Table 4 were synthesized following the above procedure. All the products were characterized by their corresponding spectroscopic data (IR, ^{1}H, ^{13}C NMR and HRMS).

Ethyl 4,6-diphenylnicotinate (3aa):[7j] White solid; Yield: 82% (49.7 mg); mp 110-112 °C; R_f = 0.85 (EtOAc:hexane = 1:4); IR (KBr) ν 1700, 1585, 1534, 1493, 1467, 1443, 1363, 1299 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 9.13 (s, 1H), 8.07 (d, *J* = 6.8 Hz, 2H), 7.72 (s, 1H), 7.44-7.51 (m, 6H), 7.37-7.39 (s, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 1.07 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 167.1, 159.8, 151.5, 151.4, 139.5, 138.6, 130.1, 129.2, 128.6, 128.5, 128.3, 127.6, 125.1, 122.0, 61.5, 14.0; HRMS (ESI) m/z calcd for $C_{20}H_{18}NO_2$ $[M+H]^+$: 304.1332, found 304.1362.

Methyl 4,6-diphenylnicotinate (3aa′):[7r] White solid; Yield: 80% (46.3 mg); mp 108-110 °C; R_f = 0.85 (EtOAc:hexane = 1:4); IR (KBr): ν 1704, 1588, 1535, 1494, 1468, 1432, 1371, 1297, 1228, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 9.13 (s, 1H), 8.06 (d, *J* = 6.8 Hz, 2H), 7.72 (s, 1H), 7.45-7.51 (m, 6H), 7.37-7.39 (m, 2H), 3.73 (s,

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3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 160.0, 151.6, 151.5, 139.3, 138.5, 130.2, 129.2, 128.8, 128.6, 128.3, 127.6, 124.6, 122.1, 52.5; HRMS (ESI) m/z calcd for $C_{19}H_{15}NO_2Na$ $[M+Na]^+$: 312.0995, found 312.0981.

Ethyl 6-phenyl-4-(4-methylphenyl)nicotinate (3ab):[7j] White solid; Yield: 81% (51.4 mg); mp 114-116 °C; R_f = 0.85 (EtOAc:hexane = 1:4); IR (KBr) ν 1696, 1594, 1573, 1534, 1468, 1444, 1373, 1299, 1231 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.04 (d, J = 6.7 Hz, 2H), 7.69 (s, 1H), 7.43-7.49 (m, 3H), 7.23-7.28 (m, 4H), 4.19 (q, J = 7.0 Hz, 2H), 2.41 (s, 3H), 1.11 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ167.2, 159.7, 151.4, 151.3, 138.6, 138.6, 136.4, 130.0, 129.3, 129.1, 128.3, 127.5, 125.1, 122.0, 61.5, 21.5, 14.1;HRMS (ESI) m/z calcd for $C_{21}H_{19}NO_2Na[M+Na]^+$: 340.1308, found 340.1312.

Ethyl 4-(4-benzyloxy-3-methoxyphenyl)-6-phenylnicotinate (3ac): White solid; Yield: 77% (67.7 mg); mp 125-127 °C; R_f = 0.62 (EtOAc:hexane = 1:4); IR (KBr) ν 1704, 1591, 1533, 1510, 1467, 1414, 1373, 1303, 1240, 1205 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ9.07 (s, 1H), 8.06 (d, J = 6.7 Hz, 2H), 7.71 (s, 1H), 7.44-7.50 (m, 5H), 7.36-7.40 (m, 2H), 7.31-7.33 (m, 1H), 6.93-6.97 (m, 2H), 6.88-6.90 (m, 1H), 5.21 (s, 2H), 4.19 (q, J = 7.2 Hz, 2H), 3.91 (s, 3H), 1.10 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ167.4, 159.6, 151.1, 150.8, 149.6, 148.8, 138.5, 137.1, 132.3(2C), 130.0, 129.1, 128.8, 128.2, 127.5, 125.3, 121.7, 120.9, 113.8, 112.2, 71.2, 61.5, 56.3, 14.1;HRMS (ESI) m/z calcd for $C_{28}H_{25}NO_4Na[M+Na]^+$: 462.1676, found 462.1664.

Ethyl 4-(4-fluorophenyl)-6-phenylnicotinate(3ad): White solid; Yield: 87% (55.9 mg); mp 118-120°C; R_f = 0.84 (EtOAc:hexane = 1:4); IR (KBr)ν 1697, 1594, 1536, 1507, 1469, 1401, 1370, 1301, 1226 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ 9.14 (s, 1H), 8.05 (d, J = 6.5 Hz, 2H), 7.67 (s, 1H), 7.46-7.52 (m, 3H), 7.33-7.36 (m, 2H), 7.14 (t, J = 8.7 Hz, 2H), 4.20 (q, J = 7.2 Hz, 2H), 1.13 (t, J = 7.2 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 163.2 (d, J_{C-F}= 246 Hz) 160.0, 151.6, 150.5, 138.4, 135.5 (d, J_{C-F}= 3.6 Hz), 130.2 (d, J_{C-F}= 8.0 Hz), 129.2, 127.6, 124.9, 122.0, 115.6 (d, J_{C-F}= 21.8 Hz), 61.6, 14.1; HRMS (ESI) m/z calcd For $C_{20}H_{16}FNO_2Na[M+Na]^+$:344.1057, found 344.1044.

Ethyl 4-(4-chlorophenyl)-6-phenylnicotinate (3ae):[7j] White solid; Yield: 85% (57.3 mg); mp 122-124 °C; R_f = 0.80 (EtOAc:hexane = 1:4); IR (KBr) ν 1696, 1596, 1573, 1532, 1490, 1468, 1399, 1371, 1296, 1230cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ9.15 (s, 1H), 8.06 (d, J = 6.8 Hz, 2H), 7.66 (s, 1H), 7.46-4.51 (m, 3H), 7.42-7.44 (m, 2H), 7.30-7.32 (m, 2H), 4.21 (q, J = 7.2 Hz, 2H), 1.14 (t, J = 7.2 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ166.7, 160.1, 151.7, 150.4, 138.4, 137.9, 134.9, 130.3, 129.8, 129.2, 128.8, 127.6, 124.6, 121.8, 61.6, 14.1; HRMS (ESI) m/z calcd for $C_{20}H_{16}ClNO_2Na[M+Na]^+$: 360.0762, found 360.0791.

Ethyl 4-(4-bromophenyl)-6-phenylnicotinate (3af): Light yellow solid; Yield: 85%(64.8 mg); mp130-132°C; R_f = 0.85 (EtOAc:hexane = 1:4);IR (KBr) ν 1697, 1597, 1573, 1531, 1489, 1469, 1446, 1394, 1376, 1361, 1298, 1233 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ9.15 (s, 1H), 8.04-8.06 (m, 2H), 7.65 (s, 1H), 7.56-7.60 (m, 2H), 7.45-7.51 (m, 3H), 7.22-7.25 (m, 2H), 4.20 (q, J = 7.2 Hz, 2H), 1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ166.6, 160.1, 151.8, 150..4, 138.4, 138.3, 131.7, 130.3, 130.0, 129.2, 127.6, 124.5, 123.0, 121.8, 61.6, 14.1; HRMS (ESI) m/z calcd for $C_{20}H_{16}{}^{79}BrNO_2Na[M+Na]^+$: 404.0257, found 404.0202; HRMS (ESI) m/z calcd for $C_{20}H_{16}{}^{81}BrNO_2Na[M+Na]^+$:406.0237, found 406.0186.

Ethyl 6-phenyl-4-(4-trifluoromethylphenyl)nicotinate(3ag): White solid; Yield: 86% (63.8 mg); mp 127-129 °C; R_f = 0.75 (EtOAc:hexane = 1:4); IR (KBr) ν 1699, 1592, 1574, 1537, 1471, 1362, 1328, 1302, 1234 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ9.22 (s, 1H), 8.06-8.08 (m, 2H), 7.72 (d, J = 8.0 Hz, 2H), 7.68 (s, 1H), 7.48-7.53 (m, 5H), 4.19 (q, J = 7.2 Hz, 2H), 1.10 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ166.2, 160.1, 151.8, 150.4, 143.3, 138.0, 131.3, 131.0, 130.6, 130.5, 130.3, 129.3, 128.8, 127.7, 125.7, 125.5, 125.5, 125.4, 125.4, 124.4, 123.0, 121.8, 61.7, 14.0; HRMS (ESI) m/z calcd for $C_{21}H_{16}F_3NO_2Na[M+Na]^+$394.1025, found 394.1025.

Ethyl 4-(4-cyanophenyl)-6-phenylnicotinate(3ah): Light yellow solid; Yield: 83%(54.5 mg); mp 130-132 °C; R_f = 0.45 (EtOAc:hexane = 1:4); IR (KBr) ν 2225, 1697, 1591, 1572, 1535, 1502, 1468, 1444, 1403, 1374, 1362, 1318, 1300, 1231 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ 9.15 (s, 1H), 7.98-8.00 (m, 2H), 7.67 (d, J = 8.0 Hz, 2H), 7.56 (s, 1H), 7.38-7.42 (m, 5H), 4.12 (q, J = 7.2 Hz, 2H), 1.06 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 160.0, 151.8, 149.6, 144.0, 137.7, 131.9, 130.2, 128.9 (2C), 127.3, 123.6, 121.1, 118.5, 112.1, 61.4, 13.8;HRMS (ESI) m/z calcd for $C_{21}H_{17}N_2O_2[M+H]^+$ 329.1285, found 329.1283.

Ethyl 4-(3-nitrophenyl)-6-phenylnicotinate(3ai): Light yellow solid; Yield: 83%(57.8 mg); mp 135-137 °C; R_f = 0.45 (EtOAc:hexane = 1:4); IR (KBr) ν 1720, 1593, 1579, 1528, 1481, 1470, 1443, 1362, 1348, 1286, 1245, 1230 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ 9.26 (s, 1H), 8.31 (d, J = 8.0 Hz, 1H), 8.26 (s, 1H), 8.07-8.09 (m, 2H), 7.62-7.70 (m, 3H), 7.48-7.53 (m, 3H), 4.22 (q, J = 6.8 Hz, 2H), 1.16 (t, J = 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 165.6, 160.2, 151.9, 149.0, 148.0, 140.9, 137.6, 134.2, 130.2, 129.1, 129.0, 127.3, 123.6, 123.2, 123.1, 121.5, 61.5, 13.8;HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2O_4[M+H]^+$ 349.1183, found 349.1189.

Methyl 4-(4-nitrophenyl)-6-phenylnicotinate(3aj): Light yellow solid; Yield: 84% (56.1 mg); mp 136-138 °C; R_f = 0.45 (EtOAc:hexane = 1:4); IR (KBr) ν 1721, 1589, 1579, 1538, 1508, 1474, 1445, 1433, 1355, 1348, 1322, 1295, 1247, 1231 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.26 (s, 1H), 8.33 (d, J = 8.8 Hz, 2H), 8.06-8.09 (m, 2H), 7.67 (s, 1H), 7.49-7.54 (m, 5H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 165.9, 160.2, 151.8, 149.5, 147.7, 145.8, 137.6, 130.3, 129.1, 129.0, 127.3, 123.4, 123.1, 121.3, 52.3; HRMS (ESI) m/z calcd for $C_{19}H_{15}N_2O_4[M+H]^+$ 335.1026, found 335.1026.

Ethyl 4-(*E*)-styryl-6-phenylnicotinate (3ak): White solid; Yield: 67% (44.1 mg); mp 74-76 °C; R_f = 0.84 (EtOAc:hexane = 1:9); IR (KBr): 1715, 1628, 1583, 1531, 1446, 1371, 1274, 1217, 1173, 1093, 1021, 961 ν cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.17 (s, 1H), 8.04-8.09 (m, 3H), 7.96 (s, 1H), 7.55-7.58 (m, 2H), 7.43-7.49 (m, 2H), 7.27-7.38 (m, 3H), 7.21 (s, 1H), 7.11-7.15 (m, 1H), 4.40 (q, J = 6.8 Hz, 2H), 1.40 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ

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166.2, 160.0, 152.4, 147.4, 138.5, 136.5, 134.8, 129.8, 128.9, 128.8 (2 C), 127.3 (2 C), 125.3, 122.1, 117.0, 61.3, 14.3; HRMS (ESI) m/z calcd for $C_{22}H_{19}NO_2[M+H]^+$: 330.1489, found 330.1502.

Ethyl 4-phenyl-6-(4-methylphenyl)nicotinate (3ba): White solid; Yield: 84% (55.2 mg); mp 114-116 °C; R_f = 0.85 (EtOAc:hexane = 1:4); IR (KBr) ν 1698, 1588, 1532, 1469, 1443, 1363, 1310, 1232 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.97 (d, J = 8.2 Hz, 2H), 7.69 (s, 1H), 7.44-7.45 (m, 3H), 7.36-7.38 (m, 2H), 7.29 (d, J = 8.0 Hz, 2H), 4.17 (q, J = 7.2 Hz, 2H), 2.41 (s, 3H), 1.07 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ167.1, 159.8, 151.4, 151.4, 140.3, 139.6, 135.7, 129.9, 128.6, 128.5, 128.3, 127.5, 124.7, 121.6, 61.4, 21.6, 14.0; HRMS (ESI) m/z calcd for $C_{21}H_{20}NO_2[M+H]^+$318.1489, found 318.1491.

Ethyl 4-(4-fluorophenyl)-6-(4-methylphenyl)nicotinate (3bd): White solid; Yield: 86% (57.7 mg); mp 125-127 °C; R_f =0.84 (EtOAc:hexane = 1:4); IR (KBr) ν 1696, 1594, 1533, 1507, 1469, 1448, 1369, 1298, 1227 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 9.12 (s, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.64 (s, 1H), 7.29-7.36 (m, 4H), 7.14 (t, J = 8.5 Hz, 2H), 4.19 (q, J = 7.2 Hz, 2H), 2.41 (s, 3H), 1.13 (t, J = 7.2 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$)δ 166.9, 163.2(d, J_{C-F}= 246.0 Hz),160.0, 151.6, 150.4, 140.5, 135.6 (d, J_{C-F}= 3.6 Hz), 130.2, 129.9, 127.5, 124.5, 121.6, 115.7, 115.4, 61.5, 21.6, 14.1; HRMS (ESI) m/z calcd for $C_{21}H_{19}FNO_2[M+H]^+$ 336.1394, found 336.1386.

Ethyl 4-(4-chlorophenyl)-6-(4-methylphenyl)nicotinate (3be): White solid; Yield: 85% (59.7 mg); mp 127-129 °C; R_f = 0.80 (EtOAc:hexane = 1:4); IR (KBr) ν 1694, 1593, 1570, 1530, 1491, 1468, 1397, 1362, 1293, 1231, 1183 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.14 (s, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.63 (s, 1H), 7.41-7.43 (m, 2H), 7.29-7.31 (m, 4H), 4.20 (q, J = 7.0 Hz, 2H), 2.41 (s, 3H), 1.14 (t, J = 7.0Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ166.7, 160.0, 151.7, 150.3, 140.5, 138.1, 135.5, 134.8, 129.9, 129.8, 128.7, 127.5, 124.3, 121.5, 61.6, 21.6, 14.1;HRMS (ESI) m/z calcd for $C_{21}H_{18}ClNO_2Na[M+Na]^+$ 374.0918, found 374.0908.

Ethyl 4-(4-bromophenyl)-6-(4-methylphenyl)nicotinate (3bf): White solid; Yield: 83% (65.7 mg); mp 135-137 °C; R_f = 0.84 (EtOAc:hexane = 1:4); IR (KBr) ν 1694, 1594, 1570, 1530, 1488, 1467, 1393, 1361, 1294, 1232cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.11 (s, 1H), 7.93 (d, J = 6.7 Hz, 2H), 7.60 (s, 1H), 7.55 (d, J = 6.7 Hz, 2H), 7.26 (d, J = 7.2 Hz, 2H), 7.20-7.22 (m, 2H), 4.17 (q, J = 7.0 Hz, 2H), 2.38 (s, 3H), 1.12 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ166.6, 160.0, 151.7, 150.3, 140.5, 138.5, 135.5, 131.6, 130.0, 129.9, 127.5, 124.2, 122.9, 121.4, 61.6, 21.6, 14.1;HRMS (ESI) m/z calcd for $C_{21}H_{19}{}^{79}BrNO_2[M+H]^+$ 396.0594, found 396.0589; HRMS (ESI) m/z calcd for $C_{21}H_{19}{}^{81}BrNO_2[M+H]^+$ 398.0574, found 398.0574.

Ethyl 6-(4-methylphenyl)-4-(4-trifluoromethylphenyl)nicotinate (3bg): White solid; Yield: 85%(65.5 mg); mp134-136 °C; R_f = 0.75 (EtOAc:hexane = 1:4); IR (KBr) ν 1698, 1592, 1571, 1536, 1470, 1363, 1327, 1296, 1233 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.20 (s, 1H), 7.97 (d, J = 8.2 Hz, 2H), 7.71 (d, J = 8.0 Hz, 2H), 7.64 (s, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 4.18 (q, J = 7.2 Hz, 2H), 2.42 (s, 3H), 1.10 (t, J = 7.2 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$)δ 166.3, 160.2, 151.9, 150.2, 143.5, 140.7, 135.4, 131.2, 130.9, 130.5, 130.2, 130.0, 128.8, 127.5, 125.7, 125.5, 125.4, 125.4, 125.3, 124.0, 123.0, 121.4, 61.6, 21.6, 14.0; HRMS (ESI) m/z calcd for $C_{22}H_{18}F_3NO_2Na[M+Na]^+$ 408.1182, found 408.1183.

Ethyl 4-(4-cyanophenyl)-6-(4-methylphenyl)nicotinate (3bh): White solid; Yield: 83% (56.8 mg); mp 134-136 °C; R_f = 0.45 (EtOAc:hexane = 1:4); IR (KBr) ν 2227, 1696, 1592, 1532, 1503, 1469, 1363, 1322, 1296, 1232 cm^{-1};^1H NMR (400 MHz, $CDCl_3$)δ9.13 (s, 1H), 7.89 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.53 (s, 1H), 7.38 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 4.11 (q, J = 7.2 Hz, 2H), 2.34 (s, 3H), 1.06 (t, J = 7.2Hz, 3H; ^{13}C NMR (100 MHz, $CDCl_3$)δ 165.7, 160.0, 151.8, 149.5, 144.2, 140.5, 134.9, 131.9, 129.7, 128.9, 127.2, 123.2, 120.8, 118.5, 112.1, 61.3, 21.3, 13.8; HRMS (ESI) m/z calcd for $C_{22}H_{19}N_2O_2[M+H]^+$ 343.1441, found 343.1449.

Methyl 4-(4-nitrophenyl)-6-(4-methylphenyl)nicotinate (3bj): White solid; Yield: 84% (58.5 mg); mp 140-142 °C; R_f = 0.45 (EtOAc:hexane = 1:4); IR (KBr) ν 1712, 1587, 1538, 1513, 1432, 1346, 1318, 1291, 1228 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 9.23 (s,1H), 8.32 (d, J = 8.0, 2H), 7.97 (d, J = 8.0 Hz, 2H), 7.63 (s, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 3.76 (s, 3H), 2.42 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$)δ 166.0, 160.2, 151.9, 149.5, 147.7, 146.0, 140.7, 134.8, 129.7, 129.1, 127.2, 123.4, 122.7, 120.9, 52.3, 21.4; HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2O_4[M+H]^+$ 349.1183, found 349.1184.

Ethyl 6-(4-methoxyphenyl)-4-phenylnicotinate (3ca):[7j] White solid; Yield: 83% (57.3 mg); mp 120-122 °C; R_f = 0.80 (EtOAc:hexane = 1:4); IR (KBr) ν 1713, 1591, 1530, 1514, 1472, 1443, 1420, 1363, 1320, 1300, 1252, 1231 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.04 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 7.43-7.44 (m, 3H), 7.36-7.37 (m, 2H), 7.00 (d, 8.5 Hz, 2H), 4.16 (q, J = 7.2 Hz, 2H), 3.86 (s, 3H), 1.07 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ167.1, 161.5, 159.4, 151.5, 151.4, 139.7, 131.1, 129.0, 128.5, 128.5, 128.3, 124.2, 121.1, 114.5, 61.4, 55.7, 14.0;HRMS (ESI) m/z calcd for $C_{21}H_{20}NO_3[M+H]^+$ 334.1438, found 334.1452.

Ethyl 4-(4-fluorophenyl)-6-(4-methoxyphenyl)nicotinate(3cd): White solid; Yield: 85% (59.7 mg); mp 131-133 °C; R_f = 0.80 (EtOAc:hexane = 1:4); IR (KBr) ν 1693, 1601, 1533, 1509, 1469, 1366, 1299, 1251, 1224 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.10 (s, 1H), 8.03 (d, J = 8.8 Hz, 2H), 7.59 (s, 1H), 7.32-7.35 (m, 2H), 7.13 (t, J = 8.5 Hz, 2H), 7.00 (d, J = 8.5 Hz, 2H), 4.18 (q, J = 7.2 Hz, 2H), 3.86 (s, 3H), 1.13 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 163.1(d, J_{C-F}= 246 Hz), 161.6, 159.6, 151.7, 150.4, 135.7 (d, J_{C-F}= 3.6 Hz), 130.9, 130.2 (d, J_{C-F}= 8.0 Hz), 129.0, 124.0, 121.1, 115.6 (d, J_{C-F}= 21.9 Hz), 114.6, 61.5, 55.7, 14.1; HRMS (ESI) m/z calcd for $C_{21}H_{18}FNO_3Na[M+Na]^+$ 374.1163, found 374.1161.

Ethyl 6-(4-methoxyphenyl)-4-(4-trifluoromethylphenyl)nicotinate (3cg): White solid; Yield: 84% (67.4 mg); mp140-142 °C; R_f = 0.67 (EtOAc:hexane = 1:4); IR (KBr) ν 1700, 1606, 1595, 1574, 1536, 1521, 1470, 1363, 1325,

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1300, 1251, 1232 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 9.17 (s, 1H), 8.04 (d, J = 8.7 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.59 (s, 1H), 7.47 (d, J = 7.7 Hz, 2H), 7.00 (d, J = 8.8 Hz, 2H), 4.17 (q, J = 7.0 Hz, 2H), 3.86 (s, 3H), 1.09 (t, J = 7.0 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ166.3, 161.7, 159.8, 151.9, 150.2, 143.5, 131.1, 130.8, 130.7, 130.4, 130.1, 129.0, 128.8, 128.4, 125.7, 125.4, 125.4, 125.3, 125.3, 123.4, 123.0, 120.8, 120.3, 114.6, 61.5, 55.6, 14.0; HRMS (ESI) m/z calcd for $C_{22}H_{18}F_3NO_3Na[M+Na]^+$ 424.1131, found 424.1127.

Ethyl 6-(4-methoxyphenyl)-4-(3-nitrophenyl)nicotinate (3ci): White solid; Yield: 82% (65.6 mg); mp 142-144 °C; R_f = 0.40 (EtOAc:hexane = 1:4); IR (KBr) ν 1704, 1586, 1535, 1466, 1442, 1347, 1297, 1255, 1223 cm^{-1};^1H NMR (400 MHz, $CDCl_3$) δ9.22 (s, 1H), 8.30 (d, J = 8.0 Hz, 1H), 8.25 (s, 1H), 8.05 (d, J = 8.8 Hz, 2H), 7.61-7.69 (m, 3H), 7.01 (d, J = 8.8 Hz, 2H), 4.20 (q, J = 6.8Hz, 2H), 3.87 (s, 3H), 1.51 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 165.6, 161.5, 159.8, 151.9, 148.9, 147.9, 141.1, 134.3, 130.1, 129.0, 128.8, 123.2, 123.0, 122.7, 120.5, 114.3, 61.3, 55.4, 13.8;HRMS (ESI) m/z calcd for $C_{21}H_{18}N_2O_5Na[M+Na]^+$ 401.1108, found 401.1121.

Methyl 6-(4-methoxyphenyl)-4-(4-nitrophenyl)nicotinate (3cj): Light yellow solid; Yield: 84% (61.2 mg); mp 144-146 °C; R_f = 0.35 (EtOAc:hexane = 1:4); IR (KBr) ν 1724, 1590, 1542, 1514, 1476, 1435, 1353, 1292, 1242 cm^{-1};^1H NMR (400 MHz, $CDCl_3$)δ 9.21 (s, 1H), 8.31 (d, J = 8.4 Hz, 2H), 8.04 (d, J = 8.8 Hz, 2H), 7.59 (s, 1H), 7.51 (d, J = 8.8 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 3.88 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 165.9, 161.5, 159.8, 151.8, 149.4, 147.6, 146.1, 130.0, 129.0, 128.8, 123.3, 122.2, 120.3, 114.3, 55.4, 52.2; HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2O_5[M+H]^+$ 365.1132, found 365.1137.

Ethyl 6-(2,5-dimethoxyphenyl)-4-(4-trifluoromethyl phenyl)nicotinate (3dg): White solid; Yield: 77% (66.4 mg); mp146-148 °C; R_f =0.63(EtOAc:hexane = 1:4); IR (KBr) ν 1720, 1587, 1541, 1502, 1466, 1424, 1370, 1326, 1285, 1229, 1205 cm^{-1};^1H NMR (400 MHz, $CDCl_3$)δ 9.19 (s, 1H), 7.89 (s, 1H), 7.70 (d, J = 8.0 Hz, 2H), 7.47-7.51 (m, 3H), 6.93-6.99 (m, 2H), 4.18 (q, J = 7.2 Hz, 2H), 3.84 (s, 3H), 3.80 (s, 3H), 1.09 (t, J = 7.2 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$)δ165.5, 157.7, 153.3, 150.9, 150.3, 148.0, 142.5, 130.1, 129.7, 129.4, 129.1, 129.0, 127.9, 127.4, 125.3, 124.7, 124.4, 124.4, 124.4, 124.3, 123.0, 122.0, 116.2, 115.1, 112.4, 60.6, 55.6, 55.2, 13.0; HRMS (ESI) m/z calcd for $C_{23}H_{21}F_3NO_4[M+H]^+$ 432.1417, found 432.1401.

Ethyl 6-(4-fluorophenyl)-4-phenylnicotinate(3ea): White solid; Yield: 77% (49.5 mg); mp 119-121 °C; R_f = 0.83 (EtOAc:hexane = 1:4); IR (KBr) ν 1697, 1584, 1534, 1514, 1468, 1366, 1297, 1230 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.05-8.08 (m, 2H), 7.66 (s, 1H), 7.44-7.45 (m, 3H), 7.36-7.37 (m, 2H), 7.17 (t, J = 8.8 Hz, 2H), 4.17 (q, J = 7.0 Hz, 2H), 1.07 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.04, 164.3(d, J_{C-F}= 248 Hz), 158.7, 151.6, 151.5, 139.4, 134.7 (d, J_{C-F}= 3.6 Hz), 129.5 (d, J_{C-F}= 8.7 Hz 128.7, 128.6, 128.3, 125.0, 121.6, 116.2 (d, J_{C-F}= 21.0 Hz), 61.5, 14.0;HRMS (ESI) m/z calcd for $C_{20}H_{17}FNO_2[M+H]^+$ 322.1238, found 322.1224.

Ethyl 6-(4-fluorophenyl)-4-(4-methylphenyl)nicotinate (3eb): White solid; Yield: 75% (50.3 mg); mp 126-128 °C; R_f = 0.83(EtOAc:hexane = 1:4); IR (KBr) ν 1692, 1598, 1535, 1510, 1468, 1363, 1323, 1300, 1231 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.07 (s, 1H), 8.03-8.06 (m, 2H), 7.64 (s, 1H), 7.26 (s, 4H), 7.15 (t, J = 8.5 Hz, 2H), 4.19 (q, J = 7.0 Hz, 2H), 2.41 (s, 3H), 1.12(t, J = 7.0Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ167.1, 164.3(d, J_{C-F}= 248 Hz), 158.6, 151.5, 151.4, 138.7, 136.3, 134.8 (d, J_{C-F}= 3.6.0 Hz), 129.5 (d, J_{C-F}= 8.0 Hz), 129.3, 128.2, 125.0, 121.6, 116.2(d, J_{C-F}= 21.0 Hz), 61.5, 21.5, 14.1;HRMS (ESI) m/z calcd for $C_{21}H_{18}FNO_2Na[M+Na]^+$358.1214, found 358.1207.

Ethyl 6-(4-fluorophenyl)-4-(4-trifluoromethylphenyl)nicotinate (3eg): White solid; Yield: 81% (66.6 mg); mp 145-147 °C; R_f = 0.72 (EtOAc:hexane = 1:4); IR (KBr)ν 1694, 1595, 1534, 1514, 1469, 1407, 1365, 1325, 1299, 1233 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.19 (s, 1H), 8.05-8.09 (m, 2H), 7.72 (d, J = 8.0 Hz, 2H), 7.62 (s, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.18 (t, J = 8.8 Hz, 2H), 4.18 (q, J = 7.2 Hz, 2H), 1.09 (t, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ166.2, 164.5 (d, J_{C-F}= 249 Hz), 159.1, 152.0, 150.4, 143.2, 134.4 (d, J_{C-F}= 3.6 Hz), 131.4, 131.0, 130.7, 130.4, 129.6 (d, J_{C-F}= 8.0 Hz), 128.8, 125.7, 125.5, 125.5, 125.5, 125.4, 124.3, 123.0, 121.4, 116.4 (d, J_{C-F}= 21.8 Hz), 61.7, 14.0; HRMS (ESI) m/z calcd for $C_{21}H_{15}F_4NO_2Na[M+Na]^+$ 412.0931, found 412.0935.

Ethyl 4-(4-benzyloxy-3-methoxyphenyl)-6-(4-fluorophenyl)nicotinate (3ec): White solid; Yield: 74% (67.7mg); mp 135-137 °C; R_f = 0.60 (EtOAc:hexane = 1:4); IR (KBr) ν 1728, 1601, 1584, 1537, 1509, 1471, 1454, 1411, 1366, 1318, 1261, 1231, 1205, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.03 (s, 1H), 8.03-8.07 (m, 2H), 7.65 (s, 1H), 7.45-7.47 (m, 2H), 7.38 (t, J = 7.0 Hz, 2H), 7.31-7.33 (m, 1H), 7.16 (t, J = 8.2 Hz, 2H), 6.86-6.97 (m, 3H), 5.2 (s, 2H), 4.18 (q, J = 7.2 Hz, 2H), 3.91 (s, 3H), 1.09 (t, J =7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ167.4, 164.2(d, J_{C-F} = 248.0 Hz), 158.6, 151.2, 150.9, 149.7, 148.8, 137.1, 134.8 (d, J_{C-F}= 3.6 Hz), 132.3, 129.5 (d, J_{C-F}= 8.7 Hz), 128.9, 128.2, 127.5, 125.3, 121.4, 120.9, 116.2 (d, J_{C-F}= 21.1 Hz), 113.9, 112.2, 71.2, 61.5, 56.4, 14.1; HRMS (ESI) m/z calcd for $C_{28}H_{24}FNO_4Na[M+Na]^+$: 480.1582, found 480.1564.

Ethyl 6-(4-chlorophenyl)-4-phenylnicotinate (3fa):[7j]White solid; Yield: 80% (53.9 mg); mp 124-126 °C; R_f = 0.85 (EtOAc:hexane = 1:4); IR (KBr) ν 1702, 1590, 15321, 1494, 1467, 1363, 1308, 1290, 1232, cm^{-1}; ^1HNMR (400 MHz, $CDCl_3$)δ9.11 (s, 1H), 8.01 (d, J = 8.5 Hz, 2H), 7.68 (s, 1H), 7.44-7.47 (m, 5H), 7.35-7.37 (m, 2H), 4.17 (q, J = 7.2 Hz, 2H), 1.07 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ167.0, 158.5, 151.6, 151.5, 139.3, 137.0, 136.4, 129.4, 128.9, 128.8, 128.6, 128.3, 125.3, 121.7, 61.6, 14.0;HRMS (ESI) m/z calcd for $C_{20}H_{16}ClNO_2Na[M+Na]^+$ 360.0762, found 360.0785.

Ethyl 6-(4-chlorophenyl)-4-(4-cyanophenyl)nicotinate(3fh): White solid; Yield: 82% (59.4 mg); mp 138-140 °C; R_f = 0.44

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(EtOAc:hexane = 1:4);IR (KBr) ν 2224, 1717, 1589, 1536, 1501, 1470, 1404, 1363, 1281, 1225, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 9.21 (s, 1H), 8.01 (d, J = 8.8 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H), 7.61 (s, 1H), 7.45-7.48 (m, 4H), 4.20 (q, J = 7.2 Hz, 2H), 1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 165.5, 158.7, 151.8, 149.7, 143.9, 136.5, 136.1, 131.9, 129.2, 128.9, 128.6, 123.8, 120.9, 118.4, 112.3, 61.5, 13.8;HRMS (ESI) m/z calcd For $C_{21}H_{16}ClNO_2[M+H]^+$ 363.0895, found 363.0916.

Methyl 6-(2-chlorophenyl)-4-(4-nitrophenyl)nicotinate(3gj): White solid; Yield: 82% (60.4 mg); mp 150-152 °C; R_f = 0.45 (EtOAc:hexane = 1:4); IR (KBr) ν 1714, 1584, 1539, 1508, 1438, 1427, 1354, 1317, 1293, 1246, 1230 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 9.26 (s, 1H), 8.31 (d, J = 8.4 Hz, 2H), 7.68-7.70 (m, 2H), 7.49-7.55 (m, 3H), 7.39-7.51 (m, 2H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 165.9, 159.7, 151.5, 148.3, 147.8, 145.3, 137.6, 132.1, 131.6, 130.5, 130.4, 129.2, 127.3, 125.9, 123.7, 123.5, 52.5; HRMS (ESI) m/z calcd for $C_{19}H_{14}ClN_2O_4[M+H]^+$: 369.0637, found 369.0640.

Ethyl 6-(4-bromophenyl)-4-phenylnicotinate (3ha): White solid; Yield: 81% (61.7mg); mp 134-136 °C; R_f= 0.85 (EtOAc:hexane = 1:4); IR (KBr) ν 1702, 1589, 1532, 1492, 1466, 1443, 1367, 1307, 1232 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.10 (s, 1H), 7.95 (d, J = 8.2 Hz, 2H), 7.68 (s, 1H), 7.62 (d, J = 8.5 Hz, 2H), 7.44-7.45 (m, 3H), 7.35-7.37 (m, 2H), 4.17 (q, J = 7.2 Hz, 2H), 1.07 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ167.0, 158.6, 151.6, 151.5, 139.3, 137.4, 132.3, 129.1, 128.8, 128.6, 128.3, 125.4, 124.8, 121.7, 61.6, 14.0;HRMS (ESI) m/z calcd for $C_{20}H_{16}{}^{79}BrNO_2Na[M+Na]^+$ 404.0257, found 404.0246.HRMS (ESI) m/z calcd for $C_{20}H_{16}{}^{81}BrNO_2Na[M+Na]^+$ 406.0237, found 406.0234.

Ethyl 6-(4-bromophenyl)-4-(4-trifluoromethylphenyl)nicotinate (3hg): White solid; Yield: 85% (76.4 mg); mp 150-152 °C; R_f = 0.74 (EtOAc:hexane = 1:4); IR (KBr) ν 1700, 1590, 1539, 1471, 1367, 1327, 1299, 1228 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.19 (s, 1H), 7.95 (d, J = 8.5 Hz, 2H), 7.72 (d, J = 8.2 Hz, 2H), 7.62-7.64 (m, 3H), 7.47 (d, J = 8.0 Hz, 2H), 4.18 (q, J = 7.2 Hz, 2H), 1.09 (t, J = 7.2 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$)δ166.2, 159.0, 152.0, 150.5, 143.1, 137.1, 132.4, 131.0, 130.7, 129.1, 128.8, 125.6, 125.5, 125.5, 125.4, 125.1, 124.7, 123.0, 121.5, 61.7, 14.0; HRMS (ESI) m/z calcd for $C_{21}H_{15}{}^{79}BrF_3NO_2Na[M+Na]^+$ 472.0130, found 472.0111.HRMS (ESI) m/z calcd for $C_{21}H_{15}{}^{81}BrF_3NO_2Na[M+Na]^+$ 474.0111, found 474.0110.

Ethyl 4-phenyl-6-(thiophen-2-yl)nicotinate (3ia): White solid; Yield: 70% (43.3 mg); mp 110-112 °C; R_f = 0.82 (EtOAc:hexane = 1:4); IR (KBr) ν 1693, 1585, 1525, 1468, 1378, 1364, 1303, 1236, 1207, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.02 (s, 1H), 7.66 (d, J = 3.5 Hz, 1H), 7.60 (s, 1H), 7.44-7.47 (m, 4H), 7.34-7.36 (m, 2H), 7.13 (t, J = 4.0 Hz, 1H), 4.15 (q, J = 7.2 Hz, 2H), 1.06 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ166.7, 154.8, 151.6, 151.5, 144.0, 139.3, 129.4, 128.7, 128.6, 128.5, 128.2, 126.4, 124.6, 120.1, 61.4, 14.0;HRMS (ESI) m/z calcd for $C_{18}H_{15}NO_2SNa[M+Na]^+$ 332.0716, found 332.0726.

Ethyl 4-(4-fluorophenyl)-6-(thiophen-2-yl)nicotinate (3id):White solid; Yield: 76% (49.7 mg); mp 1120-122 °C; R_f = 0.83 (EtOAc:hexane = 1:4); IR (KBr) ν 1707, 1587, 1527, 1508, 1471, 1374, 1299, 1226, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 9.02 (s, 1H),7.66 (d, J = 3.4 Hz, 1H), 7.55 (s, 1H), 7.47 (d, J = 4.7 Hz, 1H), 7.31-7.34 (m, 2H), 7.12-7.16 (m, 3H), 4.17 (q, J = 7.2 Hz, 2H), 1.12 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ166.5, 163.2 (d, $J_{C\text{-}F}$= 247 Hz),154.9, 151.8, 150.6, 143.8, 135.3 (d, $J_{C\text{-}F}$= 2.9 Hz), 130.1(d, $J_{C\text{-}F}$= 8.0 Hz), 129.6, 128.6, 126.5, 124.3, 120.1, 115.6 (d, $J_{C\text{-}F}$= 21.8 Hz) 61.5, 14.1; HRMS (ESI) m/z calcd for $C_{18}H_{14}FNO_2S[M+Na]^+$ 350.0621, found 350.0628.

Ethyl 4-(4-bromophenyl)-6-(thiophen-2-yl)nicotinate(3if): White solid; Yield: 72% (55.7 mg); mp127-129 °C; R_f = 0.84 (EtOAc:hexane = 1:4); IR (KBr) ν 1693, 1588, 1524, 1487, 1467, 1425, 1395, 1371, 1303, 1235, 1207, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.04 (s, 1H), 7.67 (d, J = 2.6 Hz, 1H), 7.58 (d, J = 8.2 Hz, 2H), 7.54 (s, 1H), 7.48 (d, J = 4.5 Hz, 1H), 7.22 (d, J = 8.2 Hz, 2H), 7.13-7.15 (m, 1H), 4.18 (q, J = 7.2 Hz, 2H), 1.13 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ166.3, 155.1, 152.0, 150.5, 143.8, 138.3, 131.7, 130.0, 129.7, 128.7, 126.6, 124.1, 123.1, 119.9, 61.6, 14.1; HRMS (ESI) m/z calcd for $C_{18}H_{14}{}^{79}BrNO_2SNa[M+Na]^+$ 409.9821, found 409.9821.HRMS (ESI) m/z calcdfor $C_{18}H_{14}{}^{81}BrNO_2SNa[M+Na]^+$ 411.9801, found 411.9800.

Ethyl 6-(thiophen-2-yl)-4-(4-trifluoromethylphenyl)nicotinate (3ig): White solid; Yield: 77%(58.1 mg); mp 130-132°C; R_f = 0.72 (EtOAc:hexane = 1:4); IR (KBr) ν 1707, 1588, 1530, 1473, 1366, 1330, 1231 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 9.10 (s, 1H), 7.71 (d, J = 8.2 Hz, 2H), 7.67 (d, J = 3 Hz, 1H), 7.55 (s, 1H), 7.45-7.50 (m, 3H), 7.14 (t, J = 4 Hz, 1H), 4.16 (q, J = 7.2 Hz, 2H), 1.08 (t, J = 7.2 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$)δ166.0, 155.2, 152.1, 150.4, 143.7, 143.1, 131.3, 130.9, 130.6, 130.3, 129.9, 128.7, 128.4, 126.7, 125.7, 125.5, 125.4, 125.4, 125.4, 123.8, 123.0, 119.9, 61.6, 14.0; HRMS (ESI) m/z calcd for $C_{19}H_{14}F_3NO_2SNa[M+Na]^+$ 400.0590, found 400.0588.

Ethyl 4-(3-nitrophenyl)-6-(thiophen-2-yl)nicotinate(3ii): White solid; Yield: 74% (52.4mg); mp 140-142 °C; R_f = 0.40 (EtOAc:hexane = 1:4); IR (KBr) ν 1700, 1588, 1530, 1471, 1428, 1347, 1304, 1240, 1211 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.31 (d, J = 7.6 Hz, 1H), 8.24 (s, 1H), 7.61-7.70 (m, 3H), 7.56 (s, 1H), 7.52 (d, J = 4.8 Hz, 1H), 7.14-7.16 (m, 1H), 4.20 (q, J = 7.2 Hz, 2H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 165.3, 155.2, 152.1, 149.1, 148.0, 143.2, 140.7, 134.2, 129.8, 129.1, 128.5, 126.7, 123.1(2C), 123.0, 119.6, 61.4, 13.8;HRMS (ESI) m/z calcd For $C_{18}H_{15}N_2O_4S[M+H]^+$ 355.0747, found 355.0768.

Ethyl 6-(furan-2-yl)-4-(4-(trifluoromethylphenyl)nicotinate (3jg): White solid; Yield: 72% (51.9mg); mp117-119°C; R_f = 0.70 (EtOAc:hexane = 1:4); IR (KBr) ν 1719, 1603, 1572, 1539, 1490, 1469, 1332, 1281, 1236 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ9.11 (s, 1H), 7.70 (d, J = 7.8 Hz, 2H), 7.62 (s, 1H), 7.57 (s, 1H), 7.46 (d, J = 8.0Hz, 2H), 7.23 (d, J = 3.2 Hz, 1H), 6.58-6.59 (m, 1H), 4.17 (q, J = 7.2 Hz, 2H), 1.08 (t, J = 7.2 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$)δ166.1, 152.9, 152.1, 151.7, 150.4, 144.9, 143.2, 131.3,

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130.9, 130.6, 130.3, 128.7, 128.4, 125.7, 125.5, 125.4, 125.4, 125.4, 123.8, 123.0, 119.6, 112.9, 111.7, 61.6, 14.0; HRMS (ESI) m/z calcd for $C_{19}H_{15}F_3NO_3[M+H]^+$ 362.0999, found 362.0994.

4,6-Diphenylnicotinonitrile(3al): [2b] White solid; Yield: 88% (45.1 mg).

4-(4-Methoxyphenyl)-6-phenylnicotinonitrile (3am): White solid; Yield: 86% (49.2 mg); mp 118-120°C, R_f = 0.67 (EtOAc:hexane = 1:4); IR (KBr) ν 2217, 1608, 1581, 1510, 1467, 1373, 1298, 1251 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ8.96 (s, 1H), 8.07 (d, J = 7.5 Hz, 2H), 7.84 (s, 1H), 7.65 (d, J = 8.5 Hz, 2H), 7.50-7.52 (m, 3H), 7.08 (d, J = 8.2 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ161.6, 160.7, 154.4, 152.9, 137.9, 130.8, 130.2, 129.3, 128.4, 127.7, 120.3, 117.8, 115.0, 106.5, 55.8; HRMS (ESI) m/z calcd for $C_{19}H_{14}N_2ONa[M+Na]^+$ 309.0998, found 309.0999.

4-(2,5-Dimethoxyphenyl)-6-phenylnicotinonitrile (3an): White solid; Yield: 85% (53.7 mg); mp 129-131°C; R_f = 0.57 (EtOAc:hexane = 1:4); IR (KBr) ν 2223, 1587, 1532, 1502, 1475, 1450, 1409, 1372, 1311, 1264, 1226, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ8.96 (s, 1H), 8.06 (d, J = 7.8 Hz, 2H), 7.83 (s, 1H), 7.49-7.51 (m, 3H), 6.98-7.03 (m, 2H), 6.89 (s, 1H), 3.83 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 154.0, 153.2, 150.8, 150.7, 138.0, 130.6, 129.3, 127.7, 125.9, 121.8, 117.3, 116.6, 116.3, 113.0, 109.1, 56.3, 56.2; HRMS (ESI) m/z calcd for $C_{20}H_{16}N_2O_2Na[M+Na]^+$ 339.1104, found 339.1118.

4-(4-Benzyloxy-3-methoxyphenyl)-6-phenylnicotinonitrile (3ao) :White solid; Yield:86%(67.4 mg); mp 132-134 °C; R_f = 0.35 (EtOAc:hexane = 1:4); IR (KBr) ν 2217, 1591, 1515, 1474, 1331, 1269, 1223,cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ8.96 (s, 1H), 8.06-8.08 (m, 2H), 7.85 (s, 1H), 7.46-7.54 (m, 5H), 7.40 (t, J = 7.0 Hz, 2H), 7.31-7.35 (m, 1H), 7.25-7.26 (m, 1H), 7.18-7.21 (m, 1H), 7.04 (d, J = 8.2Hz, 1H), 5.24 (s, 2H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ160.7, 154.4, 152.9, 150.3, 150.2, 137.9, 136.8, 130.8, 129.3, 129.0, 128.4, 127.7, 127.5, 121.6, 120.2, 117.8, 114.2, 112.2, 106.5, 71.3, 56.6; HRMS (ESI) m/z calcd for $C_{26}H_{20}N_2O_2Na$ $[M+Na]^+$ 415.1417, found 415.1422.

4-(4-Fluorophenyl)-6-phenylnicotinonitrile (3ap): White solid; Yield: 90% (49.3 mg); mp 124-126°C; R_f = 0.75 (EtOAc:hexane = 1:4); IR (KBr) ν 2223, 1598, 1580, 1537, 1509, 1473, 1442, 1371, 1226, 1216, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ8.99 (s, 1H), 8.07-8.09 (m, 2H), 7.84 (s, 1H), 7.65-7.68 (m, 2H), 7.51-7.52 (m, 3H), 7.26 (t, J = 8.2 Hz, 2H);^{13}C NMR (100 MHz, $CDCl_3$) δ164.2(d, J_{C-F}= 250 Hz), 160.9, 154.3, 152.2, 137.6, 132.3 (d, J_{C-F}= 3.6 Hz), 131.0, 130.8 (d, J_{C-F}= 8.0 Hz), 129.4, 127.7, 120.4, 117.3, 116.8(d, J_{C-F}= 21.8 Hz), 106.7; HRMS (ESI) m/z calcd for $C_{18}H_{11}FN_2Na$ $[M+Na]^+$ 297.0798, found 297.0796.

4-(4-Chlorophenyl)-6-phenylnicotinonitrile (3aq): White solid; Yield: 89% (51.6 mg); mp 132-134°C; R_f = 0.78 (EtOAc:hexane = 1:4); IR (KBr) ν 2222, 1534, 1493, 1470, 1441, 1369, 1243, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ8.99 (s, 1H), 8.06-8.09 (m, 2H), 7.83 (s, 1H), 7.60-7.62 (m, 2H), 7.51-7.55 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 154.3, 152.0, 137.6, 136.9, 134.6, 131.0, 130.0, 129.8, 129.4, 127.7, 120.3, 117.2, 106.6 ; HRMS (ESI) m/z calcd for $C_{18}H_{11}ClN_2Na$ $[M+Na]^+$ 313.0503, found 313.0507.

4-(4-Bromophenyl)-6-phenylnicotinonitrile (3ar): White solid; Yield: 87% (58.1 mg); mp141-143 °C; R_f = 0.77 (EtOAc:hexane = 1:4); IR (KBr)ν 2222, 1588, 1531, 1489, 1469, 1441, 1366, 1282, 1242 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ9.00 (s, 1H), 8.07-8.08 (m, 2H), 7.84 (s, 1H), 7.70 (d, J = 8.5Hz, 2H), 7.52-7.55 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ161.0, 154.3, 152.1, 137.6, 135.0, 132.8, 131.0, 130.2, 129.4, 127.7, 125.2, 120.3, 117.2, 106.6; HRMS (ESI) m/z calcd for $C_{18}H_{11}{}^{79}BrN_2Na$ $[M+Na]^+$ 356.9998, found 356.9997. HRMS (ESI) m/z calcd for $C_{18}H_{11}{}^{81}BrN_2Na$ $[M+Na]^+$ 358.9878, found 358.9982.

6-Phenyl-4-(4-trifluoromethylphenyl)nicotinonitrile (3as): White solid; Yield: 90% (58.3 mg); mp 138-140°C; R_f = 0.73 (EtOAc:hexane = 1:4); IR (KBr) ν 2226, 1586, 1537, 1474, 1443, 1369, 1324cm^{-1};^1H NMR (400 MHz, $CDCl_3$) δ9.04 (s, 1H), 8.08-8.10 (m, 2H), 7.87 (s, 1H), 7.77-7.86 (m, 4H), 7.53-7.54 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ161.1, 154.3, 151.8, 139.7, 137.5, 133.0, 132.6, 132.3, 132.0, 131.2, 129.5, 129.2, 127.8, 126.6, 126.5, 126.5, 126.5, 125.4, 122.7, 120.5, 116.9, 106.8; HRMS (ESI) m/z calcdfor $C_{19}H_{11}F_3N_2Na$ $[M+Na]^+$ 347.0767, found 347.0779.

4-(2,5-Dimethoxyphenyl)-6-(4-methylphenyl)nicotinonitrile (3bn): White solid: Yield: 83% (54.8 mg); mp 122-124°C; R_f = 0.57(EtOAc:hexane = 1:4); IR (KBr)ν 2227, 1587, 1537, 1507, 1465, 1409, 1369, 1266, 1227 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ8.93 (s, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.80 (s, 1H), 7.31 (d, J = 8.0 Hz, 2H), 6.98-7.02 (m, 2H), 6.89 (s, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 154.0, 153.2, 150.7, 150.6, 141.0, 135.2, 130.0, 127.6, 126.0, 121.4, 117.5, 116.5, 116.4, 113.0, 108.8, 56.3, 56.2, 21.7; HRMS (ESI) m/z calcd for $C_{21}H_{18}N_2O_2Na$ $[M+Na]^+$ 353.1260, found 353.1251.

4-(4-Chlorophenyl)-6-(4-methylphenyl)nicotinonitrile (3bq): White solid; Yield: 88%(53.5 mg); mp 136-138 °C; R_f = 0.80 (EtOAc:hexane = 1:4); IR (KBr)ν 2222, 1591, 1531, 1469, 1372, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ8.97 (s, 1H), 7.98 (d, J = 8.0 Hz, 2H), 7.80 (s, 1H), 7.59-7.61 (m, 2H), 7.52-7.54 (m, 2H), 7.32 (d, J = 8.0 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 154.3, 151.9, 141.5, 136.9, 134.8, 134.7, 130.1, 130.0, 129.8, 127.6, 119.9, 117.3, 106.3, 21.7; HRMS (ESI) m/z calcd for $C_{19}H_{13}ClN_2Na$ $[M+Na]^+$ 327.0659, found 327.0659.

4-(4-Bromophenyl)-6-(4-methylphenyl)nicotinonitrile (3br): White solid; Yield: 84% (58.5 mg); mp 148-150 °C; R_f = 0.77 (EtOAc:hexane = 1:4); IR (KBr)ν 2220, 1589, 1527, 1488, 1466, 1368, 1280, 1252 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ8.97 (s, 1H), 7.97 (d, J = 7.8 Hz, 2H), 7.80 (s, 1H), 7.70 (d, J = 8.2 Hz, 2H), 7.53 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 154.3, 151.9, 141.5, 135.2, 134.8, 132.7, 130.2, 130.1, 127.6, 125.21, 119.8, 117.3, 106.2, 21.7; HRMS (ESI) m/z calcd for $C_{19}H_{13}{}^{79}BrN_2Na[M+Na]^+$ 371.0154, found 371.0151.;

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HRMS (ESI) m/z calcdfor $C_{19}H_{13}{}^{81}BrN_2Na[M+Na]^+$ 371.0154, found 371.0151.

6-(4-Methoxyphenyl)-4-phenylnicotinonitrile (3cl): White solid: Yield: 88% (50.4 mg); mp 122-124 °C; R_f = 0.67 (EtOAc:hexane = 1:4); IR (KBr) ν 2220, 1585, 1530, 1469, 1418, 1370, 1319, 1283, 1244 cm^{-1};[1] H NMR (400 MHz, $CDCl_3$) δ8.93 (s, 1H), 8.05 (d, J = 8.8 Hz, 2H), 7.79 (s, 1H), 7.64-7.66 (m, 2H), 7.54-7.55 (m, 3H), 7.01 (d, J = 8.7 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ162.0, 160.3, 154.2, 153.0, 136.3, 130.3, 130.2, 129.4, 129.2, 128.6, 119.5, 117.6, 114.7, 105.9, 55.7; HRMS (ESI) m/z calcd for $C_{19}H_{14}N_2ONa$ $[M+Na]^+$309.0998, found 309.0998.

6-(4-Chlorophenyl)-4-phenylnicotinonitrile(3fl): White solid; Yield: 82% (47.6 mg,); mp 133-135 °C; R_f = 0.77 (EtOAc:hexane = 1:4); IR (KBr)ν 2220, 1591, 1528, 1468, 1405, 1369, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ8.98 (s, 1H), 8.04 (d, J = 8.5 Hz, 2H), 7.84 (s, 1H), 7.65-7.67 (m, 2H), 7.56-7.57 (m, 3H), 7.49 (d, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ159.5, 154.3, 153.5, 137.2, 136.1, 136.1, 130.6, 129.6, 129.5, 129.0, 128.6, 120.3, 117.3, 107.1;HRMS (ESI) m/z calcd for $C_{18}H_{11}ClN_2Na$ $[M+Na]^+$ 313.0503, found 313.0511.

6-(2-Chlorophenyl)-4-phenylnicotinonitrile(3gl): White solid; Yield: 80% (46.4 mg); mp 132-134 °C; R_f = 0.78 (EtOAc:hexane = 1:4); IR (KBr)ν 3068, 2923, 2221, 1590, 1525, 1463, 1434, 1368, 1257, 1079, 1032, 900, 744, 694cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ9.04 (s, 1H), 7.89 (s, 1H), 7.67-7.69 (m, 3H), 7.51-7.57 (m, 4H), 7.40-7.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ160.3, 154.1, 152.4, 137.8, 135.8, 132.4, 131.9, 131.1, 130.8, 130.6, 129.5, 128.8, 127.6, 125.3, 117.2, 107.3; HRMS (ESI) m/z calcd for $C_{18}H_{11}ClN_2Na$ $[M+Na]^+$313.0503, found 313.0498.

6-(4-Bromophenyl)-4-(2,5-dimethoxyphenyl)nicotinonitrile (3hl): White solid; Yield: 80% (63.1 mg,); mp 130-132°C;R_f = 0.63 (EtOAc:hexane = 1:4); IR (KBr) ν 2218, 1587, 1533, 1499, 1472, 1444, 1357, 1310, 1228 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ8.94 (s, 1H), 7.94 (d, J = 8.5 Hz, 2H), 7.80 (s, 1H), 7.63 (d, J = 8.5 Hz, 2H), 7.00-7.01 (m, 2H), 6.87-6.88 (m, 1H), 3.83 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ159.3, 154.0, 153.3, 151.0,150.7, 136.8, 132.5, 129.2, 125.7, 125.4, 121.5, 117.2, 116.7, 116.4, 113.0, 109.5, 56.3, 56.2; HRMS (ESI) m/z calcd for $C_{20}H_{15}BrN_2O_2Na$ $[M+Na]^+$ 417.0209, found 417.0200.

6-(4-Bromophenyl)-4-(4-chlorophenyl)nicotinonitrile(3hq): White solid; Yield: 86% (63.3 mg,); mp159-161°C; R_f = 0.77 (EtOAc:hexane = 1:4); IR (KBr)ν 2220, 1588, 1530, 1492, 1466, 1400, 1366cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.96 (d, J = 8.5 Hz, 2H), 7.81 (s, 1H), 7.65 (d, J = 8.2 Hz, 2H), 7.59-7.61 (m, 2H), 7.53-7.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ159.8, 154.4, 152.3, 137.1, 136.4, 134.4, 132.6, 130.0, 129.9, 129.2, 125.8, 120.0, 117.0, 107.0; HRMS (ESI) m/z calcd for $C_{18}H_{11}{}^{79}BrClN_2[M+H]^+$ 368.9789, found 368.9794; HRMS (ESI) m/z calcd for $C_{18}H_{11}{}^{81}BrClN_2[M+H]^+$370.9768, found 370.9773.

6-(4-Bromophenyl)-4-(4-trifluoromethylphenyl)nicotinonitrile (3hs): White solid; Yield: 87% (69.9 mg); mp 165-167 °C; R_f = 0.80 (EtOAc:hexane = 1:4); IR (KBr) ν 2221, 1587, 1536, 1476, 1368, 1331 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ9.03 (s, 1H), 7.97 (d, J = 8.2 Hz, 2H), 7.83-7.84 (m, 3H), 7.76-7.78 (m, 2H), 7.66 (d, J = 8.2 Hz, 2H);^{13}C NMR (100 MHz, $CDCl_3$)δ159.9, 154.3, 152.0, 139.5, 136.3, 132.8, 132.7, 132.4, 129.2, 129.2, 126.6, 126.6, 126.5, 126.5, 126.0, 125.3, 122.6, 120.2, 116.8, 107.1; HRMS (ESI) m/z calcd for $C_{19}H_{11}{}^{79}BrF_3N_2[M+H]^+$ 403.0052, found 403.0052; HRMS (ESI) m/z calcd for $C_{19}H_{11}{}^{81}BrF_3N_2[M+H]^+$ 405.0032, found 405.0036.

4-Phenyl-6-(thiophen-2-yl)nicotinonitrile(3il): Pale yellow solid; Yield: 80% (41.9 mg); mp116-118 °C; R_f = 0.75 (EtOAc:hexane = 1:4); IR (KBr) ν 2221, 1586, 1522, 1468, 1424, 1375, 1260, 1236 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ8.85 (s, 1H), 7.73-7.74 (m, 2H), 7.64-7.66 (m, 2H), 7.53-7.57 (m, 4H), 7.16 (t, J = 4.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ155.7, 154.3, 153.1, 143.3, 136.0, 130.7, 130.5, 129.5, 128.9, 128.6, 127.5, 118.7, 117.4, 106.2; HRMS (ESI) m/z calcd for $C_{16}H_{10}N_2ONa$ $[M+Na]^+$285.0457, found 285.0451.

4-(2,5-Dimethoxyphenyl)-6-(thiophen-2-yl)nicotinonitrile(3in): Pale yellow solid; Yield: 75%(48.3 mg); mp 134-136°C; R_f = 0.55 (EtOAc:hexane = 1:4); IR (KBr)ν 2216, 1586, 1527, 1502, 1472, 1432, 1413, 1365, 1308, 1230 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ8.81 (s, 1H), 7.70 (s, 1H), 7.68 (d, J = 3.4 Hz, 1H), 7.51 (d, J = 4.7 Hz, 1H), 7.14 (t, J = 4.2 Hz, 1H), 6.99-7.03 (m, 2H), 6.87 (d, J = 2.4Hz, 1H), 3.82 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ155.5, 154.0, 153.2, 150.7, 150.7, 143.5, 130.4, 128.8, 127.3, 125.7, 119.9, 117.3, 116.6, 116.3, 113.0, 108.6, 56.3, 56.2;HRMS (ESI) m/z calcd for $C_{18}H_{14}N_2O_2SNa$ $[M+Na]^+$345.0668, found 345.0650.

3-Acetyl-4-(4-nitrophenyl)-6-phenylpyridine(3at): Light yellow solid: Yield: 82% (52.2 mg); mp 137-139 °C; R_f = 0.40 (EtOAc:hexane = 1:4); IR (KBr) ν 1682, 1590, 1526, 1507, 1479, 1444, 1350, 1271, 1234 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ 9.06 (s, 1H), 8.34 (d, J = 7.6 Hz, 2Hz), 8.06-8.09 (m, 2H), 7.68 (s, 1H), 7.50-7.54 (m, 5H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ199.2, 159.9, 150.2, 147.9, 147.7, 145.7, 137.6, 131.8, 130.3, 129.2, 129.0, 127.3, 123.9, 121.4, 29.8; HRMS (ESI) m/z calcd for $C_{19}H_{15}N_2O_3[M+H]^+$ 319.1077, found 319.1079.

3-Acetyl-4-(4-cyanophenyl)-6-phenylpyridine(3au): White solid; Yield: 80% (47.7 mg); mp132-134 °C; R_f = 0.38 (EtOAc:hexane = 1:4); IR (KBr) ν 2226, 1681, 1587, 1525, 1480, 1441, 1414, 1361, 1328, 1276, 1235 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ9.02 (s, 1H), 8.05-8.07 (m, 2H), 7.76-7.78 (m, 2H), 7.66 (s, 1H), 7.48-7.51 (m, 4H), 7.46 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ199.8, 160.1, 150.4, 148.2, 143.9, 138.0, 132.7, 132.3, 130.5, 129.3, 129.3, 127.6, 121.6, 118.6, 112.9, 30.2; HRMS (ESI) m/z calcd for $C_{20}H_{14}N_2ONa$ $[M+Na]^+$321.0998, found 321.1008.

3-Acetyl-4-(4-cyanophenyl)-6-(4-methylphenyl)pyridine(3bu): White solid; Yield: 82% (51.2 mg); mp136-138°C; R_f = 0.39 (EtOAc:hexane = 1:4); IR (KBr)ν, 2221, 1684, 1590, 1527, 1482, 1413, 1360, 1276, 1239, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ9.00 (s, 1H), 7.96 (d, J = 8.2 Hz, 2H), 7.75-7.77 (m, 2H), 7.63 (s, 1H), 7.45-

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7.48 (m, 2H), 7.31 (d, J = 7.8 Hz, 2H), 2.42 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ199.7, 160.2, 150.4, 148.2, 144.1, 140.9, 135.2, 132.7, 132.0, 130.1, 129.3, 127.5, 121.3, 118.6, 112.9, 30.2, 21.7; HRMS (ESI) m/z calcd for $C_{21}H_{16}N_2ONa$ $[M+Na]^+$ 335.1155, found 335.1154.

3-Acetyl-4-(4-cyanophenyl)-6-(4-methoxyphenyl)pyridine (3ct): White solid; Yield: 83% (54.5 mg); mp138-140 °C; R_f = 0.35 (EtOAc:hexane = 1:4); IR (KBr) ν 2224, 1735, 1673, 1607, 1588, 1524, 1469, 1440, 1371, 1277, 1251cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ8.99 (s, 1H), 8.03-8.05 (m, 2H), 7.76 (d, J = 8.3 Hz, 2H), 7.58 (s, 1H), 7.45-7.47 (m, 2H), 7.02 (d, J = 9.0 Hz, 2H), 3.88 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 161.8, 159.8, 150.5, 148.2, 144.3, 132.7, 131.5, 130.5, 129.3, 129.1, 120.8, 118.7, 114.7, 112.8, 55.7, 30.1; HRMS (ESI) m/z calcd for $C_{21}H_{16}N_2O_2Na[M+Na]^+$ 351.1104, found 351.1101.

3-Acetyl-4-(4-nitrophenyl)-6-(4-fluorophenyl)pyridine (3et): Light yellow solid; Yield: 74% (49.8 mg); mp147-149 °C; R_f = 0.35 (EtOAc:hexane = 1:4); IR (KBr)ν 1682, 1591, 1533, 1508, 1480, 1412, 1347, 1278, 1229 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ9.03 (s, 1H), 8.33 (d, J = 8.5 Hz, 2H), 8.06-8.09 (m, 2H), 7.63 (s, 1H), 7.52 (d, J = 8.7 Hz, 2H), 7.19 (t, J = 8.5 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ199.4, 164.6(d, J_{C-F} = 249 Hz), 159.1, 150.5,148.2, 148.1, 145.9, 134.1 (d, J_{C-F} = 3.6.0 Hz), 132.1, 129.6(d, J_{C-F} = 8.7 Hz) , 129.5, 124.2, 121.3, 116.4 (d , J_{C-F} = 21.8 Hz), 30.1; HRMS (ESI) m/z calcd for $C_{19}H_{13}FN_2O_3Na[M+Na]^+$ 359.0802, found 359.0802.

3-Acetyl-4-(4-cyanophenyl)-6-(4-fluorophenyl)pyridine (3eu): White solid; Yield: 74% (46.8 mg); mp142-144 °C; R_f = 0.45 (EtOAc:hexane = 1:4); IR (KBr)ν 2219, 1683, 1593, 1528, 1481, 1412, 1362, 1277, 1228 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ8.99 (s, 1H), 8.05-8.08 (m, 2H), 7.77 (d, J = 8.0 Hz, 2H), 7.61 (s, 1H), 7.47 d, J = 8.0 Hz, 2H), 7.19 (t, J = 8.5 Hz, 2H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.7, 164.5(d, J_{C-F}= 249.0 Hz), 159.0, 150.4, 148.3, 143.9, 134.2, 134.1 132.8, 132.3, 129.6, 129.5, 129.3, 128.5, 128.4, 128.0, 127.9, 127.3, 125.9, 121.3, 118.6, 116.5, 116.2, 113.0, 30.2; HRMS (ESI) m/z calcd for $C_{20}H_{14}FN_2O$ $[M+H]^+$ 317.1085, found 317.1079.

3-Acetyl-4-(4-nitrophenyl)-6-(4-chlorophenyl)pyridine(3ft): Light yellow solid; Yield: 77% (54.2 mg); mp151-153 °C; R_f = 0.45 (EtOAc:hexane = 1:4); IR (KBr) ν 1682, 1589, 1530, 1510, 1475, 1404, 1347, 1279, 1238cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.34 (d, J = 8.2 Hz, 2H), 8.03 (d, J = 8.5 Hz, 2H), 7.65 (s, 1H), 7.47-7.53 (m, 4H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ199.4, 158.9, 150.5, 148.3, 148.1, 145.8, 137.0, 136.3, 132.4, 129.6, 129.5, 128.9, 124.2, 121.4, 30.2; HRMS (ESI) m/z calcd for $C_{19}H_{14}ClN_2O_3[M+H]^+$ 353.0687, found 353.0673.

3-Acetyl-4-(4-nitrophenyl)-6-(thiophen-2-yl)pyridine (3it): Light yellow solid; Yield: 76% (49.3 mg); mp 136-138 °C; R_f = 0.40 (EtOAc:hexane = 1:4); IR (KBr) ν 1681, 1588, 1529, 1506, 1425, 1347, 1278, 1239 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.95 (s, 1H), 8.33 (d, J = 8.4 H, 2H), 7.69 (d, J = 3.2 H, 1H), 7.49-7.55 (m, 4H), 7.15-7.17 (m, 1H), 2.39 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$)δ198.4, 155.0, 150.5, 147.9, 145.6, 143.1, 131.2, 130.0, 129.1, 128.5, 126.7, 123.8, 119.6, 29.6; HRMS (ESI) m/z calcd for $C_{17}H_{13}N_2O_3S[M+H]^+$ 325.0642, found 325.0653.

3-Acetyl-4-(4-cyanophenyl)-6-(thiophen-2-yl)pyridine (3iu): Light yellow solid; Yield: 74% (45.0 mg); mp 132-134 °C; R_f = 0.35 (EtOAc:hexane = 1:4); IR (KBr) ν 2219, 1682, 1587, 1521, 1480, 1426, 1357, 1305, 1278, 1235 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 3.2 Hz, 1H), 7.51-7.54 (m, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.14-7.17 (m, 1H), 2.34 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$)δ198.8, 154.9, 150.4, 148.1, 143.6, 143.2, 132.4, 131.5, 129.9, 128.9, 128.5, 126.6, 119.5, 118.3, 112.7, 29.7; HRMS (ESI) m/z calcd For $C_{18}H_{13}N_2OS[M+H]^+$ 305.0743, found 305.0764.

The synthesis of intermediate 5: To a stirred solution of compound **1a** (39.4 mg, 0.2 mmol) and **2a** (54.6 mg, 0.22 mmol) in 2-MeTHF (1.0 mL) was added DABCO (33.6 mg, 0.3 mmol) at room temperature. Then the reaction mixture was heated at 70 °C for 30 min O_2 atmosphere (monitored by TLC). After that, the reaction mixture was extracted with ethyl acetate (3 × 10 mL), washed with water and brine respectively, dried over Na_2SO_4. The combined organic phases were evaporated under reduced pressure to afford the crude product which was purified through column chromatography through column chromatography over silica-gel using a mixture of EtOAc/hexane (1:2, v/v) as the eluent. The intermediate **5** was fully characterized by its spectroscopic data (IR, ^{1}HNMR, ^{13}C NMR and HRMS).

Intermediate 5: Yield **(**90% combined yield of a mixture of diastereomer); IR (KBr) ν 1710, 1601, 1570, 1495, 1451, 1374, 1302, 1273, 1200, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ *(*mixture of diastereomer *dr* = 3:1*)* δ 7.84 (d, J = 7.7 Hz, 1.5H), 7.80 (d, J = 7.7 Hz, 0.5H), 7.73 (t, J = 7.2 Hz, 0.75H), 7.67 (t, J = 7.2 Hz, 0.25H), 7.59 (t, J = 7.6 Hz, 1.5H), 7.51 (t, J = 7.5 Hz, 0.5H), 7.33-7.40 (m, 1.25H), 7.19-7.29 (m, 2.25H), 6.93 (d, J = 7.2 Hz, 1.5H), 6.59 (s, 0.75H), 6.56-6.57 (m, 1H), 6.35 (d, J = 3.2 Hz, 0.25H), 6.01 (s, 0.75H), 5.71 (s, 0.25H), 4.80 (s, 0.25H), 4.72 (s, 0.75H), 4.19-4.30 (m, 1.5H), 4.00-4.15 (m, 0.5H), 1.31 (t, J = 7.2Hz, 2.25H), 1.19 (t, J = 7.2Hz, 0.75H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (major diastereomer*)* 178.4, 166.7, 138.2, 135.2, 132.5, 132.2, 130.1, 129.8, 129.5, 129.1, 128.5, 128.3, 89.0, 61.9, 49.4, 14.4; HRMS (ESI) m/z calcd for $C_{20}H_{19}NSO_5Na$ $[M+Na]^+$ 408.0876, found 408.0897.

One-pot synthesis of ethyl N-Boc-4,6-diphenyl-1,2-dihydropyridine-3-carboxylate (8): A mixture of compound **1a** (39.4 mg, 0.2 mmol), **2a** (54.6 mg, 0.22 mmol), Boc_2O (0.3 mmol) and DABCO (33.6 mg, 0.3 mmol) in 2-MeTHF (1.0 mL) was heated at 70 °C for 48h under inert atmosphere (monitored by TLC). Upon completion of the reaction, the reaction mixture was extracted with ethyl acetate (3 × 10 mL), washed with water and brine respectively, dried over Na_2SO_4. The combined organic phases were evaporated under reduced pressure to afford the crude product. Finally it was obtained in a pure form **8** through column

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chromatography over silica-gel using a mixture of EtOAc/hexane (1:4, v/v) as an eluent.

Ethyl 1-tert-butoxycarbonyl-4,6-diphenyl-1,2-dihydropyridine-3-carboxylate (8): Yield: 62% (51.0 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.42 (m, 2H), 7.33-7.37 (m, 6H), 7.27-7.29 (m, 2H), 6.00 (s, 1H), 4.79 (s, 2H), 4.03 (q, J = 7.2 Hz, 2H), 1.12 (s, 9H), 1.03 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 153.0, 146.0, 144.5, 139.6, 138.1, 128.9, 128.5, 128.2, 128.1, 128.0, 127.1, 117.5, 117.5, 81.9, 60.6, 45.5, 27.9, 14.0; HRMS (ESI) m/z calcd for $C_{25}H_{27}NO_4Na[M+Na]^+$ 428.1832, found 428.183.

Synthesis of 2-(4,6-diphenylpyridin-3-yl)-[1,2,4]triazolo[1,5-*a*]pyridine(9): A mixture of compound **3al** (0.2 mmol, 52.0 mg), 2-aminopyridine (0.24 mmol, 24 mg), CuBr (0.01 mmol, 1.5 mg), 1,10-phenanthroline (0.01 mmol, 1.8 mg) and ZnI_2 (0.02 mmol 6.4 mg) 1,2-dichlorobenzene (0.4 ml) was stirred at 130 ° C for 18 h. After cooling to room temperature, the reaction was diluted with EtOAc and filtered through celite. The filtrate was concentrated and purified by column chromatography (eluent: EtOAc:hexane = 1:3) on silica gel to afford compound **9**.

2-(4,6-Diphenylpyridin-3-yl)-[1,2,4]triazolo[1,5-*a*]pyridine(9): White solid; Yield 81% (56.3 mg); mp 173-175 °C; R_f = 0.20 (EtOAc:hexane = 1:4); IR (KBr): ν 1632, 1589, 1576, 1556, 1500, 1456, 1425, 1386, 1356, 1327, 1305, 1259, 1211; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.21 (s, 1H), 8.49 (d, J = 6.4 Hz, 1H), 8.11 (d, J = 7.6 Hz, 2H), 7.82 (s, 1H), 7.68-7.71 (m, 1H), 7.43-7.52 (m, 4H), 7.30-7.38 (m, 5H), 6.97-7.00 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5, 158.1, 151.7, 151.1, 150.0, 139.1, 138.8, 129.4, 129.3, 128.8 (2C), 128.3, 128.2, 128.1, 127.2, 124.3, 121.8, 116.6, 113.7; HRMS (ESI) m/z calcd for $C_{23}H_{17}N_4[M+H]^+$: 349.1448, found 349.1475.

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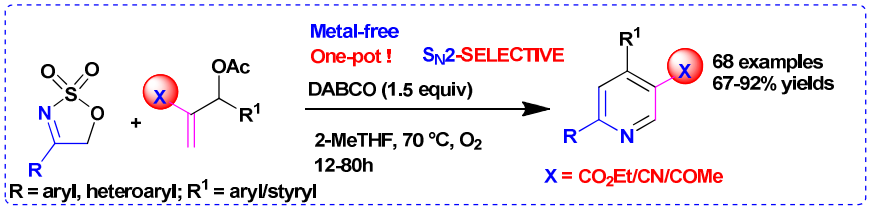
Domino reaction of cyclic sulfamidate imines with Morita-Baylis-Hillman acetates promoted by DABCO: a metal-free approach to functionalized nicotinic acid derivatives

Debashis Majee, Soumen Biswas, Shaikh M. Mobin and Sampak Samanta*

A series of 3-carboxylate/cyano/acetyl-4,6-diarylpyridines have been prepared in good to excellent yields via a domino reaction of cyclic sulfamidate imines with MBH acetates of acrylate/acrylonitrile/MVK in 2-MeTHF promoted by DABCO under O_2 atmosphere.



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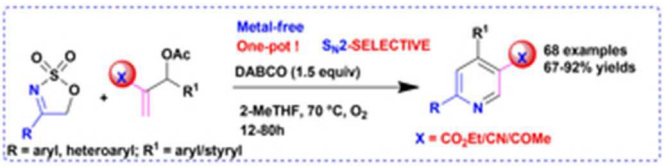

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