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FACILE SYNTHESIS OF IMIDAZO[1,2-*a*]PYRIDINES VIA TANDEM REACTION

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Abstract – An efficient method for the synthesis of 5,6,7-trisubstituted imidazo[1,2-*a*]pyridines was developed. The products were obtained in good yields under mild conditions.

Compounds containing azaindole ring systems have attracted considerable attention because of their promising biological activity and use as important building blocks in natural and synthetic bioactive compounds due to their isosterism with indole.[1] Among them, the imidazo[1,2-*a*]pyridines (IP) have been extensively studied because of their wide range of pharmacological activities such as antiviral, antibacterial, antifungal, antiulcer, and anti-inflammatory behavior.[2] Drugs containing imidazo[1,2-*a*]pyridines such as Alpidem, Zolpidem, Necopidem, Olprinone, Divalpon and Zolimidine are currently available on the market.

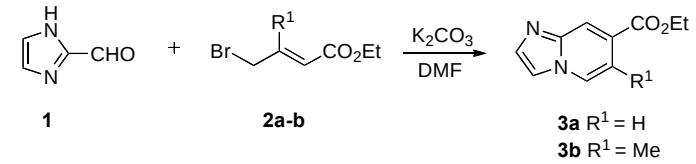
Although a number of versatile imidazo[1,2-*a*]pyridines (IP) synthesis have been reported to create heterocyclic compounds with potential therapeutic applications, the development of new methods for the synthesis of IPs remains an active area of research.[3] The classical approach involves the coupling of 2-aminopyridines with α-halocarbonyl compounds.[4] Groebke-Blackburn multi-component reaction involving the condensation of aldehydes, 2-aminopyridine, and isocyanides provides a more efficient and versatile approach.[5] This robust approach allows for the preparation of a diverse range of products. Additionally, a number of other methods were reported to evaluate their chemical and pharmacological properties.[6] However, direct introduction of a number of substituents into the pyridine moiety of the imidazo[1,2-*a*]pyridine core in synthesis was poorly studied.[7]

We recently reported a direct synthesis of indolizines and pyrazolo[1,5-a]pyridines via a new tandem reaction.[8] Our method proceeds under very mild conditions at room temperature in good yields (65-85%).

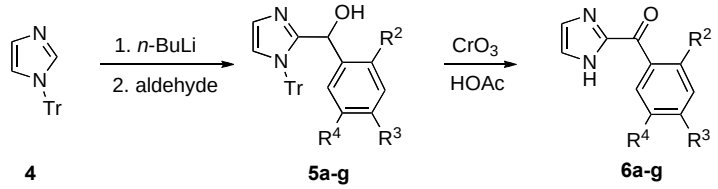
In continuation of our work on nitrogen-bridged heterocycles, we wish to expand this strategy as an convenient synthetic method for the synthesis of 5,6,7-trisubstituted imidazo[1,2-*a*]pyridines.

Imidazo[1,2-*a*]pyridines **3a-b** were synthesized through the reaction of the commercially available imidazole-2-carbaldehyde **1** and α,β-unsaturated esters **2a-b** in the presence of K_2CO_3 at room temperature in 81% and 73% yield by the established procedure (Scheme 1).[8]

This method afforded an easy and efficient way to prepare imidazo[1,2-*a*]pyridines which prompted us to extend the tandem reaction to the preparation of 5,6,7-trisubstituted imidazo[1,2-*a*]pyridines. A set of substituted 2-benzoyl imidazoles **6a-g** were readily prepared by treatment of lithium salt of imidazole **4** with 1.1 equiv of substituded phenylaldehydes, followed by oxidation of the resulting hydroxybenzylimidazoles **5a-g** (Scheme 2).[9]



Scheme 1



Scheme 2

In view of the high efficiency of K_2CO_3/DMF system on the synthesis of imidazo[1,2-*a*]pyridines, we chose it as a base to perform this one-pot reaction of poly substituted imidazo[1,2-*a*]pyridines and the results were given in Table 1. The desired imidazo[1,2-*a*]pyridines **3c-p** were obtained by the reaction of substituted 2-benzoylimidazoles **6a-g** and α,β-unsaturated esters **2a-b** in the presence of K_2CO_3 in dry DMF at room temperature for 2-6 h. A wide range of substituted 2-benzoylimidazoles **6** reacted effectively with α,β-unsaturated esters **2a-b** including a variety of electron-donating and electron-withdrawing substituents.

The structures of products **3a-p** were characterized by spectroscopic methods (^{1}H and ^{13}C NMR, IR, and HRMS). The structure of **3a** was further confirmed by X-ray crystallographic analysis as shown in Figure 1.

We believe that this reaction proceed by an intermolecular S_N2 reaction, deprotonation, and then electron pair transfer, cyclization, followed by elimination, to form the desired final products.[8]

In summary, we have developed an efficient synthetic approach to 5,6,7-trisubstituted imidazo[1,2-*a*]pyridines by a tandem reaction involving an intermolecular S_N2 reaction, deprotonation,

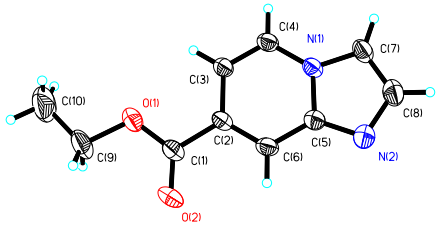
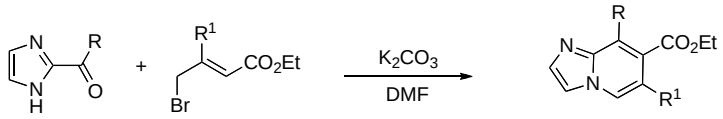


Figure 1. Crystal structure of **3a**

Table 1. Reaction of Imidazole with Unsaturated Esters to Generate Imidazo[1,2-*a*]pyridines



6a-g **2a-b** **3c-p**

Entry	R	R^1	Product	Isolated Yield(%)
1	4-MeC_6H_4	H	**3c**	80
2	4-MeC_6H_4	Me	**3d**	75
3	4-$MeOC_6H_4$	H	**3e**	75
4	4-$MeOC_6H_4$	Me	**3f**	61
5	1,3-benzodioxol-5-yl	H	**3g**	72
6	1,3-benzodioxol-5-yl	Me	**3h**	63
7	Ph	H	**3i**	80
8	Ph	Me	**3j**	72
9	4-$NO_2C_6H_4$	H	**3k**	86
10	4-$NO_2C_6H_4$	Me	**3l**	80
11	4-$NO_2C_6H_4$	H	**3m**	88
12	4-$NO_2C_6H_4$	Me	**3n**	81
13	2,4-$Cl_2C_6H_4$	H	**3o**	83
14	2,4-$Cl_2C_6H_4$	Me	**3p**	76

electron pair transfer, cyclization and elimination. These reactions proceeded under very mild conditions and a wide range of title compounds were synthesized. A study of the fluorescence properties and potential biological activity of these compounds will be presented in due course.

EXPERIMENTAL

All reagents and solvents were purchased from Sinopharm Chemical Reagent Co. Ltd and used without further purification unless otherwise noted. Starting materials were prepared according to literatures. Thin-layer chromatography (TLC) was conducted on silica gel 60 F254 plates (Merck KGaA). ^{1}H NMR spectra were recorded on a Bruker Avance 300 (300 MHz) spectrometer, using $CDCl_3$ or DMSO-d_6 as solvents and tetramethylsilane (TMS) as an internal standard. Melting points were determined on an XD-4 digital micro-melting point apparatus and are uncorrected. IR spectra were recorded with an IR

spectrophotometer Avtar 370 FT-IR (Termo Nicolet). Elemental analyses were performed on a Vario EL III (Elementar Analysensysteme GmbH) spectroanalyzer. MS spectra were recorded on a LTQ Orbitrap Hybrid mass spectrograph.

General procedure for the synthesis and analytical data of 6a-g

1-Trityl-lithioimidazole was prepared by the addition of 4.8 mL of 2.5 M *n*-butyllithium in hexane to a solution of 3.10 g (10 mmol) of 1-tritylimidazole **4** in 60 mL of tetrahydrofuran (freshly distilled from lithium aluminum hydride) at 0 °C under a nitrogen atmosphere. The solution, which gradually turned red, was stirred at room temperature for 1.5 h, was then cooled to 0 °C, and 12 mmol of aldehydes were added. After an additional 30 min at room temperature, the reaction mixture was poured into 200 mL of water and then filtered. The precipitate was collected and the crude products **5** were used in the following step without further purification.

A solution of chromium trioxide (0.60 g, 6.0 mmol) in water (2 mL) was added dropwise to a solution of hydroxybenzylimidazoles **5** (8.0 mmol) in glacial acid (20 mL) at 90 °C. The reaction mixture was heated at 100 °C for a further 5 min, and then poured into 100 mL of water and filtered. The filtrate was extracted with CH_2Cl_2 (3 x 30 mL). The combined extracts were washed with brine (2 x 20 mL), dried over $MgSO_4$ and filtered, and the solvent was removed by rotary evaporation. The crude products **6** were purified by recrystallization from EtOAc.

(1*H*-Imidazol-2-yl)(phenyl)methanone 6a[10]

^{1}H NMR (300 MHz, $CDCl_3$): δ 11.12 (s, 1H), 8.58 (d, 2H, *J* = 7.8 Hz), 7.50-7.64 (m, 3H), 7.41 (s, 1H), 7.28 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 182.2, 145.3, 135.6, 133.4, 131.9, 131.0, 128.4, 120.3.

(1*H*-Imidazol-2-yl)(*p*-tolyl)methanone 6b[10]

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.86 (s, 1H), 8.52 (d, 2H, *J* = 8.4 Hz), 7.39 (s, 1H), 7.32 (d, 2H, *J* = 8.4 Hz), 7.28 (s, 1H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 181.5, 145.5, 144.4, 133.0, 131.7, 131.2, 129.1, 119.8, 21.8.

(1*H*-Imidazol-2-yl)(4-methoxyphenyl)methanone 6c[10]

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.92 (s, 1H), 8.69 (d, 2H, *J* = 9.0 Hz), 7.38 (s, 1H), 7.27 (s, 1H), 7.00 (d, 2H, *J* = 9.0 Hz), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 180.3, 164.1, 145.6, 133.6, 131.6, 128.5, 119.6, 113.7, 55.5.

Benzo[d][1,3]dioxol-5-yl(1*H*-imidazol-2-yl)methanone 6d

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.87 (s, 1H), 8.50 (dd, 1H, *J* = 1.5, 8.4 Hz), 8.07 (d, 1H, *J* = 1.8 Hz), 7.30 (d, 3H, *J* = 8.4 Hz), 6.94 (d, 1H, *J* = 8.4 Hz), 6.06 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.7, 152.3, 147.9, 145.4, 130.0, 128.4, 127.9, 127.3, 110.5, 108.0, 101.8. HRMS: *m/z* calcd for $C_{11}H_9N_2O_3$ $[M+H]^+$ 217.0613, found 217.0616.

(2,4-Dichlorophenyl)(1*H*-imidazol-2-yl)methanone 6e

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.76 (s, 1H), 7.81 (d, 1H, *J* = 8.4 Hz), 7.51 (d, 1H, *J* = 1.8 Hz), 7.36-7.39 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 182.2, 144.7, 137.8, 134.1, 133.6,132.1, 130.5, 126.8. HRMS: *m/z* calcd for $C_{10}H_7Cl_2N_2O$ $[M+H]^+$ 240.9935, found 240.9934.

(1*H*-Imidazol-2-yl)(3-nitrophenyl)methanone 6f[11]

^{1}H NMR (300 MHz, DMSO-d_6): δ 13.69 (s, 1H), 9.40 (t, 1H, *J* = 1.8 Hz), 8.82-8.86 (m, 1H), 8.49-8.53 (m, 1H), 7.88 (t, 1H, *J* = 7.8 Hz), 7.62 (s, 1H), 7.39 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.9, 148.1, 144.8, 137.5, 136.9, 132.1, 130.5, 127.7, 125.9, 123.3.

(1*H*-Imidazol-2-yl)(4-nitrophenyl)methanone 6g[10]

^{1}H NMR (300 MHz, DMSO-d_6): δ 13.69 (s, 1H), 8.65 (d, 2H, *J* = 9.0 Hz), 8.38 (d, 2H, *J* = 9.0 Hz), 7.62 (d, 1H, *J* = 1.8 Hz), 7.37 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.9, 148.1, 144.8, 137.5, 136.9, 132.1, 130.5, 127.7, 125.9, 123.3.

General procedure for the synthesis and analytical data of 3a-3p

To a 50-mL round-bottomed flask were added **1** or **6** (1.00 mmol), enoate **2** (1.20 mmol), potassium carbonate (0.283 g, 2.05 mmol) and dry DMF (10 mL). The mixture was stirred at rt for 3 h and then filtered. The filtrate was poured into water (100 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The combined extracts were washed with water, dried over anhydrous $MgSO_4$ and filtered, and the solvent was removed by rotary evaporation. The crude products were purified by column chromatography.

Ethyl imidazo[1,2-*a*]pyridine-7-carboxylate (3a)

White solid (81% yield): mp 294-297 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.38 (s, 1H), 8.17 (d, 1H, *J* = 6.9 Hz), 7.80 (s, 1H), 7.70 (s, 1H), 7.41 (dd, 1H, *J* = 1.2, 6.9 Hz), 4.38-4.46 (q, 2H, *J* = 7.2 Hz), 1.40-1.45 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 165.2, 136.0, 126.3, 125.3, 120.6, 113.8, 111.7, 61.5, 14.3. IR (KBr) *v* = 3393, 2980, 1710, 1500, 1369, 1321, 1245, 1021, 761 cm^{-1}. HRMS: *m/z* calcd for $C_{10}H_{11}N_2O_2$ $[M+H]^+$ 191.0821, found 191.0823. *Anal*. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.16; H, 5.31; N, 14.73.

Ethyl 6-methylimidazo[1,2-*a*]pyridine-7-carboxylate (3b)

White solid (73% yield): mp 146-148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.96 (s, 1H), 7.74 (s, 1H), 7.59 (s, 1H), 4.35-4.42 (q, 2H, *J* = 7.2 Hz), 2.54 (s, 3H), 1.40-1.45 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 165.9, 135.7, 127.1, 124.6, 121.9, 121.1,112.9, 61.2, 18.5, 14.3. IR (KBr) ν = 2976, 1692, 1508, 1438, 1328, 1261, 1059, 734 cm^{-1}. HRMS: *m/z* calcd for $C_{11}H_{13}N_2O_2$ $[M+H]^+$ 205.0977, found 205.0977. *Anal*. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.67; H, 5.92; N, 13.74.

Ethyl 8-*p*-tolylimidazo[1,2-*a*]pyridine-7-carboxylate (3c)

White solid (80% yield): mp 107-110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, 1H, *J* = 7.2 Hz), 7.73 (s,

1H), 7.68 (d, 1H, *J* = 1.2 Hz), 7.35 (d, 2H, *J* = 8.1 Hz), 7.25-7.29 (m, 3H), 4.07-4.14 (q, 2H, *J* = 7.2 Hz), 2.41 (s, 3H), 0.99-1.04 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 167.0, 144.6, 135.7, 135.6, 133.1, 129.2, 128.1, 125.2, 124.4, 113.9, 112.7, 61.2, 13.5. IR (KBr) ν = 3152, 2981, 1711, 1490, 1332, 1255, 1018, 784 cm^{-1}. HRMS: *m/z* calcd for $C_{17}H_{17}N_2O_2$ $[M+H]^+$ 281.1290, Found 281.1293. *Anal*. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.88; H, 5.75; N, 9.98.

Ethyl 6-methyl-8-*p*-tolylimidazo[1,2-*a*]pyridine-7-carboxylate (3d)

White solid (75% yield): mp 86-89 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.94 (d, 1H, *J* = 0.9 Hz), 7.72 (d, 1 H, *J* = 0.9 Hz), 7.67 (d, 1H, *J* = 0.9 Hz), 7.45 (d, 2H, *J* = 8.1 Hz), 7.25 (d, 2H, *J* = 8.1 Hz), 4.06-4.16 (q, 2H, *J* = 7.2 Hz), 2.38 (s, 3H), 2.33 (d, 3H, *J* = 0.9 Hz), 0.97-1.02 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 167.9, 143.5, 138.2, 134.7, 131.9, 130.0, 129.3, 129.1, 129.0, 128.8, 123.1, 119.3, 112.8, 112.7, 61.3, 21.3, 16.7, 13.7. IR (KBr) ν = 2980, 1722, 1492, 1333, 1260, 1068, 718 cm^{-1}. HRMS: *m/z* calcd for $C_{18}H_{19}N_2O_2$ $[M+H]^+$ 295.1447, found: 295.1448. *Anal*. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C,73.48; H, 6.17; N, 9.47.

Ethyl 8-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine-7-carboxylate (3e)

Yellow oil (75% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (d, 1H, *J* = 7.2 Hz), 7.73 (d, 1H, *J* = 1.2 Hz), 7.68 (d, 1H, *J* = 1.2 Hz), 7.40-7.45 (m, 2H), 7.26 (d, 1H, *J* = 6.9 Hz), 6.98-7.03 (m, 2H), 4.09-4.16 (q, 2H, *J* = 7.2 Hz), 3.85 (s, 3H), 1.02-1.07 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 167.2, 159.7, 144.9, 135.7, 132.9, 130.6, 127.7, 125.0, 124.0, 113.8, 113.6, 112.8, 61.2, 55.3, 13.8. IR (KBr) ν = 2958, 1710, 1487, 1231, 1140, 1030, 825, 749 cm^{-1}. HRMS: *m/z* calcd for $C_{17}H_{17}N_2O_3$ $[M+H]^+$ 297.1239, found 297.1242. *Anal*. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.44; N, 9.45. Found: C, 68.95; H, 5.45; N, 9.46.

Ethyl 8-(4-methoxyphenyl)-6-methylimidazo[1,2-*a*]pyridine-7-carboxylate (3f)

Yellow oil (61% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.96 (d, 1H, *J* = 0.9 Hz), 7.63 (s, 1H), 7.58 (s, 1H), 7.50 (d, 2H, *J* = 7.2 Hz), 6.98 (d, 2H, *J* = 7.2 Hz), 7.00 (dd, 1H, *J* = 1.8, 8.1 Hz), 6.88 (d, 1H, *J* = 8.1 Hz), 5.99 (s, 2H), 4.08-4.15 (q, 2H, *J* = 7.2 Hz), 3.83 (s, 3H), 2.32 (d, 3H, *J* = 0.9 Hz), 1.00-1.05 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 167.9, 159.8, 143.4, 134.4, 130.9, 130.7, 130.2, 128.6, 127.0, 123.1, 119.4, 113.8, 113.0, 61.3, 55.3, 16.7, 13.8. IR (KBr) ν = 2928, 1721, 1609, 1501, 1249, 1031, 832, 727 cm^{-1}. HRMS: *m/z* calcd for $C_{18}H_{19}N_2O_3$ $[M+H]^+$ 311.1396, found 311.1396. *Anal*. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.69; H, 5.85; N, 9.03.

Ethyl 8-(benzo[d][1,3]dioxol-5-yl)imidazo[1,2-*a*]pyridine-7-carboxylate (3g)

White solid (72% yield): mp 147-150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (d, 1H, *J* = 6.9 Hz), 7.72 (d, 2H, *J* = 9.9 Hz), 7.26 (d, 1H, *J* = 6.9 Hz), 6.99 (s, 1H), 6.89 (s, 2H), 5.99 (s, 2H), 4.12-4.19 (q, 2H, *J* = 7.2 Hz), 1.07-1.12 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 166.9, 147.7, 147.4, 144.6, 135.5, 132.5, 131.0, 128.9, 124.3, 123.0, 113.9, 112.8, 110.1, 108.2, 101.2, 61.3, 13.8. IR (KBr) ν = 2981, 1723, 1477, 1220, 1141, 1034, 781 cm^{-1}. HRMS: *m/z* calcd for $C_{17}H_{15}N_2O_4$ $[M+H]^+$ 311.1032, found 311.1033.

Anal. Calcd for $C_{17}H_{14}N_2O_4$: C, 65.80; H, 4.55; N, 9.03. Found: C, 65.85; H, 4.56; N, 9.03.

Ethyl 8-(benzo[d][1,3]dioxol-5-yl)-6-methylimidazo[1,2-*a*]pyridine-7-carboxylate (3h)

Yellow oil (63% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, 1H, *J* = 0.9 Hz), 7.64 (d, 1H, *J* = 1.2 Hz), 7.57 (d, 1H, *J* = 0.9 Hz), 7.10 (d, 1H, *J* = 1.8 Hz), 7.00 (dd, 1H, *J* = 1.8, 8.1 Hz), 6.88 (d, 1H, *J* = 8.1 Hz), 5.99 (s, 2H), 4.12-4.19 (q, 2H, *J* = 7.2 Hz), 2.33 (d, 3H, *J* = 0.9 Hz), 1.06-1.11 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 167.8, 147.9, 147.6, 143.4, 134.7, 130.2, 128.6, 128.4, 123.2, 123.2, 119.3, 112.9, 110.2, 108.3, 101.2, 61.4, 16.7, 13.9. IR (KBr) ν = 2980, 1723, 1671, 1490, 1238, 1037, 811 cm^{-1}. HRMS: *m/z* calcd for $C_{18}H_{17}N_2O_4$ $[M+H]^+$ 325.1188, found 325.1188. *Anal*. Calcd for $C_{18}H_{16}N_2O_4$: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.68; H, 4.97; N, 8.64.

Ethyl 8-phenylimidazo[1,2-*a*]pyridine-7-carboxylate (3i)

Yellow oil (80% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (d, 1H, *J* = 7.2 Hz), 7.72 (s, 1H), 7.68 (d, 1H, *J* = 0.6 Hz), 7.43-7.47 (m, 5H), 7.27 (d, 1H, *J* = 7.2 Hz), 4.04-4.11 (q, 2H, *J* = 7.2 Hz), 0.93-0.98 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 167.0, 144.6, 135.7, 135.6, 133.1, 129.2, 128.1, 125.2, 124.4, 113.9, 112.7, 61.2, 13.5. IR (KBr) ν = 2982, 1711, 1487, 1334, 1267, 1150, 1023, 766, 702 cm^{-1}. HRMS: *m/z* calcd for $C_{16}H_{15}N_2O_2$ $[M+H]^+$ 267.1134, found 267.1137. *Anal*. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.19; H, 5.30; N, 10.53.

Ethyl 6-methyl-8-phenylimidazo[1,2-*a*]pyridine-7-carboxylate (3j)

White solid (72% yield): mp 105-108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (s, 1H), 7.66 (s, 1H), 7.54-7.59 (m, 3H), 7.37-7.48 (m, 3H), 4.02-4.10 (q, 2H, *J* = 7.2 Hz), 2.35 (s, 3H), 0.93-0.97 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 167.8, 143.4, 134.9, 134.8, 130.1, 129.4, 129.3, 128.4, 128.3, 123.3, 119.3, 112.9, 61.3, 16.8, 13.6. IR (KBr) ν = 2983, 1720, 1491, 1256, 1181, 1064, 698 cm^{-1}. HRMS: *m/z* calcd for $C_{17}H_{17}N_2O_2$ $[M+H]^+$ 281.1290, found 281.1291. *Anal*. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.84; H, 5.76; N, 10.01.

Ethyl 8-(4-nitrophenyl)imidazo[1,2-*a*]pyridine-7-carboxylate (3k)

Yellow solid (86% yield): mp 138-139 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.35-8.37 (m, 2H), 7.33 (d, 1H, *J* = 4.5 Hz), 7.77 (s, 2H), 7.61-7.65 (m, 2H), 7.43 (d, 1H, *J* = 6.9 Hz), 4.11-4.18 (q, 2H, *J* = 7.2 Hz), 1.04-1.08 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 165.7, 147.6, 144.0, 142.7, 136.3, 131.3, 130.4, 125.2, 124.7, 123.3, 114.2, 112.8, 61.6, 13.7. IR (KBr) ν = 2990, 1729, 1513, 1344, 1240, 1154, 1028, 740 cm^{-1}. HRMS: *m/z* calcd for $C_{16}H_{14}N_3O_4$ $[M+H]^+$ 312.0984, found 312.0986. *Anal*. Calcd for $C_{16}H_{13}N_3O_4$: C, 61.73; H, 4.21; N, 13.50. Found: C, 61.78; H, 4.22; N, 13.51.

Ethyl 6-methyl-8-(4-nitrophenyl)imidazo[1,2-*a*]pyridine-7-carboxylate (3l)

Yellow solid (80% yield): mp 132-134 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.31-8.35 (m, 2H), 8.06 (s, 1H), 7.74-7.79 (m, 2H), 7.65-7.68 (m, 2H), 4.08-4.15 (q, 2H, *J* = 7.2 Hz), 2.38 (s, 3H), 1.00-1.05 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 167.1, 147.7, 142.6, 141.8, 135.2, 130.7, 130.3, 126.8, 124.4,

123.4, 119.5, 113.3, 61.7, 16.8, 13.8. IR (KBr) ν = 2981, 1738, 1519, 1347, 1251, 1181, 1063, 847, 709 cm^{-1}. HRMS: *m/z* calcd for $C_{17}H_{16}N_3O_4$ $[M+H]^+$ 326.1141, found 326.1145. *Anal*. Calcd for $C_{17}H_{15}N_3O_4$: C, 62.76; H, 4.65; N, 12.92. Found: C, 62.77; H, 4.66; N, 12.93.

Ethyl 8-(3-nitrophenyl)imidazo[1,2-*a*]pyridine-7-carboxylate (3m)

Yellow solid (88% yield): mp 146-147 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.30-8.34 (m, 2H), 8.24 (d, 1H, *J* = 7.2 Hz), 7.77-7.82 (m, 3H), 7.63-7.69 (m, 1H), 7.44 (d, 1H, *J* = 7.2 Hz), 4.10-4.17 (q, 2H, *J* = 7.2 Hz), 1.02-1.07 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 165.7, 148.1, 144.3, 137.3, 136.3, 135.6, 131.1, 128.9, 125.1, 124.9, 124.7, 123.1, 114.3, 112.9, 61.5, 13.7. IR (KBr) ν = 2991, 1718, 1531, 1346, 1231, 1153, 1030, 740 cm^{-1}. HRMS: *m/z* calcd for $C_{16}H_{14}N_3O_4$ $[M+H]^+$ 312.0984, found 312.0986. *Anal*. Calcd for $C_{16}H_{13}N_3O_4$: C, 61.73; H, 4.21; N, 13.50. Found: C, 61.74; H, 4.21; N, 13.53.

Ethyl 6-methyl-8-(3-nitrophenyl)imidazo[1,2-*a*]pyridine-7-carboxylate (3n)

Yellow oil (81% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.46 (s, 1H), 8.29 (d, 1H, *J* = 8.1 Hz), 8.06 (s, 1H), 7.94 (d, 1H, *J* = 7.5 Hz), 7.63-7.67 (m, 3H), 4.10-4.17 (q, 2H, *J* = 7.2 Hz), 2.38 (s, 3H), 1.03-1.08 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 167.1, 148.1, 142.7, 136.6, 135.8, 135.1, 129.3, 126.4, 124.7, 124.4, 123.3, 119.4, 113.4, 61.6, 16.8, 13.8. IR (KBr) ν = 2977, 1719, 1533, 1347, 1251, 1068, 748 cm^{-1}. HRMS: *m/z* calcd for $C_{17}H_{16}N_3O_4$ $[M+H]^+$ 326.1141, found 326.1145. *Anal*. Calcd for $C_{17}H_{15}N_3O_4$: C, 62.76; H, 4.65; N, 12.92. Found: C, 62.78; H, 4.66; N, 12.93.

Ethyl 8-(2,4-dichlorophenyl)imidazo[1,2-*a*]pyridine-7-carboxylate (3o)

Yellow oil (83% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (d, 1H, *J* = 7.2 Hz), 7.75 (d, 1H, *J* = 0.9 Hz), 7.73 (d, 1H, *J* = 0.9 Hz), 7.53 (d, 1H, *J* = 2.1 Hz), 7.48(d, 1H, *J* = 7.2 Hz), 7.37 (dd, 1H, *J* = 2.1, 8.1 Hz), 7.29 (d, 1H, *J* = 8.1 Hz), 4.14-4.18 (q, 2H, *J* = 7.2 Hz), 1.05-1.10 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 165.3, 144.1, 136.2, 134.7, 134.0, 133.7, 131.3, 129.9, 129.2, 126.9, 125.1, 125.0, 114.1. 112.7. 61.4. 13.6. IR (KBr) ν = 2982, 1717, 1589, 1492, 1372, 1333, 1023, 749 cm^{-1}. HRMS: *m/z* calcd for $C_{16}H_{13}Cl_2N_2O_2$ $[M+H]^+$ 335.0354, found 335.0357. *Anal*. Calcd for $C_{16}H_{12}Cl_2N_2O_2$: C, 57.33; H, 3.61; N, 8.36. Found: C, 57.36; H, 3.60; N, 8.36.

Ethyl 8-(2,4-dichlorophenyl)-6-methylimidazo[1,2-*a*]pyridine-7-carboxylate (3p)

White solid (76% yield): mp 152-154 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.03 (d, 1H, *J* = 1.2 Hz), 7.66 (d, 1H, *J* = 1.2 Hz), 7.60 (d, 1H, *J* = 1.2 Hz), 7.53 (d, 1H, *J* = 1.8 Hz), 7.26-7.35 (m, 2H), 4.05-4.13 (q, 2H, *J* = 7.2 Hz), 2.40 (d, 3H, *J* = 0.9 Hz), 0.98-1.03 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 166.5, 142.7, 135.2, 135.1, 134.9, 132.9, 131.9, 130.3, 129.5, 126.9, 126.5, 124.4, 119.6, 113.0, 61.3, 17.1, 13.6. IR (KBr) ν = 2958, 1732, 1497, 1336, 1182, 1050, 731 cm^{-1}. HRMS: *m/z* calcd for $C_{17}H_{14}Cl_2N_2O_2$ $[M+H]^+$ 349.0511, found 349.0511. *Anal*. Calcd for $C_{17}H_{15}Cl_2N_2O_2$: C, 58.47; H, 4.04; N, 8.02. Found: C, 58.49; H, 6.45; N, 8.03.

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