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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%).

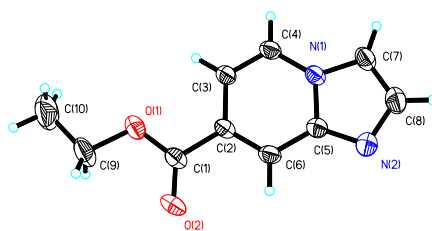
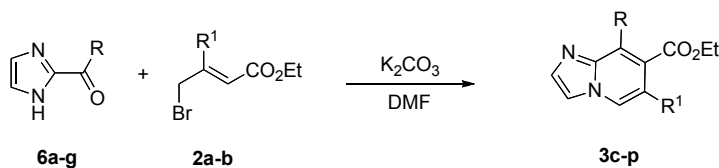


Table 1. Reaction of Imidazole with Unsaturated Esters to Generate Imidazo[1,2-*a*]pyridines



Entry	R	R ¹	Product	Isolated Yield(%)
1	4-MeC ₆ H ₄	H	3c	80
2	4-MeC ₆ H ₄	Me	3d	75
3	4-MeOC ₆ H ₄	H	3e	75
4	4-MeOC ₆ H 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 ₂ C ₆ H ₄	H	3k	86
10	4-NO ₂ C ₆ H ₄	Me	3l	80
11	4-NO ₂ C ₆ H ₄	H	3m	88
12	4-NO ₂ C ₆ H ₄	Me	3n	81
13	2,4-Cl ₂ C ₆ H ₄	H	3o	83
14	2,4-Cl ₂ C ₆ H ₄	Me	3p	76

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). ¹H NMR spectra were recorded on a Bruker Avance 300 (300 MHz) spectrometer, using CDCl₃ 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 CH₂Cl₂ (3 x 30 mL). The combined extracts were washed with brine (2 x 20 mL), dried over MgSO₄ 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

¹H NMR (300 MHz, CDCl₃): 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). ¹³C NMR (75 MHz, CDCl₃): 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

¹H NMR (300 MHz, CDCl₃): 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). ¹³C NMR (75 MHz, CDCl₃): 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

¹H NMR (300 MHz, CDCl₃): 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). ¹³C NMR (75 MHz, CDCl₃): 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**

¹H NMR (300 MHz, CDCl₃): 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). ¹³C NMR (75 MHz, CDCl₃): 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 C₁₁H₉N₂O₃ [M+H]⁺ 217.0613, found 217.0616.

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

¹H NMR (300 MHz, CDCl₃): 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). ¹³C NMR (75 MHz, CDCl₃): δ 182.2, 144.7, 137.8, 134.1, 133.6, 132.1, 130.5, 126.8. HRMS: *m/z* calcd for C₁₀H₇Cl₂N₂O [M+H]⁺ 240.9935, found 240.9934.

(1*H*-Imidazol-2-yl)(3-nitrophenyl)methanone 6f¹¹

¹H 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). ¹³C NMR (75 MHz, CDCl₃): 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 6g¹⁰

¹H 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). ¹³C NMR (75 MHz, CDCl₃): 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 CH₂Cl₂ (3 x 30 mL). The combined extracts were washed with water, dried over anhydrous MgSO₄ 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. ¹H NMR (300 MHz, CDCl₃): 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). ¹³C NMR (75.4 MHz, CDCl₃): δ 165.2, 136.0, 126.3, 125.3, 120.6, 113.8, 111.7, 61.5, 14.3. IR (KBr) ν = 3393, 2980, 1710, 1500, 1369, 1321, 1245, 1021, 761 cm⁻¹. HRMS: *m/z* calcd for C₁₀H₁₁N₂O₂ [M+H]⁺ 191.0821, found 191.0823. *Anal.* Calcd for C₁₀H₁₀N₂O₂: 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. ¹H NMR (300 MHz, CDCl₃): 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). ¹³C NMR (75.4 MHz, CDCl₃): 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 C₁₁H₁₃N₂O₂ [M+H]⁺ 205.0977, found 205.0977. *Anal.* Calcd for C₁₁H₁₂N₂O₂: 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. ¹H NMR (300 MHz, CDCl₃): 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) $\nu = 3152, 2981, 1711, 1490, 1332, 1255, 1018, 784\text{ cm}^{-1}$. HRMS: m/z calcd for $\text{C}_{17}\text{H}_{17}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 281.1290, Found 281.1293. *Anal.* Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_2$: 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. ^1H NMR (300 MHz, CDCl_3): δ 7.94 (d, 1H, $J = 0.9$ Hz), 7.72 (d, 1H, $J = 0.9$ 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) $\nu = 2980, 1722, 1492, 1333, 1260, 1068, 718\text{ cm}^{-1}$. HRMS: m/z calcd for $\text{C}_{18}\text{H}_{19}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 295.1447, found: 295.1448. *Anal.* Calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_2$: 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). ^1H 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) $\nu = 2958, 1710, 1487, 1231, 1140, 1030, 825, 749\text{ cm}^{-1}$. HRMS: m/z calcd for $\text{C}_{17}\text{H}_{17}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 297.1239, found 297.1242. *Anal.* Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_3$: 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). ^1H 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) $\nu = 2928, 1721, 1609, 1501, 1249, 1031, 832, 727\text{ cm}^{-1}$. HRMS: m/z calcd for $\text{C}_{18}\text{H}_{19}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 311.1396, found 311.1396. *Anal.* Calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_3$: 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. ^1H 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) $\nu = 2981, 1723, 1477, 1220, 1141, 1034, 781\text{ cm}^{-1}$. HRMS: m/z calcd for $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$ 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). 1H 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) $\nu = 2980, 1723, 1671, 1490, 1238, 1037, 811\text{ cm}^{-1}$. 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). 1H 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) $\nu = 2982, 1711, 1487, 1334, 1267, 1150, 1023, 766, 702\text{ cm}^{-1}$. 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. 1H 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) $\nu = 2983, 1720, 1491, 1256, 1181, 1064, 698\text{ cm}^{-1}$. 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. 1H 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) $\nu = 2990, 1729, 1513, 1344, 1240, 1154, 1028, 740\text{ cm}^{-1}$. 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. 1H 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 $\text{C}_{17}\text{H}_{16}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 326.1141, found 326.1145. *Anal.* Calcd for $\text{C}_{17}\text{H}_{15}\text{N}_3\text{O}_4$: 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. ^1H 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 $\text{C}_{16}\text{H}_{14}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 312.0984, found 312.0986. *Anal.* Calcd for $\text{C}_{16}\text{H}_{13}\text{N}_3\text{O}_4$: 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). ^1H 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 $\text{C}_{17}\text{H}_{16}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 326.1141, found 326.1145. *Anal.* Calcd for $\text{C}_{17}\text{H}_{15}\text{N}_3\text{O}_4$: 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). ^1H 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 $\text{C}_{16}\text{H}_{13}\text{Cl}_2\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 335.0354, found 335.0357. *Anal.* Calcd for $\text{C}_{16}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}_2$: 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. ^1H 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 $\text{C}_{17}\text{H}_{14}\text{Cl}_2\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 349.0511, found 349.0511. *Anal.* Calcd for $\text{C}_{17}\text{H}_{15}\text{Cl}_2\text{N}_2\text{O}_2$: C, 58.47; H, 4.04; N, 8.02. Found: C, 58.49; H, 6.45; N, 8.03.

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