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The synthesis of imidazo[1,5-*a*]quinolines via a decarboxylative cyclization under metal-free conditions†

Zicong Yan,^a Changfeng Wan,^b Yu Yang,^a Zhenggen Zha^{*a} and Zhiyong Wang^{ID}^{*a}

An iodine-mediated decarboxylative cyclization was developed from α -amino acids and 2-methylquinolines under metal-free conditions, affording a variety of imidazo[1,5-*a*]quinolines with moderate to good yields.

Introduction

The imidazo[1,5-*a*]quinoline moiety is an important class of fused *N*-heterocyclic compounds such as skeletons of NK1 receptor ligands,¹ antitumor drug C-1311,² potential antimicrobial natural product cribrostatin 6,³ inhibitor targeting phosphodiesterase 10A⁴ and highly efficient ligands of central benzodiazepine receptors.⁵ As the structure for the precursors of *N*-heterocyclic carbene⁶ and other transformations,⁷ much effort has been done for the synthesis of imidazo[1,5-*a*]quinolines. The previous strategies mainly focused in Vilsmeier-type cyclizations using *N*-2-pyridylmethylamides as starting materials.⁸ Subsequently, various new protocols have also been developed to synthesize these compounds.⁹ Recently, Zeng and Xu groups independently reported copper-catalyzed imidazole synthesis *via* the oxidative C–H amination reactions (Scheme 1a and b).¹⁰ These elegant protocols led to new reactivity pathways and made great progress in imidazole synthesis. However, these reported methods still suffered from the usage of transition-metal catalysts. Our group also developed previously some oxidative C–H amination reactions for imidazole synthesis under metal-free conditions.¹¹ The main drawbacks are the narrow scope of the substrates and the difficulty of the available starting materials. Therefore, a more environmental-friendly methodology with readily available starting materials for the preparation of imidazo[1,5-*a*]quinolines is also highly desirable.

On the other hand, decarboxylative reactions were widely used in organic synthesis, especially in pericyclic reactions for

heterocycles.¹² Recently, a series of cascade decarboxylative reactions involving azomethine ylides have been developed to construct C–C and C–N bonds.¹³ As a facile, stable and cheap starting materials, amino acids has long been neglected in organic synthesis.¹⁴ Our group also developed some decarboxylative cyclization reactions from amino acids.¹⁵ As our continuing interest in the decarboxylative reaction for the synthesis of *N*-heterocycles, herein we report a new decarboxylative cascade reaction for the synthesis of imidazo[1,5-*a*]quinolines starting from readily available materials under metal-free condition (Scheme 1c and d).

Results and discussion

Initially, we employed 2-methylquinoline (**1a**) and valine (**2a**) as model substrates. The results are summarized in Table 1. Firstly, the reaction of 1 equiv. of **1a** and 1.5 equiv. of **2a** was carried out in the presence of 1 equiv. of I₂ in *N,N*-dimethylformamide (DMF) at 80 °C for 3 h to give rise to a 20% yield of the expected product 1-isopropylimidazo[1,5-*a*]quinoline (**3aa**) (Entry 1, Table 1). Then the influence of oxidants on this reaction was investigated (Entries 2–6, Table 1). It was found that the yield could be improved to 84% by using 3 equiv. of *tert*-butyl hydroperoxide (TBHP) while the other oxidants, such as di-*tert*-butyl peroxide (DTBP), dioxygen and peroxyulfates had little influence on the reaction or deteriorated the reaction.

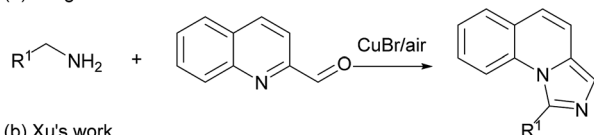
Afterwards several solvents were also examined (Entries 7–16, Table 1). *N,N*-Dimethylacetamide (DMA) had a little negative influence on the reaction (Entry 7, Table 1) while dimethyl sulfoxide (DMSO) reduced the reaction yield remarkably. Other solvents, such as ethyl nitrile, toluene, tetrahydrofuran (THF), methanol, 1,4-dioxane and water would result in the failure of the reaction (Entries 9–14, Table 1). The mixed solvents deteriorated the reaction either (Entries 15–16, Table 1). Subsequently the different temperature was examined for this reaction. When the reaction temperature was increased to 100 °C, the corresponding product can be obtained with a yield of 83%. (Entry 19, Table 1). Further increase of the temperature could not

^aHefei National Laboratory for Physical Sciences at Microscale, CAS Key Laboratory of Soft Matter Chemistry & Center for Excellence in Molecular Synthesis of Chinese Academy of Sciences, Collaborative Innovation Center of Suzhou Nano Science and Technology & School of Chemistry and Materials Science, University of Science and Technology of China, 230026, Hefei, Anhui, P. R. China. E-mail: zhang3@ustc.edu.cn; Tel: +86-551-6360-3185

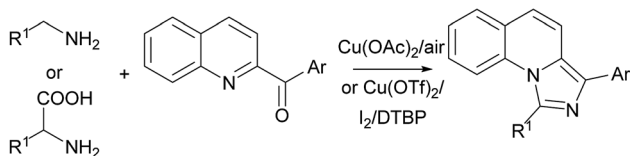
^bCollege of Chemistry and Chemical Engineering, Jiangxi Normal University, 330022, Nanchang, P. R. China. E-mail: wanfeng@jxnu.edu.cn

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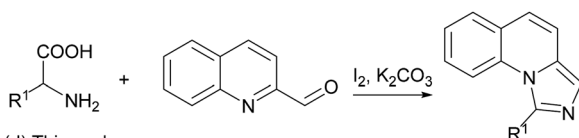
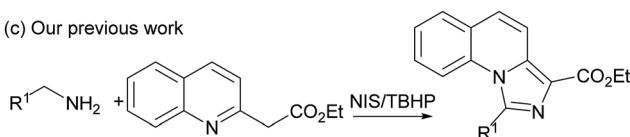
(a) Zeng's work



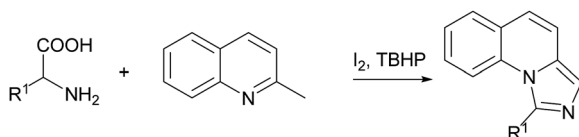
(b) Xu's work



(c) Our previous work



(d) This work



Scheme 1 Previous study and this work for the synthesis of imidazo [1,5-*a*]quinolines.

improve the yield (Entry 20, Table 1). The product **3aa** was obtained with the yields of 25% and 43% when the reactions were carried out at 25 °C and 50 °C, respectively (Entry 17–18, Table 1). This indicated that reducing the reaction temperature would destroy this reaction. The reaction could not proceed without I₂ and the yield of the product decreased to 17% while only 20% of the I₂ was added (Entries 21–22, Table 1). Finally, the optimized reaction conditions were obtained as described in entry 2 of Table 1: 1.0 equiv. of 2-methyl quinoline **1a** and 1.5 equiv. of α -amino acid **2a** as the reaction substrates, 1.0 equiv. of iodine and 3.0 equiv. of TBHP as the oxidants, the reaction being carried out in 0.5 mL of DMF at 80 °C for 3 h.

With the optimized conditions in hand, we explored the scope of the reaction substrates. Firstly, different substrates with groups on R¹ and R² were examined, and the results were listed in Table 2. Generally, 6-substituted 2-methylquinolines could be converted to the corresponding products in moderate to good yields (**3ba–3ia**). The substrates with electron-withdrawing groups presented more efficient than that with the electron-donating groups in this reaction. For example, 2-methyl-6-methoxyquinoline only afforded the product (**3ha**) with 44% yield while 2-methyl-6-nitroquinoline gave the product with a high yield of 81% (**3ga**). Subsequently, the substitution position of methoxyl group was investigated. The yields between 4-methoxyl and 6-methoxyl product were almost

Table 1 Optimization of reaction conditions^a

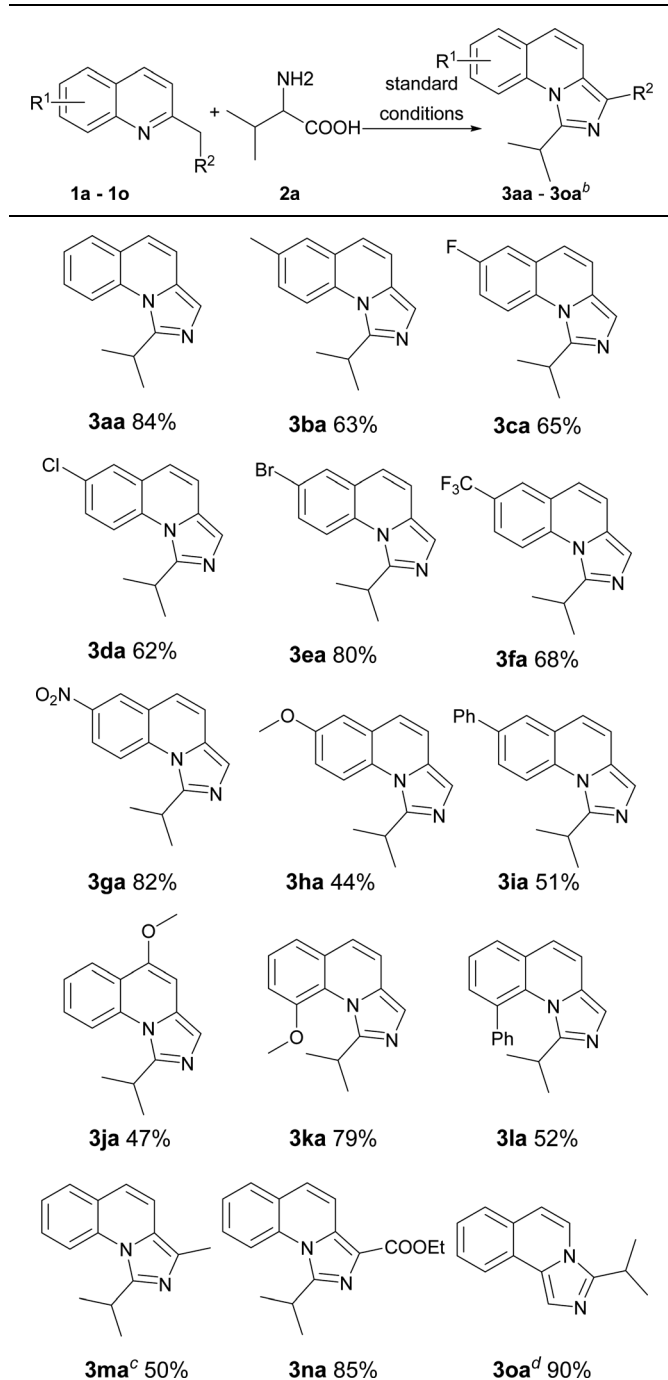
Entry	Oxidant	Solvent	Temp. (°C)	Yield ^b (%)
1	—	DMF	80	20
2	TBHP	DMF	80	84
3	O ₂	DMF	80	84
4	DTBP	DMF	80	18
5	K ₂ S ₂ O ₈	DMF	80	0
6	(NH ₄) ₂ S ₂ O ₈	DMF	80	Trace
7	TBHP	DMA	80	81
8	TBHP	DMSO	80	57
9	TBHP	H ₂ O	80	n. d.
10	TBHP	Tol.	80	n. d.
11	TBHP	MeCN	80	Trace
12	TBHP	MeOH	80	n. d.
13	TBHP	THF	80	n. d.
14	TBHP	1,4-Dioxane	80	n. d.
15	TBHP	DMF/H ₂ O	80	37
16	TBHP	DMF/MeOH	80	49
17	TBHP	DMF	25	25
18	TBHP	DMF	50	43
19	TBHP	DMF	100	83
20	TBHP	DMF	120	83
21 ^c	TBHP	DMF	80	0
22 ^d	TBHP	DMF	80	17

^a Reaction conditions: **1a** (1.0 equiv., 0.2 mmol), **2a** (1.5 equiv., 0.3 mmol), I₂ (1.0 equiv.), oxidant (3 equiv.) in solvent (0.5 mL). ^b Isolated yield. ^c The reaction was carried out without I₂. ^d The reaction was carried out with 20% of I₂.

the same. However, the 8-methoxyl product was obtained with an abnormal yield of 79% (**3ha**, **3ja** and **3ka**). This implied that steric hindrance had little influence on the reaction when 2-methyl-8-phenylquinoline was employed (**3ia** vs. **3la**). The 2-ethylquinoline showed lower reactivity. We could not obtain the desired product under the standard conditions but only the corresponding ketone was obtained. The desired imidazo[1,5-*a*]quinoline can be obtained with a yield of 50% when the reaction temperature was increased to 120 °C (**3ma**). Agreeing with former reports,^{11b} an electron-withdrawing substituent on the carbon of methyl at 2-position favoured the reaction (**3na**). 1-Methylisoquinoline could also converted to the desired product well under standard conditions (**3oa**).

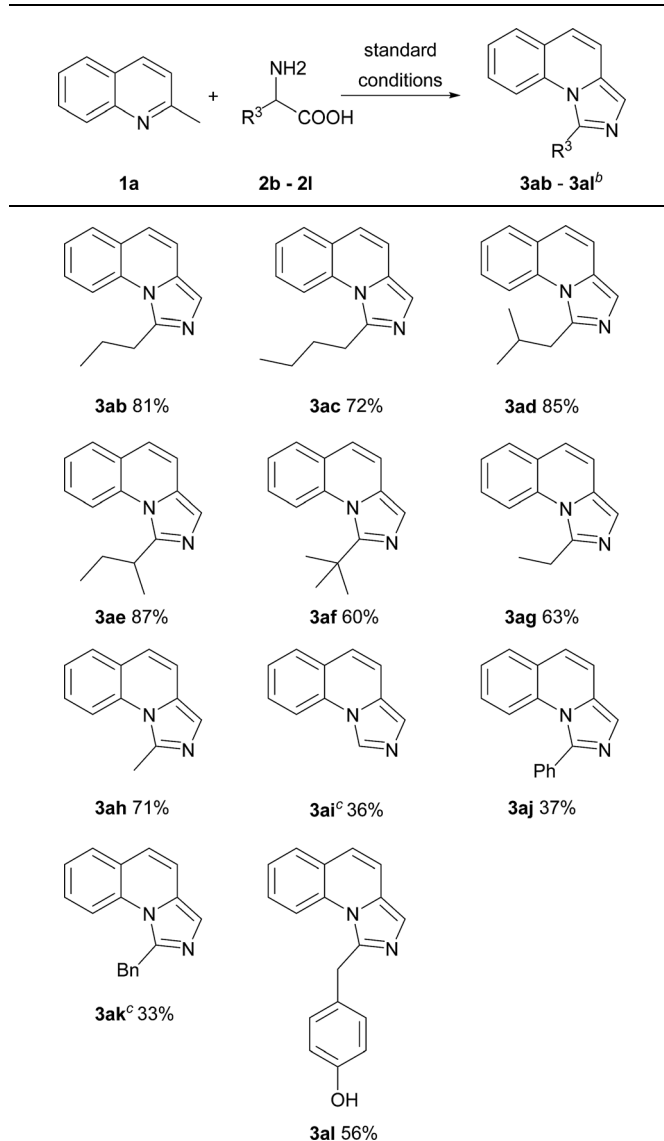
On the other hand, the scope of the amino acids were investigated (Table 3). Alkyl amino acids worked well in this reaction to afford the desired products with moderate to good yields (**3ab–3ah**), while the aromatic amino acids, such as phenylglycine and phenylalanine, can also be employed as the substrate to afford the corresponding products with lower yields (**3aj–3ak**). This may be due to the fact that under these conditions, aromatic amino acids are more active and some side reactions can occur. For instance, part of the amino acids might



Table 2 Substrate scope of various quinolines^a

^a Reaction conditions: **1a-1o** (1.0 equiv., 0.2 mmol), **2a** (1.5 equiv., 0.3 mmol), I₂ (1.0 equiv.), oxidant (3 equiv.) in solvent (0.5 mL). ^b Isolated yield. ^c This reaction was carried out at 120 °C. ^d This product was obtained with the starting material of 1-methylisoquinoline so the structure was different from **3** as shown.

be decarboxylated first, which could not convert to desired products. As for tyrosine, the phenolic hydroxyl group could tolerate the reaction conditions to give the desired product with good yield (**3al**). To our delight, non-substituted imidazo

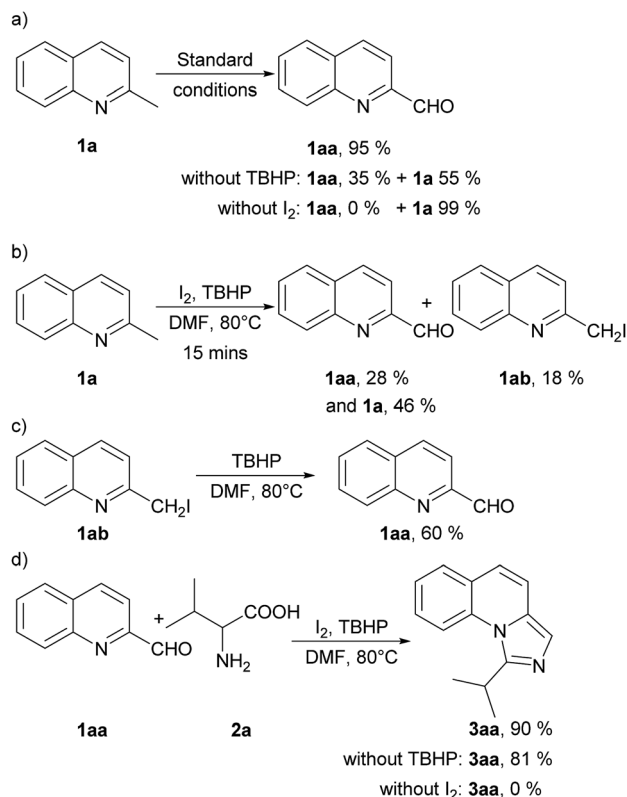
Table 3 Substrate scope of various amino acids^a

^a Reaction conditions: **2b-2o** (1.0 equiv., 0.2 mmol), **2a** (1.5 equiv., 0.3 mmol), I₂ (1.0 equiv.), oxidant (3 equiv.) in solvent (0.5 mL). ^b Isolated yield. ^c This reaction was carried out at 120 °C.

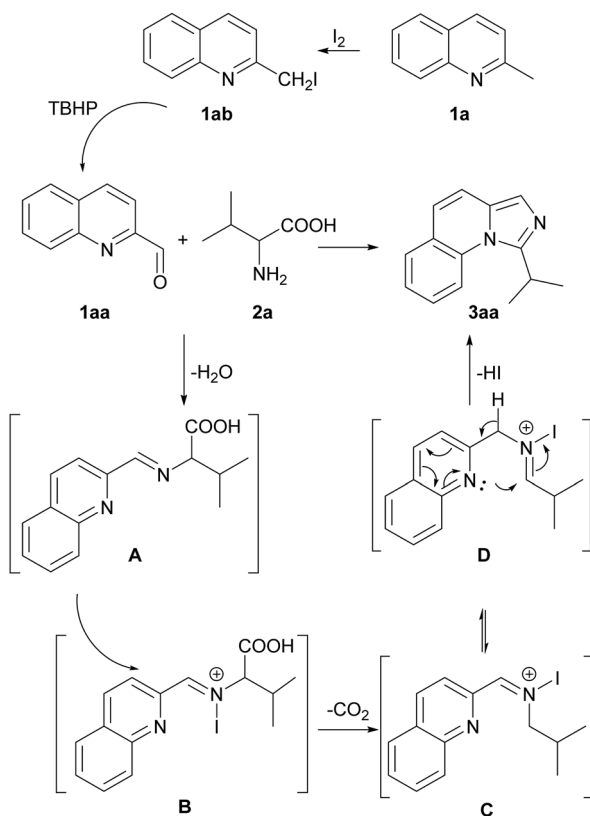
[1,5-*a*]quinoline (**3ai**) can be obtained at 120 °C by virtue of this method, which was challenging from other methods.^{9a,11a}

To get an insight into the mechanism of this process, we conducted several control experiments (Scheme 2). Firstly, only 2-methylquinoline (**1a**) was employed under the standard conditions and quinoline-2-carbaldehyde (**1aa**) was obtained with a yield of 95%. The yield decreased when TBHP was absent with 55% of **1a** recovered, and no corresponding aldehyde was found without iodine (Scheme 2a). Besides, the aldehyde (**1aa**) and 2-(iodomethyl) quinoline (**1ab**) could be detected at 15 minutes of the model reaction (Scheme 2b). Moreover, 2-(iodomethyl) quinoline (**1ab**) was employed under the standard conditions without I₂ and **1aa** was obtained with a yield of 60% (Scheme 2c). When quinoline-2-carbaldehyde (**1aa**) and valine





Scheme 2 Control experiments.



Scheme 3 The proposed reaction mechanism.

(**2a**) were used as the reaction substrates under standard conditions, 90% of **3aa** could be afforded. It should be noted that the yield decreased slightly when TBHP was absent, but no corresponding product **3aa** was detected without iodine (Scheme 2d). These experiments indicated that **1aa** might be an intermediate of this reaction under the promotion of iodine and TBHP. In the subsequent transformation, TBHP might not be important but I_2 is needed.

Based on the experimental results above and the previous reports,^{10c,11a} a possible reaction pathway was proposed as shown in Scheme 3. Initially, 2-methylquinoline (**1a**) is quickly substituted with iodine to afford 2-(iodomethyl)quinoline (**1ab**) and subsequently oxidized to quinoline-2-carbaldehyde (**1aa**). Thereafter, **1aa** produces imine **A** with the amino acid **2a**. The imine **A** goes through *N*-iodination process, generating intermediate **B**. Afterward, the intermediate **B** undergoes a decarboxylative pathway to generate intermediate **C** at high temperature. Finally, **C** transforms to **D** and then cyclization happens easily through an intramolecular nucleophilic attack to give the final product **3aa**.

Conclusions

In summary, we developed a facile decarboxylative cyclization to construct imidazo[1,5-*a*]quinolines with readily available starting material under metal-free condition. Compared to previous reports, the substrate scope of the primary α -amino acid was largely extended. In particular, the synthesis avoids the metal residues in the products, which provides a useful method for the pharmaceutical synthesis.

Experimental

Materials and methods

Products were purified by flash chromatography on 200–300 mesh silica gels using petroleum ether/ethyl acetate as eluent. NMR spectra were recorded on 400 MHz (101 MHz for ¹³C NMR) Bruker NMR spectrometer with CDCl₃ or DMSO-*d*₆ as the solvent and tetramethylsilane (TMS) as the internal standard. High resolution mass spectra (ESI) were recorded on a WatersTM Q-TOF Premier. Melting points were determined on a melting point apparatus and are uncorrected.

General procedure for the synthesis of imidazo[1,5-*a*]quinolines (**3**)

2-Methylquinoline (**1a**, 28 mg, 0.2 mmol), valine (**2a**, 35 mg, 0.3 mmol) and iodine (51 mg, 0.2 mmol) were added to 0.5 mL of *N,N*-dimethylformamide. Then 60 μ L of *tert*-butyl hydroperoxide was added and the solution was kept at 80 °C for 3 h. After the reaction was finished, the reaction mixture was washed and extracted by CH₂Cl₂. The organic phase was dried by Na₂SO₄ and then evaporated under reduced pressure. The resulting residue was purified by silica gel column chromatography (PE/EtOAc) to afford the desired product **3**.



1-Isopropyl imidazo[1,5-*a*]quinoline (3aa)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow oil. Silica gel TLC Rf = 0.6 (PE : EtOAc = 3 : 1); ^1H NMR (400 MHz, CDCl_3) δ 8.07–8.05 (d, J = 8.5 Hz, 1H), 7.52–7.50 (d, J = 7.7 Hz, 1H), 7.41–7.37 (t, J = 7.9 Hz, 1H), 7.27–7.24 (m, 2H), 7.15–7.12 (d, J = 9.6 Hz, 1H), 6.81–6.79 (d, J = 9.3 Hz, 1H), 3.77–3.67 (sept, J = 6.6 Hz, 1H), 1.47–1.45 (d, J = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 149.3, 133.1, 130.2, 128.7, 127.7, 126.0, 124.8, 120.6, 117.5, 116.9, 30.0, 21.6; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{15}\text{N}_2$ [$\text{M} + \text{H}$] $^+$ 211.1235, found 211.1236.

1-Isopropyl-7-methyl-imidazo[1,5-*a*]quinoline (3ba)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a brown oil. Silica gel TLC Rf = 0.45 (PE : EtOAc = 3 : 1); ^1H NMR (400 MHz, CDCl_3) δ 8.06–8.04 (d, J = 8.6 Hz, 1H), 7.40 (s, 1H), 7.35 (s, 1H), 7.31–7.29 (d, J = 8.6 Hz, 1H), 7.21 (d, J = 8.1 Hz, 1H), 6.86–6.84 (d, J = 9.4 Hz, 1H), 3.85–3.75 (sept, J = 6.7 Hz, 1H), 2.44 (s, 3H), 1.56–1.54 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 149.0, 134.4, 131.0, 130.0, 128.7, 128.7, 126.0, 120.5, 117.4, 116.8, 29.8, 21.5, 20.7; HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2$ [$\text{M} + \text{H}$] $^+$ 225.1392, found 225.1390.

7-Fluoro-1-isopropyl-imidazo[1,5-*a*]quinoline (3ca)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid. Silica gel TLC Rf = 0.6 (PE : EtOAc = 3 : 1); mp = 74–76 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.16–8.12 (dd, J = 9.1, 4.4 Hz, 1H), 7.40 (s, 1H), 7.31–7.27 (m, 2H), 7.25–7.20 (m, 1H), 6.87–6.84 (d, J = 9.3 Hz, 1H), 3.81–3.71 (sept, J = 6.7 Hz, 1H), 1.56 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 160.4, 157.9 (d, $^1J_{\text{CF}}$ = 251.5 Hz), 149.2, 129.9, 129.5, 129.5 (d, $^4J_{\text{CF}}$ = 2.2 Hz), 127.9, 127.8 (d, $^3J_{\text{CF}}$ = 8.3 Hz), 121.2, 119.7, 119.7 (d, $^4J_{\text{CF}}$ = 2.7 Hz), 118.8, 118.6, 118.5 (d, $^3J_{\text{CF}}$ = 8.5 Hz), 115.0, 114.8 (d, $^2J_{\text{CF}}$ = 23.5 Hz), 114.0, 113.7 (d, $^2J_{\text{CF}}$ = 22.3 Hz), 29.9, 21.4; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{F}$ [$\text{M} + \text{H}$] $^+$ 229.1141, found 229.1138.

7-Chloro-1-isopropyl-imidazo[1,5-*a*]quinoline (3da)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow oil. Silica gel TLC Rf = 0.6 (PE : EtOAc = 2 : 1); ^1H NMR (400 MHz, CDCl_3) δ 8.10–8.08 (d, J = 9.0 Hz, 1H), 7.59 (s, 1H), 7.46–7.44 (d, J = 9.0 Hz, 1H), 7.39 (s, 1H), 7.30–7.27 (d, J = 9.6 Hz, 1H), 6.84–6.82 (d, J = 9.4 Hz, 1H), 3.80–3.70 (sept, J = 6.7 Hz, 1H), 1.57–1.55 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 149.5, 131.5, 130.17, 130.0, 127.8, 127.5, 127.5, 121.3, 119.4, 118.8, 118.3, 30.0, 21.4; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{Cl}$ [$\text{M} + \text{H}$] $^+$ 245.0846, found 245.0844.

7-Bromo-1-isopropyl-imidazo[1,5-*a*]quinoline (3ea)

The title compound was prepared according to the general working procedure and purified by column chromatography to

give the product as a yellow oil. Silica gel TLC Rf = 0.15 (PE : EtOAc = 10 : 1); ^1H NMR (400 MHz, CDCl_3) δ 8.03 (m, 1H), 7.75–7.74 (d, J = 2.3 Hz, 1H), 7.60–7.57 (m, 1H), 7.39 (s, 1H), 7.29–7.27 (m, 1H), 6.83–6.80 (m, 1H), 3.80–3.69 (sept, J = 6.6 Hz, 1H), 1.56–1.54 (d, J = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 149.5, 131.9, 130.9, 130.3, 130.0, 127.9, 121.3, 119.3, 118.8, 118.5, 117.8, 30.0, 21.3; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{Br}$ [$\text{M} + \text{H}$] $^+$ 289.0340, found 289.0340.

1-Isopropyl-7-(trifluoromethyl)-imidazo[1,5-*a*]quinoline (3fa)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow needle solid. Silica gel TLC Rf = 0.5 (PE : EtOAc = 3 : 1); mp = 60–62 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.27–8.24 (d, J = 8.9 Hz, 1H), 7.88 (s, 1H), 7.74–7.72 (d, J = 8.9 Hz, 1H), 7.41 (s, 1H), 7.34–7.32 (d, J = 9.3 Hz, 1H), 6.95–6.92 (d, J = 9.3 Hz, 1H), 3.84–3.74 (sept, J = 6.6 Hz, 1H), 1.57 (d, J = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 150.0, 135.0, 130.2, 127.8, 125.1, 122.4, 119.7 (q, $^1J_{\text{CF}}$ = 272.0 Hz), 127.4, 127.0, 126.7, 126.4 (q, $^2J_{\text{CF}}$ = 33.0 Hz), 126.1, 125.8, 125.7, 125.7 (q, J_{CF} = 3.9 Hz), 124.2, 124.2, 124.1, 124.1 (q, J_{CF} = 3.4 Hz), 121.5, 119.9, 119.1, 117.4, 30.1, 21.4; HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{F}_3$ [$\text{M} + \text{H}$] $^+$ 279.1109, found 279.1107.

1-Isopropyl-7-nitro-imidazo[1,5-*a*]quinoline (3ga)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as an orange needle solid. Silica gel TLC Rf = 0.45 (PE : EtOAc = 3 : 1); mp = 190–192 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.47–8.24 (m, 3H), 7.44–7.43 (d, J = 4.8 Hz, 1H), 7.40–7.36 (dd, J = 9.3, 5.5 Hz, 1H), 7.00–6.96 (m, 1H), 3.79–3.74 (sept, J = 6.4 Hz, 1H), 1.57 (d, J = 6.5, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 150.5, 143.9, 136.7, 130.2, 126.5, 123.8, 122.3, 122.1, 120.0, 119.8, 117.6, 30.2, 21.4; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{14}\text{N}_3\text{O}_2$ [$\text{M} + \text{H}$] $^+$ 256.1086, found 256.1083.

1-Isopropyl-7-methoxy-imidazo[1,5-*a*]quinoline (3ha)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a brown oil. Silica gel TLC Rf = 0.30 (PE : EtOAc = 3 : 1); ^1H NMR (400 MHz, CDCl_3) δ 8.11–8.08 (d, J = 8.8 Hz, 1H), 7.37 (s, 1H), 7.26–7.24 (d, J = 9.6 Hz, 1H), 7.10–7.08 (m, 2H), 6.88–6.86 (d, J = 9.3 Hz, 1H), 3.90 (s, 3H), 3.84–3.74 (sept, J = 6.7 Hz, 1H), 1.56 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 156.3, 148.7, 129.9, 127.4, 127.3, 120.6, 120.4, 118.2, 118.0, 115.1, 111.2, 55.5, 29.8, 21.5; HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}$ [$\text{M} + \text{H}$] $^+$ 241.1341, found 241.1342.

1-Isopropyl-7-phenyl-imidazo[1,5-*a*]quinoline (3ia)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow oil. Silica gel TLC Rf = 0.15 (PE : EtOAc = 10 : 1); ^1H NMR (400 MHz, CDCl_3) δ 8.24–8.22 (d, J = 8.8 Hz, 1H), 7.82 (s, 1H), 7.75–7.73 (d, J = 8.8 Hz, 1H), 7.67–7.65 (d, J = 7.5 Hz, 4H), 7.50–7.46 (t, J = 7.5 Hz, 2H), 7.40–7.37



(m, 2H), 7.28–7.26 (t, $J = 6.8$ Hz, 1H), 6.98–6.96 (d, $J = 9.3$ Hz, 2H), 3.90–3.80 (sept, $J = 6.6$ Hz, 1H), 1.59 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 149.4, 139.7, 137.6, 130.2, 128.9, 127.6, 127.0, 126.8, 126.5, 126.4, 120.8, 120.7, 117.9, 117.3, 30.0, 21.5. HRMS (ESI) m/z calcd for $\text{C}_{20}\text{H}_{19}\text{N}_2$ $[\text{M} + \text{H}]^+$ 287.1548, found 287.1550.

1-Isopropyl-5-methoxy-imidazo[1,5-*a*]quinoline (3ja)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a green oil. Silica gel TLC Rf = 0.50 (PE : EtOAc = 3 : 1); ^1H NMR (400 MHz, CDCl_3) δ 8.15–8.12 (d, $J = 8.7$ Hz, 1H), 8.08–8.06 (d, $J = 8.1$ Hz, 1H), 7.57–7.53 (m, 1H), 7.42–7.38 (m, 1H), 7.17 (s, 1H), 6.50 (s, 1H), 3.94 (m, 3H), 3.80–3.71 (sept, $J = 6.5$ Hz, 1H), 1.54 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 148.5, 147.9, 133.4, 130.1, 128.5, 124.4, 123.4, 121.3, 117.9, 116.7, 91.9, 55.3, 30.0, 21.5; HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}$ $[\text{M} + \text{H}]^+$ 241.1341, found 241.1338.

1-Isopropyl-9-methoxy-imidazo[1,5-*a*]quinoline (3ka)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a green oil. Silica gel TLC Rf = 0.55 (PE : EtOAc = 3 : 1); ^1H NMR (400 MHz, CDCl_3) δ 7.41 (s, 1H), 7.33–7.29 (m, 1H), 7.18–7.16 (d, $J = 8.3$ Hz, 2H), 7.00–6.98 (d, $J = 8.1$ Hz, 1H), 6.79–6.77 (d, $J = 9.2$ Hz, 1H), 3.92 (m, 3H), 3.75–3.65 (sept, $J = 6.7$ Hz, 1H), 1.36 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 154.6, 149.7, 130.5, 129.1, 125.7, 122.7, 121.6, 119.7, 118.0, 109.9, 55.3, 30.2, 22.9; HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}$ $[\text{M} + \text{H}]^+$ 241.1341, found 241.1345.

1-Isopropyl-9-phenyl-imidazo[1,5-*a*]quinoline (3la)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow oil. Silica gel TLC Rf = 0.35 (PE : EtOAc = 10 : 1); ^1H NMR (400 MHz, CDCl_3) δ 7.56–7.53 (m, 1H), 7.45–7.43 (d, $J = 9.2$ Hz, 3H), 7.40–7.36 (t, $J = 7.4$ Hz, 2H), 7.32–7.28 (t, $J = 7.4$ Hz, 1H), 7.26–7.24 (d, $J = 9.4$ Hz, 1H), 7.20–7.18 (d, $J = 6.9$ Hz, 2H), 6.92–6.90 (d, $J = 9.2$ Hz, 1H), 2.83–2.73 (sept, $J = 6.7$ Hz, 1H), 0.69–0.67 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 154.5, 141.0, 133.0, 131.0, 130.9, 129.5, 129.2, 129.0, 127.60, 127.6, 126.5, 125.6, 122.1, 120.3, 117.7, 29.8, 21.3; HRMS (ESI) m/z calcd for $\text{C}_{20}\text{H}_{19}\text{N}_2$ $[\text{M} + \text{H}]^+$ 287.1548, found 287.1552.

1-Isopropyl-3-methyl-imidazo[1,5-*a*]quinoline (3ma)

The title compound was prepared according to the general working procedure except the temperature was 120 °C and purified by column chromatography to give the product as a yellow solid. Silica gel TLC Rf = 0.25 (PE : EtOAc = 5 : 1); mp = 110–112 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.13–8.11 (d, $J = 8.5$ Hz, 1H), 7.60–7.58 (d, $J = 7.6$ Hz, 1H), 7.49–7.45 (t, $J = 7.4$ Hz, 1H), 7.36–7.33 (t, $J = 7.4$ Hz, 1H), 7.20–7.17 (d, $J = 9.4$ Hz, 1H), 6.84–6.81 (d, $J = 9.4$ Hz, 1H), 3.86–3.76 (sept, $J = 6.7$ Hz, 1H), 2.49 (s, 3H), 1.57–1.55 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (101 MHz,

CDCl_3) δ 148.0, 133.3, 128.6, 128.5, 127.5, 126.2, 126.1, 124.6, 118.8, 117.1, 116.9, 29.7, 21.7, 12.5; HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{17}\text{N}_2$ $[\text{M} + \text{H}]^+$ 225.1392, found 225.1390.

Ethyl 1-isopropyl-imidazo[1,5-*a*]quinoline-3-carboxylate (3na)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a pale yellow solid. Silica gel TLC Rf = 0.2 (PE : DCM = 2 : 1); mp = 118–120 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.30–8.28 (d, $J = 8.5$ Hz, 1H), 8.15–8.13 (d, $J = 9.3$ Hz, 1H), 7.77–7.75 (d, $J = 7.5$ Hz, 1H), 7.65–7.61 (t, $J = 7.6$ Hz, 1H), 7.57–7.41 (t, $J = 7.4$ Hz, 1H), 7.33–7.31 (d, $J = 9.5$ Hz, 1H), 4.51–4.46 (q, $J = 7.0$ Hz, 2H), 3.93–3.83 (sept, $J = 6.3$ Hz, 1H), 1.64–1.62 (d, $J = 6.4$ Hz, 6H), 1.48–1.45 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 163.8, 150.0, 134.6, 132.8, 129.2, 128.9, 125.8, 125.7, 125.6, 121.9, 118.1, 117.3, 60.6, 30.3, 21.5, 14.6; HRMS (ESI) m/z calcd for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_2\text{Na}$ $[\text{M} + \text{Na}]^+$ 305.1266, found 305.1265.

3-Isopropyl-imidazo[5,1-*a*]isoquinoline (3oa)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a pale yellow solid, mp = 73–75 °C, silica gel TLC Rf = 0.3 (PE : EtOAc = 3 : 1); ^1H NMR (400 MHz, CDCl_3) δ 8.00–7.98 (d, $J = 7.9$ Hz, 1H), 7.77 (s, 1H), 7.65–7.63 (d, $J = 7.5$ Hz, 1H), 7.57–7.55 (d, $J = 7.7$ Hz, 1H), 7.52–7.48 (t, $J = 7.5$ Hz, 1H), 7.42–7.38 (t, $J = 7.4$ Hz, 1H), 6.82–6.80 (d, $J = 7.4$ Hz, 1H), 3.41–3.31 (sept, $J = 6.8$ Hz, 1H), 1.48 (d, $J = 6.8$ Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 146.0, 128.4, 128.1, 127.0, 127.7, 126.6, 125.1, 122.3, 119.5, 118.2, 113.5, 26.1, 20.8; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{15}\text{N}_2$ $[\text{M} + \text{H}]^+$ 211.1235, found 211.1235.

1-Propyl-imidazo[1,5-*a*]quinoline (3ab)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow oil. Silica gel TLC Rf = 0.40 (PE : EtOAc = 2 : 1); ^1H NMR (400 MHz, CDCl_3) δ 8.15–8.13 (d, $J = 8.1$ Hz, 1H), 7.65–7.63 (d, $J = 7.5$ Hz, 1H), 7.54–7.50 (m, 1H), 7.41–7.36 (m, 2H), 7.27–7.25 (m, 1H), 6.94–6.92 (d, $J = 9.5$ Hz, 1H), 3.38–3.34 (t, $J = 7.4$ Hz, 2H), 2.07–1.99 (m, 2H), 1.17–1.13 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 144.1, 133.2, 130.3, 128.7, 127.7, 125.9, 124.8, 120.6, 117.4, 116.6, 34.3, 20.6, 14.0; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{15}\text{N}_2$ $[\text{M} + \text{H}]^+$ 211.1235, found 211.1230.

1-Butyl-imidazo[1,5-*a*]quinoline (3ac)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as an orange oil. Silica gel TLC Rf = 0.65 (PE : EtOAc = 6 : 1); ^1H NMR (400 MHz, CDCl_3) δ 8.14–8.12 (d, $J = 8.5$ Hz, 1H), 7.63–7.61 (d, $J = 7.7$ Hz, 1H), 7.53–7.49 (t, $J = 7.8$ Hz, 1H), 7.40–7.35 (m, 2H), 7.25–7.23 (m, 1H), 6.92–6.90 (d, $J = 9.4$ Hz, 1H), 3.38–3.35 (t, $J = 7.7$ Hz, 2H), 2.02–1.95 (m, 2H), 1.61–1.54 (m, 2H), 1.05–1.00 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 144.2, 133.2, 130.3, 128.7, 127.7, 125.9, 124.8,



120.6, 120.6, 117.5, 116.6, 32.1, 29.3, 22.6, 13.9; HRMS (ESI) m/z calcd for $C_{15}H_{17}N_2$ $[M + H]^+$ 225.1392, found 225.1391.

1-Isobutyl-imidazo[1,5-*a*]quinoline (3ad)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow oil. Silica gel TLC Rf = 0.25 (PE : EtOAc = 5 : 1); 1H NMR (400 MHz, $CDCl_3$) δ 8.13–8.10 (d, J = 8.5 Hz, 1H), 7.65–7.63 (d, J = 7.7 Hz, 1H), 7.54–7.50 (t, J = 7.8 Hz, 1H), 7.41–7.37 (m, 2H), 7.27–7.25 (m, 1H), 6.95–6.92 (d, J = 9.4 Hz, 1H), 3.28–3.26 (d, J = 7.0 Hz, 2H), 2.47–2.35 (m, 1H), 1.10–1.09 (d, J = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 133.1, 130.3, 128.7, 127.7, 125.9, 124.9, 120.6, 120.6, 117.5, 116.6, 41.1, 26.6, 22.6; HRMS (ESI) m/z calcd for $C_{15}H_{17}N_2$ $[M + H]^+$ 225.1392, found 225.1393.

1-(*sec*-Butyl)-imidazo[1,5-*a*]quinoline (3ae)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a brown oil. Silica gel TLC Rf = 0.70 (PE : EtOAc = 3 : 1); 1H NMR (400 MHz, $CDCl_3$) δ 8.15–8.13 (d, J = 8.6 Hz, 1H), 7.63–7.61 (d, J = 7.7 Hz, 1H), 7.52–7.49 (t, J = 7.9 Hz, 1H), 7.38–7.35 (m, 2H), 7.27–7.23 (m, 1H), 6.92–6.89 (d, J = 9.3 Hz, 1H), 3.64–3.56 (m, 1H), 2.24–2.14 (m, 1H), 1.86–1.75 (m, 1H), 1.55–1.53 (d, J = 6.7 Hz, 3H), 1.05–1.01 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.7, 133.2, 130.1, 128.7, 127.6, 126.1, 124.7, 120.7, 120.5, 117.5, 116.9, 36.7, 28.5, 18.9, 11.9; HRMS (ESI) m/z calcd for $C_{15}H_{17}N_2$ $[M + H]^+$ 225.1392, found 225.1396.

1-(*tert*-Butyl)-imidazo[1,5-*a*]quinoline (3af)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow oil. Silica gel TLC Rf = 0.55 (PE : EtOAc = 3 : 1); 1H NMR (400 MHz, $CDCl_3$) δ 8.42–8.40 (d, J = 8.7 Hz, 1H), 7.63–7.61 (d, J = 7.7 Hz, 1H), 7.54–7.50 (t, J = 7.9 Hz, 1H), 7.40–7.37 (m, 2H), 7.28–7.26 (d, J = 9.1 Hz, 1H), 6.95–6.92 (d, J = 9.3 Hz, 1H), 1.75 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.5, 133.2, 131.8, 128.7, 126.7, 126.5, 124.8, 120.8, 120.4, 120.3, 117.9, 34.8, 30.5; HRMS (ESI) m/z calcd for $C_{15}H_{17}N_2$ $[M + H]^+$ 225.1392, found 225.1391.

1-Ethyl-imidazo[1,5-*a*]quinoline (3ag)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a brown oil. Silica gel TLC Rf = 0.35 (PE : EtOAc = 10 : 1); 1H NMR (400 MHz, $CDCl_3$) δ 8.18–8.16 (d, J = 8.5 Hz, 1H), 7.64–7.62 (d, J = 7.9 Hz, 1H), 7.53–7.50 (t, J = 7.8 Hz, 1H), 7.41–7.37 (m, 2H), 7.27–7.25 (m, 1H), 6.95–6.92 (d, J = 9.1 Hz, 1H), 3.44–3.39 (q, J = 6.9 Hz, 2H), 1.60–1.56 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 133.2, 130.4, 128.7, 127.8, 125.9, 124.9, 120.7, 120.5, 117.4, 116.6, 25.8, 11.8; HRMS (ESI) m/z calcd for $C_{13}H_{13}N_2$ $[M + H]^+$ 197.1079, found 197.1079.

1-Methyl-imidazo[1,5-*a*]quinoline (3ah)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow oil. Silica gel TLC Rf = 0.30 (PE : EtOAc = 6 : 1); 1H NMR (400 MHz, $CDCl_3$) δ 8.23–8.21 (d, J = 8.5 Hz, 1H), 7.65–7.63 (dd, J = 7.7, 1.4 Hz, 1H), 7.54–7.49 (m, 1H), 7.41–7.37 (m, 1H), 7.33 (s, 1H), 7.26–7.24 (m, 1H), 6.95–6.92 (d, J = 9.4 Hz, 1H), 3.09 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 133.3, 130.3, 128.6, 127.7, 125.7, 124.9, 120.6, 120.5, 117.3, 116.2, 19.6; HRMS (ESI) m/z calcd for $C_{12}H_{11}N_2$ $[M + H]^+$ 183.0922, found 183.0923.

Imidazo[1,5-*a*]quinoline (3ai)

The title compound was prepared according to the general working procedure except the temperature was 120 °C and purified by column chromatography to give the product as a brown oil. Silica gel TLC Rf = 0.15 (PE : EtOAc = 3 : 1); 1H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.98–7.96 (d, J = 8.3 Hz, 1H), 7.68–7.66 (d, J = 7.8 Hz, 1H), 7.58–7.54 (m, 1H), 7.48–7.41 (m, 2H), 7.34–7.32 (d, J = 9.5 Hz, 1H), 7.05–7.03 (d, J = 9.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 130.9, 128.8, 128.6, 127.8, 125.6, 124.2, 122.4, 121.3, 116.8, 114.6; HRMS (ESI) m/z calcd for $C_{11}H_9N_2$ $[M + H]^+$ 169.0766, found 169.0765.

1-Phenyl-imidazo[1,5-*a*]quinoline (3aj)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a pale yellow solid. Silica gel TLC Rf = 0.30 (PE : EtOAc = 6 : 1); mp = 113–115 °C; 1H NMR (400 MHz, $CDCl_3$) δ 7.66–7.60 (m, 3H), 7.54–7.50 (m, 5H), 7.34–7.26 (m, 2H), 7.19–7.14 (m, 1H), 7.03–7.00 (d, J = 9.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.3, 133.7, 132.3, 130.5, 129.5, 129.2, 128.7, 128.6, 127.3, 125.5, 125.1, 122.3, 121.4, 117.4, 117.1; HRMS (ESI) m/z calcd for $C_{17}H_{13}N_2$ $[M + H]^+$ 245.1079, found 245.1082.

1-Benzyl-imidazo[1,5-*a*]quinoline (3ak)

The title compound was prepared according to the general working procedure except the temperature was 120 °C and purified by column chromatography to give the product as a pale yellow solid. Silica gel TLC Rf = 0.40 (PE : EtOAc = 3 : 1); mp = 95–97 °C; 1H NMR (400 MHz, $CDCl_3$) δ 8.00–7.98 (d, J = 7.7 Hz, 1H), 7.61–7.59 (m, 1H), 7.47 (s, 1H), 7.35–7.25 (m, 5H), 7.23–7.15 (m, 3H), 6.98–6.96 (d, J = 9.4 Hz, 1H), 4.83 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.4, 136.9, 132.6, 130.7, 128.9, 128.5, 128.2, 127.8, 126.7, 125.7, 125.0, 121.2, 121.0, 117.3, 116.9, 37.8; HRMS (ESI) m/z calcd for $C_{18}H_{15}N_2$ $[M + H]^+$ 259.1235, found 259.1230.

4-(Imidazo[1,5-*a*]quinolin-1-ylmethyl)-phenol (3al)

The title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a brown solid, mp = 224–225 °C. Silica gel TLC Rf = 0.55 (DCM : MeOH = 10 : 1); 1H NMR (400 MHz, DMSO) δ 9.26 (s, 1H), 8.09–8.07 (d, J = 8.2 Hz, 1H), 7.75–7.74 (d,



$J = 7.4$ Hz, 1H), 7.47–7.38 (m, 4H), 7.12–7.10 (d, $J = 9.1$ Hz, 1H), 6.91–6.89 (d, $J = 8.1$ Hz, 2H), 6.66–6.64 (d, $J = 8.0$ Hz, 2H), 4.68 (s, 2H); ^{13}C NMR (101 MHz, DMSO) δ 155.9, 141.9, 131.8, 130.2, 129.0, 128.5, 128.0, 127.1, 125.1, 125.08, 121.0, 120.6, 117.4, 117.0, 115.5, 36.1; HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{15}\text{N}_2\text{O}$ $[\text{M} + \text{H}]^+$ 275.1184, found 275.1185.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

- 1 A. Cappelli, G. Giuliani, M. Anzini, D. Riitano, G. Giorgi and S. Vomero, *Bioorg. Med. Chem.*, 2008, **16**, 6850.
- 2 A. Wiśniewska, A. Chrapkowska, A. Kot-Wasik, J. Konopa and Z. Mazerska, *Acta Biochim. Pol.*, 2007, **54**, 831.
- 3 (a) G. R. Pettit, J. C. Collins, J. C. Knight, D. L. Herald, R. A. Nieman, M. D. Williams and R. K. Pettit, *J. Nat. Prod.*, 2003, **66**, 544; (b) M. D. Markey and T. R. Kelly, *J. Org. Chem.*, 2008, **73**, 7441; (c) D. Knueppel and S. F. Martin, *Angew. Chem., Int. Ed.*, 2009, **48**, 2569; (d) M. Mohamed, T. P. Gonçalves, R. J. Whitby, H. F. Sneddon and D. C. Harrowven, *Chem.-Eur. J.*, 2011, **17**, 13698.
- 4 M. S. Malamas, Y. Ni, J. Erdei, H. Stange, R. Schindler, H.-J. Lankau, C. Grunwald, K. Y. Fan, K. Parris, B. Langen, U. Egerland, T. Hage, K. L. Marquis, S. Grauer, J. Brennan, R. Navarra, R. Graf, B. L. Harrison, A. Robichaud, T. Kronbach, M. N. Pangalos, N. Hoefgen and N. J. Brandon, *J. Med. Chem.*, 2011, **54**, 7621.
- 5 A. Cappelli, M. Anzini, F. Castriconi, G. Grisci, M. Paolino, C. Braile, S. Valenti, G. Giuliani, S. Vomero, A. D. Capua, L. Betti, G. Giannaccini, A. Lucacchini, C. Ghelardini, L. D. C. Mannelli, M. Frosini, L. Ricci, G. Giorgi, M. P. Mascia and G. Biggio, *J. Med. Chem.*, 2016, **59**, 3353.
- 6 (a) M. Alcarazo, S. J. Roseblade, A. R. Cowley, R. Fernández, J. M. Brown and J. M. Lassaletta, *J. Am. Chem. Soc.*, 2005, **127**, 3290; (b) F. E. Hahn, *Angew. Chem., Int. Ed.*, 2006, **45**, 1348; (c) K. G. Kishore, O. Ghashghaei, C. Estarellas, M. M. Mestre, C. Monturiol, N. Kielland, J. M. Kelly, A. F. Francisco, S. Jayawardhana, D. Muñoz-Torrero, B. Pérez, F. J. Luque, R. Gámez-Montaña and R. Lavilla, *Angew. Chem., Int. Ed.*, 2016, **55**, 8994; (d) H. Erguven, D. C. Leitch, E. N. Keyzer and B. A. Arndtsen, *Angew. Chem., Int. Ed.*, 2017, **56**, 6078.
- 7 (a) D. S. Roman, V. Poirer, G. Pelletier and A. B. Charette, *Eur. J. Org. Chem.*, 2015, 67; (b) Z. Tan, H. Zhao, C. Zhou, H. Jiang and M. Zhang, *J. Org. Chem.*, 2016, **81**, 9939; (c) S.-S. Wu, C.-T. Feng, D. Hu, Y.-K. Huang, Z. Li, Z.-G. Luo and S.-T. Ma, *Org. Biomol. Chem.*, 2017, **15**, 1680.
- 8 (a) J. D. Bower and G. R. Ramage, *J. Chem. Soc.*, 1955, 2834; (b) K. Winterfeld and H. Franzke, *Angew. Chem.*, 1963, **75**, 1101.
- 9 (a) D. C. Mohan, S. N. Rao, C. Ravi and S. Adimurthy, *Org. Biomol. Chem.*, 2015, **13**, 5602; (b) Z. Li, S.-S. Wu, Z.-G. Luo, W.-K. Liu, C.-T. Feng and S.-T. Ma, *J. Org. Chem.*, 2016, **81**, 4386.
- 10 (a) M. Li, Y. Xie, Y. Ye, Y. Zou, H. Jiang and W. Zeng, *Org. Lett.*, 2014, **16**, 6232; (b) H. Wang, W. Xu, Z. Wang, L. Yu and K. Xu, *J. Org. Chem.*, 2015, **80**, 2431; (c) H. Wang, W. Xu, L. Xin, W. Liu, Z. Wang and K. Xu, *J. Org. Chem.*, 2016, **81**, 3681.
- 11 (a) Q. Wang, S. Zhang, F. Guo, B. Zhang, P. Hu and Z. Wang, *J. Org. Chem.*, 2012, **77**, 11161; (b) Y. Yan, Y. Zhang, Z. Zha and Z. Wang, *Org. Lett.*, 2013, **15**, 2274.
- 12 (a) N. Rodríguez and L. J. Goossen, *Chem. Soc. Rev.*, 2011, **40**, 5030; (b) Y. Wei, P. Hu, M. Zhang and W. Su, *Chem. Rev.*, 2017, **117**, 8864.
- 13 (a) D. Seidel, *Acc. Chem. Res.*, 2015, **48**, 317; (b) L. Zheng, F. Yang, Q. Dang and X. Bai, *Org. Lett.*, 2008, **10**, 889; (c) H.-P. Bi, L. Zhao, Y.-M. Liang and C.-J. Li, *Angew. Chem., Int. Ed.*, 2009, **48**, 792; (d) C. Zhang and D. Seidel, *J. Am. Chem. Soc.*, 2010, **132**, 1798; (e) H.-P. Bi, Q. Teng, M. Guan, W.-W. Chen, Y.-M. Liang, X. Yao and C.-J. Li, *J. Org. Chem.*, 2010, **75**, 783; (f) Y. Kang and D. Seidel, *Org. Lett.*, 2016, **18**, 4277; (g) D. Singh, V. Kumar, N. Devi, C. C. Malakar, R. Shankar and V. Singh, *Adv. Synth. Catal.*, 2017, **359**, 1213.
- 14 (a) D. Zhao, T. Wang, Q. Shen and J.-X. Li, *Chem. Commun.*, 2014, **50**, 4302; (b) K. Xu, Z. Wang, J. Zhang, L. Yu and J. Tan, *Org. Lett.*, 2015, **17**, 4476; (c) A. Joshi, D. C. Mohan and S. Adimurthy, *Org. Lett.*, 2016, **18**, 464; (d) P. Olsén, M. Oschmann, E. V. Johnston and B. Åkermær, *Green Chem.*, 2018, **20**, 469; (e) P. Peng, J. Xiong, B. Li, G. Mo, R. Chen and Z. Wang, *Chin. J. Org. Chem.*, 2013, **33**, 1891.
- 15 (a) Z. Zhang, J. Zhang, J. Tan and Z. Wang, *J. Org. Chem.*, 2008, **73**, 5180; (b) Q. Wang, C. Wan, Y. Gu, J. Zhang, L. Gao and Z. Wang, *Green Chem.*, 2011, **13**, 578; (c) Y. Yan and Z. Wang, *Chem. Commun.*, 2011, **47**, 9513; (d) Y. Li, F. Guo, Z. Zha and Z. Wang, *Sustainable Chem. Processes*, 2013, **1**, 8.

