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Copper-Catalyzed Oxidative Multicomponent Reaction: Synthesis of Imidazo Fused Heterocycles with Molecular Oxygen

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Xianwei Li,[*a] Tianzhang Wang,[a] Yu-Jing Lu,[*a] Shaomin Ji,[a] Yanping Huo,[a] Bifu Liu*[b]

An oxidative cascade that involves multicomponent reaction comprising terminal alkyne, 2-amino N-heterocycle, benzyl or allylic bromide with molecular oxygen, delivering densely functionalized imidazo fused heterocycles, is described. This reaction features that cheap catalyst, green oxidant, readily available starting materials, which makes the overall synthetic applicable in the quick access to relevant pharmaceutical molecules with imidazole derived heterocycles.

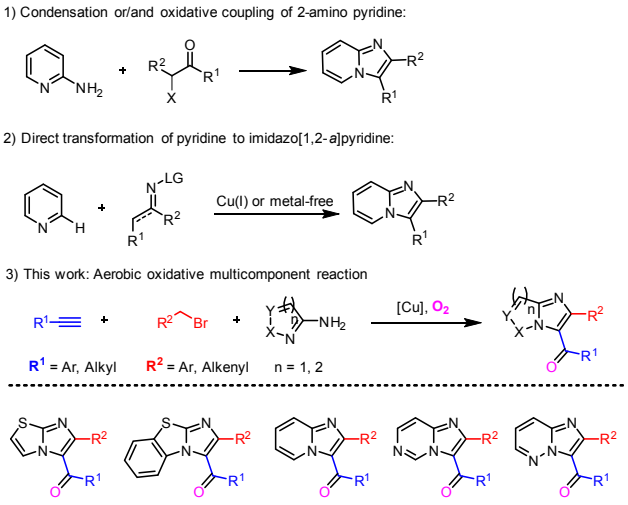
Introduction

Sequential and selective assembly of target molecules enables quick access to complex skeletons, which can be applicable in pharmaceutical and material science. In this context, the development of multicomponent reactions (MCRs)[1] provides an expedient platform for the construction of versatile building blocks as well as complex natural products in a single reaction. By rapidly increasing molecular complexity, MCRs can provide convenience for the study of structure-reactivity relationship. Nevertheless, the rational design of cascade reactions that transform readily available substrates into complex structures remained a formidable challenge.[2]

Selective oxidative functionalization of organic molecules that leads to valuable scaffolds is a great strategy in the lab and industry. Oxidative cascade reaction that take advantages of metal catalyst and oxidant that enables the multiple bond formations in one single operation has also met the demand of green and sustainable chemistry. However, commonly used stoichiometric unfriendly oxidants for the overall efficiency often minimized the practical applications. Molecular oxygen is a green, abundant and sustainable oxidant.[3] Thus in our opinion, oxidative cascade reactions in combination of molecular oxygen activation that delivers valuable complex structures represents one ideal process.

On our continuous quest to molecular oxygen participated oxygenation reactions,[4] we envisioned that by combining selective aerobic oxidation and multicomponent reaction, an efficient and green reaction utilizing transition metal catalysis and molecular oxygen for the quick access of complex molecules[5] such as imidazo[1,2-a]pyridines can be developed and find application in pharmaceutical industries.

Imidazo[1,2-a]pyridines serve as key structure motifs occurred in numerous bioactive molecules, such as Alpidem, Zolpidem, Saripidem, and Necopidem.[6] General method toward their synthesis includes condensation of 2-amino pyridine with carbonyl derivatives,[7] further functionalization of existed imidazo[1,2-a]pyridine core structures,[8] as well as dehydrogenative cross-couplings of pyridines.[9] Govergyan reported a three component reaction, comprising 2-amino pyridine, alkyne and aldehyde for the synthesis of imidazo[1,2-a]pyridine derived pharmaceuticals.[7a] Jiang developed an elegant example on imidazo[1,2-a]pyridine synthesis via copper-catalyzed aerobic oxidative cyclization of pyridines with ketone oxime esters.[9c]



Scheme 1. Strategies for the Rapid Construction of Imidazo fused N-heterocycles.

We envisioned that the development of efficient methods is still desired with the following concerns in mind: 1) readily available precursors should be used that enable the rapid increase in the

[a] School of Chemical Engineering and Light Industry, Guangdong University of Technology, No. 100 Waihuan Xi Road Guangzhou Higher Education Mega Center, Guangzhou, 510006, China. Email: xwli@gdut.edu.cn; luyj@gdut.edu.cn;
[b] School of Chemistry and Material Engineering, Huizhou University, No. 46 Yanda Avenue, Huizhou, 516007, China. Email: liubf@hzu.edu.cn

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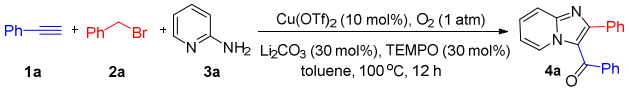
molecular diversity; 2) general methodologies enable the divergent products are in great emergency. Herein, we report multicomponent participated copper-catalyzed oxidative cascade reactions of terminal alkynes, benzyl or allylic bromides, 2-amino *N*-heterocycles, delivering diverse structures based on imidazoles, which hold the synthetic potential for the quick access to bioactive molecules.

Results and Discussions

Inspired by the previous strategies on oxidative MCRs, we commenced our studies by performing the reaction of terminal alkyne **1a**, benzylic bromide **2a** and 2-amino pyridine **3a** under oxidative conditions (Table 1). To our delight, the results of optimization revealed that with $Cu(OTf)_2$ as the catalyst, Li_2CO_3 as the base, TEMPO and molecular oxygen as the oxidant in toluene with the ratio of **1a**:**2a**:**3a** was 1:1:1.5, the desired product imidazo[1,2-a]pyridine (IP) **4a** could be isolated in 87% yield. Cu(I) and Fe(III) exhibited lower efficiency than that of Cu(II), while Pd(II) and Mn(II) delivered no desired product (entries 2-5). No product **4a** was obtained when HOTf was used instead of $Cu(OTf)_2$, indicating the essential role of copper salt (entry 6). Other oxidants such as $K_2S_2O_8$ and DTBP also displayed certain catalytic efficiency, and moderated yield of **4a** was detected. Lower yield was obtained with increased relative ratio of terminal alkyne (entry 9), or with pyridine as the base (entry 10), or with decreased temperature (entry 13). Toluene was proved to be optimal solvent in this transformation, while DMSO and 1,4-dioxane showed inferior results (entries 11-12). Lower the temperature led to dramatically reduced yield (entry 13). Significantly, trace amount of product **4a** was detected when the reaction was conducted under N_2 atmosphere (entry 14), which indicate the critical role of molecular oxygen in this transformation. Control experiment by replacing benzaldehyde to benzylic bromide **2a** led to much lower efficiency of this transformation (entry 15).

Table 1. Optimization of Reaction Conditions. [a]



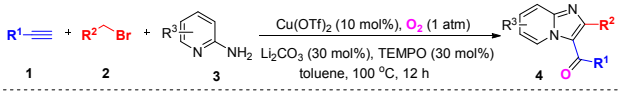
Entry	Variation of optimal conditions	Yield (%)
1	None	90 (87)
2	$PdCl_2$ instead of $Cu(OTf)_2$	-
3	CuI instead of $Cu(OTf)_2$	45
4	$FeCl_3$ instead of $Cu(OTf)_2$	< 10
5	$Mn(OAc)_2$ instead of $Cu(OTf)_2$	-
6	HOTf instead of $Cu(OTf)_2$	-
7	$K_2S_2O_8$ instead of TEMPO	30
8	DTBP instead of TEMPO	71
9	**1a** : **2a** : **3a** = 2 : 1 : 1	43
10	pyridine instead of Li_2CO_3	16
11	DMSO	22
12	1,4-dioxane	trace
13	80°C	37
14	under N_2	trace
15	benzaldehyde instead of **2a**	-

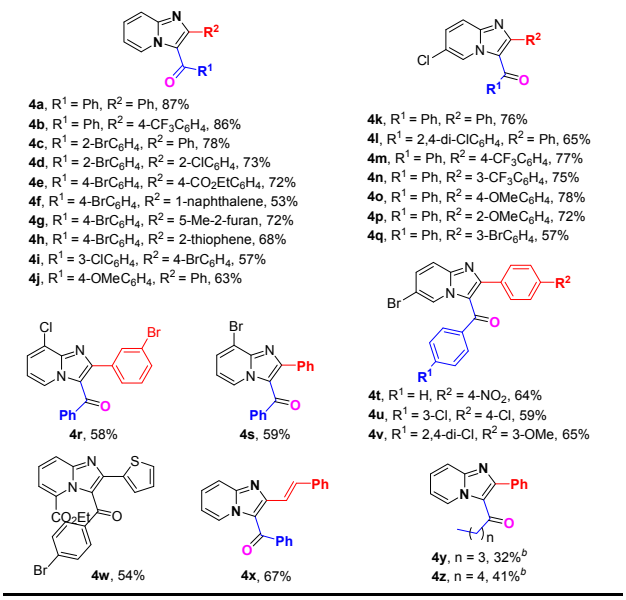
[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), **3a** (0.3 mmol), catalyst (10 mol%), solvent (1.0 mL) at the given temperature for 12 h. [b] Yields were determined by GC-MS with *n*-dodecane as the internal standard. Yield in the parentheses is the isolated yield.

With the optimal reaction condition, we next explored the generality of this oxidative cascade reaction. As depicted in Table 2, halogens such as chloro (**4d**, **4i**, **4l**)and bromo (**4c**, **4e**, **4q**) exhibited great chemoselectivity, which provide new opportunities for further derivation via cross-coupling reactions. It is worthy to note that, fused arenes or heterocyclic (including naphthalene (**4f**), furan (**4g**) and thiophene (**4h**)) bromomethyl **2**, could also be transformed into the corresponding IPs in good yields. Versatile functionalities, such as methoxyl (**4j**, **4o**, **4p**), trifluomethyl (**4b**, **4m**, **4n**) and ester (**4w**) moieties at different positions are compatible, which enable the facile further transformations. The reaction with component **3** revealed that 2-amino pyridines with electron-donating groups exhibited better performance than that of electron-withdrawing groups. Halogens, fluoro, chloro and bromo at C3, C5 position on pyridines could be well tolerated, delivering multiple functionalized IPs (**4r**-**4v**).

Notably, allylic bromides such as (*E*)-(3-bromoprop-1-en-1-yl)benzene, could participate in this oxygenative cascade, affording to highly functionalized IP ptorudct **4x** with C=C double bond intact. Significantly, aliphatic terminal alkynes, which are challenging substrates in related oxygenative reactions with molecular oxygen, could also give the desired IPs (**4y**, **4z**) in moderate yields.

Table 2. Substrate Scope for Oxidative Cascade Reaction for the Construction of Imidazo[1,2-a]pyridines [a]





[a] Reaction conditions: **1** (0.2 mmol), **2** (0.2 mmol), **3** (0.3 mmol), $Cu(OTf)_2$ (10 mol%), Li_2CO_3 (30 mol%), TEMPO (30 mol%), toluene

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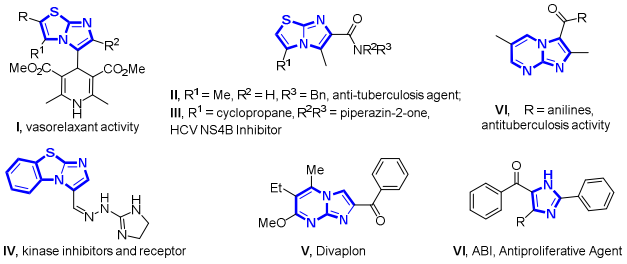
(1.0 mL) at 100 °C for 12 h under 1 atm of oxygen atmosphere. [b] Addition of 1 equivalent of KI.

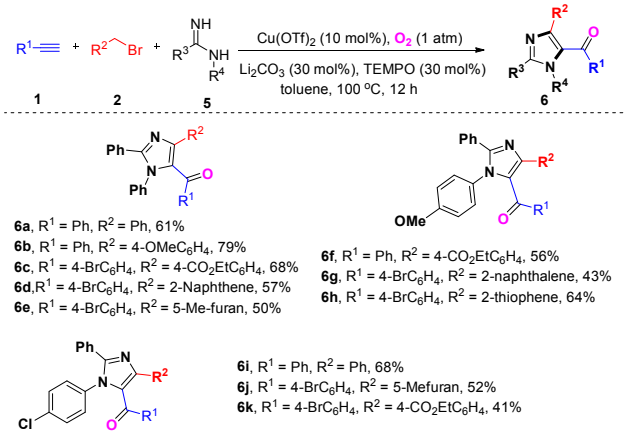
Due to the wide utilities of imidazoles and their fused heterocycles in pharmaceuticals and material science, for instance, thioxazole, benzoxazole and related *N*-heterocycles derived fused heterocycles exhibited great bioactivities[11] (Scheme 2). Thus, it would be of great synthetic desire to develop a general and efficient methodology for the rapid delivery of imidazole derived skeletons.[12]



Scheme 2. Selected bioactive molecules contained imidazole and their fused heterocycles skeletons.

To our satisfaction, this process was also successfully applied to the synthesis of densely substituted imidazoles,[10] which are widely existed in bioactive molecules and functional materials. With slight modification of reaction condition, this transformation could well proceed. As shown in Table 3, readily transformable functionalities on the aryl rings, eg. al., methoxyl (**6b**), ester (**6f**), chloro (**6i**) and bromo (**6h, 6k**) were tolerated, which hold the potential for the further derivation. Fused ring system and heterocycles, such as naphthalene (**6d**, **6g**), furan (**6e, 6j**) and thiophene (**6h**), were well compatible in this multicomponent reaction. This protocol allowed for the quick access to polysubstituted imidazoles, providing new opportunities for the late-stage modifications of related bioactive imidazole derivatives.

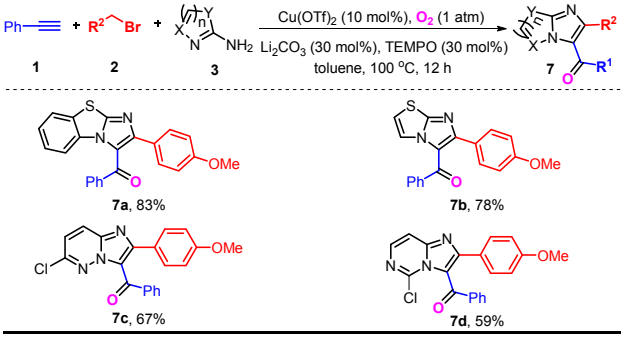
Table 3. Oxidative Cascade for the Construction of Imidazoles[a]



[a] Reaction conditions: **1** (0.2 mmol), **2** (0.2 mmol), **5** (0.3 mmol), $Cu(OTf)_2$ (10 mol%), Li_2CO_3 (30 mol%), KI (30 mol%), TEMPO (30 mol%), toluene (1.0 mL) at 100 °C for 8 h under 1 atm of oxygen atmosphere.

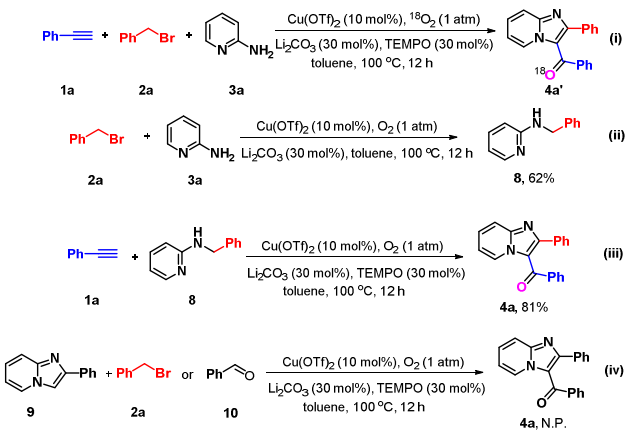
We select other 2-amino *N*-heterocycles to test the synthetic utility of this multicomponent reaction in related fused heterocycles. As depicted in Table 4, this process can be applied to the synthesis of benzo[d]imidazo[2,1-b]thiazole (**7a**), imidazo[2,1-b]thiazole (**7b**), imidazo[1,2-b]pyridazine (**7c**) and imidazo[1,2-c]pyrimidine (**7d**), which might find their synthetic utility in the quick access to related bioactive molecules synthesis.

Table 4. Synthetic Applications for the Synthesis of Imidazole Fused Heterocycles.



[a] Reaction conditions: **1** (0.2 mmol), **2** (0.2 mmol), **3** (0.3 mmol), $Cu(OTf)_2$ (10 mol%), Li_2CO_3 (30 mol%), TEMPO (30 mol%), toluene (1.0 mL) at 100 °C for 12 h under 1 atm of oxygen atmosphere.

To gain mechanistic insights into the present reaction, the following experiments were performed (Scheme 3): (i) isotopic experiments demonstrated the oxygen atom of the product **4a'** derived from molecular oxygen; (ii) when the standard reaction was conducted without terminal alkyne and TEMPO, S_N2 product **8** was obtained in 62% yield; (iii) the desired IP product **4a** was obtained in 81% yield when **1a** and **8** were subjected into the standard conditions; (iv) With the synthesized heterocycle **9**,[8c] together and benzylic bromide **2a** or benzaldehyde **10** under the standard condition, no desired product **4a** was detected. This result rule out the possibility that oxidative coupling of terminal alkyne **1a** and **3a** that led to heterocycle **9**, which further underwent substitution reaction with benzylic bromide **2a** or benzaldehyde **10**, to give the desired IP product **4a** (See Supporting Information for details).



Scheme 3. Mechanistic studies.

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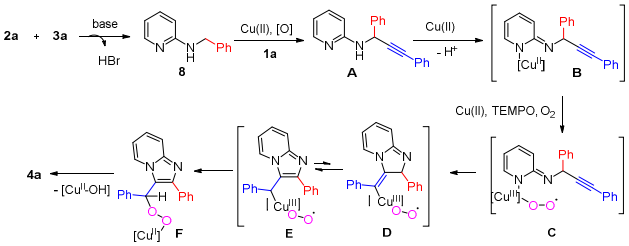
On the basis of these findings and previous results,[8e, 13-14] one possible pathway is proposed in Scheme 4. Initially, S_N2 reaction of benzylic bromide with 2-amino pyridine **3** took place, delivering intermediate **8**; further CDC (cross dehydrogenative coupling) reaction of **8** with terminal alkyne **2a** under Cu(II)-catalyzed oxidative conditions led to intermediate **A**. Coordination of **A** with Cu(II) catalyst to form complex **B**. Considering the experimental results in eq. (ii) and eq. (iii).), we envisioned that subsequent SET process occurs with molecular oxygen, which might be assisted by TEMPO,[15] delivering peroxy-Cu(III) intermediate **C**. Following by a sequence of intramolecular amino-cuperation of alkynes and oxygenative carbonylation,[16] affording to acylated heterocycle **4a**.



Scheme 4. Proposed mechanism.

Conclusions

In summary, we have developed a general and efficient oxidative cascade reaction for the sequential assembly of densely functionalized imidazo fused *N*-heterocycles, which might find utility in the rapid synthesis of bioactive analogues. This reaction provides a concise route that utilized readily available starting materials, delivering divergent *N*-heterocycles using cheap catalyst and green oxidant. Further explorations on the oxidative cascade based on MCRs and application in biochemistry are underway in our laboratory.

Experimental

General Information

^{1}H NMR, ^{13}C NMR data were obtained on AVANCE III Bruker 400 MHz nuclear resonance spectrometers unless otherwise noted. Chemical shifts (in ppm) were referenced to tetramethylsilane (TMS) (δ = 0.00 ppm) in $CDCl_3$ or dimethyl sulfoxide (δ = 2.50 ppm) in DMSO-d6 as an internal standard. ^{13}C NMR spectra were obtained by the same NMR spectrometers and were calibrated with $CDCl_3$ (δ = 77.16 ppm). The data of HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF).

Typical procedure for the preparation of imidazo[1,2-a]pyridines 4:

To a Schlenk tube was added sequentially $Cu(OTf)_2$ (4.5 mg, 0.02 mmol), TEMPO (3.2 mg, 0.02 mmol), phenylacetylene **1a** (22.4 mg, 0.20 mmol), benzylic bromide **2a** (34.0 mg, 0.20 mmol), pyridin-2-amine **3a** (28.0 mg, 0.30 mmol) in toluene (1.0 mL) under O_2 (1 atm). The reaction mixture was vigorously stirred at 100 °C for 12 h. After cooling down to room temperature and concentrating in vacuum, the residue was purified by flash chromatography on a short silica gel (eluent: petroleum ether/ethyl acetate = 5:1) to afford 67 mg (87%) of Phenyl(2-phenylimidazo[1,2-a]pyridin-3-yl)methanone (**4a**)[17a] 51.8 mg (87%), yellow solid, mp 124-127 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (d, J = 7.2 Hz, 1H), 7.80 (d, J = 8.8 Hz, 1H), 7.54-7.50 (m, 3H), 7.34-7.31 (m, 2H), 7.27-7.23 (m, 1H), 7.15-7.06 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.3, 154.8, 147.3, 138.6, 133.9, 131.7, 130.2, 129.5, 129.1, 128.2, 127.7, 120.0, 117.4, 114.5.

Phenyl(2-(4-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridin-3-yl) methanone (4b), 62.9 mg (86%), yellow solid, mp 166-169 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (d, J = 6.8 Hz, 1H), 7.83 (d, J = 8.8 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.47 (d, J = 7.6 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.29 (t, J = 7.6 Hz, 1H), 7.16-7.08 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.0, 153.2, 147.4, 138.5, 137.7, 132.0, 130.4, 130.2, 129.9, 129.5, 129.4, 128.3, 127.9 (q, J_{C-F} = 3.8 Hz), 125.2, 124.5 (q, J_{C-F} = 271.6 Hz), 122.5 (q, J_{C-F} = 33.7 Hz), 120.4, 117.6, 115.0; ^{19}F NMR (300 MHz, $CDCl_3$) δ -62.9. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{13}F_3N_2ONa^+$: 389.0872; found: 389.0876.

(2-Bromophenyl)(2-phenylimidazo[1,2-a]pyridin-3-yl)methanone (4c), 58.6 mg (78%), yellow solid, mp 156-160 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (d, J = 6.8 Hz, 1H), 7.82 (d, J = 8.8 Hz, 1H), 7.63-7.58 (m, 1H), 7.32-7.27 (m, 3H), 7.18 (t, J = 7.2 Hz, 1H), 7.13-7.04 (m, 4H), 7.00-6.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.2, 157.3, 147.7, 140.5, 133.6, 132.8, 130.9, 130.1, 129.6, 129.5, 129.1, 128.2, 127.3, 126.5, 120.6, 120.2, 117.4, 115.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{14}BrN_2O^+$: 377.0284; found: 377.0284.

(2-Bromophenyl)(2-(2-chlorophenyl)imidazo[1,2-a]pyridin-3-yl) methanone (4d), 60.0 mg (73%), yellow solid, mp 185-188 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (d, J = 6.8 Hz, 1H), 7.84 (d, J = 8.8 Hz, 1H), 7.63 (t, J = 7.2 Hz, 1H), 7.30-7.21 (m, 4H), 7.10 (d, J = 7.2 Hz, 1H), 7.07-7.02 (m, 2H), 6.98 (d, J = 7.2 Hz, 1H), 6.93 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.0, 154.0, 147.8, 140.1, 133.3, 133.1, 132.4, 131.2, 130.8, 130.1, 129.7, 129.2, 128.9, 128.8, 126.5, 125.9, 121.2, 120.1, 117.7, 115.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{13}BrClN_2O^+$: 410.9894; found: 410.9893.

Ethyl 4-(3-(4-bromobenzoyl)imidazo[1,2-a]pyridin-2-yl)benzoate (4e), 64.5 mg (72%), light yellow solid, mp 172-175 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22-8.19 (m, 2H), 8.13 (d, J = 8.2 Hz, 2H), 8.06 (d, J = 6.8 Hz, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.66-7.59 (m, 4H), 7.36-7.32 (m, 1H), 6.89 (t, J = 6.8 Hz, 1H), 4.43 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.7, 165.9, 140.1, 136.4, 132.7, 132.4, 131.4, 131.2, 130.4, 130.3, 130.2, 130.1, 128.0, 126.5, 123.8, 119.3, 114.2, 61.2, 14.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{18}BrN_2O_3^+$: 449.0495; found: 449.0491.

(4-Bromophenyl)(2-(naphthalen-2-yl)imidazo[1,2-a]pyridin-3-yl) methanone (4f), 45.1 mg (53%), yellow solid, mp 152-155 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 2H), 7.95-7.91 (m, 1H), 7.87(d, J = 8.0 Hz, 1H), 7.72 (d, J = 9.2 Hz, 1H), 7.53-7.51 (m, 2H), 7.47 (d, J = 7.6 Hz, 1H), 7.45-7.41 (m, 3H), 7.33-7.29 (m, 1H), 7.26-7.18 (m, 2H), 6.67 (t, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.5, 144.2, 140.9, 136.6, 133.8, 132.2, 131.9, 131.2, 130.2, 129.9, 128.9, 127.8, 127.6, 127.1, 126.4, 126.2, 125.7, 125.6, 124.65,

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124.57, 119.1, 113.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{16}BrN_2O^+$: 427.0440; found: 427.0439.

(4-Bromophenyl)(2-(5-methylfuran-2-yl)imidazo[1,2-a]pyridin-3-yl)methanone (4g), 54.7 mg (72%), yellow solid, mp 116-119 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 6.8 Hz, 1H), 8.02 (d, J = 8.8 Hz, 2H), 7.69 (d, J = 9.2 Hz, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.34-7.30 (m, 1H), 7.17 (d, J = 3.2 Hz, 1H), 6.93 (t, J = 6.8 Hz, 1H), 6.18 (d, J = 2.4 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.8, 153.4, 143.9, 140.7, 139.7, 136.7, 132.3, 131.3, 127.7, 126.4, 126.2, 118.9, 115.1, 114.0, 107.9, 100.0, 13.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{14}BrN_2O_2^+$: 381.0233; found: 381.0229.

(4-Bromophenyl)(2-(thiophen-2-yl)imidazo[1,2-a]pyridin-3-yl) methanone (4h), 51.9 mg (68%), yellow solid, mp 112-115 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (d, J = 1.2 Hz, 1H), 7.65 (d, J = 9.6 Hz, 1H), 7.59-7.56 (m, 1H), 7.53 (t, J = 6.4 Hz, 1H), 7.51 (t, J = 2.0 Hz, 1H), 7.40-7.37 (m, 3H), 7.31 (dd, J = 0.8 Hz, 4.8 Hz, 1H), 6.74(dd, J = 3.6 Hz, 5.2 Hz, 1H), 6.63 (dd, J = 1.2 Hz, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.6, 147.7, 145.7, 136.9, 135.0, 132.9, 131.5, 130.9, 130.5, 128.4, 128.1, 127.44, 127.39, 119.2, 117.8, 109.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{12}BrN_2OS^+$: 382.9848; found: 382.9846.

(2-(4-Bromophenyl)imidazo[1,2-a]pyridin-3-yl)(3-chlorophenyl) methanone (4i), 46.7 mg (57%), yellow solid, mp 186-189 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.47 (d, J = 6.8 Hz, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.28 (d, J = 8.4 Hz, 2H), 7.24-7.19 (m, 3H), 7.14-7.06 (m, 3H), 6.99 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.8, 153.5, 147.5, 137.5, 135.5, 134.0, 131.2, 130.8, 130.2, 129.7, 129.1, 128.5, 128.3, 126.8, 117.6, 115.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{13}BrClN_2O^+$: 410.9894; found: 410.9893.

(4-Methoxyphenyl)(2-phenylimidazo[1,2-a]pyridin-3-yl) methanone (4j)[17b], 41.3 mg (63%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.36 (d, J = 6.8 Hz, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.51 (d, J = 8.8 Hz, 2H), 7.47-7.42 (m, 1H), 7.37-7.35 (m, 2H), 7.13-7.09 (m, 3H), 7.03-6.99 (m, 1H), 6.57 (d, J = 8.8 Hz, 2H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.0, 162.6, 153.6, 147.1, 134.0, 131.8, 131.0, 130.1, 128.6, 128.1, 127.9, 127.7, 119.9, 117.3, 114.1, 113.0, 55.2.

(6-Chloro-2-phenylimidazo[1,2-a]pyridin-3-yl)(phenyl) methanone (4k)[17c], 50.5 mg (76%), yellow solid, mp 135-137 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (s, 1H), 7.72 (d, J = 9.6 Hz, 1H), 7.51-7.46 (m, 3H), 7.31-7.24 (m, 3H), 7.14 (t, J = 7.2 Hz, 1H), 7.10-7.07 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.1, 154.9, 145.5, 138.0, 133.4, 131.9, 130.2, 130.0, 129.4, 128.3, 127.67, 127.66, 126.1, 122.7, 120.0, 117.5.

(6-Chloro-2-phenylimidazo[1,2-a]pyridin-3-yl)(2,4-dichlorophenyl) methanone (4l), 52.0 mg (65%), yellow solid, mp 191-193 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.75 (d, J = 9.6 Hz, 1H), 7.52 (d, J = 9.2 Hz, 1H), 7.45 (d, J = 7.6 Hz, 2H), 7.30 (t, J = 7.2 Hz, 1H), 7.19 (d, J = 8.0 Hz, 1H), 7.12 (t, J= 7.6 Hz, 3H), 7.06 (d, J= 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.9, 150.9, 145.6, 138.0, 135.2, 134.2, 132.8, 132.1, 131.9, 130.6, 129.1, 129.0, 127.5, 126.7, 126.4, 123.5, 121.5, 117.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{12}Cl_3N_2O^+$: 401.0010; found: 401.0010.

(6-Chloro-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridin-3-yl) (phenyl)methanone (4m), 61.6 mg (77%), yellow solid, mp 174-176 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.57-7.52 (m, 2H), 7.48 (t, J = 7.2 Hz, 3H), 7.40 (d, J = 8.0 Hz, 1H), 7.31-7.24 (m, 2H), 7.11 (t, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.0, 153.2, 145.6, 137.9, 134.4, 133.0, 132.3, 130.7, 129.4, 128.4, 127.9, 127.0 (q, J = 3.8 Hz), 126.2, 125.0 (q, J_{C-F} = 32.3 Hz), 124.5, 123.2, 122.6, 120.4 (q, J_{C-F} =32.8 Hz), 117.7; ^{19}F NMR (300 MHz, $CDCl_3$) δ -62.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{13}ClF_3N_2O^+$: 401.0663; found: 401.0663.

(4-Chloro-2-(3-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridin-3-yl)(phenyl)methanone (4n), 60.0 mg (75%), yellow solid, mp 172-175 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (s, 1H), 7.73 (d, J = 7.2 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.51-7.45 (m, 4H), 7.40 (d, J = 8.0 Hz, 1H), 7.29-7.22 (m, 2H), 7.09 (t, J = 3.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.7, 153.0, 145.4, 137.8, 134.3, 132.9, 132.1, 130.6, 130.5, 130.4, 130.2, 130.0, 129.2, 128.2, 128.0, 127.8, 126.9 (q, J_{C-F} = 3.0 Hz), 126.1, 124.9 (q, J_{C-F} = 269.4 Hz), 124.4, 123.1 (q, J_{C-F} = 32.3 Hz), 122.6, 120.3, 117.6; ^{19}F NMR (300 MHz, $CDCl_3$) δ -62.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{13}ClF_3N_2O^+$: 401.0663; found: 401.0663.

(6-Chloro-2-(4-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl) (phenyl)methanone (4o), 56.5 mg (78%), yellow solid, mp 156-158 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (s, 1H), 7.61 (d, J = 9.2 Hz, 1H), 7.44-7.36 (m, 3H), 7.23-7.15 (m, 3H), 7.04 (t, J = 7.6 Hz 2H), 6.53 (d, J = 8.8 Hz, 2H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.2, 159.8, 154.8, 145.5, 138.1, 131.9, 131.4, 130.2, 129.5, 127.8, 126.1, 125.8, 122.5, 119.7, 117.3, 113.3, 55.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}ClN_2O_2^+$: 363.0895; found: 363.0893.

(6-Chloro-2-(2-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl) (phenyl)methanone (4p), 52.1 mg (72%), yellow solid, mp 155-157 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.68 (d, J = 9.2 Hz, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 7.6 Hz, 2H), 7.39 (dd, J = 1.2 Hz, 9.2 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.10 (t, J = 7.6 Hz, 1H), 7.04 (t, J = 8.0 Hz, 2H), 6.91 (t, J = 7.2 Hz, 1H), 6.32 (d, J = 8.4 Hz, 1H), 3.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.1, 155.6, 150.3, 145.5, 137.8, 131.6, 130.6, 130.3, 129.3, 128.6, 127.0, 125.8, 123.3, 122.4, 120.8, 120.4, 117.4, 109.6, 54.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}ClN_2O_2^+$: 363.0895; found: 363.0893.

(2-(3-Bromophenyl)-6-chloroimidazo[1,2-a]pyridin-3-yl) (phenyl)methanone (4q), 46.7 mg (57%), yellow solid, mp 192-194 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52 (d, J = 0.8 Hz, 1H), 7.65 (d, J = 9.6 Hz, 1H), 7.44-7.41 (m, 3H), 7.38 (s, 1H), 7.25 (t, J = 7.6 Hz, 1H), 7.19 (d, J = 7.2 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 7.08 (t, J = 7.6 Hz, 2H), 6.87 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.0, 153.2, 145.6, 138.1, 135.5, 133.0, 132.3, 131.4, 130.6, 129.3, 129.2, 128.6, 128.0, 126.2, 123.1, 121.8, 120.3, 117.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{13}BrClN_2O^+$: 410.9894; found: 410.9893.

(2-(3-Bromophenyl)-8-chloroimidazo[1,2-a]pyridin-3-yl) (phenyl)methanone (4r), 47.6 mg (58%), yellow solid, mp 196-198 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (d, J = 6.8 Hz, 1H), 7.81 (d, J = 7.2 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.52 (s, 1H), 7.47 (d, J = 7.6 Hz, 2H), 7.39 (d, J = 7.6 Hz, 1H), 7.28 (dd, J = 8.4 Hz, 2H), 7.11 (t, J = 7.6 Hz, 2H), 7.01 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.0, 153.2, 145.6, 138.1, 135.5, 133.0, 132.3, 131.4, 130.6, 129.3, 129.2, 128.6, 128.0, 126.2, 123.1, 121.8, 120.3, 117.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{13}BrClN_2O^+$: 410.9894; found: 410.9893.

(8-Bromo-2-phenylimidazo[1,2-a]pyridin-3-yl)(phenyl)

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methanone (4s), 44.6 mg (59%), yellow solid, mp 166-168 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.48 (d, J = 6.8 Hz, 1H), 7.77 (d, J = 7.6 Hz, 1H), 7.51 (d, J = 7.2 Hz, 2H), 7.36 (d, J = 7.2 Hz, 2H), 7.28 (d, J = 7.6 Hz, 1H), 7.15-7.10 (m, 2H), 7.10-7.07 (m, 3H), 6.97 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.6, 154.9, 145.3, 138.2, 133.5, 132.1, 131.4, 130.4, 129.6, 128.4, 127.82, 127.77, 127.3, 121.3, 114.5, 111.5. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{20}H_{14}BrN_2O^+$: 377.0284; found: 377.0284.

(6-Bromo-2-(4-nitrophenyl)imidazo[1,2-a]pyridin-3-yl)(phenyl) methanone (4t), 53.5 mg (64%), yellow solid, mp 254-257 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.93 (d, J = 8.4 Hz, 2H), 7.79 (d, J = 9.6 Hz, 1H), 7.63 (d, J = 9.6 Hz, 1H), 7.43-7.40 (m, 2H), 7.32-7.30 (m, 1H), 7.16-7.08 (m, 2H), 7.07-6.99 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.8, 154.4, 147.5, 146.1, 140.1, 139.7, 133.1, 131.8, 131.7, 130.6, 130.5, 130.0, 127.1, 126.9, 124.4, 117.9. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{20}H_{13}BrN_3O_3^+$: 422.0135; found: 422.0130.

(6-Bromo-2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl)(3-chlorophenyl)methanone (4u), 52.8 mg (59%), yellow solid, mp 265-267 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (d, J = 5.2 Hz, 1H), 7.71-7.68 (m, 1H), 7.64-7.61 (m, 1H), 7.35-7.34 (m, 2H), 7.28 (d, J = 8.8 Hz, 3H), 7.20 (t, J = 3.2 Hz, 1H), 7.14 (d, J = 6.4 Hz, 1H), 7.09-7.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.7, 153.3, 145.8, 136.9, 134.9, 134.0, 133.0, 131.2, 130.7, 130.1, 129.2, 128.7, 128.3, 128.2, 127.2, 119.9, 118.0, 109.9. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{20}H_{12}BrCl_2N_2O^+$: 444.9505; found: 444.9504.

(6-Bromo-2-(3-methoxyphenyl)imidazo[1,2-a]pyridin-3-yl)(2,4-dichlorophenyl)methanone (4v)[17d], 61.6 mg (65%), yellow solid, mp 225-227 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1H), 7.70 (d, J = 9.2 Hz, 1H), 7.62 (d, J = 9.6 Hz, 1H), 7.19 (d, J = 8.8 Hz, 2H), 7.07 (d, J = 8.0 Hz, 1H), 7.02-6.98 (m, 3H), 6.85-6.84 (m, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.5, 158.9, 150.7, 145.7, 139.4, 135.1, 134.2, 132.70, 132.68, 132.1, 129.1, 128.6, 128.5, 126.6, 121.7, 121.4, 118.1, 117.9, 113.8, 110.0, 55.3.

Ethyl 3-(4-bromobenzoyl)-2-(thiophen-2-yl)imidazo[1,2-a] pyridine-5-carboxylate (4w), 49.0 mg (54%), yellow solid, mp 203-205 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.10-8.07 (m, 2H), 7.87 (dd, J = 1.6 Hz, 9.6 Hz, 1H), 7.73 (d, J = 9.2 Hz, 1H), 7.63-7.59 (m, 3H), 7.43 (dd, J = 0.8 Hz, 3.6Hz, 1H), 7.27-7.24 (m, 1H), 4.41 (q, J = 7.2 Hz, 2H), 1.40 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.2, 164.3, 144.6, 142.2, 136.0, 132.2, 131.4, 130.7, 129.1, 128.7, 128.2, 127.7, 126.7, 126.1, 118.6, 118.3, 61.8, 14.2. HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{21}H_{15}BrN_2O_3SNa^+$: 476.9879; found: 476.9877.

(*E*)-Phenyl(2-styrylimidazo[1,2-a]pyridin-3-yl)methanone (4x), 43.4 mg (67%), yellow solid, mp 131-134 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, J = 7.2 Hz, 1H), 8.16 (d, J = 8.4 Hz, 2H), 7.79-7.70 (m, 3H), 7.63 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 7.2 Hz, 2H), 7.42-7.36 (m, 3H), 7.34-7.29 (m, 2H), 6.98 (t, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.6, 144.4, 140.3, 134.3, 132.8, 132.4, 131.4, 128.8, 127.9, 126.8, 126.2, 125.1, 119.6, 118.9, 116.3, 115.1, 114.2, 113.1; HRMS (ESI-TOF) m/z: [M + H]$^+$Calcd for $C_{22}H_{17}N_2O^+$: 325.1335; found: 325.1335.

1-(2-Phenylimidazo[1,2-a]pyridin-3-yl)pentan-1-one (4y), 18.0 mg (32%), yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (d, J = 7.2 Hz, 1H), 7.74 (d, J = 9.2 Hz, 1H), 7.59-7.57 (m, 2H), 7.53-7.48 (m, 4H), 7.08 (t, J = 6.8 Hz, 1H), 2,46 (t, J = 7.6 Hz, 2H), 1.57-1.49 (m, 2H), 1.15-1.06 (m, 2H), 0.73 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 154.7, 130.5, 129.7, 129.2, 129.1, 129.0, 128.7, 128.4, 128.2, 117.3, 114.8, 40.8, 27.2, 22.2, 13.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{18}H_{19}N_2O^+$: 279.1492; found: 279.1490.

1-(2-Penylimidazo[1,2-a]pyridin-3-yl)hexan-1-one (4z), 23.9 mg (41%), yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.81-7.73 (m, 1H), 7.64-7.59 (m, 2H), 7.53-7.47 (m, 4H), 7.10-7.06 (m, 1H), 2.45 (t, J = 7.6 Hz, 2H), 1.58-1.51 (m, 2H), 1.17-1.10 (m, 2H), 1.08-1.02 (m, 2H), 0.79 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 129.6, 129.1, 128.4, 117.3, 114.8, 100.0, 41.1, 31.3, 24.9, 22.3, 13.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{19}H_{20}N_2O^+$: 293.1648; found: 293.1649.

Phenyl (1,2,4-triphenyl-1*H*-imidazol-5-yl)methanone (6a)[17e], 48.8 mg (61%), yellow solid, m.p. = 218-219 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 7.6 Hz, 2H), 7.48 (t, J = 7.6 Hz, 1H), 7.42-7.39 (m, 4H), 7.33-7.23 (m, 7H), 7.20 (s, 4H), 7.05 (d, J = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9, 146.6, 140.4, 138.2, 137.5, 136.3, 132.1, 130.8, 130.7, 129.9, 129.3, 129.1, 128.8, 128.4, 128.3, 128.1, 127.8, 127.7.

(4-(4-Mthoxyphenyl)-1,2-diphenyl-1*H*-imidazol-5-yl)(phenyl) methanone (6b), 67.9 mg (79%), yellow solid, mp 184-185 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 7.2 Hz, 2H), 7.46-7.42 (m, 4H), 7.36-7.32 (m, 4H),7.31-7.28 (m, 1H), 7.27-7.22 (m, 4H), 7.18 (t, J = 8.0 Hz, 2H), 6.68 (d, J = 8.8 Hz, 2H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.5, 159.3, 149.6, 146.3, 137.6, 137.0, 132,9, 130.3, 132.1, 129.8, 129.3, 129.13, 129.11, 128.7, 128.5, 128.2, 128.1, 127.7, 125.7, 113.4, 55.1. HRMS (ESI-TOF) m/z: [M + H]$^+$Calcd for $C_{29}H_{23}N_2O_2^+$: 431.1754; found: 431.1751.

Ethyl 4-(5-(4-bromobenzoyl)-1,2-diphenyl-1*H*-imidazol-4-yl) benzoate (6c), 74.8 mg (68%), yellow solid, mp 168-170 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.4 Hz, 2H), 7.58 (t, J = 8.8 Hz, 3H), 7.46-7.44 (m, 2H), 7.38-7.32 (m, 6H), 7.29 (d, J = 8.4 Hz, 1H), 7.27-7.21 (m, 4H), 4.35 (q, J = 7.2 Hz, 2H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.4, 166.8, 166.3, 150.0, 144.8, 137.6, 137.4, 136.6, 136.2, 131.7, 131.2, 129.7, 129.43, 129.39, 129.3, 129.1, 129.0, 128.63, 128.57, 128.3, 127.7, 60.9, 14.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{31}H_{24}BrN_2O_3^+$: 551.0965; found: 551.0964.

(4-Bromophenyl)(4-(naphthalen-2-yl)-1,2-diphenyl-1*H*-imidazol-5-yl)methanone (6d)[17e], 60.2 mg (57%), yellow solid, mp 256-258 ℃ ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.8 Hz, 1H), 7.73 (d, J = 7.6 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.51 (dd, J = 1.2 Hz, 8.0 Hz, 2H), 7.45-7.40 (m, 5H), 7.37-7.34 (m, 3H), 7.32-7.28 (m, 2H), 7.26-7.23 (m, 4H), 6.88 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) ***δ*** 185.7, 150.5, 147.5, 137.2, 136.4, 133.4, 132.1, 131.0, 130.6, 130.4, 130.2, 129.30, 129.26, 129.24, 129.19, 128.9, 128.8, 128.2, 128.1, 127.7, 127.1, 126.4, 125.7, 125.6, 124.7, 120.2.

(4-Bromophenyl)(4-(5-methylfuran-2-yl)-1,2-diphenyl-1*H*-imidazol-5-yl)methanone (6e), 47.9 mg (50%), yellow solid, mp 189-191 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.4 Hz, 2H), 7.61-7.57 (m, 2H), 7.44-7.41 (m, 3H), 7.40-7.37 (m, 2H), 7.29-7.27 (m, 1H), 7.26-7.23 (m, 3H), 7.22-7.21 (m, 1H), 6.60 (d, J = 4.0 Hz, 1H), 5.90 (dd, J = 1.2 Hz, 3.2 Hz, 1H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.4, 153.5, 147.2, 140.1, 137.4, 137.2, 137.1, 132.1, 131.3, 131.1, 129.5, 129.2, 129.1, 128.98, 128.97, 128.2, 128.1, 127.1, 115.4, 107.2, 13.2. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{27}H_{20}BrN_2O_2^+$: 483.0703; found: 483.0700.

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Ethyl 4-(5-benzoyl-1-(4-methoxyphenyl)-2-phenyl-1*H*-imidazol-4-yl)benzoate (6f), 56.2 mg (56%), yellow solid, mp 167-169 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.8 Hz, 2H), 7.59 -7.56 (m, 4H), 7.49 (dd, J = 1.2 Hz, 8.0 Hz, 2H), 7.35 (dd, J = 2.0 Hz, 8.8 Hz, 2H), 7.33-7.30 (m, 2H), 7.28-7.26 (m, 2H), 7.15 (d, J = 9.2 Hz, 2H), 6.85 (d, J = 9.2 Hz, 2H), 4.34 (q, J = 7.2 Hz, 2H), 3.80 (s, 3H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 186.6, 166.3, 159.7, 150.2, 144.5, 137.5, 136.2, 131.7, 131.2, 129.6, 129.43, 129.38, 129.24, 129.21, 129.0, 128.9, 128.7, 128.6, 128.5, 128.3, 114.4, 61.0, 55.4, 14.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{32}H_{27}N_2O_4^+$: 503.1965; found: 503.1999.

(4-Bromophenyl)(1-(4-methoxyphenyl)-4-(naphthalen-2-yl)-2-phenyl-1*H*-imidazol-5-yl)methanone (6g), 48.0 mg (43%), yellow solid, mp 254-256 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 7.6 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 6.8 Hz, 2H),7.47-7.39 (m, 3H), 7.33 (d, J = 7.2 Hz, 1H), 7,32-7.30 (m, 2H), 7.29-7.27 (m, 2H), 7.25-7.22 (m, 2H), 7.22-7.18 (m, 1H), 6.92 (dd, J = 4.0 Hz, 6.8 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.8, 159.6, 150.6, 147.3, 136.5, 133.4, 132.10, 131.07, 130.8, 130.3, 130.2, 129.9, 129.3, 129.22, 129.19, 129.16, 128.8, 128.7, 128.2, 128.1, 127.0, 126.4, 125.68, 125.65, 124.7, 114.4, 55.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{33}H_{23}BrN_2O_2^+$: 559.1016; found: 559.1011.

(4-Bromophenyl)(1-(4-methoxyphenyl)-2-phenyl-4-(thiophen-2-yl)-1*H*-imidazol-5-yl)methanone (6h)[17f], 65.8 mg (64%), yellow solid, mp 146-148 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, J = 1.6 Hz, 6.8 Hz, 2H), 7.40-7.38 (m, 2H), 7.32 (dd, J = 1.6 Hz, 6.8 Hz, 2H), 7.23-7.13 (m, 4H), 7.05-7.01 (m, 2H), 6.86 (dd, J = 0.8 Hz, 3.6 Hz, 1H), 6.75-6.72 (m, 3H), 3.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.2, 159.6, 149.9, 140.1, 136.5, 135.8, 131.6, 131.1, 129.3, 129.2, 129.1, 129.0, 128.9, 128.8, 128.22, 128.19, 127.30, 127.26, 126.3, 114.4, 55.4.

(1-(4-Chlorophenyl)-2,4-diphenyl-1*H*-imidazol-5-yl)(phenyl) methanone (6i)[17f], 59.0 mg (68%), yellow solid, mp 206-208 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, J = 0.8 Hz, 8.0 Hz, 2H), 7.47-7.45 (m, 4H), 7.36-7.34 (m, 2H), 7.33-7.31 (m, 3H), 7.29 (s, 1H), 7.28-7.25 (m, 1H), 7.20-7.17 (m, 3H), 7.16-7.13 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.4, 149.9, 147.0, 137.5, 135.6, 134.8, 133.1, 133.0, 129.8, 129.4, 129.3, 129.2, 129.1, 129.0, 128.9, 128.3, 128.1, 128.0, 127.9.

(4-Bromophenyl)(1-(4-chlorophenyl)-4-(5-methylfuran-2-yl)-2-phenyl-1*H*-imidazol-5-yl)methanone (6j), 52.6 mg (52%), yellow solid, mp 167-169 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.8 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 7.40-7.35 (m, 4H), 7.30-7.25 (m, 3H), 7.16 (dd, J = 1.6 Hz, 6.4 Hz, 2H), 6.71 (d, J = 3.2 Hz, 1H), 5.93 (d, J = 3.2 Hz, 1H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.2, 153.7, 147.1, 139.8, 137.6, 137.0, 135.7, 135.1, 132.1, 131.2, 129.4, 129.3, 129.20, 129.18, 129.0, 128.3, 127.2, 115.8, 107.3, 13.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{19}BrClN_2O_2^+$: 517.0313; found: 517.0313.

Ethyl 4-(5-(4-bromobenzoyl)-1-(4-chlorophenyl)-2-phenyl-1*H*-imidazol-4-yl) benzoate (6k), 47.9 mg (41%), yellow solid, mp 258-260 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, J = 1.6 Hz, 8.4 Hz, 2H), 7.59-7.54 (m, 4H), 7.46-7.44 (m, 2H), 7.37-7.28 (m, 7H), 7.17 (dd, J = 2.0 Hz, 6.8 Hz, 2H), 4.34 (1, J = 7.2 Hz, 2H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.1, 166.6, 166.2, 150.2, 145.2, 137.2, 136.0, 135.13, 135.07, 131.7, 131.1, 129.8, 129.5, 129.4, 129.3, 129.1, 128.79, 128.77, 128.71, 128.66, 128.4, 61.0, 14.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{31}H_{23}BrClN_2O_3^+$: 585.0575; found: 585.0576.

(2-(4-Methoxyphenyl)benzo[d]imidazo[2,1-b]thiazol-3-yl) (phenyl)methanone (7a), 63.7 mg (83%), yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, J = 0.8 Hz, 8.4 Hz, 1H), 7.77 (dd, J = 2.0 Hz, 6.8 Hz, 2H), 7.72 (dd, J = 0.8 Hz, 7.6 Hz, 1H), 7.44-7.36 (m, 4H), 7.15 (t, J = 2.8 Hz, 3H), 7.71-7.67 (m, 2H), 3.76 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.4, 163.7, 152.9, 151.6, 133.6, 133.3, 133.2, 132.6, 130.3, 130.2, 129.4, 128.1, 128.0, 126.4, 125.3, 123.9, 116.5, 113.5, 55.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{17}N_2O_2S^+$: 385.1005; found: 385.1003.

(6-(4-Methoxyphenyl)imidazo[2,1-b]thiazol-5-yl)(phenyl) methanone (7b), 52.1 mg (78%), yellow oil, mp 124-127 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.8 Hz, 2H), 7.59 (d, J = 7.6 Hz, 2H), 7.47 (d, J = 5.2 Hz, 2H), 7.43 (t, J = 6.8 Hz, 2H), 6.97 (d, J = 4.8 Hz, 1H), 6.92 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.7, 163.1, 148.3, 141.8, 132.9, 131.2, 130.8, 129.4, 129.1, 129.0, 128.7, 117.5, 115.3, 113.3, 55.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{14}N_2O_2SNa^+$: 357.0668; found: 357.0665.

(6-Chloro-2-(4-methoxyphenyl)imidazo[1,2-b]pyridazin-3-yl) (phenyl)methanone (7c), 48.6 mg (67%), yellow solid, mp 210-212 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, J = 1.6 Hz, 6.8 Hz, 2H), 7.79 (d, J = 15.6 Hz, 1H), 7.65-7.62 (m, 2H), 7.54 (d, J = 15.6 Hz, 1H), 7.44-7.40 (m, 3H), 6.99-6.97 (m, 2H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 163.4, 143.9, 135.0, 131.0, 130.8, 130.3, 128.9, 128.3, 121.8, 113.8, 55.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{15}ClN_3O_2^+$: 364.0847; found: 364.0843.

(5-Chloro-2-(4-methoxyphenyl)imidazo[1,2-c]pyrimidin-3-yl) (phenyl)methanone (7d), 42.8 mg (59%), yellow solid, mp 206-208 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, J = 2.0 Hz, 6.8 Hz, 2H), 7.79 (d, J = 16.0 Hz, 1H), 7.65-7.62 (m, 2H), 7.54 (d, J = 15.6 Hz, 1H), 7.43-7.39 (m, 3H), 6.99-6.96 (m, 2H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 163.4, 143.8, 135.0, 131.0, 130.7, 130.2, 128.8, 128.3, 121.8, 113.8, 55.4; HRMS (ESI-TOF) m/z: $[M + H]^+$Calcd for $C_{20}H_{15}ClN_3O_2^+$: 364.0847; found: 364.0843.

2-Phenylimidazo[1,2-a]pyridine (8)[8c], ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97-7.92 (m, 3H), 7.73 (s, 1H), 7.59 (d, J = 9.0 Hz, 1H), 7.41 (t, J = 7.4 Hz, 2H), 7.32 (d, J = 6.9 Hz, 1H), 7.09 (t, J = 7.8 Hz, 1H), 6.66 (t, J = 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 145.9, 134.0, 128.9, 128.2, 126.3, 125.8, 124.9, 117.7, 112.6, 108.4.

Conflicts of interest

There are no conflicts to declare.

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