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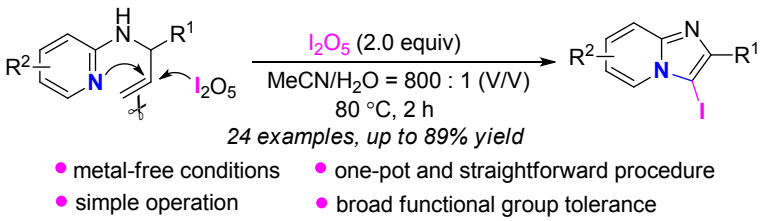
# $I_2O_5$-Mediated Iodocyclization Cascade of N-(1-arylallyl)pyridine-2-amines with Concomitant C=C Bond Cleavage: A Synthesis of 3-Iodoimidazo[1,2-a]pyridines

Bingwei Zhou, Yuan Yuan, Hongwei Jin,* and Yunkui Liu*

State Key Laboratory Breeding Base of Green Chemistry-Synthesis Technology, College of Chemical Engineering, Zhejiang University of Technology, Zhejiang University of Technology, Hangzhou 310014, People's Republic of China

E-mail: ykuiliu@zjut.edu.cn; jhwei828@zjut.edu.cn

TOC graphic




## ABSTRACT

A facile method for the synthesis of 3-iodoimidazo[1,2-a]pyridines has been successfully developed involving an $I_2O_5$-mediated iodocyclization cascade of *N*-(1-arylallyl)pyridin-2-amines with concomitant C=C bond cleavage. Preliminary mechanistic studies reveal that this protocol might undergo an oxidative cyclization/decarboxylation/iodination sequence in which $I_2O_5$ is used as both an

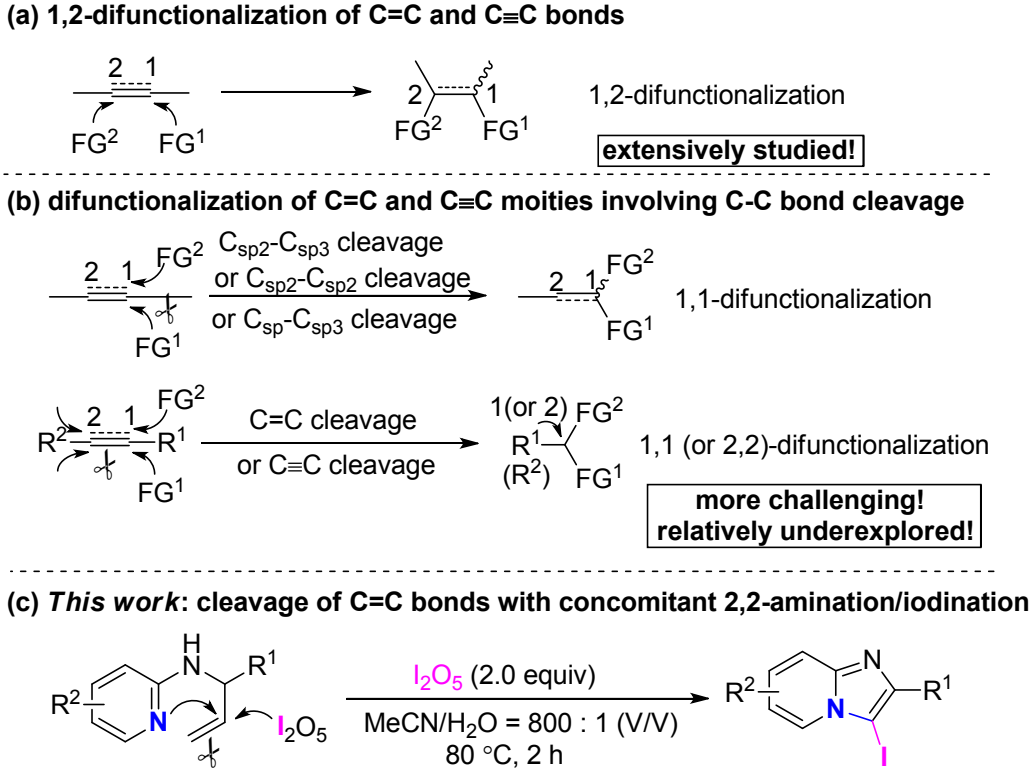
oxidant and an iodine source. The present protocol has advantages of wide substrate scope, simple operation, and metal-free conditions.

## Introduction

Alkenes and alkynes are ubiquitous structural units in organic molecules, and they serve as useful building blocks for the construction of molecule diversities due to their easy availability and high reactivity.[1,2] In this regard, recently, the 1,2-difunctionalizations of C=C and C≡C bonds have received special attention because such reactions usually allow for the synthesis of complex molecules in simple operation and step-economy manner (Scheme 1-a).[3,4] As compared to the extensive studies on the 1,2-difunctionalizations of C=C and C≡C bonds, the 1,1 (or 2,2)-difunctionalizations of C=C and C≡C moieties involving C–C bond cleavage ($C_{sp2}$–$C_{sp3}$, $C_{sp2}$–$C_{sp2}$, $C_{sp}$–$C_{sp3}$, C=C, or C≡C bond, Scheme 1-b), however, have been relatively underexplored[5-8] because the cleavage of C–C bond remains a great challenge owing to the extraordinarily large bond association energy of C–C bonds.[9] Yet this type of strategy would provide an alternative way to make fully use of alkenes and alkynes as synthetic platforms in organic synthesis (Scheme 1-b).[5-8] Regarding difunctionalization with concomitant C=C bond cleavage, for example, we[7a] and Zhao's group[7b] independently realized a splitting of C=C bonds in chalcones with concomitant 2,2-oxygenation/arylation of the cleaved $sp^2$-carbon resulting in the formation of 9,10-phenanthraquinones and α-ketoamides (esters), respectively; Meldal and

co-workers[7c] reported a cleavage of C=C bonds in solid-supported peptide olefins followed by 2,2-amination/arylation of the scissored $sp^2$-carbon to afford pyrroloisoquinolines; very recently, Wu and Liu[7d] reported a palladium-catalyzed oxidative cleavage of C=C bonds with a concomitant double amination of the resulting $sp^2$-carbon fragments to yield quinazolinones; Xu and Liu[7e,8a] described a transition-metal-free cleavage of C=C or C≡C bonds followed by reassembling the cleaved fragments with $S_8$ and amides to access aryl thioamides. Despite some progress made in this field, it is still highly desirable to further explore novel reactions for the multifunctionalization of C=C and C≡C moieties involving concomitant C–C bond cleavage.

**Scheme 1. Difunctionalization of C=C and C≡C bonds**



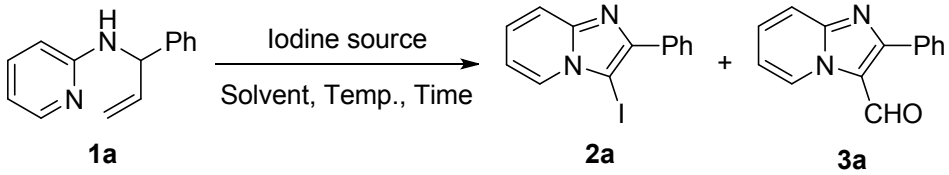
Imidazo[1,2-a]pyridines represent one class of valuable pharmacophores exhibiting unique biological and pharmaceutical activities.[10] They thus have broad applications in drug designs including zolpidem,[11] olprinone,[12] zolimidine,[13] necopidem,[14] and saripidem,[14] etc. In addition, they are widely used in optoelectronic materials[15] and abnormal NHC ligand synthesis.[16] Among imidazo[1,2-a]pyridine family, 3-halogenated imidazo[1,2-a]pyridines have received special attention because they are versatile intermediates enabling the late-stage elaboration with the C–X (X = Cl, Br, I) bonds.[17] The traditional methods for the preparation of 3-halogenated imidazo[1,2-a]pyridines relied on stepwise synthesis via 3-halogenation of preformed imidazo[1,2-a]pyridines with certain halogen sources.[18] Several straightforward methods have been explored including $CuO_x$/OMS-2-catalyzed three-component reaction of 2-aminopyridine, acetophenones and iodine,[19a] copper-catalyzed oxidative coupling between 2-aminopyridine and alkenes in the presence of iodine,[19b] copper-mediated aerobic oxidative coupling/cyclization of pyridines and enamides,[19c] and transition-metal-free chlorocyclization cascade of 2-aminopyridines with aliphatic carboxylic acids or ketones.[19d] Despite their merits in organic synthesis, these reactions have one or more limitations in terms of multiple steps, transition metal participation, and the use of toxic halogen sources. Thus, there is high demand to develop direct and efficient methods for the synthesis of 3-halogenated imidazo[1,2-a]pyridines using non-toxic halogen sources under metal-free conditions. As our ongoing interests in carbon-carbon bond cleavage reactions[6,7a,20] and $I_2O_5$-mediated efficient tandem reactions,[21] we herein describe a facile method for

the construction of 3-iodoimidazo[1,2-a]pyridines through an $I_2O_5$-mediated iodocyclization cascade of *N*-(1-arylallyl)-pyridin-2-amines with concomitant C=C bond cleavage (Scheme 1-c).[22]

## Results and Discussion

Initially, *N*-(1-phenylallyl)pyridin-2-amine **1a** was chosen as the model substrate for the optimization of the reaction conditions (Table 1). When **1a** was treated with 2 equivalents of $I_2O_5$ in newly purchased acetonitrile at 80 ºC for 2 h, 3-iodoimidazo[1,2-a]pyridine **2a** could be obtained in 45% yield along with **3a** in 28% yield as a side product (entry 1, Table 1). It was found that switching the iodine source to $I_2$ or $PhI(OAc)_2$ failed to give the desired product, and most of **1a** was recovered (entries 2, 3, Table 1). The use of 3 equivalents of $I_2O_5$ slightly decreased the yield of **2a** (43%, entry 4, Table 1). Solvent screening experiments revealed that a solvent mixture with a ratio of $MeCN/H_2O$ = 800:1 (V/V) gave the best yield of **2a** (entries 1, 5-11, Table 1). The present reaction was quite sensitive to temperature. Either lowering or elevating the temperature reduced the yield of **2a** (60 ºC: 25%, entry 12; 100 ºC: 11%, entry 13, Table 1). Prolonging the reaction time had no obvious effect on the yield of **2a** (entry 14 vs 10), while shortening the reaction time significantly reduced the yield of **2a** (36%, entry 15, Table 1). When the dehydrated MeCN was used, the reaction could still give a small amount of **2a** (< 15%, entry 16, Table 1). We think it is possibly because it is hard to completely remove water in MeCN. The direct use of $HIO_3$ could also give **2a** in 35% yield, albeit much lower than that of $I_2O_5$ (entry 17 vs 10, Table 1).

**Table 1. Optimization of the Reaction Conditions**[a]



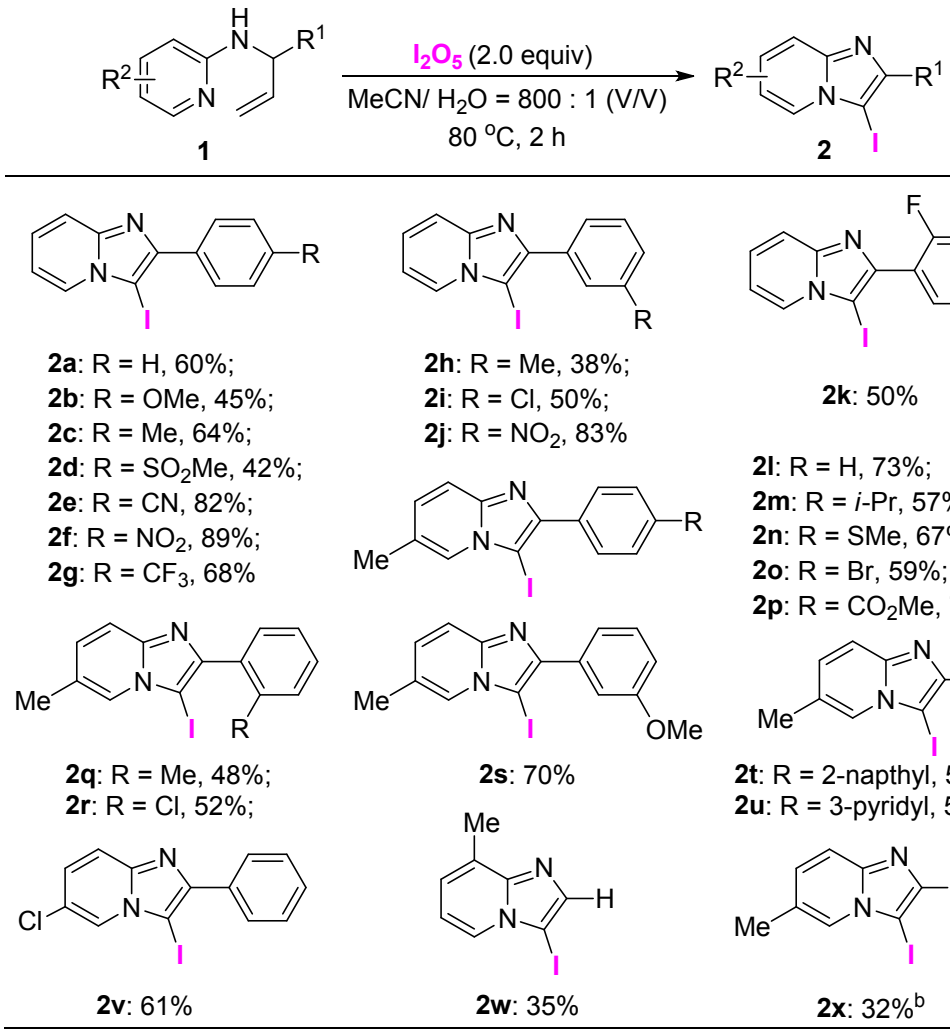

**1a** **2a** **3a**

| entry | iodine source (mo%) | solvent | temp (ºC) | time [h] | yield (%) | |
|---|---|---|---|---|---|---|
| | | | | | **2a** | **3a** |
| 1 | $I_2O_5$ | MeCN[b] | 80 | 2 | 45 | 28 |
| 2 | $I_2$ | MeCN[b] | 80 | 2 | 0 | 0 |
| 3 | $PhI(OAc)_2$ | MeCN[b] | 80 | 2 | 0 | 0 |
| 4 | $I_2O_5$[c] | MeCN[b] | 80 | 2 | 43 | 25 |
| 5 | $I_2O_5$ | DMF | 80 | 2 | 40 | 20 |
| 6 | $I_2O_5$ | DCE | 80 | 2 | 38 | 13 |
| 7 | $I_2O_5$ | toluene | 80 | 2 | 22 | 5 |
| 8 | $I_2O_5$ | 1,4-dioxane | 80 | 2 | 33 | 9 |
| 9 | $I_2O_5$ | MeCN/$H_2O$ = 500:1 (V/V) | 80 | 2 | 53 | 34 |
| 10 | $I_2O_5$ | MeCN/$H_2O$ = 800:1 (V/V) | 80 | 2 | 60 | 26 |
| 11 | $I_2O_5$ | MeCN/$H_2O$ = 1000:1 (V/V) | 80 | 2 | 42 | 18 |
| 12[d] | $I_2O_5$ | MeCN/$H_2O$ = 800:1 (V/V) | 60 | 2 | 25 | 10 |
| 13[e] | $I_2O_5$ | MeCN/$H_2O$ = 800:1 (V/V) | 100 | 2 | 11 | 4 |
| 14[f] | $I_2O_5$ | MeCN/$H_2O$ = 800:1 (V/V) | 80 | 1 | 36 | 15 |
| 15 | $I_2O_5$ | MeCN/$H_2O$ = 800:1 (V/V) | 80 | 6 | 59 | 27 |
| 16 | $I_2O_5$ | MeCN[g] | 80 | 2 | <15 | <10 |
| 17 | $HIO_3$[h] | MeCN/$H_2O$ = 800:1 (V/V) | 80 | 6 | 35 | 10 |

[a]Reaction conditions: **1a** (0.2 mmol), iodine source (0.4 mmol, 2.0 equiv based on **1a**), solvent (2 mL), at 60-100 °C for 1-6 h. [b]New purchased MeCN was used (water content < 0.05 w/w %) was used. [c]$I_2O_5$ (0.6 mmol, 3.0 equiv). [d]Most of **1a** was recovered. [e]The reaction resulted in a complicated mixture which is hard to be separated. [f](2-phenylimidazo[1,2-a]pyridin-3-yl)methanol (**4a**) was obtained in 25% yield. [g]Dehydrated MeCN was used. [h]4 equivalents (0.8 mmol) were used.

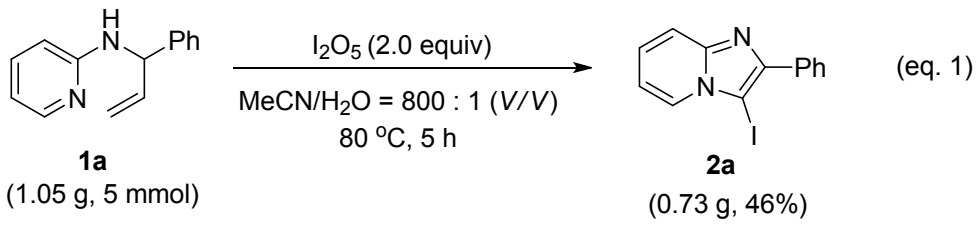
The substrate scope of *N*-(1-arylallyl)pyridine-2-amines **1** was then investigated under the optimized reaction conditions (Table 2). First, the generality of **1** with various aryl groups at the 3-position of the allyl moiety of **1** was examined ($R^1$ = Ar). It was found that **1** containing a range of aryl groups with various substitution patterns (*para*-, *meta*-, or *ortho*-) underwent the iodocyclization smoothly to afford the desired products in modest to good yields (38%-89%, **2a**-**2v**). The functional groups on the aryl rings ($R^1$) could be electron-donating groups (**2b**, **2c**, **2h**, **2m**, **2n**, **2q**, **2s**) as well as electron-withdrawing ones (**2d**-**2g**, **2i**-**2k**, **2o**, **2p**, **2r**). Note that the reaction is compatible with a wide variety of functional groups including alkanyl, ether, sulfuryl, cyano, nitro, trifluoromethyl, halo (F, Cl, Br), ester, and even thiomethyl groups. Gratifyingly, 3-pyridyl group was fully tolerated as well (**2u**). In addition, it was found that substrates with $R^1$ as H or an alkanyl group (cyclohexanyl) were also workable under the standard reaction conditions, albeit affording relatively lower yields of products (**2w** and **2x**). Finally, the substituents $R^2$ on the pyridine ring were investigated. Pyridine bearing either electron-donating or electron-withdrawing groups could undergo the iodocyclization smoothly and afford the desired products in modest to good yields (**2l**-**2x**).

**Table 2. Substrate scope of *N*-(1-arylallyl)pyridine-2-amines 1.**[a]




[a]Reaction conditions: **1** (0.3 mmol), $I_2O_5$ (0.6 mmol), MeCN/ $H_2O$ = 800 : 1 (2 mL, V/V) at 80 °C for 2 h. [b]The reaction time is 6 h.

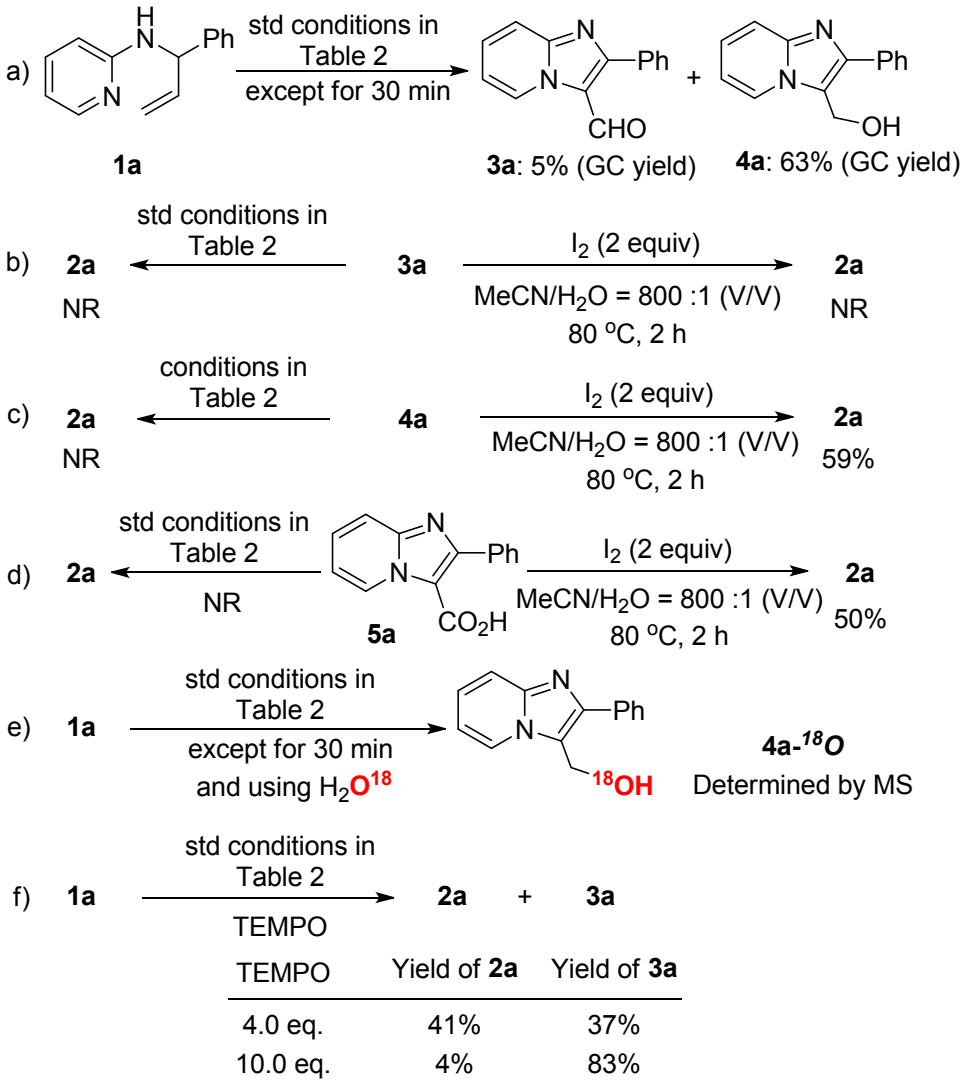
To make this protocol synthetically valuable, a gram-scale (5 mmol of **1a** used) synthesis of **2a** was also studied, and the desired 3-iodoimidazo[1,2-a]pyridine **2a** was obtained in 46% yield (eq. 1).




(eq. 1)

To gain insight into the possible mechanism, several mechanistic experiments were carried out (Scheme 2). When the reaction of **1a** proceeded for 30 min under the standard reaction conditions, sample analysis indicated that both intermediate **3a** and **4a** were detected in 5% and 63% GC yield, respectively (Scheme 2-a). When **3a** was subjected to the standard reaction conditions or was treated with 2 equivalents of iodine, both cases failed to give **2a**, suggesting **3a** is not likely the key intermediate for the formation of **2a** (Scheme 2-b). Treatment of **4a** or **5a** under the standard reaction conditions failed to give **2a**; while in the presence of 2 equivalents of iodine, both **4a** and **5a** were converted to **2a** in 59% and 50% yield, respectively (Scheme 2-c,d). These results implied that **4a** and **5a** might be the key intermediates for the formation of **2a** and $I_2$ might be in situ generated in the reaction process. To probe the oxygen source in intermediate **4a**, **1a** was subjected to the standard reaction conditions except using a $MeCN/H_2O^{18}$ = 800: 1 (V/V) system (Scheme 2-e). The $^{18}O$-incorporated product **4a-O$^{18}$** ($[M+H]^+$ *m/z* = 227) was detected by the MS analysis (Scheme 1-e, also see the Supporting Information), which disclosed that the oxygen atom in **4a** was originated from $H_2O$. In addition, radical scavenging experiments were performed by adding extra TEMPO[23] into the model reaction (Scheme 2-f). The reaction could still give **2a** in 41% yield along with **3a** in 37% yield in the presence of 4 equivalents of TEMPO; while the reaction only gave **2a** in 4% yield along with a large amount of **3a** in 83% yield. We presume that TEMPO may undergo redox reaction with $I_2O_5$ under the reaction conditions;[21b,24] thus, the formation of **2a** was suppressed.

**Scheme 2. Mechanistic Studies**

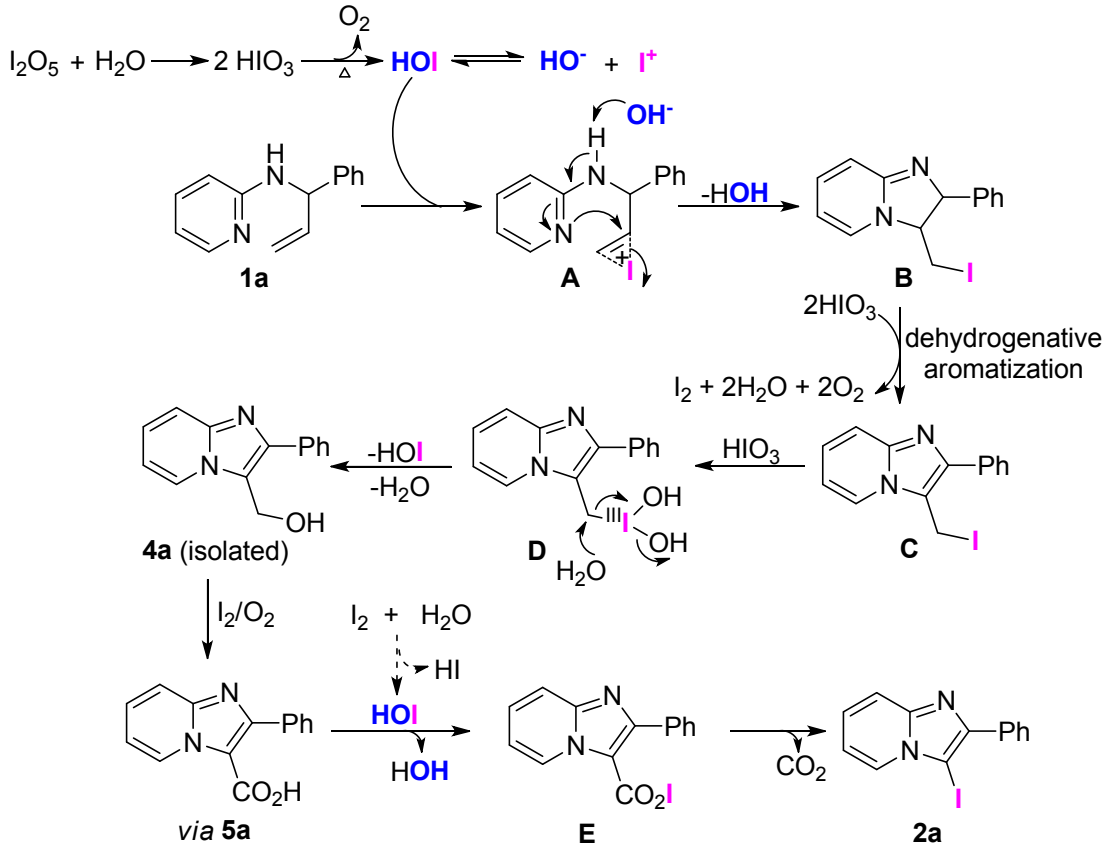



| TEMPO | Yield of **2a** | Yield of **3a** |
|---|---|---|
| 4.0 eq. | 41% | 37% |
| 10.0 eq. | 4% | 83% |

On the basis of the preliminary mechanistic experiments and previous literature,[21,25-28] a plausible reaction mechanism is proposed in Scheme 3. First, HOI was generated from the hydrolysis of $I_2O_5$ with water followed by the decomposition of the resulting $HIO_3$ under thermal conditions.[21b,25] HOI may release $I^+$ and $OH^-$ species in solution. Then activation of the alkene moiety in **1a** by $I^+$ species followed by a *5-exo-trig* cyclization to give intermediate **B**.[21] **B** might undergo dehydrogenative aromatization to deliver intermediate **C** promoted by $HIO_3$, and $I_2$ might be generated in the process.[26]

Oxidation of **C** with $HIO_3$ delivered a vinyl-$\lambda^3$-iodane intermediate **D** that underwent substitution by $H_2O$ to generate alcohol **4a**.[21,27] According to the abovementioned mechanistic studies (Scheme 2, *vide supra*), the in situ generated $I_2$ may promote the conversion of **4a** to the final product **2a** where C=C bond cleavage occurred possibly via a decarboxylation reaction of intermediate **5a**.[28]

**Scheme 3. Proposed mechanism**




## Conclusion

In summary, we have developed the synthesis of 3-iodoimidazo[1,2-a]pyridines involving an $I_2O_5$-mediated *5-exo-trig* iodocyclization of *N*-(1-arylallyl)pyridin-2-amines with concomitant C=C

bond cleavage. The present protocol has competitive advantages as follows: (1) the use of inexpensive, easily handled, and environmentally benign $I_2O_5$ as the oxidant and the iodine source, (2) transition-metal-free reaction conditions, (3) broad functional group tolerance, and (4) simple operation.

## Experimental Section

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without purification. The $^1H$ and $^{13}C$ NMR spectra were recorded on a spectrometer at 25 °C in $CDCl_3$ or DMSO-$d_6$ at 500 MHz and 125 MHz, respectively. Proton chemical shifts (δ) are relative to tetramethylsilane (TMS, δ = 0.00) as internal standard and expressed in ppm. Chemical shifts of $^{13}C$ NMR were reported relative to the solvent signal ($CDCl_3$: δ = 77.16 ppm; DMSO-$d_6$: δ = 39.51 ppm). GC-MS experiments were performed with an Agilent 6890N GC system equipped with a 5973N mass-selective detector with EI source; High resolution mass spectra (HRMS) were obtained on a TOF MS instrument with EI or ESI source. Acetonitrile is dehydrated by $CaH_2$ before preparation of the combined MeCN/$H_2O$ solvent system. Flash column chromatography was performed on silica gel (100-200 mesh) with the indicated solvent mixtures.

### General Procedure for the Synthesis of Substrate 1.

**General procedure A.**[14c]: A mixture of 2-aminopyridine (3.0 mmol), aldehyde (3.0 mmol), *p*-toluenesulfonic acid (10 mg, 0.06 mmol), and 4Å molecular sieve powders (2.0 g) in anhydrous THF

(20 mL) was refluxed under argon for 18 h. The mixture was then cooled to -78 °C before addition of vinylmagnesium bromide (6 mL, 1.0 M in THF, 2.0 equiv). The reaction mixture was maintained at -78 °C for 30 min and then warmed up to room temperature gradually. The reaction was quenched with saturated aqueous $NH_4Cl$ (1 mL) and then water (30 mL). The resulting mixture was extracted with EtOAc (2 × 30 mL). The combined organic layer was washed with brine, and dried over anhydrous $Na_2SO_4$. The concentrated crude product was purified by flash chromatography to afford the corresponding product. Substrates **1a**,[14c] **1l**,[14c], **1p**,[14c] **1r**,[14c] **1s**,[14c] **1u**[14c] and **1x**[14c] are known compounds and their spectra data are in line with those reported in previous literature.

**General procedure B**.[14c]: A mixture of 3-methylpyridin-2-amine (3.0 mmol), *t*-BuOK (504 mg, 4.5 mmol, 1.5 equiv) in anhydrous THF (10 mL) was stirred at room temperature under argon for 1 h. Allylbromide (3.6 mmol, 1.2 equiv, diluted in 2 mL of THF) was added dropwise to the resulting brown and transparent solution. The reaction was stirred for another 2 h at room temperature and then quenched with water (30 mL). The reaction mixture was extracted with EtOAc (2 × 30 mL). The combined organic layer was washed with brine, and dried over anhydrous $Na_2SO_4$. The concentrated crude product was purified by flash chromatography to afford the corresponding product **1w**.

**Characterization of unknown substrates.**

***N*-(1-(4-methoxyphenyl)allyl)pyridin-2-amine (1b)**: Following the general procedure A. White solid (0.36 g, 50%). m.p. 80-82 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.08 (dd, $J_1$ = 4.5 Hz, $J_2$ = 1.0 Hz, 1H), 7.40-7.37 (m, 1H), 7.32-7.29 (m, 2H), 6.90-6.88 (m, 2H), 6.59-6.57 (m, 1H), 6.35 (d, $J$ = 8.5 Hz,

1H), 6.10-6.03 (m, 1H), 5.28-5.22 (m, 3H), 5.04 (d, $J$ = 6.5 Hz, 1H), 3.80 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 158.9, 157.9, 148.2, 138.7, 137.4, 133.4, 128.3, 115.5, 114.0, 113.2, 107.0, 57.9, 55.2. HRMS (ESI) for $C_{15}H_{17}N_2O$ $[M+H]^+$: calcd 241.1335, found 241.1340.

***N*-(1-(p-tolyl)allyl)pyridin-2-amine (1c)**: Following the general procedure A. White solid (0.51g, 71%). m.p. 47-49 °C. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.11-8.09 (m, 1H), 7.40-7.37 (m, 1H), 7.30-7.28 (m, 2H), 7.18-7.17 (m, 2H), 6.60-6.57 (m, 1H), 6.35 (d, $J$ = 8.5 Hz, 1H), 6.12-6.06 (m, 1H), 5.31-5.23 (m, 3H), 5.07 (d, $J$ = 6.0 Hz, 1H), 2.36 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 158.0, 148.2, 138.8, 138.5, 137.4, 137.1, 129.4, 127.0, 115.6, 113.3, 107.0, 58.3, 21.1. HRMS (ESI) for $C_{15}H_{17}N_2$ $[M+H]^+$: calcd 225.1386, found 225.1380.

***N*-(1-(4-(methylsulfonyl)phenyl)allyl)pyridin-2-amine (1d)**: Following the general procedure A. White solid (0.42 g, 49%). m.p. 54-56 °C. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.04 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.0 Hz, 1H), 7.90-7.87 (m, 2H), 7.58(d, $J$ = 8.5 Hz, 2H), 7.39-7.36 (m, 1H), 6.60-6.58 (m, 1H), 6.34 (d, $J$ = 8.0 Hz, 1H), 6.08-6.01 (m, 1H), 5.49 (t, $J$ = 6.5 Hz, 1H), 5.28-5.21 (m, 3H), 3.04 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 157.3, 148.2, 148.1, 139.3, 137.5, 137.5, 128.0, 127.7, 117.2, 113.7, 107.5, 57.8, 44.4. HRMS (ESI) for $C_{15}H_{17}N_2O_2S$ $[M+H]^+$: calcd 289.1005, found 289.1012.

**4-(1-(pyridin-2-ylamino)allyl)benzonitrile (1e)**: Following the general procedure A. Pale yellow solid (0.47 g, 66%). m.p. 72-74 °C. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.05 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.0 Hz, 1H), 7.61 (d, $J$ = 8.5 Hz, 2H), 7.50 (d, $J$ = 8.5 Hz, 2H), 7.40-7.36 (m, 1H), 6.61-6.59 (m, 1H), 6.33 (d, $J$ = 8.5 Hz, 1H), 6.07-6.01 (m, 1H), 5.45 (t, $J$ = 6.0 Hz, 1H), 5.29-5.23 (m, 2H), 5.17 (d, $J$ = 6.5 Hz, 1H).

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 157.3, 148.1, 147.3, 137.5, 137.5, 132.4, 127.8, 118.7, 117.2, 113.8, 111.1, 107.4, 58.0. HRMS (ESI) for $C_{15}H_{14}N_3$ $[M+H]^+$: calcd 236.1182, found 236.1189.

**N-(1-(4-nitrophenyl)allyl)pyridin-2-amine (1f)**: Following the general procedure A. Yellow solid (0.37 g, 48%). m.p. 92-94 °C. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.20-8.17 (m, 2H), 8.06 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.0 Hz, 1H), 7.56 (d, $J$ = 8.5 Hz, 2H), 7.41-7.38 (m, 1H), 6.62-6.60 (m, 1H), 6.34 (d, $J$ = 8.5 Hz, 1H), 6.10-6.03 (m, 1H), 5.51 (t, $J$ = 6.5 Hz, 1H), 5.31-5.25 (m, 2H), 5.15 (d, $J$ = 6.5 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 157.2, 149.3, 148.2, 147.2, 137.6, 137.4, 127.9, 123.9, 117.5, 113.9, 107.5, 57.8. HRMS (ESI) for $C_{14}H_{14}N_3O_2$ $[M+H]^+$: calcd 256.1081, found 256.1075.

***N*-(1-(4-(trifluoromethyl)phenyl)allyl)pyridin-2-amine (1g)**: Following the general procedure A. White solid (0.30 g, 36%). m.p. 51-53 °C. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.09 (d, $J$ = 4.5 Hz, 1H), 7.61 (d, $J$ = 8.0 Hz, 2H), 7.52 (d, $J$ = 8.0 Hz, 2H), 7.41-7.38 (m, 1H), 6.63-6.60 (m, 1H), 6.33 (d, $J$ = 8.5 Hz, 1H), 6.11-6.04 (m, 1H), 5.43 (t, $J$ = 6.5 Hz, 1H), 5.29-5.25 (m, 2H), 5.09 (d, $J$ = 5.0 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 157.5, 148.3, 145.7, 137.9, 137.6, 129.6 (q, $J$ = 32.5 Hz), 127.43, 125.6 (q, $J$ = 3.8 Hz), 124.1 (q, $J$ = 277.5 Hz), 116.9, 113.7, 107.2, 58.1. HRMS (ESI) for $C_{15}H_{14}F_3N_2$ $[M+H]^+$: calcd 279.1104, found 279.1111.

***N*-(1-(m-tolyl)allyl)pyridin-2-amine (1h)**: Following the general procedure A. White solid (0.35 g, 52%). m.p. 49-51 °C. $^{1}H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.10 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.0 Hz, 1H), 7.41-7.37 (m, 1H), 7.28-7.19 (m, 3H), 7.11 (d, $J$ = 7.5 Hz, 1H), 6.60-6.58 (m, 1H), 6.36 (d, $J$ = 8.5 Hz, 1H), 6.12-6.05 (m, 1H), 5.31-5.23 (m, 3H), 5.04 (d, $J$ = 6.0 Hz, 1H), 2.36 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz,

$CDCl_3$): $\delta$ 158.0, 148.2, 141.4, 138.7, 138.4, 137.4, 128.6, 128.2, 127.8, 124.1, 115.6, 113.3, 107.0, 58.6, 21.4. HRMS (ESI) for $C_{15}H_{17}N_2$ $[M+H]^+$: calcd 225.1386, found 225.1380.

***N*-(1-(3-chlorophenyl)allyl)pyridin-2-amine (1i)**: Following the general procedure A. White solid (0.33 g, 45%). m.p. 68-70 °C. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.08-8.07 (m, 1H), 7.41-7.37 (m, 2H), 7.28-7.23 (m, 3H), 6.61-6.58 (m, 1H), 6.33 (d, $J$ = 8.5 Hz, 1H), 6.08-6.01 (m, 1H), 5.31 (t, $J$ = 6.5 Hz, 1H), 5.28-5.16 (m, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 157.6, 148.2, 143.7, 137.9, 137.5, 134.5, 129.9, 127.6, 127.2, 125.3, 116.5, 113.5, 107.1, 57.9. HRMS (ESI) for $C_{14}H_{14}ClN_2$ $[M+H]^+$: calcd 245.0840, found 245.0832.

***N*-(1-(3-nitrophenyl)allyl)pyridin-2-amine (1j)**: Following the general procedure A. Yellow solid (0.44 g, 57%). m.p. 53-55 °C. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.26 (s, 1H), 8.12 (dd, $J_1$ = 8.5 Hz, $J_2$ = 1.5 Hz, 1H), 8.06 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.0 Hz, 1H), 7.74 (d, $J$ = 7.5 Hz, 1H), 7.50 (t, $J$ = 8.0 Hz, 1H), 7.41-7.38 (m, 1H), 6.62-6.60 (m, 1H), 6.37 (d, $J$ = 8.0 Hz, 1H), 6.1-6.05 (m, 1H), 5.54 (t, $J$ = 6.0 Hz, 1H), 5.32-5.26 (m, 2H), 5.14 (d, $J$ = 6.5 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 157.2, 148.5, 148.2, 144.2, 137.6, 137.5, 133.3, 129.5, 122.4, 122.0, 117.4, 113.9, 107.6, 57.6. HRMS (ESI) for $C_{14}H_{14}N_3O_2$ $[M+H]^+$: calcd 256.1081, found 256.1089.

***N*-(1-(2-fluorophenyl)allyl)pyridin-2-amine (1k)**: Following the general procedure A. White solid (0.27 g, 40%). m.p. 60-62 °C. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.10-8.08 (m, 1H), 7.41-7.37 (m, 2H), 7.28-7.23 (m, 1H), 7.13-7.05 (m, 2H), 6.60-6.57 (m, 1H), 6.37 (d, $J$ = 8.5 Hz, 1H), 6.14-6.08 (m, 1H), 5.67-5.64 (m, 1H), 5.28-5.22 (m, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 160.1 (d, $J$ = 245.0 Hz),

157.6, 148.2, 137.5 (d, $J$ = 11.3 Hz), 129.0 (d, $J$ = 7.5 Hz), 128.5, 128.4 (d, $J$ = 3.8 Hz), 124.4 (d, $J$ = 3.8 Hz), 115.9, 115.7, 115.5, 113.5, 106.8, 52.5 (d, $J$ = 2.5 Hz).

***N*-(1-(4-isopropylphenyl)allyl)-5-methylpyridin-2-amine (1m)**: Following the general procedure A. Yellow solid (0.60 g, 75%). m.p. 41-43 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.93 (d, $J$ = 1.5 Hz, 1H), 7.33 (d, $J$ = 8.0 Hz, 2H), 7.23 (d, $J$ = 8.0 Hz, 3H), 6.32 (d, $J$ = 8.5 Hz, 1H), 6.12-6.05 (m, 1H), 5.3-5.21 (m, 3H), 4.96 (d, $J$ = 6.5 Hz, 1H), 2.95-2.18 (m, 1H), 2.18 (s, 3H), 1.27 (d, $J$ = 7.0 Hz, 3H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 156.2, 147.9, 147.8, 139.0, 138.9, 138.3, 127.0, 126.7, 121.9, 115.3, 106.6, 58.4, 33.7, 23.9, 17.3. HRMS (ESI) for $C_{18}H_{23}N_2$ $[M+H]^+$: calcd 267.1856, found 267.1863.

**5-methyl-*N*-(1-(4-(methylthio)phenyl)allyl)pyridin-2-amine (1n)**: Following the general procedure A. White solid (0.36 g, 44%). m.p. 55-57 °C. $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.89 (d, $J$ = 1.5 Hz, 1H), 7.31-7.29 (m, 2H), 7.24-7.22 (m, 3H), 6.29 (d, $J$ = 8.5 Hz, 1H), 6.08-6.02 (m, 1H), 5.28-5.20 (m, 3H), 5.06 (d, $J$ = 6.0 Hz, 1H), 2.47 (s, 3H), 2.16 (s, 3H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 155.8, 147.2, 138.7, 138.5, 138.5, 137.5, 127.6, 126.9, 122.2, 115.9, 106.9, 58.4, 17.3, 15.9. HRMS (ESI) for $C_{16}H_{19}N_2S$ $[M+H]^+$: calcd 271.1263, found 271.1272.

***N*-(1-(4-bromophenyl)allyl)-5-methylpyridin-2-amine (1o)**: Following the general procedure A. White solid (0.55 g, 60%). m.p. 96-98 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.89 (d, $J$ = 1.5 Hz, 1H), 7.47-7.44 (m, 2H), 7.26 (d, $J$ = 8.5 Hz, 2H), 7.21 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.5 Hz, 1H), 6.25 (d, $J$ = 8.5 Hz, 1H), 6.07-6.00 (m, 1H), 5.26-5.22 (m, 3H), 5.03 (d, $J$ = 6.5 Hz, 1H), 2.16 (s, 3H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 155.8, 147.8, 140.8, 138.4, 138.3, 131.7, 128.8, 122.3, 121.1, 116.2, 106.8, 58.1, 17.3.

HRMS (ESI) for $C_{15}H_{16}BrN_2$ $[M+H]^+$: calcd 303.0491, found 303.0484.

**5-methyl-*N*-(1-(o-tolyl)allyl)pyridin-2-amine (1q)**: Following the general procedure A. Yield: 37%. White solid (0.26 g, 37%). m.p. 85-87 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.91 (d, $J$ = 1.5 Hz, 1H), 7.40-7.38 (m, 1H), 7.23-7.19 (m, 4H), 6.24 (d, $J$ = 8.0 Hz, 1H), 6.15-6.08 (m, 1H), 5.47-5.45 (m, 1H), 5.28-5.23 (m, 2H), 4.97 (d, $J$ = 6.5 Hz, 1H), 2.42 (s, 3H), 2.17 (s, 3H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 156.1, 147.8, 139.3, 138.3, 137.8, 136.1, 130.6, 127.3, 126.5, 126.2, 121.8, 115.7, 106.2, 55.1, 19.1, 17.3. HRMS (ESI) for $C_{16}H_{19}N_2$ $[M+H]^+$: calcd 239.1543, found 239.1551.

**5-methyl-*N*-(1-(naphthalen-2-yl)allyl)pyridin-2-amine (1t)**: Following the general procedure A. White solid (0.51 g, 62%). m.p. 87-89 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.94-7.93 (m, 1H), 7.85-7.82 (m, 4H), 7.52 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.0 Hz, 1H), 7.50-7.46 (m, 2H), 7.21 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.0 Hz, 1H), 6.32 (d, $J$ = 8.5 Hz, 1H), 6.20-6.14 (m, 1H), 5.43 (t, $J$ = 6.0 Hz, 1H), 5.44-5.27 (m, 2H), 5.07 (d, $J$ = 6.5 Hz, 1H), 2.16 (s, 3H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 156.1, 147.8, 139.0, 138.7, 138.5, 133.4, 132.8, 128.5, 127.9, 127.6, 126.1, 125.8, 125.7, 125.4, 122.2, 116.1, 106.7, 58.9, 17.4. HRMS (ESI) for $C_{19}H_{19}N_2$ $[M+H]^+$: calcd 275.1543, found 275.1543.

**5-chloro-*N*-(1-phenylallyl)pyridin-2-amine (1v)**: Following the general procedure A. White solid (0.35 g, 48%). m.p. 106-108 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.00 (d, $J$ = 2.0 Hz, 1H), 7.39-7.37 (m, 4H), 7.35-7.29 (m, 2H), 6.30 (d, $J$ = 9.0 Hz, 1H), 6.11-6.05 (m, 1H), 5.29-5.23 (m, 4H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 156.2, 146.5, 141.0, 138.2, 137.2, 128.8, 127.6, 127.1, 120.1, 116.1, 107.8, 58.7. HRMS (ESI) for $C_{14}H_{14}ClN_2$ $[M+H]^+$: calcd 245.0840, found 245.0840.

**Preparation of 3-iodoimidazo[1,2-a]pyridines 2 from the reaction of *N*-(1-arylallyl)pyridin-2-amines with $I_2O_5/H_2O$.** Typical procedure (**2a** as example): (1-phenylallyl)pyridin-2-amine **1a** (63.0 mg, 0.3 mmol), $I_2O_5$ (200.4 mg, 0.6 mmol) were stirred and heated at 80 ºC in an oil bath for 2 h in mixed solvent (MeCN : $H_2O$ = 800 : 1 (V/V), 2 mL). After completion, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (10 mL) and EtOAc (10 mL) were added to the reaction mixture. The organic phase was separated, and the aqueous phase was further extracted with EtOAc (2×10 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$. The solvent was removed and the residue was purified by column chromatography (eluted with petroleum ether/ethyl acetate = 6:1) to give a pure product **2a** ( 57.6 mg, 60%). Other compounds **2b**-**x** were synthesized according to this typical procedure.

**Characterization of the products.**

**3-iodo-2-phenylimidazo[1,2-a]pyridine (2a)**[19a]: White solid (57.6 mg, 60%). m.p. 145-147 ºC. $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 8.25 (d, $J$ = 7.0 Hz, 1H), 8.09-8.08 (m, 2H), 7.64 (d, $J$ = 9.0 Hz, 1H), 7.52-7.49 (m, 2H), 7.44-7.40 (m, 1H), 7.30-7.26 (m, 1H), 6.96-6.93 (m, 1H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 148.2, 148.1, 133.6, 128.5, 128.4, 128.4, 126.5, 125.6, 117.6, 113.2, 59.5.

**3-iodo-2-(4-methoxyphenyl)imidazo[1,2-a]pyridine (2b)**[19a]: White solid (47.3 mg, 45%). m.p. 116-118 ºC. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.23-8.21 (m, 1H), 8.04-8.01 (m, 2H), 7.63-7.61 (m, 1H), 7.27-7.24 (m, 1H), 7.04-7.02 (m, 2H), 6.94-6.91 (m, 1H), 3.88 (s, 3H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 159.8, 148.1, 147.9, 129.8, 126.4, 126.0, 125.5, 117.4, 113.8, 113.0, 58.8, 55.3.

**3-iodo-2-(p-tolyl)imidazo[1,2-a]pyridine (2c)**[19a]: White solid (64.1 mg, 64%). m.p. 143-145 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.23 (d, $J$ = 7.0 Hz, 1H), 7.98 (d, $J$ = 8.0 Hz, 2H), 7.63(d, $J$ = 9.0 Hz, 1H), 7.31(d, $J$ = 8.0 Hz, 2H), 7.28-26 (m, 1H), 6.95-6.92 (m, 1H), 2.43 (s, 3H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 148.2, 148.1, 138.2, 130.7, 129.1, 128.4, 126.5, 125.5, 117.5, 113.1, 59.2, 21.4.

**3-iodo-2-(4-(methylsulfonyl)phenyl)imidazo[1,2-a]pyridine (2d)**[18b]: White solid (50.2 mg, 42%). m.p. 151-153 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.33-8.31 (m, 2H), 8.25 (d, $J$ = 7.0 Hz, 1H), 8.06-8.04 (m, 2H), 7.64 (d, $J$ = 9.5 Hz, 1H), 7.34-7.31 (m, 1H), 7.01-6.98 (m, 1H), 3.12 (s, 3H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 148.3, 145.8, 139.8, 139.1, 129.1, 127.4, 126.7, 126.3, 117.9, 113.8, 60.7, 44.6.

**4-(3-iodoimidazo[1,2-a]pyridin-2-yl)benzonitrile (2e)**:[19a] White solid (84.9 mg, 82%). m.p. 181-183 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.24-8.22 (m, 3H), 7.76 (d, $J$ = 7.0 Hz, 2H), 7.63 (d, $J$ = 9.0 Hz, 1H), 7.33-7.28 (m, 1H), 6.99-6.96 (m, 1H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 148.3, 145.8, 138.1, 132.1, 128.8, 126.6, 126.3, 118.9, 117.9, 113.7, 111.6, 60.5.

**3-iodo-2-(4-nitrophenyl)imidazo[1,2-a]pyridine (2f)**: Yellow solid (97.5 mg, 89%). m.p. 192-194 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.36-8.31 (m, 4H), 8.28-8.26 (m, 1H), 7.66 (d, $J$ = 9.0 Hz, 1H), 7.36-7.33 (m, 1H), 7.03-7.00 (m, 1H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 148.4, 147.5, 145.6, 140.1, 129.0, 126.7, 126.5, 123.7, 118.0, 113.9, 60.9. HRMS (ESI) for $C_{13}H_9IN_3O_2$ $[M+H]^+$: calcd 365.9734, found 365.9741.

**3-iodo-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridine (2g)**:[19a] White solid (79.2 mg, 68%). m.p. 123-125 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.26-8.22 (m, 3H), 7.75 (d, $J$ = 8.0 Hz, 2H), 7.65 (d, $J$ = 9.0 Hz, 1H), 7.33-7.29 (m, 1H), 6.99-6.96 (m, 1H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $^{13}$C{$^1$H}

NMR (125 MHz, $CDCl_3$): $\delta$ 148.3, 146.5, 137.2, 130.1 (q, $J$ = 32.5 Hz), 128.7, 126.6, 126.0, 125.3 (q, $J$ = 3.8 Hz), 124.2 (q, $J$ = 271.25 Hz), 117.8, 113.6, 60.1.

**3-iodo-2-(m-tolyl)imidazo[1,2-a]pyridine (2h)**: White solid (38.1 mg, 38%). m.p. 107-109 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.23-8.21 (m, 1H), 7.89 (d, $J$ = 7.0 Hz, 2H), 7.64-7.61 (m, 1H), 7.40-7.37 (m, 1H), 7.27-7.22 (m, 2H), 6.93-6.90 (m, 1H), 2.46 (s, 3H). $^{13}$C{$^{1}$H} NMR (125 MHz, $CDCl_3$): $\delta$ 148.1, 148.0, 138.0, 133.4, 129.2, 129.1, 128.1, 126.4, 125.5, 125.5, 117.5, 113.1, 59.5, 21.4. HRMS (ESI) for $C_{14}H_{12}IN_2$ $[M+H]^+$: calcd 335.0040, found 335.0030.

**2-(3-chlorophenyl)-3-iodoimidazo[1,2-a]pyridine (2i)**[19a]: Pale yellow solid (53.2 mg, 50%). m.p. 147-149 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.22-8.20 (m, 1H), 8.10 (t, $J$ = 1.5 Hz, 1H), 7.99-7.97 (m, 1H), 7.63-7.61 (m, 1H), 7.4-7.40 ( m, 1H), 7.38-7.36 (m, 1H), 7.29-7.26 (m, 1H), 6.95-6.92 (m, 1H). $^{13}$C{$^{1}$H} NMR (125MHz, $CDCl_3$): $\delta$ 148.1, 146.5, 135.4, 134.3, 129.6, 128.5, 128.3, 126.5, 126.5, 125.9, 117.7, 113.4, 59.8.

**3-iodo-2-(3-nitrophenyl)imidazo[1,2-a]pyridine (2j)**: Yellow solid (90.7 mg, 83%). m.p. 151-153 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 9.03 (s 1H), 8.46 (d, $J$ = 8.0 Hz, 1H), 8.27-8.25 (m, 2H), 7.67 (t, $J$ = 8.5 Hz, 2H), 7.36-7.32 (m, 1H), 7.02-6.99 (m, 1H). $^{13}$C{$^{1}$H} NMR (126 MHz, $CDCl_3$): $\delta$ 148.3, 147.3, 145.5, 135.4, 134.2, 129.4, 126.7, 126.3, 123.2, 123.0, 117.9, 113.8, 60.2. HRMS (ESI) for $C_{13}H_9IN_3O_2$ $[M+H]^+$: calcd 365.9734, found 365.9742.

**2-(2-fluorophenyl)-3-iodoimidazo[1,2-a]pyridine (2k)**: White solid (50.7 mg, 50%). 186-188 $^{o}$C. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.19 (d, $J$ = 7.0 Hz, 1H), 7.69-7.66 (m, 1H), 7.63 (d, $J$ = 9.0 Hz, 1H), 7.44-7.39 (m, 1H), 7.28-7.24 (m, 2H), 7.21 (t, $J$ = 9.0 Hz, 2H), 6.94-6.91 (m, 1H). $^{13}$C{$^{1}$H} NMR (125

MHz, $CDCl_3$): $\delta$ 159.8 (d, $J$ = 248.8 Hz), 147.9, 145.3, 132.1 (d, $J$ = 3.8 Hz), 130.4 (d, $J$ = 7.5 Hz), 126.4, 125.5, 124.0 (d, $J$ = 3.8 Hz), 121.9 (d, $J$ = 15.0 Hz), 117.7, 116.0 (d, $J$ = 22.5 Hz), 113.3, 63.1. HRMS (ESI) for $C_{13}H_9FIN_2$ $[M+H]^+$: calcd 338.9789, found 338.9785.

**3-iodo-6-methyl-2-phenylimidazo[1,2-a]pyridine (2l)**[29]: White solid (73.1 mg, 73%). m.p. 111-113 $^oC$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.08-8.06 (m, 2H), 7.99 (s, 1H), 7.54-7.47 (m, 3H), 7.41-7.38 (m, 1H), 7.10 (dd, $J_1$ = 9.5 Hz, $J_2$ = 1.5 Hz, 1H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 147.7, 147.2, 133.7, 128.7, 128.4, 128.3, 128.2, 124.3, 123.0, 116.9, 59.0, 18.3.

**3-iodo-2-(4-isopropylphenyl)-6-methylimidazo[1,2-a]pyridine (2m)**: Pale yellow solid (64.7 mg, 57%). m.p. 148-150 $^oC$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.02-8.00 (m, 3H), 7.52 (d, $J$ = 9.0 Hz, 1H), 7.35 (d, $J$ = 8.0 Hz, 2H), 7.10 (dd, $J_1$ = 9.5 Hz, $J_2$ = 2.0 Hz, 1H), 3.01-2.95 (m, 1H), 2.41 (s, 3H), 1.31 (d, $J$ = 7.0 Hz, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 149.0, 147.8, 147.1, 131.2, 128.5, 128.3, 126.4, 124.2, 122.8, 116.8, 58.6, 34.0, 23.9, 18.4. HRMS (ESI) for $C_{17}H_{18}IN_2$ $[M+H]^+$: calcd 377.0509, found 377.0505.

**3-iodo-6-methyl-2-(4-(methylthio)phenyl)imidazo[1,2-a]pyridine (2n)**: White solid (76.4 mg, 67%). m.p. 152-154 $^oC$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.02-7.99 (m ,3H), 7.51 (d, $J$ = 9.5 Hz, 1H), 7.37-7.35 (m, 2H), 7.11 (dd, $J_1$ = 9.5 Hz, $J_2$ = 2.0 Hz, 1H), 2.54 (s, 3H), 2.41 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 147.2, 147.2, 138.7, 130.4, 128.7, 128.7, 126.2, 124.2, 123.0, 116.8, 58.7, 18.4, 15.7. HRMS (ESI) for $C_{15}H_{14}IN_2S$ $[M+H]^+$: calcd 380.9917, found 380.9915.

**2-(4-bromophenyl)-3-iodo-6-methylimidazo[1,2-a]pyridine (2o)**: White solid (73.1 mg, 59%). m.p.

150-152 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.98 (s, 1H), 7.97-7.94 (m, 2H), 7.61-7.58 (m, 2H), 7.51 (d, $J$ = 10.0 Hz, 1H), 7.11 (dd, $J_1$ = 10.0 Hz, $J_2$ = 5.0 Hz, 1H), 2.40 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 147.2, 146.6, 132.7, 131.5, 129.9, 128.9, 124.3, 123.2, 122.4, 116.9, 59.0, 18.4. HRMS (ESI) for $C_{14}H_{11}BrIN_2$ $[M+H]^+$: calcd 412.9145, found 412.9139.

**methyl 4-(3-iodo-6-methylimidazo[1,2-a]pyridin-2-yl)benzoate (2p)**: White solid (84.7 mg, 72%). 134-136 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.16 (dd, $J_1$ = 16.0 Hz, $J_2$ = 8.5 Hz, 4H), 8.01 (s, 1H), 7.53 (d, $J$ = 9.5 Hz, 1H), 7.13 (dd, $J_1$ = 9.0 Hz, $J_2$ = 1.0 Hz, 1H), 3.95 (s, 3H), 2.41 (s, 3H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 167.0, 147.3, 146.5, 138.2, 129.6, 129.5, 129.2, 128.2, 124.3, 123.34, 117.1, 59.8, 52.1, 18.4. HRMS (ESI) for $C_{16}H_{14}IN_2O_2$ $[M+H]^+$: calcd 393.0094, found 393.0090.

**3-iodo-6-methyl-2-(o-tolyl)imidazo[1,2-a]pyridine (2q)**: White solid (50. 1 mg, 48%). m.p. 180-182 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.97 (s, 1H), 7.51 (d, $J$ = 9.5 Hz, 1H), 7.40 (d, $J$ = 7.5 Hz, 1H), 7.35-7.30 (m, 2H), 7.28-7.25 (m, 1H), 7.11 (dd, $J_1$ = 9.0 Hz, $J_2$ = 1.5 Hz, 1H), 2.41 (s, 1H), 2.33 (s, 1H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 150.1, 146.8, 137.5, 133.5, 130.8, 130.2, 128.5, 128.3, 125.3, 124.1, 122.8, 116.9, 62.1, 20.2, 18.3. HRMS (ESI) for $C_{15}H_{14}IN_2$ $[M+H]^+$: calcd 349.0196, found 349.0191.

**2-(2-chlorophenyl)-3-iodo-6-methylimidazo[1,2-a]pyridine (2r)**: White solid (57.5 mg, 52%). m.p. 132-134 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.97 (s, 1H), 7.55-7.49 (m, 3H), 7.39-7.34 (m, 2H), 7.13 (dd, $J_1$ = 9.5 Hz, $J_2$ = 2.0 Hz, 1H), 2.42 (s, 3H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 147.9, 146.8, 134.0, 133.2, 132.5, 129.9, 129.8, 128.6, 126.4, 124.1, 123.2, 117.2 , 63.0, 18.3. HRMS (ESI) for

$C_{14}H_{11}ClIN_2$ $[M+H]^+$: calcd 368.9650, found 368.9647.

**3-iodo-2-(3-methoxyphenyl)-6-methylimidazo[1,2-a]pyridine (2s)**: White solid (76.5 mg, 70%). m.p. 141-143 °C. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.00 (s, 1H), 7.66 (d, $J$ = 8.0 Hz, 1H), 7.62 (t, $J$ = 2.5 Hz, 1H), 7.52 (d, $J$ = 9.5 Hz, 1H), 7.39 (t, $J$ = 7.0 Hz, 1H), 7.11 (dd, $J_1$ = 9.0 Hz, $J_2$ = 1.5 Hz, 1H), 6.96-6.94 (m, 1H), 3.90 (s, 3H), 2.40 (s, 3H). $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 159.5, 147.5, 147.1, 135.0, 129.3, 128.7, 124.3, 123.0, 120.9, 116.9, 114.5, 113.4, 59.2, 55.4, 18.3. HRMS (ESI) for $C_{15}H_{14}IN_2O$ $[M+H]^+$: calcd 365.0145, found 365.0141.

**3-iodo-6-methyl-2-(naphthalen-2-yl)imidazo[1,2-a]pyridine (2t)**: White solid (65.7 mg, 57%). m.p. 215-217 °C. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.57 (s, 1H), 8.22 (dd, , $J_1$ = 8.5 Hz, $J_2$ = 1.5 Hz, 1H), 8.05 (s, 1H), 7.97-7.95 (m, 2H), 7.90-7.88 (m, 1H), 7.58 (d, $J$ = 9.0 Hz, 1H), 7.53-52 (m, 2H), 7.14 (dd, , $J_1$ = 9.0 Hz, $J_2$ = 1.0 Hz, 1H), 2.43 (s, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 147.7, 147.3, 133.3, 133.1, 131.2, 128.8, 128.5, 127.9, 127.7, 127.7, 126.3, 126.2, 126.2, 124.3, 123.1, 117.0, 59.3, 18.4. HRMS (ESI) for $C_{18}H_{14}IN_2$ $[M+H]^+$: calcd 385.0193, found 385.0193.

**3-iodo-6-methyl-2-(pyridin-3-yl)imidazo[1,2-a]pyridine (2u)**: White solid (50.2 mg, 50%). m.p. 123-125 °C. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 9.33 (d, $J$ = 1.5 Hz, 1H), 8.63 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 8.36-8.34 (m, 1H), 8.00 (s, 1H), 7.53 (d, $J$ = 9.0 Hz, 1H), 7.42-7.40 (m, 1H), 7.14 (dd, $J_1$ = 9.0 Hz, $J_2$ = 1.5 Hz, 1H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): $\delta$ 149.4, 149.1, 147.4, 145.0, 135.6, 129.8, 129.1, 124.3, 123.4, 123.2, 117.0, 59.4, 18.4. HRMS (ESI) for $C_{13}H_{11}IN_3$ $[M+H]^+$: calcd 335.9992, found 335.9993.

**6-chloro-3-iodo-2-phenylimidazo[1,2-a]pyridine (2v)**[18b]: White solid (64.8 mg, 61%). m.p. 122-124 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.27-8.26 (m, 1H), 8.06-8.04 (m, 2H), 7.56 (d, $J$ = 9.5 Hz, 1H), 7.50-7.47 (m, 2H), 7.43-7.40 (m, 1H), 7.21 (dd, $J_1$ = 9.5 Hz, $J_2$ = 2.0 Hz, 1H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 148.9, 146.5, 133.1, 128.6, 128.4, 128.4, 126.9, 124.5, 121.5, 117.9, 60.1.

**3-iodo-8-methylimidazo[1,2-a]pyridine (2w)**[18b]: White solid (27.1 mg, 35%). m.p. 92-194 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.98 (d, $J$ = 6.5 Hz, 1H), 7.67 (s, 1H), 7.02-7.00 (m, 1H), 6.82 (t, $J$ = 7.0 Hz, 1H), 2.61 (s, 1H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 148.0, 139.4, 127.6, 123.8, 123.7, 113.1, 61.1, 16.5.

**2-cyclohexyl-3-iodo-6-methylimidazo[1,2-a]pyridine (2x)**: White solid (32.7 mg, 32%). m.p. 131-133 °C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.85 (s, 1H), 7.43 (d, $J$ = 9.0 Hz, 1H), 7.01 (dd, $J_1$ = 8.5 Hz, $J_2$ = 1.5 Hz, 1H), 2.81-2.75 (m, 1H), 2.35 (s, 3H), 1.87-1.85 (m, 4H), 1.80-1.71 (m, 3H), 1.47-1.29 (m, 3H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 154.9, 146.8, 127.6, 123.7, 122.3, 116.5, 59.6, 38.0, 32.3, 26.6, 25.9, 18.2. HRMS (ESI) for $C_{14}H_{18}IN_2$ $[M+H]^+$: calcd 341.0509, found 341.0515.

**Gram-scale synthesis of 2a. 1a** (1.05 g, 5.0 mmol), $I_2O_5$ (3.33 g, 10.0 mmol) were stirred and heated at 80 ºC in an oil bath for 5 h in mixed solvent (MeCN : $H_2O$ = 800 : 1 (V/V), 30 mL). After completion, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (60 mL) and EtOAc (100 mL) were added to the reaction mixture. The organic phase was separated, and the aqueous phase was further extracted with EtOAc (2×50 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$. The solvent was removed and the residue was purified by column chromatography (eluted

with petroleum ether/ethyl acetate = 6:1) to give a pure product **2a** (0.73 g, 46%).

**Mechanistic studies.**

**Probe the possible reaction intermediates.**

**Synthesis of 2-phenylimidazo[1,2-a]pyridine-3-carbaldehyde (3a).** *N*-(1-phenylallyl)pyridin-2-amine (63.0 mg, 0.3 mmol), $I_2O_5$ (200.4 mg, 0.6 mmol), TEMPO (468.1 mg, 3 mmol) were stirred for 2 h in mixed solvent (MeCN : $H_2O$ = 800 : 1 (V/V), 2 mL) at 80 ºC. After completion, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (10 mL) and EtOAc (10 mL) were added to the reaction mixture. The organic phase was separated, and the aqueous phase was further extracted with EtOAc (2×10 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$. The solvent was removed and the residue was purified by column chromatography (eluted with petroleum ether/ethyl acetate = 5:1) to give a pure product **3a**[30] (50.0 mg, 75%). White solid. m.p. 144-145 ºC (lit.[5] m.p. 141-143 ºC). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 10.08 (s, 1H), 9.68 (d, $J$ = 7.0 Hz, 1H), 7.85-7.82 (m, 3H), 7.62-7.58 (m, 1H), 7.56-7.52 (m, 3H), 7.16-7.13 (m, 1H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 179.6, 158.3, 147.7, 132.3, 130.4, 129.8, 128.9, 128.2, 120.8, 117.4, 115.3.

**Synthesis of (2-phenylimidazo[1,2-a]pyridin-3-yl)methanol (4a).** N-(1-phenylallyl)pyridin-2-amine (63 mg, 0.3 mmol), $I_2O_5$ (200.4 mg, 0.6 mmol) were stirred and heated at 80 ºC in an oil bath for 0.5 h in mixed solvent (MeCN : $H_2O$ = 800 : 1 (V/V), 2 mL). After completion, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (10 mL) and EtOAc (10 mL) were added to the reaction mixture. The organic phase was separated, and the aqueous phase was further extracted with EtOAc (2×10 mL). The

combined organic layer was dried over anhydrous $Na_2SO_4$. The solvent was removed and the residue was purified by column chromatography (eluted with petroleum ether/ethyl acetate = 1:1) to give a pure product **4a** (36.0 mg, 50%, ). m.p. 143-145 °C. $^1$H NMR (500 MHz, DMSO): $\delta$ 8.47 (d, $J$ = 7.0 Hz, 1H), 7.86 (d, $J$ = 7.5 Hz, 2H), 7.63 (d, $J$ = 9.0 Hz, 1H), 7.50 (t, $J$ = 7.5 Hz, 2H), 7.41-7.31 (m, 2H), 7.01-6.98 (m, 1H), 5.45 (s, 1H), 4.93 (s, 2H). $^{13}$C NMR (125 MHz, DMSO): $\delta$ 144.0, 142.8, 134.4, 128.5, 128.2, 127.6, 125.2, 125.0, 120.6, 116.7, 112.1, 52.2. HRMS (ESI) for $C_{14}H_{13}N_2O$ $[M+H]^+$: calcd 225.1022, found 225.1026.

**Synthesis of 2-phenylimidazo[1,2-a]pyridine-3-carboxylic acid (5a).**[31,32] A mixture of pyridin-2-amine (1.41 g, 15 mmol), ethyl benzoylacetate (0.96 g, 5 mmol) and $CBr_4$ (3.3 g, 10 mmol) in 20 mL of acetonitrile was stirred and heated at 80 °C in an oil bath for 6 h. The reactions were completed as monitored by TLC. Product **5a'** was isolated by silica gel column chromatography using petroleum ether/acetone (50:1 to 5:1 (V/V)) in 90% yield as a white solid. Next, to a solution of **5a'** (565.0 mg, 2.5 mmol) in EtOH (3 mL), THF (3 mL) and $H_2O$ (3 mL) was added NaOH (200.0 mg, 5 mmol). The mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure. The residue was acidified by HCl (1N) until pH = 4. The precipitate solid **5a** was collected without further purification (476.0 mg, yield 80%).

**Treatment of 3a (or 4a, or 5a) under the standard reaction conditions.** A mixture of substrate **3a** (or **4a**, or **5a**) (0.6 mmol), $I_2O_5$ (400.8 mg, 1.2 mmol, 2.0 equiv) in mixed solvent (MeCN : $H_2O$ = 800 : 1 (V/V), 6 mL) was stirred and heated at 80 °C in an oil bath for 2 h. After completion, the reaction

mixture was detected by TLC and GC-MS analysis. Unfortunately, no product was found in three reactions.

**Treatment of 3a (or 4a, or 5a) in MeCN-water mixture in the presence of $I_2$.** A mixture of substrate **3a** (or **4a**, or **5a**) (0.6 mmol), $I_2$ (304.8 mg, 1.2 mmol, 2.0 equiv.) in mixed solvent ($CH_3CN$ : $H_2O$ = 800 : 1 (V/V), 6 mL) was stirred and heated at 80 °C in an oil bath for 2 h. The reaction was cooled down to room temperature. Saturated aqueous $Na_2S_2O_3$ (10 mL), and EtOAc (10 mL) were added to the reaction mixture successively. The organic phase was separated, and the aqueous phase was further extracted with EtOAc (2×10 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$ and concentrated. The residue was separated by column chromatography (eluted with petroleum ether/ethyl acetate = 6:1) to give a pure product **2a** (in case of **3a**, **2a**: 0%; in case of **4a**, **2a**: 59%; in case of **5a**, **2a**: 50%).

**Isotope experiment.** N-(1-phenylallyl)pyridin-2-amine **1a** (63 mg, 0.3 mmol), $I_2O_5$ (200.4 mg, 0.6 mmol) were stirred and heated at 80 ºC in an oil bath for 0.5 h in mixed solvent (MeCN : $H_2{}^{18}O$ = 800 : 1 (V/V), 2 mL). After completion, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (10 mL) and EtOAc (10 mL) were added to the reaction mixture. The organic phase was separated, and the aqueous phase was further extracted with EtOAc (2×10 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$. The solvent was removed and the residue was purified by column chromatography (eluted with petroleum ether/ethyl acetate = 1:1) to give a mixture of **4a-$^{18}$*O*** and **4a** (originated from $H_2O$ because water can not be completely excluded). The ESI/APCI-MS spectra of

**4a-$^{18}O$** and **4a** were indicated in Figure *1S* and Figure *2S*, respectively.

**Radical scavenging experiment.** N-(1-phenylallyl)pyridin-2-amine **1a** (63.0 mg, 0.3 mmol), $I_2O_5$ (200.4 mg, 0.6 mmol, ), TEMPO were stirred and heated at 80 ºC in an oil bath for 2 h in mixed solvent (MeCN : $H_2O$ = 800 : 1 (V/V), 2 mL). After completion, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (10 mL) and EtOAc (10 mL) were added to the reaction mixture. The organic phase was separated, and the aqueous phase was further extracted with EtOAc (2×10 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$. The residue was purified by flash chromatography to provide **2a** and **3a**, respectively.

## ASSOCIATED CONTENT

### Supporting Information

Charts for mechanistic studies as well as copies of $^1H$ and $^{13}C$ NMR spectra of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

## AUTHOR INFORMATION

### Corresponding Author

*E-mail: ykuiliu@zjut.edu.cn; jhwei828@zjut.edu.cn

### Notes

The authors declare no competing financial interest.

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**References**

1. (a) Bender, M. *ChemBioEng Rev.* An Overview of Industrial Processes for the Production of Olefins-C4 Hydrocarbons. **2014**, *1*, 136-147. (b) Mohr, J.; Oestreich, M. Balancing C=C Functionalization and C=O Reduction in Cu-H Catalysis. *Angew. Chem., Int. Ed.* **2016**, *55*, 12148-12149. (c) Dong, Y.; Matson, J. B.; Edgar, K. J. Olefin Cross-Metathesis in Polymer and Polysaccharide Chemistry: A Review. *Biomacromolecules* **2017**, *18*, 1661-1676. (d) Wan, J.-P.; Gao, Y.; Wei, L. Recent Advances in Transition-Metal-Free Oxygenation of Alkene C=C Double Bonds for Carbonyl Generation. *Chem. Asian J.* **2016**, *11*, 2092-2102. (e) Nolan, S. P.; Clavier, H. Chemoselective olefin metathesis transformations mediated by ruthenium complexes. *Chem. Soc. Rev.* **2010**, *39*, 3305-3316.

2. (a) Diederich, F.; Stang, P. J.; Tykwinski, R. R. *Acetylene Chemistry: Chemistry, Biology and Material Science*; Wiley-VCH: Weinheim, 2005. (b) Chinchilla, R.; Nájera, C. Chemicals from Alkynes with Palladium Catalysts. *Chem. Rev.* **2014**, *114*, 1783-1826.

3. (a) Wang, F.; Chen, P.; Liu, G. Copper-Catalyzed Radical Relay for Asymmetric Radical Transformations. *Acc. Chem. Res.* **2018**, *51*, 2036-2046. (b) Yin, G.; Mu, X.; Liu, G. Palladium(II)-Catalyzed Oxidative Difunctionalization of Alkenes: Bond Forming at a High-Valent Palladium Center. *Acc. Chem. Res.* **2016**, *49*, 2413-2423. (c) Wang, X.; Studer, A. Iodine(III) Reagents

in Radical Chemistry. *Acc. Chem. Res.* **2017**, *50*, 1712-1724. (d) Merino, E.; Nevado, C. Addition of $CF_3$ across unsaturated moieties: a powerful functionalization tool. *Chem. Soc. Rev.* **2014**, *43*, 6598-6608. (e) Charpentier, J.; Früh, N.; Togni, A. Electrophilic Trifluoromethylation by Use of Hypervalent Iodine Reagents. *Chem. Rev.* **2015**, *115*, 650-682. (f) Tang, S.; Liu, K.; Liu, C.; Lei, A. Olefinic C-H functionalization through radical alkenylation. *Chem. Soc. Rev.* **2015**, *44*, 1070-1082.

4. (a) Gao, P.; Song, X.-R.; Liu, X.-Y.; Liang, Y.-M. Recent Developments in the Trifluoromethylation of Alkynes. *Chem. Eur. J.* **2015**, *21*, 7648-7661. (b) Besset, T.; Poisson, T.; Pannecoucke, X. Direct Vicinal Difunctionalization of Alkynes: An Efficient Approach Towards the Synthesis of Highly Functionalized Fluorinated Alkenes. *Eur. J. Org. Chem.* **2015**, 2765-2789. (c) Chemler, S. R.; Bovino, M. T. Catalytic Aminohalogenation of Alkenes and Alkynes. *ACS Catal.* **2013**, *3*, 1076-1091. (d) Hartrampf, F.; Toombs-Ruane, H. Diaryliodonium Salts: Aryl Transfer Reagents for Alkyne Difunctionalization. *Aust. J. Chem.* **2015**, *68*, 699-702.

5. Difunctionalizations of $sp^2$-carbon involving $C_{sp2}$–$C_{sp3}$ or $C_{sp2}$–$C_{sp2}$ bond cleavage, see: (a) Farid, U.; Malmedy, F.; Claveau, R.; Albers, L.; Wirth, T. Stereoselective Rearrangements with Chiral Hypervalent Iodine Reagents. *Angew. Chem., Int. Ed.* **2013**, *52*, 7018-7022. (b) Guntreddi, T.; Vanjari, R.; Singh, K. N. Decarboxylative Thioamidation of Arylacetic and Cinnamic Acids: A New Approach to Thioamides. *Org. Lett.* **2014**, *16*, 3624-3627. (c) Kumar, S.; Vanjari, R.; Guntreddi, T.; Singh, K. N. Sulfur promoted decarboxylative thioamidation of carboxylic acids using formamides as amine proxy. *Tetrahedron* **2016**, *72*, 2012-2017.

6. Difunctionalizations of sp-carbon involving $C_{sp}$–$C_{sp3}$ bond cleavage, see: (a) Zhang, J.; Wang, H.; Ren, S.; Zhang, W.; Liu, Y. Cu(0)/Selectfluor System-Mediated Mild Synthesis of Fluorinated Fluorenones from Nonaromatic Precursors (1,6-Enynes) Involving C-C Single Bond Cleavage. *Org. Lett.* **2015**, *17*, 2920-2923. (b) Zhang, J.; Zhang, H.; Shi, D.; Jin, H.; Liu, Y. Facile and Diverse Synthesis of Benzo[b]fluorenone Derivatives via Copper/Selectfluor System-Catalyzed Tandem Annulation of 1,6-Enynes. *Eur. J. Org. Chem.* **2016**, 5545-5558.

7. (a) Bao, H.; Xu, Z.; Wu, D.; Zhang, H.; Jin, H.; Liu, Y. Copper(0)/Selectfluor System-Promoted Oxidative Carbon-Carbon Bond Cleavage/Annulation of o-Aryl Chalcones: An Unexpected Synthesis of 9,10-Phenanthraquinone Derivatives. *J. Org. Chem.* **2017**, *82*, 109-118. (b) Liu, L.; Du, L.; Zhang-Negrerie, D.; Du, Y.; Zhao, K.Metal-Free Tandem Oxidative Aryl Migration and C-C Bond Cleavage: Synthesis of α-Ketoamides and Esters from Acrylic Derivatives. *Org. Lett.* **2014**, *16*, 5772-5775. (c) Nielsen, T. E.; Meldal, M. Highly Efficient Solid-Phase Oxidative Cleavage of Olefins by OsO4-$NaIO_4$ in the Intramolecular N-Acyliminium Pictet-Spengler Reaction. *Org. Lett.* **2005**, *7*, 2695-2698. (d) Liu, W.; Wu, G.; Gao, W.; Ding, J.; Huang, X.; Liu, M.; Wu, H. Palladium-catalyzed oxidative C=C bond cleavage with molecular oxygen: one-pot synthesis of quinazolinones from 2-amino benzamides and alkenes. *Org. Chem. Front.* **2018**, *5*, 2734-2738. (e) Liu, L.; Gao, Z.; Xu, K.; Hui, S.; Zhao, X.; Wu, Y. Transition-metal-free cleavage of C-C double bonds: a three-component reaction of aromatic alkenes with S8 and amides towards aryl thioamides. *Org. Chem. Front.* **2018**, *5*, 3315-3318. (f) Cen, J.; Liu, J.; Zhang, Y.; Zhu, Z.; Yang, S.; Jiang, H. Direct Assembly of

4-Substituted Quinolines with Vinyl Azides as a Dual Synthon via C=C and C-N Bond Cleavage. *Org. Lett.* **2018**, *20*, 4434-4438.

8. For selected difunctionalizations of $sp^2$-carbon involving C=C bond cleavage, see: (a) Xu, K.; Li, Z.; Cheng, F.; Zuo, Z.; Wang, T.; Wang, M.; Liu, T. Transition-Metal-Free Cleavage of C-C Triple Bonds in Aromatic Alkynes with S8 and Amides Leading to Aryl Thioamides. *Org. Lett.* **2018**, *20*, 2228-2231. (b) Liu, Y.; Song, F.; Guo, S. Cleavage of a Carbon-Carbon Triple Bond via Gold-Catalyzed Cascade Cyclization/Oxidative Cleavage Reactions of (Z)-Enynols with Molecular Oxygen. *J. Am. Chem. Soc.* **2006**, *128*, 11332-11333. (c) Park, S.; Jeon, W. H.; Yong, W.-S.; Lee, P. H. Synthesis of Azulen-1-yl Ketones via Oxidative Cleavage of C-C Multiple Bonds in N-Sulfonyl Enamides and 1-Alkynes under Air and Natural Sunlight. *Org. Lett.* **2015**, *17*, 5060-5063. (d) Ni, J.; Jiang, Y.; An, Z.; Yan, R. Cleavage of C-C Bonds for the Synthesis of C2-Substituted Quinolines and Indoles by Catalyst-Controlled Tandem Annulation of 2-Vinylanilines and Alkynoates. *Org. Lett.* **2018**, *20*, 1534-1537. (e) Liu, Q.; Chen, P.; Liu, G. Palladium-Catalyzed C-C Triple Bond Cleavage: Efficient Synthesis of 4H-Benzo[d][1,3]oxazin-4-ones. *Acs Catal.* **2013**, *3*, 178-181. (f) Jiang, Q.; Zhao, A.; Xu, B.; Jia, J.; Liu, X.; Gao, C. PIFA-Mediated Esterification Reaction of Alkynes with Alcohols via Oxidative Cleavage of Carbon Triple Bonds. *J. Org. Chem.* **2014**, *79*, 2709-2715. (g) Sun, J.; Wang, F.; Hu, H.; Wang, X.; Wu, H.; Liu, Y. Copper(II)-Catalyzed Carbon-Carbon Triple Bond Cleavage of Internal Alkynes for the Synthesis of Annulated Indolizines. *J. Org. Chem.* **2014**, *79*, 3992-3998. (h) Long, Z; Yang, Y.; You, J. Rh(III)-Catalyzed [4 + 1]-Annulation of Azoxy Compounds with Alkynes:

A Regioselective Approach to 2H-Indazoles. *Org. Lett.* **2017**, *19*, 2781-2784. (i) Wang, A.; Jiang, H. Palladium-Catalyzed Cleavage Reaction of Carbon-Carbon Triple Bond with Molecular Oxygen Promoted by Lewis Acid. *J. Am. Chem. Soc.* **2008**, *130*, 5030-5031.

9. For some reviews on the carbon-carbon bond cleavage, see: (a) Fumagalli, G.; Stanton, S.; Bower, J. F. Recent Methodologies that Exploit C-C Single Bond Cleavage of Strained Ring System by Transition Metal Complexes. *Chem. Rev.* **2017**, *117*, 9404-9432, and references cited therein. (b) Souillart, L.; Cramer, N. Catalytic C-C Bond Activations via Oxidative Addition to Transition Metals. *Chem. Rev.* **2015**, *115*, 9410-9464, and refereces cited therein. (c) Jiao, N. Recent Advances in Transition-Metal-Catalyzed Functionalization of Unstrained Carbon-Carbon Bonds. *Chem. Rev.* **2014**, *114*, 8613-8661, and references cited therein.

10. (a) Bagdi, A. K.; Santra, S.; Monir, K.; Hajra, A. Synthesis of imidazo[1,2-a] Pyridines: a decade update. *Chem. Commun.* **2015**, *51*, 1555-1575. (b) Bagdi, A. K.; Hajra, A. Design, Synthesis, and Functionalization of Imidazoheterocycles. *Chem. Rec.* **2016**, *16*, 1868-1885. (c) Fisher, M. H.; Lusi, A. Imidazo[1,2-a]pyridine anthelmintic and antifungal agents. *J. Med. Chem.* **1972**, *15*, 982-985. (d) Gueiffier, A.; Lhassani, M.; Elhakmaoui, A.; Snoeck, R.; Andrei, G.; Chavignon, O.; Teulade, J.-C.; Kerbal, A.; Essassi, E. M.; Debouzy, J.-C.; Witvrouw, M.; Blache, Y.; Balzarini, J.; De Clercq, E.; Chapat, J.-P. Synthesis of Acyclo-C-nucleosides in the Imidazo[1,2-a]-pyridine and Pyrimidine Series as Antiviral Agents. *J. Med. Chem*. **1996**, *39*, 2856-2859. (e) Lhassani, M.; Chavignon, O.; Chezal, J.-M.; Teulade, J.-C.; Chapat, J.-P.; Snoeck, R.; Andrei, G.; Balzarini, J.; De Clercq, E.; Gueiffier, A.

Synthesis and antiviral activity of imidazo[1,2-a]pyridines. *Eur. J. Med. Chem.* **1999**, *34*, 271-274. (f) Hranjec, M.; Piantanida, I.; Kralj, M. Šuman, L.; Pavelić, K.; Karminski-Zamola, G. Novel Amidino-Substituted Thienyl- and Furylvinylbenzimidazole: Derivatives and Their Photochemical Conversion into Corresponding Diazacyclopenta[c]fluorenes. Synthesis, Interactions with DNA and RNA, and Antitumor Evaluation. 4. *J. Med. Chem*. **2008**, *51*, 4899-4910. (g) Hirayama, T.; Okaniwa, M.; Banno H.; Kakei, H.; Ohashi, A.; Iwai, K.; Ohori, M.; Mori, K.; Gotou, M.; Kwawamoto, T.; Yokota, A. Synthetic Studies on Centromere-Associated Protein-E (CENP-E) Inhibitors: 2. Application of Electrostatic Potential Map (EPM) and Structure-Based Modeling to Imidazo[1,2-a]pyridine Derivatives as Anti-Tumor Agents. *J. Med. Chem.* **2015**, *58*, 8036-8053.

11. (a) Amorim, E.; McDade, E. M. Rapidly-progressive catatonia responsive to zolpidem in a patient with ovarian teratoma-associated paraneoplastic encephalitis. *J. Clin. Neurosci.* **2016***, 30*, 136-138. (b) Mierzejewski, P.; Kolaczkowski, M.; Marcinkowska, M.; Wesolowska, A.; Samochowiec J.; Pawlowski, M.; Bienkowski, P. Antipsychotic-like effects of zolpidem in Wistar rats. *Eur. J. Pharmacol.* **2016**, *773*, 51-58.

12. (a) Mizushige, K.; Ueda, T.; Yukiiri, K.; Suzuki, H. Olprinone: a phosphodiesterase III inhibitor with positive inotropic and vasodilator effects. *Cardiovasc. Drug Rev.* **2002**, *20*, 163-174. (b) Yamanaka, H.; Hayashi, Y.; Kamibayashi, T.; Mashimo, T. Effect of Olprinone, a Phosphodiesterase III Inhibitor, on Balance of Cerebral Oxygen Supply and Demand During Cardiopulmonary Bypass. *J. Cardiovasc. Pharmacol.* **2011**, *57*, 579-583.

13. Almirante, L.; Polo, L.; Mugnaini, A.; Provinciali, E.; Rugarli, P.; Biancotti, A.; Gamba, A.; Murmann, W. Derivatives of imidazole. I. Synthesis and reactions of imidazo[1,2-a]pyridines with analgesic, antiinflammatory, antipyretic, and anticonvulsant activity. *J. Med. Chem.* **1965**, *8*, 305-312.

14. (a) Stasyuk, A. J.; Banasiewicz, M.; Cyrański, M. K.; Gryko. D. T. Imidazo[1,2-a]pyridines Susceptible to Excited State Intramolecular Proton Transfer: One-Pot Synthesis via an Ortoleva-King Reaction. *J. Org. Chem.* **2012**, *77*, 5552-5558. (b) Shao, N.; Pang, G.-X.; Yan, C.-X.; Shi, G.-F.; Cheng, Y. Reaction of β-Lactam Carbenes with 2-Pyridyl Isonitriles: A One-Pot Synthesis of 2-Carbonyl-3-(pyridylamino)imidazo[1,2-a]pyridines Useful as Fluorescent Probes for Mercury Ion. *J. Org. Chem*. **2011**, *76*, 7458-7465. (c) Wang, H.; Wang, Y,; Liang, D.; Liu, L.; Zhang, J.; Zhu, Q. Copper-Catalyzed Intramolecular Dehydrogenative Aminooxygenation: Direct Access to Formyl-Substituted Aromatic N-Heterocycles. *Angew. Chem. Int. Ed*. **2011**, *50*, 5678-5681.

15. Boerner, R. J.; Möller, H. J. *Depression und Angststörungen-Epidemiologie, theoretische Konzepte und Therapiemöglichkeiten bei Komorbidität*. In book Depressionsstationen/Stationäre Depressionsbehandlung: Konzepte, Erfahrungen, Möglichkeiten, heutiger Depressionsbehandlung. **1997**, pp 210-235.

16. John, A.; Shaikh, M. M.; Ghosh, P. Palladium complexes of abnormal N-heterocyclic carbenes as precatalysts for the much preferred Cu-free and amine-free Sonogashira coupling in air in a mixed-aqueous medium. *Dalton Trans.* **2009**, 10581-10591. (b) Song, G.; Zhang, Y.; Li, X. Rhodium and Iridium Complexes of Abnormal N-Heterocyclic Carbenes Derived from Imidazo[1,2-a]pyridine.

*Organometallics* **2008**, *27*, 1936-1943.

17. (a) Gudmundsson, K. S.; Drach J. C.; Townsend, L. B. Synthesis of the First C3 Ribosylated Imidazo[1,2-a]pyridine C-Nucleoside by Enantioselective Construction of the Ribose Moiety. *J. Org. Chem.* **1998**, *63*, 984-989. (b) Gudmundsson, K. S.; Williams J. D.; Drach, J. C.; Townsend, L. B. Synthesis and Antiviral Activity of Novel Erythrofuranosyl Imidazo[1,2-a]pyridine C-Nucleosides Constructed via Palladium Coupling of Iodoimidazo[1,2-a]pyridines and Dihydrofuran. *J. Med. Chem.* **2003**, *46*, 1449-1455. (c) Miller, J. F.; Chong, P. Y.; Shotwell, J. B.; Catalano, J. G.; Tai, V. W.-F.; Fang, J.; Banka, A. L.; Roberts, C. D.; Youngman, M.; Zhang, H.; Xiong, Z.; Mathis, A.; Pouliot, J. J.; Hamatake, R. K.; Price, D. J.; Seal, J. W.; Stroup, L. L.; Creech, K. L.; Carballo, L. H.; Todd, D.; Spaltenstein, A.; Furst, S.; Hong, Z.; Peat, A. J. Hepatitis C Replication Inhibitors That Target the Viral NS4B Protein. *J. Med. Chem*. **2014**, *57*, 2107-2120.

18. (a) Marhadour, S.; Bazin, M. A.; Marchand, P. An efficient access to 2,3-diarylimidazo[1,2-a]pyridines via imidazo[1,2-a]pyridin-2-yl triflate through a Suzuki cross-coupling reaction-direct arylation sequence. *Tetrahedron Lett*. **2012**, *53*, 297-300. (b) Mondal, S.; Samanta, S.; Singsardar, M.; Mishra, S.; Mitra, S.; Hajra, A. Zwitterionic-Type Molten Salt Catalyzed Iodination in Water: Synthesis of Iodoimidazoheterocycles. *Synthesis* **2016**, *48*, 4009-4015. (c) Li, J.; Tang, J.; Wu, Y.; He, Q.; Yu, Y. Transition-metal-free regioselective C–H halogenation of imidazo[1,2-a]pyridines: sodium chlorite/bromite as the halogen source. *RSC Adv.* **2018**, *8*, 5058-5062. (d) Zhao, C.; Li, F.; Yang, S.; Liu, L.; Huang, Z.; Chai, H. Chemoselective iodination of 6-substituted

imidazo[1,2-a]pyridine. *Chem. Heterocycycl. Comp.* **2018**, *54*, 568-571.

19. (a) Meng, X.; Yu, C.; Chen, G.; Zhao, P. Heterogeneous biomimetic aerobic synthesis of 3-iodoimidazo[1,2-a]pyridines via CuOx/OMS-2-catalyzed tandem cyclization/iodination and their late-stage functionalization. *Catal. Sci. Technol.* **2015**, *5*, 372-379. (b) Samanta, S.; Jana, S.; Mondal, S.; Monir, K.; Chandra, S. K.; Jajra, A. Switching the regioselectivity in the copper-catalyzed synthesis of iodoimidazo[1,2-a]pyridines. *Org. Biomol. Chem.* **2016**, *14*, 5073-5078. (c) Zhou, X.; Yan, H.; Ma, C.; He, Y.; Li, Y.; Cao, J.; Yan, R.; Huang, G. *J. Org. Chem.* Copper-Mediated Aerobic Oxidative Synthesis of 3-Bromo-imidazo[1,2-a]pyridines with Pyridines and Enamides. **2016**, *81*, 25-31. (d) Xiao, X.; Xie, Y.; Bai, S.; Deng, Y.; Jiang, H.; Zeng, W. Transition-Metal-Free Tandem Chlorocyclization of Amines with Carboxylic Acids: Access to Chloroimidazo[1,2-α]pyridines. *Org. Lett.* **2015**, *17*, 3998-4001.

20. (a) Zhang, J.; Wu, D.; Chen, X.; Liu, Y.; Xu, Z. Copper-Catalyzed Oxidative Cyclization of 1,5-Enynes with Concomitant C-C Bond Cleavage: An Unexpected Access to 3-Formyl-1-indenone Derivatives. *J. Org. Chem.* **2014**, *79*, 4799-4808. (b) Wang, H.; Ren, S.; Zhang, J.; Zhang, W.; Liu, Y. Selectfluor-Mediated Simultaneous Cleavage of C-O and C-C Bonds in α,β-Epoxy Ketones Under Transition-Metal-Free Conditions: A Route to 1,2-Diketones. *J. Org. Chem.* **2015**, *80*, 6856-6863.

21. (a) Zheng, L.; Zhou, B.; Jin, H.; Li, T.; Liu, Y. Radical-Triggered Tandem Cyclization of 1,6-Enynes with H2O: A Way to Access Strained 1H-Cyclopropa[b]naphthalene-2,7-diones. *Org. Lett.* **2018**, *20*, 7053-7056. (b) Zhou, B.; Yang, H.; Jin, H.; Liu, Y. $I_2O_5$-Mediated 1,5-Cyclization of

Aryldiynes with $H_2O$: A Way To Access 3-Acyl-1-indenone Derivatives. *J. Org. Chem.* **2019**, *84*, 2169-2177.

22. Miyamoto, K.; Tada, N.; Ochiai, M. Activated Iodosylbenzene Monomer as an Ozone Equivalent: Oxidative Cleavage of Carbon-Carbon Double Bonds in the Presence of Water. *J. Am. Chem. Soc.* **2007**, *129*, 2722-2773.

23. (a) Albéniz, A. C.; Espinet, P.; López-Fernández, R.; Sen, A. A Warning on the Use of Radical Traps as a Test for Radical Mechanisms: They React with Palladium Hydrido Complexes. *J. Am. Chem. Soc.* **2002**, *124*, 11278-11279. (b) Winterle, J. S.; Mill, T. Free-radical dynamics in organized lipid bilayers. *J. Am. Chem. Soc.* **1980**, *102*, 6336-6338.

24. Liu, Z.-Q.; Shang, X.; Chai, L.; Sheng, Q. An Atom-Efficient Catalytic Oxidation of Alcohols Using TEMPO/I2O5 in Water. *Catal. Lett.* **2008**, *123*, 317-320.

25. (a) Smith, D. K.; Pantoya, M. L.; Parkey, J. S.; Kesmez, M. The water-iodine oxide system: a revised mechanism for hydration and dehydration. *RSC Adv.* **2017**, *7*, 10183-10191. (b) Zhang, M.-Z.; Wang, X.; Gong, M.-Y.; Chen, L.; Shi, W.-B.; He, S.-H.; Jiang, Y.; Chen, T. An efficient iodine pentoxide-triggered iodocarbocyclization for the synthesis of iodooxindoles in water. *Org. Biomol. Chem.* **2018**, *16*, 5197-5202, and references cited therein.

26. (a) Chai, L.; Zhao, Y.; Sheng, Q.; Liu, Z.-Q. Aromatization of Hantzsch 1,4-dihydropyridines and 1,3,5-trisubstituted pyrazolines with HIO3 and I2O5 in water. *Tetrahedron Lett.* **2006**, 47, 9283-9285. (b) Wen, J.; Wei, W.; Xue, S.; Yang, D.; Lou, Y.; Gao, C.; Wang, H. Metal-Free Oxidative

Spirocyclization of Alkynes with Sulfonylhydrazides Leading to 3-Sulfonated Azaspiro[4,5]trienones. *J. Org. Chem.* **2015**, *80*, 4966-4972.

27. (a) Kiyokawa, K.; Ito, R.; Takemoto, K.; Minakata, S. C-H oxygenation at tertiary carbon centers using iodine oxidant. *Chem. Commun.* **2018**, *54*, 7609-7612. (b) Guo, W.; Vallcorba, O.; Vallribera, A.; Shafir, A.; Pleixats, R.; Rius, J. Oxidative Breakdown of Iodoalkanes to Catalytically Active Iodine Species: A Case Study in the α-Tosyloxylation of Ketones. *ChemCatChem* **2014**, *6*, 468-472.

28. (a) Perry, G. J. P.; Quibell, J. M.; Panigrahi, A.; Larrosa, I. T. Transition-metal-free decarboxylative iodination: New routes for decarboxylative oxidative cross-couplings. *J. Am. Chem. Soc.* **2017**, *139*, 11527-11536. (b) Uemura, S.; Tanaka, S.; Okano, M. Decarboxylative ipso halogenation of mercury(II) pyridinecarboxylates. Facile formation of 3-iodo- and 3-bromopyridines. *J. Org. Chem.* **1983**, *48*, 3297-3301.

29. Hiebel, M.; Berteina-Raboin, S. Iodine-catalyzed regioselective sulfenylation of imidazoheterocycles in PEG400. *Green Chem.* **2015**, *17*, 937-944.

30. Oehler, E.; Zbirab, E.; El-Badawi, M. A novel and versatile synthesis of heterocyclic aldehydes using dialkyl 3-oxo-1-alkenyl-phosphonates. *Tetrahedron Lett.* **1983**, *24*, 5599-5602.

31. Huo, C.; Tang, J.; Xie, H.; Wang, Y.; Dong, J. $CBr_4$ Mediated Oxidative C–N Bond Formation: Applied in the Synthesis of Imidazo[1,2-α]pyridines and Imidazo[1,2-α]pyrimidines. *Org. Lett.* **2016**, *18*, 1016-1019.

32. Abignente, E.; De Caprariis, P.; Fattorusso, E.; Mayol, L. Research on heterocyclic compounds.

XXIII. Phenyl derivatives of fused imidazole systems. *J. Heterocycl. Chem.* **1989,** *26*, 1875-1880.