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Selective synthesis of pyrrolidin-2-ones and 3-iodopyrroles *via* the ring contraction and deformylative functionalization of piperidine derivatives†

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In this paper, a selective synthesis of pyrrolidin-2-ones and 3-iodopyrroles *via* the cascade reactions of *N*-substituted piperidines is presented. Mechanistically, the formation of pyrrolidin-2-ones involves a domino process including the *in situ* formation of pyrrolidine-2-carbaldehyde followed by carboxylic acid formation, decarboxylation and *ipso*-oxidation. On the other hand, 3-iodopyrroles are believed to be formed *via* the initial generation of pyrrolidine-2-carbaldehyde followed by carboxylic acid formation, decarboxylation, dehydrogenation, iodination and aromatization. Interestingly, either pyrrolidin-2-ones or 3-iodopyrroles could be obtained selectively from the same substrates, and the selectivity was easily tuned by using a specific oxidant and additive.

Introduction

Pyrrolidin-2-ones (γ-lactams) are common structural motifs widely encountered in natural products and synthetic compounds possessing potent biological activities and diverse functional properties (Fig. 1).[1,2] In addition, pyrrolidin-2-ones are routinely used as versatile synthons in organic synthesis due to their inherently rich reactivity.[1,3] Owing to their importance, a number of synthetic approaches toward pyrrolidin-2-ones have been established, which mainly included: (1) amination and cyclization of functionalized acyclic substrates,[1,4] (2) oxidation of pyrrolidine derivatives,[5] (3) ring expansion of β-lactams[6] or cyclopropylamides,[7] *etc*.[8] Meanwhile, iodo-substituted pyrroles are highly valuable intermediates in the synthesis of drugs, dyes, pigments and other fine chemicals.[9] Traditionally, iodopyrroles are accessed either by electrophilic iodination of the existing pyrrole unit[10] or through electrophilic iodocyclization of functionalized acyclic substrates.[11] While these above-mentioned synthetic methods toward pyrrolidin-2-one and iodopyrrole derivatives are generally efficient and reliable, some of them suffer from poor regioselectivity, require multi-step preparation of the highly functionalized substrates, or employ expensive transition-metal catalysts. Therefore, the development of more selective and easy-to-run methods starting from simple and readily obtainable substrates without using precious metal catalysts is highly desirable.

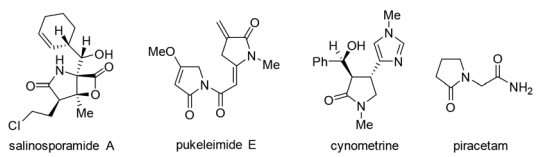

Fig. 1 Some important pyrrolidin-2-one derivatives.

Recently, direct functionalization of the inert C(sp^3)–H bond has attracted much attention owing to its elimination of substrate pre-activation and minimization of by-product formation. In particular, C(sp^3)–H bond functionalization of inactivated cyclic amines is a highly promising strategy in the preparation of diversely functionalized N-heterocyclic compounds.[12,13] In this regard, we have recently disclosed a novel synthesis of 1-phenylpyrrolidine-2-carbaldehyde (**A**, Scheme 1, (1)) through the oxidative ring contraction of 1-phenylpiperidine (**1a**) under the promotion of a combination of $Cu(OAc)_2$ with O_2 and KI.[13b] During this study, we have been trying to use Oxone[14] as a co-oxidant or DMAP as a co-additive in order to improve the yield of **A**. To our surprise, in the presence of Oxone or DMAP, the reaction of **1a** mainly afforded 1-phenyl-

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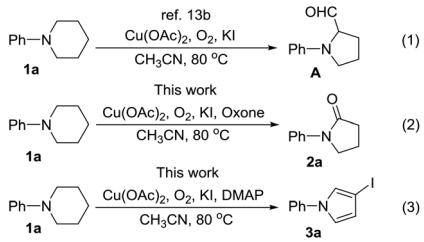
† Electronic supplementary information (ESI) available: Experimental procedure, characterization data and NMR spectra of all products, and the X-ray crystal structures and data of **3d**. CCDC 1859829. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c8ob02640h



Scheme 1 Transformations of 1-phenylpiperidine under different conditions.

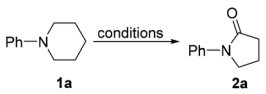
pyrrolidin-2-one (**2a**, Scheme 1, (2)) or 3-iodo-1-phenyl-1*H*-pyrrole (**3a**, Scheme 1, (3)) instead of the expected **A**.

Notwithstanding that we did not obtain our initially expected results, it occurred to us that the facile formation of pyrrolidin-2-ones and 3-iodopyrroles directly from piperidine is synthetically significant. This is not only owing to the importance of pyrrolidin-2-one and 3-iodopyrrole derivatives, but also due to the shortage of selective and sustainable synthetic methods for their preparation. Under this circumstance, we decided to carry out a systematic study of these serendipitously found transformations with the aim to develop them into efficient and reliable synthetic methods toward pyrrolidin-2-ones and 3-iodopyrroles. Herein we report the detailed results we obtained on this aspect.

Results and discussion

At the outset of our investigation, the reaction conditions for the formation of pyrrolidin-2-ones **2** were optimized by using 1-phenylpiperidine (**1a**) as the model substrate. Initially, **1a** was treated with $Cu(OAc)_2$ (1 equiv.), KI (1 equiv.) and Oxone (1 equiv.) in CH_3CN under O_2 at 80 °C for 12 h. From this reaction, 1-phenyl pyrrolidin-2-one (**2a**) was obtained in 31% yield (Table 1, entry 1). Increasing the loading of $Cu(OAc)_2$ from 1 equiv. to 2 equiv. could improve the yield of **2a** slightly (entry 2). On the other hand, reducing it from 1 equiv. to 0.5 equiv. diminished the reaction efficiency dramatically (entry 3). Our study on the suitable loading of Oxone showed that the reaction using 2 equiv. of Oxone gave the best yield of **2a** (entry 4 *vs.* 1 and 5). Next, $CuSO_4$, $CuBr_2$ and $CuCl_2$ were tried to replace $Cu(OAc)_2$. However, they were found to be much less effective compared to $Cu(OAc)_2$ (entries 6–8 *vs.* 4). When $K_2S_2O_8$, TEMPO or TBHP was used to replace Oxone as the co-oxidant, the yield of **2a** decreased significantly (entries 9–11). Next, screening of different solvents including DMF, DCE and dioxane revealed that CH_3CN is the most efficient in mediating this reaction (entries 12–14 *vs.* 4). Delightfully, increasing the loading of $Cu(OAc)_2$ from 1 equiv. to 2 equiv. in the presence of 2 equiv. of Oxone could further improve the yield of **2a** (entry 15). When the loading of KI was also increased to 2 equiv., **2a** could be obtained in a yield of 58% (entry 16). Finally, control experiments showed that in the absence of either $Cu(OAc)_2$ or Oxone the formation of **2a** was not observed (entries 17 and 18).

Table 1 Optimization study for the formation of **2a**[a]

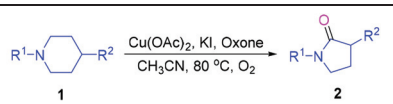


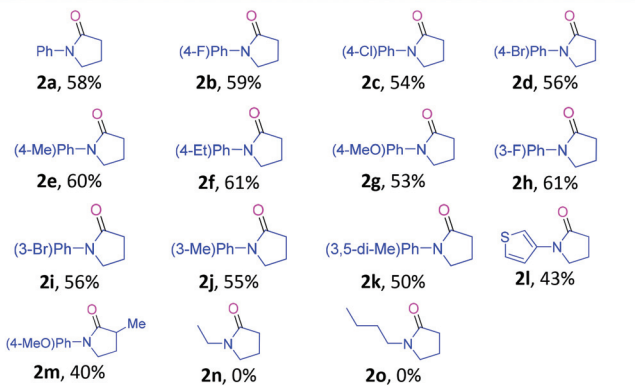
Entry	Cu(II) salt (eq.)	Co-oxidant (eq.)	Solvent	Yield[b] (%)
1	$Cu(OAc)_2$ (1)	Oxone (1)	CH_3CN	31
2	$Cu(OAc)_2$ (2)	Oxone (1)	CH_3CN	32
3	$Cu(OAc)_2$ (0.5)	Oxone (1)	CH_3CN	23
4	$Cu(OAc)_2$ (1)	Oxone (2)	CH_3CN	50
5	$Cu(OAc)_2$ (1)	Oxone (3)	CH_3CN	41
6	$CuSO_4$ (1)	Oxone (2)	CH_3CN	Trace
7	$CuBr_2$ (1)	Oxone (2)	CH_3CN	20
8	$CuCl_2$ (1)	Oxone (2)	CH_3CN	21
9	$Cu(OAc)_2$ (1)	$K_2S_2O_8$ (2)	CH_3CN	8
10	$Cu(OAc)_2$ (1)	TEMPO (2)	CH_3CN	Trace
11	$Cu(OAc)_2$ (1)	TBHP (2)	CH_3CN	Trace
12	$Cu(OAc)_2$ (1)	Oxone (2)	DMF	14
13	$Cu(OAc)_2$ (1)	Oxone (2)	DCE	13
14	$Cu(OAc)_2$ (1)	Oxone (2)	Dioxane	13
15	$Cu(OAc)_2$ (2)	Oxone (2)	CH_3CN	53
16[c]	$Cu(OAc)_2$ (2)	Oxone (2)	CH_3CN	58
17[c]	—	Oxone (2)	CH_3CN	—
18[c]	$Cu(OAc)_2$ (2)	—	CH_3CN	—

[a] Reaction conditions: **1** (0.5 mmol), KI (0.5 mmol), solvent (5 mL), 80 °C, O_2 (1 atm, balloon), 12 h. [b] Isolated yield. [c] KI (1 mmol).

With the optimum conditions established, the scope and generality of this novel transformation was studied, and the results are included in Table 2. First, a range of 1-phenylpiperidines **1** bearing different substituents on the *para*-position of the phenyl ring underwent this cascade reaction smoothly to give products **2b–2g** in yields ranging from 53–61%. Notably, a number of functional groups, from the electron-donating

Table 2 Substrate scope for the synthesis of **2**[a,b]





[a] Reaction conditions: **1** (0.5 mmol), $Cu(OAc)_2$ (1 mmol), KI (1 mmol), Oxone (1 mmol), CH_3CN (5 mL), 80 °C, O_2 (1 atm, balloon), 12 h. [b] Isolated yield.

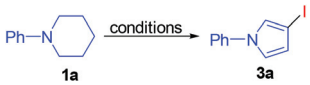
methyl, ethyl and methoxy to the electron-withdrawing fluoro and chloro, were well compatible with the reaction conditions. In addition, substrates with *meta* substitutions on the phenyl ring were also compatible with this transformation to give **2h–2k**. Interestingly, 1-(thiophen-3-yl)-piperidine was a suitable substrate to give **2l**. In addition, **1** bearing a methyl group on the *para*-position of the piperidine ring could also take part in this cascade reaction to give a 1,3-disubstituted pyrrolidin-2-one derivative **2m** in moderate yield. Unfortunately, when 1-ethylpiperidine and 1-butylpiperidine were tried as substrates for this reaction, the formation of the desired products (**2n**, **2o**) was not observed.

After having established a convenient synthesis of pyrrolidin-2-ones **2** *via* the cascade reactions of **1** under the promotion of $Cu(OAc)_2$/KI/Oxone/O_2, we then moved forward to search for the suitable reaction conditions for the efficient formation of 3-iodopyrroles **3**. Initially, **1a** was treated with $Cu(OAc)_2$ (1 equiv.), KI (1 equiv.) and DMAP (0.5 equiv.) in CH_3CN under O_2 at 80 °C for 10 h. From this reaction, 3-iodo-1-phenyl-1*H*-pyrrole (**3a**) was obtained in 30% yield (Table 3, entry 1). To our pleasure, increasing the loading of DMAP resulted in an obvious increase in the yield of **3a** (entries 2 and 3). When DMAP was replaced by triethylamine or pyridine, the formation of **3a** was not observed (entries 4 and 5). On the other hand, when KI was replaced by I_2, the yield of **3a** improved (entries 6–8). Next, $CuBr_2$, $CuCl_2$ and $CuSO_4$ were found to be much less effective compared to $Cu(OAc)_2$ (entries 9–11). When DCE, dioxane or DMSO was used as the solvent, the yield of **3a** decreased (entries 12–14). Our further optimization showed that increasing the loading of $Cu(OAc)_2$ from 1 equiv. to 2 equiv. could improve the yield of **3a** (entry 15). More promisingly, when a combination of 2 equiv. of $Cu(OAc)_2$ and 1 equiv. of I_2 was used, **3a** could be obtained in a yield of 65% (entry 16).

With the optimum reaction conditions in hand, the substrate scope for the preparation of 3-iodopyrroles **3** was explored. The results included in Table 4 demonstrated that 1-phenylpiperidines bearing either the electron-withdrawing or the electron-donating groups on the *para*-, *meta*- or *ortho*-position of the phenyl ring were well suitable for this reaction, affording 3-iodopyrrole derivatives **3b–3l** in moderate to good yields. In addition, 1-(3,5-dimethylphenyl)piperidine could also take part in this reaction to give **3m**. In another aspect, this reaction proceeded smoothly when the substrate bearing a phenyl group on the *para*-position of the piperidine ring gave 3-iodo-1,4-diphenyl-1*H*-pyrrole (**3n**). It is worth noting that the structure of **3d** was unambiguously confirmed by its X-ray single crystal diffraction analysis.[15]

To gain some insight into the reaction mechanism accounting for the formation of **2a**, the following control experiments were conducted. First, **1a** was subjected to the optimum reaction conditions (Table 1, entry 16) used for the preparation of **2** for 2 h. From the resulting mixture, **A** and **2a** were isolated in 35% and 15% yields (Scheme 2, (1)). Second, **A** was subjected to the same reaction conditions for 6 h to give **2a** in a yield of 82% (Scheme 2, (2)). These results indicated that **A** should be a key intermediate in the formation of **2a** from **1a**. Third, **A** was treated with KI and Oxone in the absence of $Cu(OAc)_2$. Under this circumstance, the formation of **2a** was not observed (Scheme 2, (3)). Fourth, **A** was treated with $Cu(OAc)_2$, KI and Oxone under nitrogen instead of oxygen. From this reaction, **2a** was formed only in a trace amount (Scheme 2, (4)). These results showed that in addition to Oxone and $Cu(OAc)_2$, O_2 is also indispensable for the efficient formation of **2a** from **A**.

Table 3 Optimization study for the formation of **3a**[a]

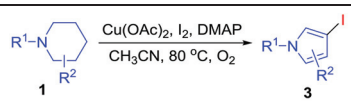


1a **3a**

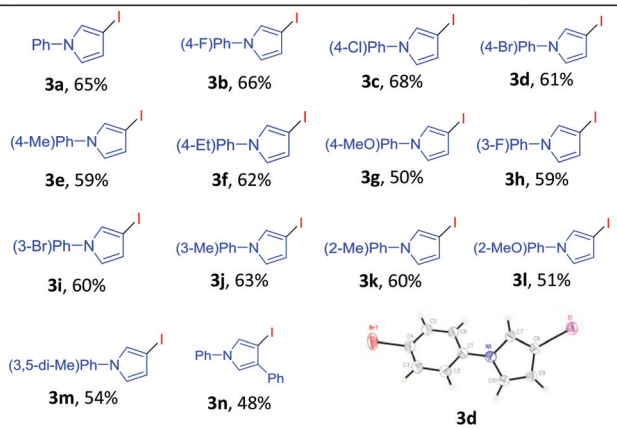
Entry	Cu(II) salt (eq.)	Additive 1 (eq.)	Additive 2 (eq.)	Solvent	Yield[b] (%)
1	$Cu(OAc)_2$ (1)	KI (1)	DMAP (0.5)	CH_3CN	30
2	$Cu(OAc)_2$ (1)	KI (1)	DMAP (1)	CH_3CN	40
3	$Cu(OAc)_2$ (1)	KI (1)	DMAP (2)	CH_3CN	39
4	$Cu(OAc)_2$ (1)	KI (1)	Et_3N (1)	CH_3CN	—
5	$Cu(OAc)_2$ (1)	KI (1)	Pyridine (1)	CH_3CN	—
6	$Cu(OAc)_2$ (1)	I_2 (0.5)	DMAP (1)	CH_3CN	51
7	$Cu(OAc)_2$ (1)	I_2 (0.25)	DMAP (1)	CH_3CN	25
8	$Cu(OAc)_2$ (1)	I_2 (1)	DMAP (1)	CH_3CN	45
9	$CuBr_2$ (1)	I_2 (0.5)	DMAP (1)	CH_3CN	Trace
10	$CuCl_2$ (1)	I_2 (0.5)	DMAP (1)	CH_3CN	Trace
11	$CuSO_4$ (1)	I_2 (0.5)	DMAP (1)	CH_3CN	10
12	$Cu(OAc)_2$ (1)	I_2 (0.5)	DMAP (1)	DCE	13
13	$Cu(OAc)_2$ (1)	I_2 (0.5)	DMAP (1)	Dioxane	15
14	$Cu(OAc)_2$ (1)	I_2 (0.5)	DMAP (1)	DMSO	17
15	$Cu(OAc)_2$ (2)	I_2 (0.5)	DMAP (1)	CH_3CN	57
16	$Cu(OAc)_2$ (2)	I_2 (1)	DMAP (1)	CH_3CN	65

[a] Reaction conditions: **1a** (0.5 mmol), solvent (5 mL), 80 °C, O_2 (1 atm, balloon), 10 h. [b] Isolated yield.

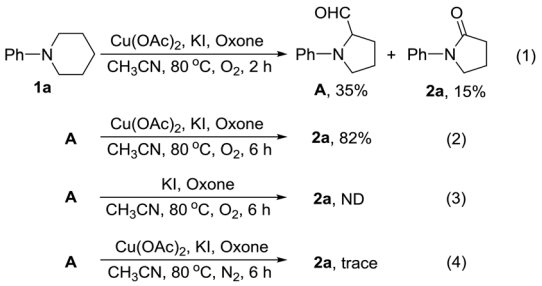
Table 4 Substrate scope for the synthesis of **3**[a,b]



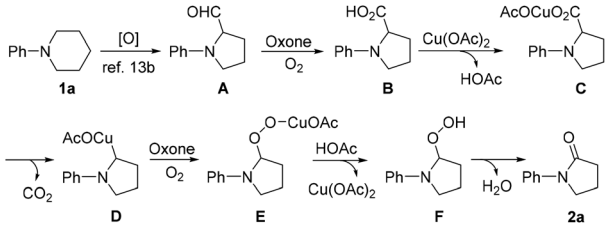
1 **3**



[a] Reaction conditions: **1** (0.5 mmol), $Cu(OAc)_2$ (1 mmol), I_2 (0.5 mmol), DMAP (0.5 mmol), CH_3CN (5 mL), 80 °C, O_2 (1 atm, balloon), 10 h. [b] Isolated yield.



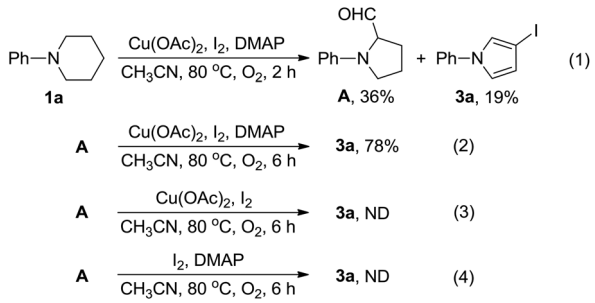
Scheme 2 Control experiments (I).



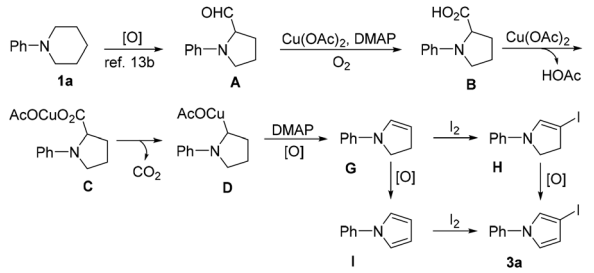
Scheme 3 Plausible mechanism accounting for the formation of **2a**.

Based on our experimental results and literature reports, a plausible pathway accounting for the formation of **2a** is proposed in Scheme 3. Initially, an oxidative ring contraction occurs with **1a** to give **A**,[13b] which is then oxidized by Oxone/O_2 to give intermediate **B**.[14] Next, **B** undergoes a decarboxylation and *ipso*-oxidation under the reaction conditions to give **2a**, presumably *via* the formation of intermediates **C**, **D**, **E** and **F**.[16] As for the role played by KI, it is postulated that it might be firstly converted into I_2, which can activate the C–N bond of **1a**, and thus facilitate the C–N bond cleavage to give **A**.[13b]

To elucidate the reaction mechanism accounting for the formation of **3a**, another set of control experiments were carried out. First, **1a** was subjected to the optimum reaction conditions (Table 3, entry 16) used for the preparation of **3** for 2 h. From the resulting mixture, **A** and **3a** were isolated in 36% and 19% yields (Scheme 4, (1)). Second, **A** was subjected to the same reaction conditions for 6 h to give **3a** in a yield of 78% (Scheme 4, (2)). These results indicated that **A**



Scheme 4 Control experiments (II).

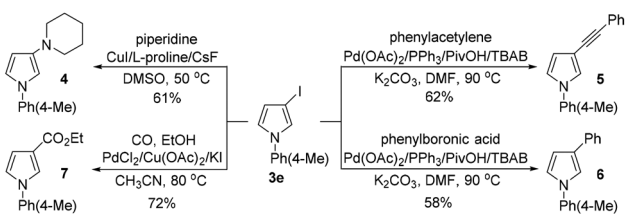


Scheme 5 Plausible mechanism accounting for the formation of **3a**.

should be a key intermediate in the formation of **3a** from **1a**. Third, **A** was treated with $Cu(OAc)_2$ and I_2 in the absence of DMAP. Under this circumstance, the formation of **3a** was not observed (Scheme 4, (3)). Fourth, **A** was treated with I_2 and DMAP but in the absence of $Cu(OAc)_2$. From this reaction, the formation of **3a** was not observed (Scheme 4, (4)). These results showed that the presence of DMAP and Cu $(OAc)_2$ is indispensable for the formation of **3a** from intermediate **A**.

Based on the above-described control experiments and literature reports, a plausible pathway accounting for the formation of **3a** from **1a** is proposed in Scheme 5. Initially, **A** is formed through an oxidative ring contraction of **1a**,[13b] and then oxidized by Cu(II)/O_2/DMAP to give **B**. The following decarboxylation and dehydrogenation of **B** under the reaction conditions afforded dihydropyrrole **G**. Since the *in situ* formed enamine moiety in intermediate **G** is nucleophilic on the β-position, it then undergoes a regioselective iodination with I_2 to give **H**. Finally, an oxidative aromatization occurs with **H** to give **3a**. As for the role played by DMAP, it is postulated that it may help to facilitate this cascade reaction by activating the Cu(II) catalyst through coordination[17] and promoting the dehydrogenation of **D** to form **G** *via* hydrogen abstraction.[18,19] Alternatively, **G** may be firstly oxidized to give **I**, which is then iodinated to give **3a**.

To showcase the utility of the 3-iodopyrroles obtained above, **3e** was reacted with piperidine, phenylacetylene and phenylboronic acid under different reaction conditions to give diversely functionalized pyrrole derivatives **4**, **5**, and **6** in moderate yields (Scheme 6). Interestingly, a Pd-catalyzed carbonylation and esterification of **3e** with CO and ethanol proceeded smoothly to give pyrrole-3-carboxylate **7** in 72% yield (Scheme 6).



Scheme 6 Structural elaboration of **3e**.

Conclusions

In summary, we have developed a novel and selective synthesis of pyrrolidin-2-one and 3-iodopyrrole derivatives *via* the cascade reactions of piperidine derivatives under different conditions. To the best of our knowledge, this is the first example in which pyrrolidin-2-ones and 3-iodopyrroles were directly and selectively synthesized from inactivated cyclic amines featuring with an oxidative ring contraction and deformylative functionalization. The use of simple and inactivated cyclic amines as the substrates, air-stable and low-cost copper salt as the promoter, non-poisonous and cost-effective Oxone as the oxidant and DMAP as the additive makes this approach an attractive and practical method for the preparation of the title compounds. A further study on the detailed reaction mechanism and application of these methods is in progress.

Experimental section

Typical procedure for the synthesis of 2a

A tube containing 1-phenylpiperidine (**1a**, 81 mg, 0.5 mmol), $Cu(OAc)_2$ (181 mg, 1 mmol), KI (166 mg, 1 mmol) and Oxone (615 mg, 1 mmol) was evacuated and back-filled with O_2 three times. Then, CH_3CN (5 mL) was added, and the mixture was stirred at 80 °C under O_2 (balloon) for 12 h. Upon completion, it was quenched with saturated brine, and extracted with EtOAc (10 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (3 : 1) as the eluent to give **2a** in 58% yield. **2b–2m** were obtained in a similar manner.

1-Phenylpyrrolidin-2-one (2a).[7] White solid (47 mg, 58%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.09 (quint, J = 7.8 Hz, 2H), 2.54 (t, J = 7.8 Hz, 2H), 3.80 (t, J = 7.2 Hz, 2H), 7.07 (t, J = 7.2 Hz, 1H), 7.30 (t, J = 7.8 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 18.1, 32.8, 48.8, 120.0, 124.5, 128.8, 139.4, 174.2. HRMS calcd for $C_{10}H_{11}NNaO$: 184.0733 $[M + Na]^+$, found: 184.0735.

1-(4-Fluorophenyl)pyrrolidin-2-one (2b).[8c] White solid (53 mg, 59%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.10 (quint, J = 7.8 Hz, 2H), 2.53 (t, J = 7.8 Hz, 2H), 3.77 (t, J = 7.2 Hz, 2H), 6.98 (t, J = 8.4 Hz, 2H), 7.48–7.51 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 18.0, 32.5, 49.0, 115.5 (d, $^2J_{C-F}$ = 21.9 Hz), 121.7 (d, $^3J_{C-F}$ = 7.7 Hz), 135.5 (d, $^4J_{C-F}$ = 2.3 Hz), 159.5 (d, $^1J_{C-F}$ = 242.7 Hz), 174.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ −117.77. HRMS calcd for $C_{10}H_{11}FNO$: 180.0819 $[M + H]^+$, found: 180.0818.

1-(4-Chlorophenyl)pyrrolidin-2-one (2c).[8c] White solid (53 mg, 54%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.10 (quint, J = 7.8 Hz, 2H), 2.54 (t, J = 7.8 Hz, 2H), 3.77 (t, J = 7.2 Hz, 2H), 7.25 (d, J = 9.0 Hz, 2H), 7.50 (d, J = 9.0 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.9, 32.7, 48.7, 121.0, 128.8, 129.6, 138.0, 174.3. HRMS calcd for $C_{10}H_{11}ClNO$: 196.0524 $[M + H]^+$, found: 196.0527.

1-(4-Bromophenyl)pyrrolidin-2-one (2d).[8b] White solid (67 mg, 56%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.10 (quint, J = 7.8 Hz, 2H), 2.54 (t, J = 7.8 Hz, 2H), 3.77 (t, J = 7.2 Hz, 2H), 7.40 (d, J = 9.0 Hz, 2H), 7.45 (d, J = 9.0 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.9, 32.7, 48.6, 117.3, 121.3, 131.8, 138.5, 174.2. HRMS calcd for $C_{10}H_{10}BrNNaO$: 261.9838 $[M + Na]^+$, found: 261.9841.

1-(*p*-Tolyl)pyrrolidin-2-one (2e).[7] White solid (53 mg, 60%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.08 (quint, J = 7.8 Hz, 2H), 2.25 (s, 3H), 2.53 (t, J = 7.8 Hz, 2H), 3.77 (t, J = 7.2 Hz, 2H), 7.09 (d, J = 7.8 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 18.1, 20.9, 32.7, 49.0, 120.2, 129.4, 134.3, 136.9, 174.2. HRMS calcd for $C_{11}H_{14}NO$: 176.1070 $[M + H]^+$, found: 176.1064.

1-(4-Ethylphenyl)pyrrolidin-2-one (2f).[20] White solid (58 mg, 61%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.15 (t, J = 7.8 Hz, 3H), 2.09 (quint, J = 7.8 Hz, 2H), 2.52–2.57 (m, 4H), 3.78 (t, J = 7.2 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 9.0 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 15.7, 18.1, 28.3, 32.7, 49.1, 120.3, 128.2, 137.0, 140.8, 174.2. HRMS calcd for $C_{12}H_{15}NNaO$: 212.1046 $[M + Na]^+$, found: 212.1043.

1-(4-Methoxyphenyl)pyrrolidin-2-one (2g).[8c] White solid (51 mg, 53%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.08 (quint, J = 7.8 Hz, 2H), 2.52 (t, J = 7.8 Hz, 2H), 3.73 (s, 3H), 3.75 (t, J = 7.2 Hz, 2H), 6.83 (d, J = 9.0 Hz, 2H), 7.42 (d, J = 9.0 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 18.0, 32.5, 49.2, 55.5, 114.1, 121.9, 132.6, 156.6, 174.0. HRMS calcd for $C_{11}H_{14}NO_2$: 192.1019 $[M + H]^+$, found: 192.1018.

1-(3-Fluorophenyl)pyrrolidin-2-one (2h).[7] White solid (55 mg, 61%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.11–2.19 (m, 2H), 2.58–2.62 (m, 2H), 3.80–3.84 (m, 2H), 6.80–6.85 (m, 1H), 7.28–7.31 (m, 2H), 7.52–7.56 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.7, 32.8, 48.6, 107.1 (d, $^2J_{C-F}$ = 26.3 Hz), 111.0 (d, $^2J_{C-F}$ = 21.9 Hz), 114.7 (d, $^4J_{C-F}$ = 3.2 Hz), 129.9 (d, $^3J_{C-F}$ = 8.4 Hz), 141.0 (d, $^3J_{C-F}$ = 9.9 Hz), 162.8 (d, $^1J_{C-F}$ = 242.9 Hz), 174.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ −92.23. HRMS calcd for $C_{10}H_{11}FNO$: 180.0819 $[M + H]^+$, found: 180.0816.

1-(3-Bromophenyl)pyrrolidin-2-one (2i).[8c] White solid (67 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11 (quint, J = 7.6 Hz, 2H), 2.55 (t, J = 7.6 Hz, 2H), 3.77 (t, J = 7.2 Hz, 2H), 7.14–7.21 (m, 2H), 7.54 (d, J = 8.0 Hz, 1H), 7.73 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.9, 32.7, 48.6, 118.2, 122.5, 122.6, 127.3, 130.1, 140.7, 174.4. HRMS calcd for $C_{10}H_{11}BrNO$: 240.0019 $[M + H]^+$, found: 240.0019.

1-(*m*-Tolyl)pyrrolidin-2-one (2j).[21] White solid (48 mg, 55%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.09 (quint, J = 7.8 Hz, 2H), 2.29 (s, 3H), 2.54 (t, J = 7.8 Hz, 2H), 3.79 (t, J = 7.2 Hz, 2H), 6.90 (d, J = 7.8 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 7.29 (d, J = 8.4 Hz, 1H), 7.36 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 18.1, 21.6, 32.8, 49.1, 117.4, 121.0, 125.6, 128.7, 138.7, 139.3, 174.3. HRMS calcd for $C_{11}H_{13}NNaO$: 198.0889 $[M + Na]^+$, found: 198.0881.

1-(3,5-Dimethylphenyl)pyrrolidin-2-one (2k).[22] White solid (47 mg, 50%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.07 (quint, J = 7.8 Hz, 2H), 2.25 (s, 6H), 2.52 (t, J = 7.8 Hz, 2H), 3.76 (t, J = 7.2 Hz, 2H), 6.73 (s, 1H), 7.14 (s, 2H). ^{13}C NMR (150 MHz,

$CDCl_3$) δ 18.1, 21.5, 32.8, 49.1, 118.1, 126.4, 138.5, 139.3, 174.2. HRMS calcd for $C_{12}H_{15}NNaO$: 212.1046 $[M + Na]^+$, found: 212.1040.

1-(Thiophen-3-yl)pyrrolidin-2-one (2l).[8c] White solid (36 mg, 43%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.12 (quint, J = 7.8 Hz, 2H), 2.52 (t, J = 7.8 Hz, 2H), 3.78 (t, J = 7.2 Hz, 2H), 7.19–7.21 (m, 2H), 7.45 (d, J = 3.6 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 18.0, 32.0, 48.9, 108.9, 120.4, 124.8, 138.0, 173.1. HRMS calcd for C_8H_9NNaOS: 190.0297 $[M + Na]^+$, found: 190.0299.

1-(4-Methoxyphenyl)-3-methylpyrrolidin-2-one (2m).[23] White solid (41 mg, 40%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.29 (d, J = 7.2 Hz, 3H), 1.74–1.78 (m, 1H), 2.34–2.37 (m, 1H), 2.63–2.67 (m, 1H), 3.70–3.76 (m, 2H), 3.80 (s, 3H), 6.90 (dd, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 2H), 7.52 (dd, J_1 = 7.2 Hz, J_2 = 2.4 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 16.3, 27.1, 38.1, 47.0, 55.5, 114.0, 121.5, 133.0, 156.4, 176.4. HRMS calcd for $C_{12}H_{15}NNaO_2$: 228.0995 $[M + Na]^+$, found: 228.0996.

Typical procedure for the synthesis of 3a

A tube containing 1-phenylpiperidine (**1a**, 81 mg, 0.5 mmol), $Cu(OAc)_2$ (181 mg, 1 mmol), I_2 (127 mg, 0.5 mmol) and DMAP (61 mg, 0.5 mmol) was evacuated and back-filled with O_2 three times. Then, CH_3CN (5 mL) was added, and the mixture was stirred at 80 °C under O_2 (balloon) for 10 h. Upon completion, it was quenched with saturated ammonium chloride (5 mL), and extracted with EtOAc (10 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (100 : 1) as the eluent to give **3a** in 65% yield. **3b–3n** were obtained in a similar manner.

3-Iodo-1-phenyl-1*H*-pyrrole (3a).[13b] Syrup (87 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.42 (t, J = 1.2 Hz, 1H), 6.96 (t, J = 2.0 Hz, 1H), 7.13 (t, J = 2.0 Hz, 1H), 7.28 (t, J = 7.2 Hz, 1H), 7.34 (d, J = 7.6 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.0, 117.6, 120.6, 121.2, 124.2, 126.4, 129.7, 139.9. MS (EI): 269 $[M]^+$. HRMS (APCI) calcd for $C_{10}H_9IN$: 269.9774 $[M + H]^+$, found: 269.9760.

1-(4-Fluorophenyl)-3-iodo-1*H*-pyrrole (3b). Brown solid (95 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.33 (d, J = 1.6 Hz, 1H), 6.80 (t, J = 2.4 Hz, 1H), 6.97 (s, 1H), 7.02–7.06 (m, 2H), 7.20–7.23 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 62.0, 116.5 (d, $^2J_{C-F}$ = 23.1 Hz), 117.7, 121.5, 122.5 (d, $^3J_{C-F}$ = 8.9 Hz), 124.5, 136.3 (d, $^4J_{C-F}$ = 2.3 Hz), 161.0 (d, $^1J_{C-F}$ = 245.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −115.78. MS (EI): 287 $[M]^+$. HRMS (APCI) calcd for $C_{10}H_8FIN$: 287.9680 $[M + H]^+$, found: 287.9687.

1-(4-Chlorophenyl)-3-iodo-1*H*-pyrrole (3c). Syrup (103 mg, 68%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.42 (d, J = 0.6 Hz, 1H), 6.91 (t, J = 2.4 Hz, 1H), 7.08 (s, 1H), 7.27 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 9.0 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 62.5, 118.0, 121.1, 121.7, 124.1, 129.8, 131.9, 138.4. MS (EI): 303, 305 $[M]^+$. HRMS (APCI) calcd for $C_{10}H_8ClIN$: 303.9385 $[M + H]^+$, found: 303.9393.

1-(4-Bromophenyl)-3-iodo-1*H*-pyrrole (3d). Syrup (106 mg, 61%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.42 (s, 1H), 6.91 (s, 1H), 7.09 (s, 1H), 7.21 (d, J = 7.2 Hz, 2H), 7.54 (d, J = 7.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.6, 118.1, 119.5, 121.0, 122.0, 124.0, 132.8, 138.8. MS (EI): 347, 349 $[M]^+$. HRMS (APCI) calcd for $C_{10}H_8BrIN$: 347.8879 $[M + H]^+$, found: 347.8886.

3-Iodo-1-(*p*-tolyl)-1*H*-pyrrole (3e). Syrup (83 mg, 59%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.37 (s, 3H), 6.39 (dd, J_1 = 3.0 Hz, J_2 = 1.2 Hz, 1H), 6.91 (t, J = 2.4 Hz, 1H), 7.08 (d, J = 1.8 Hz, 1H), 7.22 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 61.5, 117.3, 120.5, 121.3, 124.2, 130.2, 136.2, 137.6. MS (EI): 283 $[M]^+$. HRMS (APCI) calcd for $C_{11}H_{11}IN$: 283.9931 $[M + H]^+$, found: 283.9940.

1-(4-Ethylphenyl)-3-iodo-1*H*-pyrrole (3f). Syrup (92 mg, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.25 (t, J = 7.8 Hz, 3H), 2.67 (q, J = 7.8 Hz, 2H), 6.40 (t, J = 1.8 Hz, 1H), 6.92 (d, J = 2.4 Hz, 1H), 7.09 (s, 1H), 7.24 (s, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 15.6, 28.3, 61.5, 117.3, 120.7, 121.3, 124.3, 129.0, 137.8, 142.6. MS (EI): 297 $[M]^+$. HRMS (APCI) calcd for $C_{12}H_{13}IN$: 298.0087 $[M + H]^+$, found: 298.0100.

3-Iodo-1-(4-methoxyphenyl)-1*H*-pyrrole (3g). Syrup (75 mg, 50%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.76 (s, 3H), 6.32 (dd, J_1 = 3.0 Hz, J_2 = 1.2 Hz, 1H), 6.79 (t, J = 2.4 Hz, 1H), 6.87 (dd, J_1 = 6.6 Hz, J_2 = 1.8 Hz, 2H), 6.96 (t, J = 1.8 Hz, 1H), 7.18 (d, J = 6.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.6, 61.1, 114.7, 117.1, 121.6, 122.3, 124.5, 133.6, 158.2. MS (EI): 299 $[M]^+$. HRMS (APCI) calcd for $C_{11}H_{11}INO$: 299.9880 $[M + H]^+$, found: 299.9883.

1-(3-Fluorophenyl)-3-iodo-1*H*-pyrrole (3h). Syrup (85 mg, 59%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.43 (s, 1H), 6.95–6.99 (m, 2H), 7.06 (d, J = 9.6 Hz, 1H), 7.13–7.14 (m, 2H), 7.37–7.41 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 62.7, 107.9 (d, $^2J_{C-F}$ = 25.2 Hz), 113.1 (d, $^2J_{C-F}$ = 20.9 Hz), 115.8 (d, $^4J_{C-F}$ = 3.3 Hz), 118.1, 121.0, 124.1, 131.0 (d, $^3J_{C-F}$ = 9.9 Hz), 141.2 (d, $^3J_{C-F}$ = 9.9 Hz), 163.3 (d, $^1J_{C-F}$ = 246.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −110.55. MS (EI): 287 $[M]^+$. HRMS (APCI) calcd for $C_{10}H_8FIN$: 287.9680 $[M + H]^+$, found: 287.9674.

1-(3-Bromophenyl)-3-iodo-1*H*-pyrrole (3i). Syrup (104 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (s, 1H), 6.86 (t, J = 2.4 Hz, 1H), 7.04 (s, 1H), 7.19–7.23 (m, 2H), 7.32–7.34 (m, 1H), 7.44 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.8, 118.2, 118.9, 121.0, 123.2, 123.6, 124.0, 129.3, 131.0, 140.9. MS (EI): 347 349 $[M]^+$. HRMS (APCI) calcd for $C_{10}H_8BrIN$: 347.8879 $[M + H]^+$, found: 347.8877.

3-Iodo-1-(*m*-tolyl)-1*H*-pyrrole (3j). Syrup (89 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H), 6.32 (s, 1H), 6.85 (s, 1H), 7.00 (d, J = 7.2 Hz, 1H), 7.03–7.06 (m, 3H), 7.21 (t, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 61.8, 117.4, 117.7, 121.2, 121.3, 124.2, 127.1, 129.5, 139.8, 139.9. MS (EI): 283 $[M]^+$. HRMS (APCI) calcd for $C_{11}H_{11}IN$: 283.9931 $[M + H]^+$, found: 283.9909.

3-Iodo-1-(*o*-tolyl)-1*H*-pyrrole (3k). Syrup (85 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 3H), 6.31 (t, J = 2.4 Hz, 1H), 6.59 (t, J = 2.4 Hz, 1H), 6.76 (t, J = 2.0 Hz, 1H), 7.12–7.13 (m, 1H), 7.15–7.23 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.7, 60.1, 116.2, 123.9, 126.6, 126.7, 128.1, 131.2, 133.8, 139.7. MS (EI): 283 $[M]^+$. HRMS (APCI) calcd for $C_{11}H_{11}IN$: 283.9931 $[M + H]^+$, found: 283.9903.

3-Iodo-1-(2-methoxyphenyl)-1*H*-pyrrole (3l). Syrup (76 mg, 51%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.77 (s, 3H), 6.30 (s, 1H),

6.79 (t, J = 2.4 Hz, 1H), 6.92–6.96 (m, 3H), 7.16–7.18 (m, 1H), 7.20–7.23 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.8, 60.4, 112.3, 116.1, 121.0, 123.9, 125.6, 126.7, 128.1, 129.3, 152.6. MS (EI): 299 $[M]^+$. HRMS (APCI) calcd for $C_{11}H_{11}INO$: 299.9880 $[M + H]^+$, found: 299.9877.

1-(3,5-Dimethylphenyl)-3-iodo-1*H*-pyrrole (3m). Syrup (81 mg, 54%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.35 (s, 6H), 6.39 (s, 1H), 6.91–6.95 (m, 4H), 7.10 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 61.5, 117.2, 118.4, 121.2, 124.2, 128.0, 139.5, 139.9. MS (EI): 297 $[M]^+$. HRMS (APCI) calcd for $C_{12}H_{13}IN$: 298.0087 $[M + H]^+$, found: 298.0079.

3-Iodo-1,4-diphenyl-1*H*-pyrrole (3n). Syrup (83 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.55 (d, J = 3.2 Hz, 1H), 7.16 (d, J = 3.2 Hz, 1H), 7.27–7.32 (m, 1H), 7.39–7.51 (m, 7H), 7.60–7.63 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.9, 111.6, 126.57, 126.62, 127.4, 128.16, 128.24, 128.5, 128.9, 132.1, 136.4, 141.3. MS (EI): 345 $[M]^+$. HRMS (APCI) calcd for $C_{16}H_{13}IN$: 346.0087 $[M + H]^+$, found: 346.0052.

Synthetic applications of 3e

Synthesis of 1-(1-(*p*-tolyl)-1*H*-pyrrol-3-yl)piperidine (4) and its spectroscopic data. A tube containing **3e** (141 mg, 0.5 mmol), CuI (9.5 mg, 0.05 mmol), L-proline (5.8 mg, 0.05 mmol) and CsF (152 mg, 1 mmol) was evacuated and back-filled with N_2 three times. Then, piperidine (85 mg, 1 mmol) and DMSO (5 mL) were added. The resulting mixture was stirred at 50 °C under N_2 for 24 h. Upon completion, it was quenched with saturated brine (5 mL), and extracted with EtOAc (10 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (20 : 1) as the eluent to give **4** in 61% yield.

1-(1-(p-Tolyl)-1H-pyrrol-3-yl)piperidine (4). Yellow oil (73 mg, 61%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.45–1.49 (m, 2H), 1.63–1.67 (m, 4H), 2.27 (s, 3H), 2.88 (t, J = 5.4 Hz, 4H), 6.02 (t, J = 2.4 Hz, 1H), 6.46 (t, J = 1.8 Hz, 1H), 6.85 (t, J = 2.4 Hz, 1H), 7.10 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 8.4 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.8, 24.2, 25.7, 52.1, 101.9, 103.4, 118.1, 119.4, 130.0, 134.3, 138.7, 142.5. HRMS calcd for $C_{16}H_{20}N_2Na$: 263.1519 $[M + Na]^+$, found: 263.1521.

Synthesis of 3-(phenylethynyl)-1-(*p*-tolyl)-1*H*-pyrrole (5) and its spectroscopic data. A tube containing **3e** (141 mg, 0.5 mmol), phenylacetylene (153 mg, 1.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), PivOH (51 mg, 0.5 mmol), PPh_3 (13 mg, 0.05 mmol), TBAB (161 mg, 0.5 mmol) and K_2CO_3 (69 mg, 0.5 mmol) was evacuated and back-filled with N_2 three times. Then, DMF (5 mL) was added, and the resulting mixture was stirred at 90 °C under N_2 for 20 h. Upon completion, it was quenched with saturated sodium hydrogen carbonate (5 mL), and extracted with EtOAc (10 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (50 : 1) as the eluent to give **5** in 62% yield.

3-(Phenylethynyl)-1-(p-tolyl)-1H-pyrrole (5). Brown solid (80 mg, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.31 (s, 3H), 6.41 (dd, J_1 = 3.0 Hz, J_2 = 1.2 Hz, 1H), 6.90 (t, J = 2.4 Hz, 1H), 7.15–7.26 (m, 8H), 7.42–7.43 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.9, 84.6, 88.5, 106.2, 113.6, 119.8, 120.6, 123.2, 124.1, 127.6, 128.3, 130.2, 131.3, 136.1, 137.8. HRMS calcd for $C_{19}H_{15}NNa$: 280.1097 $[M + Na]^+$, found: 280.1097.

Synthesis of 3-phenyl-1-(*p*-tolyl)-1*H*-pyrrole (6) and its spectroscopic data. A tube containing **3e** (141 mg, 0.5 mmol), phenylboronic acid (183 mg, 1.5 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), PivOH (51 mg, 0.5 mmol), PPh_3 (13 mg, 0.05 mmol), TBAB (161 mg, 0.5 mmol) and K_2CO_3 (69 mg, 0.5 mmol) was evacuated and back-filled with N_2 three times. Then DMF (5 mL) was added, and the resulting mixture was stirred at 90 °C under N_2 for 20 h. Upon completion, it was quenched with saturated sodium hydrogen carbonate (5 mL), and extracted with EtOAc (10 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (100 : 1) as the eluent to give **6** in 58% yield.

3-Phenyl-1-(p-tolyl)-1H-pyrrole (6). Yellow oil (68 mg, 58%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.28 (s, 3H), 6.27 (t, J = 3.6 Hz, 1H), 6.35 (dd, J_1 = 3.6 Hz, J_2 = 1.8 Hz, 1H), 6.84 (dd, J_1 = 2.4 Hz, J_2 = 1.8 Hz, 1H), 6.97–6.99 (m, 2H), 7.03–7.05 (m, 2H), 7.06–7.09 (m, 3H), 7.12–7.14 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.0, 109.0, 110.4, 124.5, 125.6, 126.2, 128.0, 128.3, 129.6, 133.1, 133.8, 136.4, 138.1. HRMS calcd for $C_{17}H_{16}N$: 234.1277 $[M + H]^+$, found: 234.1270.

Synthesis of ethyl 1-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (7) and its spectroscopic data. A tube containing **3e** (141 mg, 0.5 mmol), $PdCl_2$ (8.9 mg, 0.05 mmol), $Cu(OAc)_2$ (91 mg, 0.5 mmol), and KI (83 mg, 0.5 mmol) was evacuated and back-filled with CO three times. Then EtOH (292 μL, 5 mmol) and CH_3CN (5 mL) were added, and the resulting mixture was stirred at 80 °C under CO (balloon) for 12 h. Upon completion, it was quenched with saturated brine (5 mL), and extracted with EtOAc (10 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (50 : 1) as the eluent to give **7** in 72% yield.

Ethyl 1-(p-tolyl)-1H-pyrrole-3-carboxylate (7).[13a] Yellow oil (82 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.28 (t, J = 7.2 Hz, 3H), 2.31 (s, 3H), 4.23 (q, J = 7.2 Hz, 2H), 6.67 (s, 1H), 6.90 (s, 1H), 7.17 (d, J = 7.8 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 7.58 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 20.9, 59.8, 111.4, 118.0, 120.6, 120.9, 124.4, 130.2, 136.8, 137.6, 164.8. HRMS calcd for $C_{14}H_{15}NNaO_2$: 252.0995 $[M + Na]^+$, found: 252.0998.

Control experiments

Control experiment (I). A tube containing 1-phenylpiperidine (**1a**, 81 mg, 0.5 mmol), $Cu(OAc)_2$ (181 mg, 1 mmol), KI (166 mg, 1 mmol) and Oxone (615 mg, 1 mmol) was evacuated and back-filled with O_2 three times. Then, CH_3CN (5 mL) was added, and the mixture was stirred at 80 °C under O_2 (balloon)

for 2 h. It was quenched with saturated brine, and extracted with EtOAc (10 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (20 : 1 to 3 : 1) as the eluent to give **A** and **2a** in 35% and 15% yields, respectively.

*1-Phenylpyrrolidine-2-carbaldehyde (**A**).*[13b] Oil (31 mg, 35%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.96–2.01 (m, 2H), 2.09–2.14 (m, 2H), 3.26–3.32 (m, 1H), 3.56–3.62 (m, 1H), 3.95–3.99 (m, 1H), 6.52 (d, J = 8.0 Hz, 2H), 6.69 (t, J = 7.2 Hz, 1H), 7.14–7.18 (m, 2H), 9.47 (d, J = 3.6 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 23.4, 27.2, 48.1, 65.9, 111.1, 116.3, 128.4, 146.1, 202.6. HRMS calcd for $C_{11}H_{14}NO$: 176.1070 $[M + H]^+$, found: 176.1070.

A tube containing **A** (88 mg, 0.5 mmol), $Cu(OAc)_2$ (181 mg, 1 mmol), KI (166 mg, 1 mmol) and Oxone (615 mg, 1 mmol) was evacuated and back-filled with O_2 three times. Then CH_3CN (5 mL) was added, and the mixture was stirred at 80 °C under O_2 (balloon) for 6 h. Upon completion, it was quenched with saturated brine, and extracted with EtOAc (10 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (3 : 1) as the eluent to give **2a** in 82% yield.

A tube containing **A** (88 mg, 0.5 mmol), KI (166 mg, 1 mmol) and Oxone (615 mg, 1 mmol) was evacuated and back-filled with O_2 three times. Then CH_3CN (5 mL) was added, and the mixture was stirred at 80 °C under O_2 (balloon) for 6 h, from which the formation of **2a** was not observed (TLC).

A tube containing **A** (88 mg, 0.5 mmol), $Cu(OAc)_2$ (181 mg, 1 mmol), KI (166 mg, 1 mmol) and Oxone (615 mg, 1 mmol) was evacuated and back-filled with N_2 three times. Then CH_3CN (5 mL) was added, and the mixture was stirred at 80 °C under N_2 (balloon) for 6 h, from which **2a** was formed in a trace amount (TLC).

Control experiment (II). A tube containing 1-phenylpiperidine (**1a**, 81 mg, 0.5 mmol), $Cu(OAc)_2$ (181 mg, 1 mmol), I_2 (127 mg, 0.5 mmol) and DMAP (61 mg, 0.5 mmol) was evacuated and back-filled with O_2. Then CH_3CN (5 mL) was added, and the mixture was stirred at 80 °C under O_2 (balloon) for 2 h. It was quenched with saturated ammonium chloride (5 mL), and extracted with EtOAc (10 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (100 : 1 to 20 : 1) to afford **A** and **3a** in 36% and 19% yields, respectively.

A tube containing **A** (88 mg, 0.5 mmol), $Cu(OAc)_2$ (181 mg, 1 mmol), I_2 (127 mg, 0.5 mmol) and DMAP (61 mg, 0.5 mmol) was evacuated and back-filled with O_2. Then, CH_3CN (5 mL) was added, and the resulting mixture was stirred at 80 °C under O_2 (balloon) for 6 h. Upon completion, it was quenched with saturated ammonium chloride (5 mL), and extracted with EtOAc (10 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (100 : 1) to afford **3a** in 78% yield.

A tube containing **A** (88 mg, 0.5 mmol), $Cu(OAc)_2$ (181 mg, 1 mmol) and I_2 (127 mg, 0.5 mmol) was evacuated and back-filled with O_2. Then CH_3CN (5 mL) was added, and the resulting mixture was stirred at 80 °C under O_2 (balloon) for 6 h, from which the formation of **3a** was not observed (TLC).

A tube containing **A** (88 mg, 0.5 mmol), I_2 (127 mg, 0.5 mmol) and DMAP (61 mg, 0.5 mmol) was evacuated and back-filled with O_2. Then CH_3CN (5 mL) was added, and the resulting mixture was stirred at 80 °C under O_2 (balloon) for 6 h, from which the formation of **3a** was not observed (TLC).

Conflicts of interest

There are no conflicts to declare.

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