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Regioselective Synthesis of Acylated *N*-Heterocycles via the Cascade Reactions of Saturated Cyclic Amines with 2-Oxo-2-arylacetic Acids

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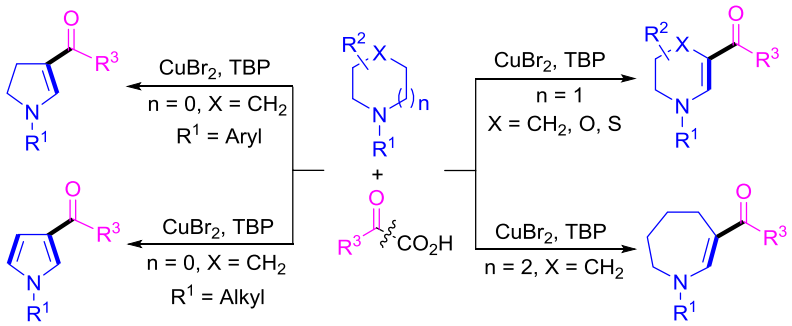
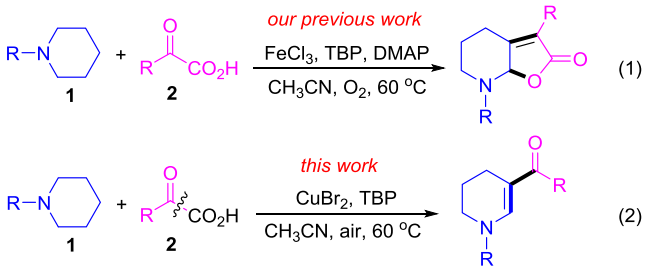


Abstract: A highly regioselective and versatile synthesis of acylated *N*-heterocycles from the cascade reactions of saturated cyclic amines with 2-oxo-2-arylacetic acids is presented. Mechanistically, the formation of the title compounds involves firstly a C(sp^3)–H bond dehydrogenation of cyclic amine to give an enamine intermediate followed by its cross coupling with the acyl species in situ generated through the decarboxylation of 2-oxo-2-arylacetic acid. Interestingly, in this cascade process the copper catalyst is believed to play a crucial role not only in dehydrogenation, but also in decarboxylation and cross coupling reaction. To the best of our knowledge, this is the first example in which different classes of acylated *N*-heterocycles were directly prepared from the readily available saturated cyclic amines by using 2-oxo-2-arylacetic acids as the non-corrosive and easy to handle acylating reagents. Compared with literature methods, this new protocol has the advantages such as readily obtainable substrates, broad substrate scope, high efficiency and good selectivity.

INTRODUCTION

Acyl *N*-heterocycles are ubiquitous in natural products and man-made compounds possessing biological and pharmaceutical activities. They are also important synthons widely used in synthetic chemistry.[1,2] Notwithstanding of their importance, reliable methods for the preparation of acyl *N*-heterocycles are still very limited.[3-4] In addition, some of these literature methods might be plagued by poor regioselectivity, expensive catalysts, corrosive reagents, and sophisticated starting materials. Therefore, the development of new methods for the regioselective synthesis of acyl *N*-heterocycles starting from easily obtainable substrates without using toxic and moisture-sensitive acylation reagents is highly desirable.

Direct C(sp^3)–H bond functionalization of inactivated cyclic amines is flourishing as an atom-economic synthetic approach to functionalized *N*-heterocycles since it can eliminate substrate(s) pre-activation and minimize byproduct(s) production.[5] In this regard, we have recently developed an efficient synthesis of furan-2(5*H*)-one fused *N*,*O*-containing bicyclic compounds *via* $FeCl_3$-catalyzed cascade reactions of cyclic amines (**1**) with 2-oxo-2-arylacetic acids (**2**) (Scheme 1, (1)).[5g] In our following study, we serendipitously found that when $FeCl_3$ was replaced by $CuBr_2$ as the catalyst, **1** underwent an oxidative acylation process with **2** to afford an acylated heterocycles rather than the bicyclic products (Scheme 1, (2)). It occurred to us that this is an interesting finding since although decarboxylative C–H functionalization with carboxylic acids has been developed as a highly useful tool for C–C bond formation owing to its high efficiency and step-economy,[6-8] direct synthesis of acyl heterocycles through the oxidative C(sp^3)–H bond acylation of saturated cyclic amines by using 2-oxo-2-arylacetic acid as easily obtainable, generally stable and convenient to handle acylation reagents has not been reported previously. Therefore, we set to have a systematic study on this promising new transformation.

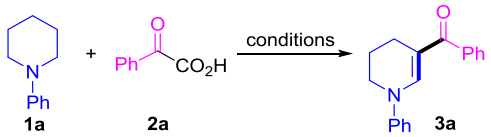


Scheme 1. Functionalizations of Cyclic Amines

RESULTS AND DISCUSSION

Our study was commenced by treating a mixture of 1-phenylpiperidine (**1a**) and 2-oxo-2-phenylacetic acid (**2a**) with $Cu(OAc)_2$ and *tert*-butylperoxide (TBP) in CH_3CN at 60 ℃ for 24 h. From this reaction, 3-benzoyl-1-phenyltetrahydropyridine (**3a**) was obtained in 40% yield (Table 1, entry 1). To improve the efficiency, different copper catalysts such as $CuCl_2$, $CuBr_2$, $CuSO_4$ $5H_2O$, CuBr and CuI were tried. Among them, $CuBr_2$ was the most efficient (entries 1-6). Following study on the effect of different oxidants indicated that Ag_2CO_3 gave a comparable yield of **3a** as that with TBP. However, $(NH_4)_2S_2O_8$ and O_2 were much less effective (entries 7-9). It was also found that when the loading of TBP reduced from 2 equiv to 1 equiv, the yield of **3a** diminished (entry 10). To study the solvent effect, dioxane, DCE, THF and TFE were tried. With these solvents, the yield of **3a** was not improved compared with CH_3CN (entries 11-14). Further screening showed that reaction temperatures higher or lower than 60 ℃ had an adverse effect on the efficiency (entries 15-16). It was also observed that in the absence of the copper catalyst or the oxidant, **3a** could not be obtained or was formed only in trace amount (entries 17-18). Notably, the structure of **3a** was confirmed by its single crystal X-ray diffraction analysis.[9]

Table 1. Optimization Studies [a]



Entry	Catalyst	Oxidant (eq)	Solvent	T/°C	Yield (%)[b]
1	$Cu(OAc)_2$	TBP(2)	CH_3CN	60	40
2	$CuCl_2$	TBP(2)	CH_3CN	60	15
3	$CuBr_2$	TBP(2)	CH_3CN	60	75
4	$CuSO_4$ $5H_2O$	TBP(2)	CH_3CN	60	35
5	CuBr	TBP(2)	CH_3CN	60	50
6	CuI	TBP(2)	CH_3CN	60	32
7	$CuBr_2$	$(NH_4)_2S_2O_8$(2)	CH_3CN	60	30
8	$CuBr_2$	Ag_2CO_3(2)	CH_3CN	60	74
9	$CuBr_2$	O_2	CH_3CN	60	48
10	$CuBr_2$	TBP(1)	CH_3CN	60	64
11	$CuBr_2$	TBP(2)	dioxane	60	47

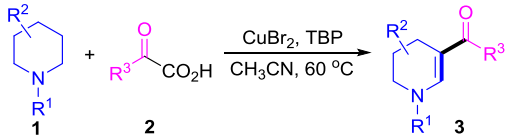
12	$CuBr_2$	TBP(2)	DCE	60	72
13	$CuBr_2$	TBP(2)	THF	60	40
14	$CuBr_2$	TBP(2)	TFE	60	48
15	$CuBr_2$	TBP(2)	CH_3CN	70	72
16	$CuBr_2$	TBP(2)	CH_3CN	50	55
17	-	TBP(2)	CH_3CN	60	-
18	$CuBr_2$	-	CH_3CN	60	trace

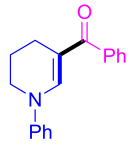
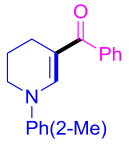
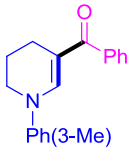
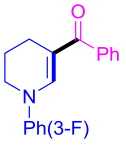
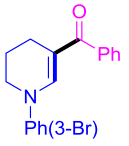
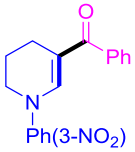
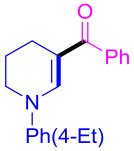
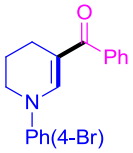
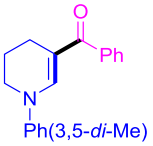
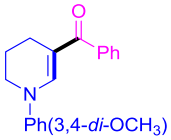
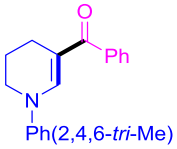
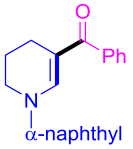
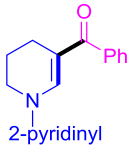
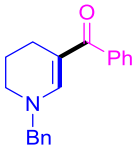
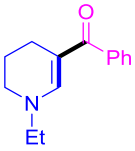
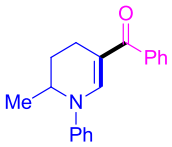
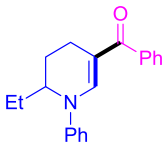
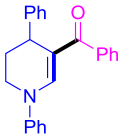
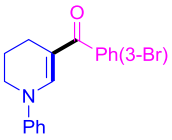
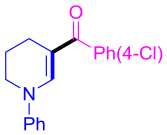
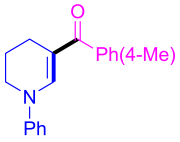
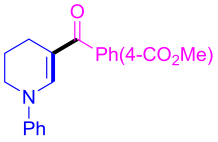
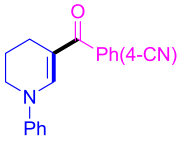
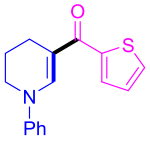
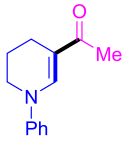
[a] Reaction conditions: 0.5 mmol of **1a**, 0.6 mmol of **2a**, 0.05 mmol of catalyst, 3 mL of solvent, 60 ℃, 24 h. [b] Isolated yields.

With the optimum reaction conditions established (Table 1, entry 3), the substrate scope of this 3-acyltetrahydropyridine forming reaction was explored. First, a number of *N*-phenylpiperidines **1** bearing various functional groups on the phenyl ring were tried by using **2a** as a model substrate. It turned out they took part in this reaction smoothly to give **3a**-**3k** in moderate to good yields (Table 2). Meanwhile, **1** with an *ortho*, *meta*, or *para*-substituent on the phenyl unit afforded the corresponding products with almost equally good efficiency. In addition, the reactions did not show an obvious electronic effect in that **1** bearing either electron-donating group(s) or electron-withdrawing group(s) on the phenyl ring gave their products in good yields. Remarkably, functional groups such as methyl, ethyl, methoxy, fluoro, bromo and nitro were well tolerated. Notably, 1-(naphthalene-1-yl)piperidine and 2-(piperidin-1-yl)pyridine could take part in this reaction to afford **3l** and **3m** in 60% and 69% yields. In addition to *N*-aryl piperidines, some *N*-alkylpiperidines also reacted with **2a** smoothly to give **3n** and **3o**, albeit the yields were somewhat lower. Promisingly, the diversity of the substrate structure was further underlined by the successful participation of 2-methyl-1-phenylpiperidine, 2-ethyl-1-phenylpiperidine and 1,4-diphenyl piperidine in this reaction to afford **3p**-**3r**. Notably, the reaction of 2-methyl- or 2-ethyl-1-phenylpiperidine took place regioselectively on the less sterically hindered side to give **3p** or **3q** exclusively, and the formation of other possible regioisomer was not observed. Second, we surveyed the substrate scope and functional group compatibility of 2-oxo-2-arylacetic acids **2**. It was thus found that **2** with either a bromo group attached on the *meta*-position, or a chloro, methyl, ester or cyano unit on the *para*-position of the phenyl unit reacted with **1a** smoothly to afford **3s**-

3w in 45%-64% yields. Moreover, heteroaromatic and aliphatic α-keto acids such as 2-oxo-2-(thiophen-2-yl)acetic acid and 2-oxopropanoic acid could also react with **1a** to give **3x** and **3y**.

Table 2. Substrate Scope for the Synthesis of **3** [a,b]



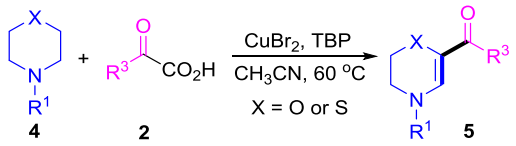
 **3a**, 75%	 **3b**, 66%	 **3c**, 73%	 **3d**, 62%	 **3e**, 64%
 **3f**, 69%	 **3g**, 75%	 **3h**, 72%	 **3i**, 72%	 **3j**, 70%
 **3k**, 67%	 **3l**, 60%	 **3m**, 69%	 **3n**, 51%	 **3o**, 29%
 **3p**, 54%	 **3q**, 44%	 **3r**, 59%	 **3s**, 63%	 **3t**, 64%
 **3u**, 57%	 **3v**, 45%	 **3w**, 51%	 **3x**, 71%	 **3y**, 23%

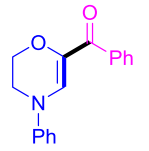
[a] Reaction conditions: 0.5 mmol of **1**, 0.6 mmol of **2**, 0.05 mmol of $CuBr_2$, 1 mmol of TBP, 3 mL of CH_3CN, 60 ℃, 24 h. [b] Isolated yields.

Next, given the importance of 1,4-oxazine derivatives,[10] we tried to extend the substrate scope from piperidines **1** to morpholines **4** to establish a novel synthesis of acylated 1,4-oxazines. Thus, 4-phenylmorpholine (**4a**) was treated with **2a** under the optimized conditions. To our delight, the desired product **5a** was obtained in 65% yield (Table 3). Encouraged by this preliminary result, 4-(3-fluorophenyl)morpholine and 4-(4-methylphenyl)morpholine were tried to react with **2a**. From these reactions, **5b** and **5c** were obtained in yields of 62% and 51%, respectively. Next, the

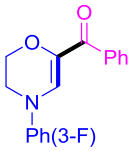
suitability of different 2-oxo-2-arylacetic acids **2** for this reaction was explored. It turned out that all of them took part in this reaction smoothly to give **5d**-**5g** in good yields. Promisingly, in addition to morpholines, thiomorpholines were also suitable partners for this reaction to afford acylated 1,4-thiazine derivatives **5h**-**5j** in moderate yields.

Table 3. Substrate Scope for the Synthesis of **5** [a,b]

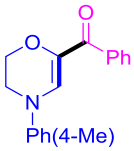




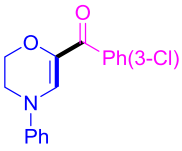
5a, 65%



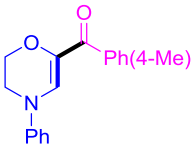
5b, 62%



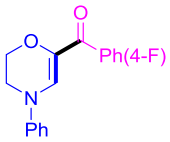
5c, 51%



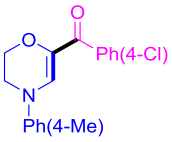
5d, 59%



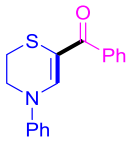
5e, 68%



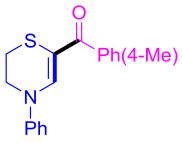
5f, 58%



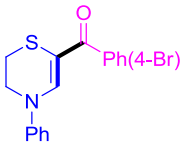
5g, 72%



5h, 62%



5i, 51%



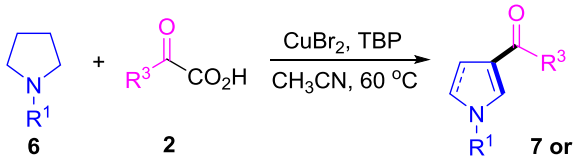
5j, 52%

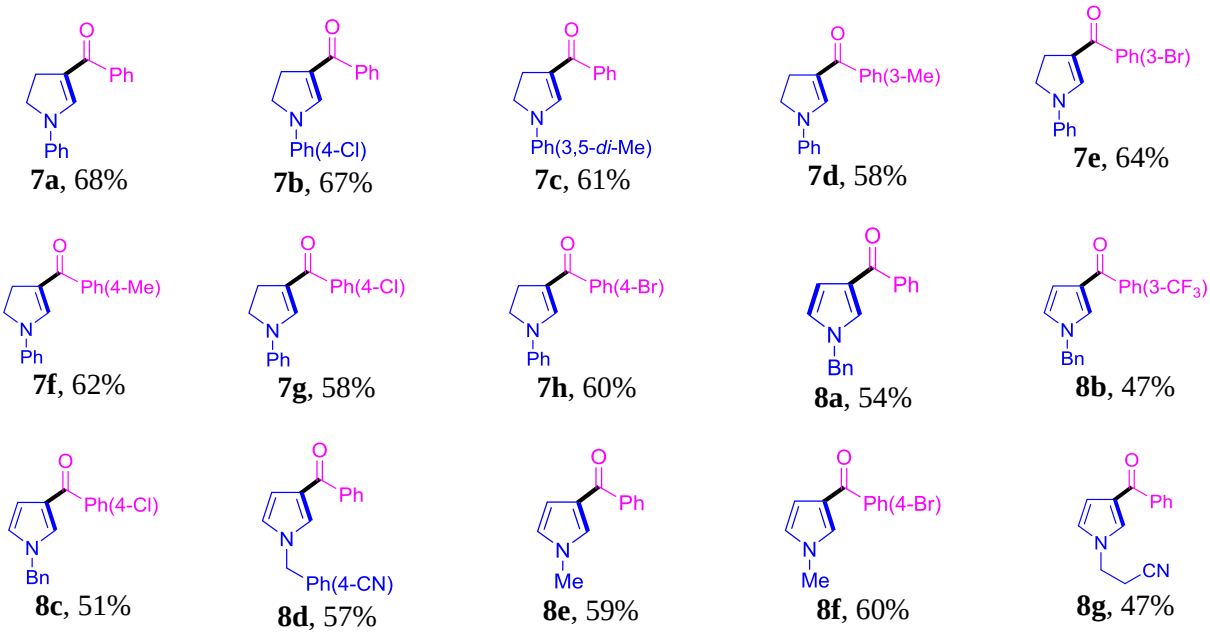
[a] Reaction conditions: 0.5 mmol of **4**, 0.6 mmol of **2**, 0.05 mmol of $CuBr_2$, 1 mmol of TBP, 3 mL of CH_3CN, 60 ℃, 24 h. [b] Isolated yields.

After establishing a novel protocol for the preparation of acylated 6-membered heterocycles, we then explored the suitability of pyrrolidines as substrates for this reaction to develop an access to 3-acyldihydropyrroles. It is well known that dihydropyrrole is an essential structural fragment embedded in various natural products and pharmaceuticals. While some elegant methods for the preparation of dihydropyrroles have been established,[11,12] to our knowledge, regioselective synthesis of 3-acyldihydropyrroles directly from pyrrolidines has not been realized previously. Thus, 1-phenylpyrrolidine (**6a**) was treated with **2a** under the optimized reaction conditions. From this reaction, the desired 3-acyldihydropyrrole **7a** was obtained in 68% yield(Table 4). Further study showed that 1-(4-chlorophenyl)pyrrolidine (**6b**) and 1-(3,5-dimethylphenyl)pyrrolidine (**6c**) participated in this reaction smoothly to afford **7b** and **7c** in yields of 67% and 61%, respectively. Next, with **6a** as a model substrate, the suitability of several 2-oxo-2-arylacetic acids **2** was studied. It was thus found that **2** with either a methyl or bromo unit attached on the *meta*-position, or a

methyl, chloro or bromo unit on the *para*-position of the phenyl unit reacted with **6a** efficiently to afford **7d**-**7h** in yields ranging from 58%-64%.

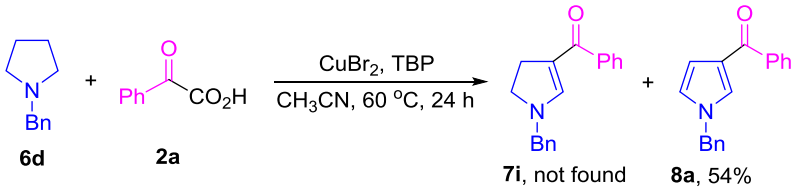
Table 4. Substrate Scope for the Synthesis of **7** and **8** [a,b]





[a] Reaction conditions: 0.5 mmol of **6**, 0.6 mmol of **2**, 0.05 mmol of $CuBr_2$, 1 mmol of TBP, 3 mL of CH_3CN, 60 ℃, 24 h. [b] Isolated yields.

Next, 1-benzylpyrrolidine (**6d**) as a *N*-alkyl substituted pyrrolidine was tried to react with **2a**. To our surprise, the expected 3-acyldihydropyrrole **7i** was not obtained from this reaction. On the other hand, **8a**, the dehydrogenative counterpart of **7i**, was isolated in 54% yield (Scheme 2).



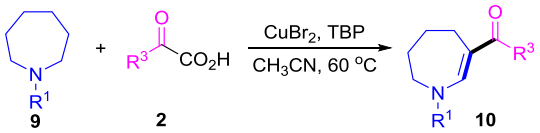
Scheme 2. Reaction of 1-Benzylpyrrolidine

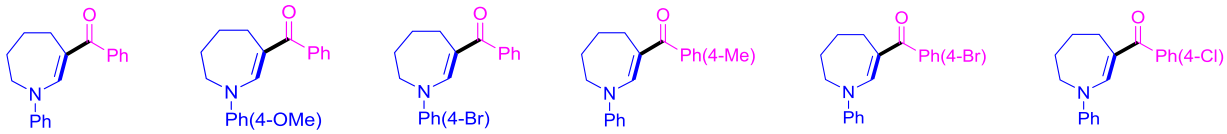
We postulated that this is probably owing to the presence of the electron-donating 1-alkyl substituent in the in situ formed **7i**, which makes **7i** have substantially high electron density on the pyrrole unit to undergo a simultaneous oxidative aromatization to give **8a**. In order to get **7i**, this reaction was then carried out in shorter reaction periods and under lower reaction temperatures.

However, under these reaction conditions **8a** was still obtained as a dominating product. Under this circumstance, we turned our focus from **7** to **8**, and explored the substrate generality of this 3-acylpyrrole forming reaction. We were pleased to find that in addition to **6d**, 4-(pyrrolidin-1-ylmethyl)benzonitrile (**6e**), 1-methylpyrrolidine (**6f**) and 3-(pyrrolidin-1-yl)propanenitrile (**6g**) could react with different 2-oxo-2-arylacetic acids **2** smoothly to afford the corresponding 3-acylpyrrole derivatives **8b-8g** in yields from 47% to 60% (Table 4).

Promisingly, further study revealed that this novel protocol for the dehydrogenation and acylation of saturated cyclic amines could be applied to azepanes **9**.[13] To be specific, treating 1-phenylazepane (**9a**) with **2a** under the optimized reaction conditions as described above afforded acylated azepine **10a** in 66% yield (Table 5). Through similar procedure, a series of 3-acylazepine derivatives **10b**-**10f** were synthesized in moderate to good yields from the corresponding azepanes and 2-oxo-2-arylacetic acids.

Table 5. Substrate Scope for the Synthesis of **10** [a,b]



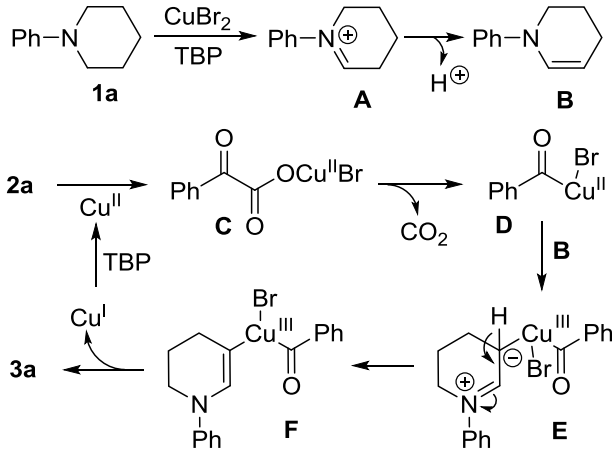


10a, 66% **10b**, 71% **10c**, 65% **10d**, 63% **10e**, 59% **10f**, 61%

[a] Reaction conditions: 0.5 mmol of **9**, 0.6 mmol of **2**, 0.05 mmol of $CuBr_2$, 1 mmol of TBP, 3 mL of CH_3CN, 60 ℃, 24 h. [b] Isolated yields.

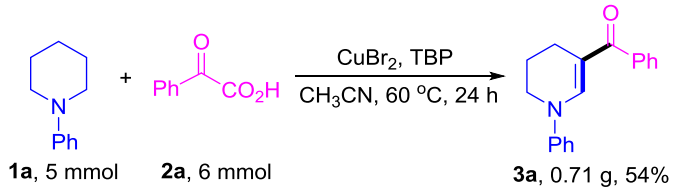
Based on previous reports[5-8] and our own observations, a plausible mechanism accounting for the formation of **3a** was proposed in Scheme 3. Initially, **1a** is oxidized by Cu(II)/TBP to give an iminium intermediate **A**. Subsequently, an isomerization occurs with **A** to produce enamine **B** through an elimination of a proton. Meanwhile, **2a** reacts with Cu(II) to form Cu(II) carboxylate **C**, which then undergoes a decarboxylation to afford an acyl Cu(II) species **D**. Next, a complexation of the central metal (copper) of **D** with the electron-rich β-carbon of the in situ formed enamine intermediate **B** generates a Cu(III) complex **E**. Isomerization of **E** gives another Cu(III) complex **F**.

Finally, a reductive elimination of **F** occurs to afford **3a** with the release of Cu(I), which is then oxidized by TBP to give Cu(II) for the next catalytic cycle.



Scheme 3. Proposed Mechanism for the Formation of **3a**

Finally, to see if this new method is suitable for a large scale synthetic mission, 5 mmol of **1a** was treated with 6 mmol of **2a** under the standard reaction conditions. The corresponding reaction proceeded smoothly to afford **3a** in a yield of 54% (Scheme 4).



Scheme 4. Gram-scale Synthesis of **3a**

In summary, we have developed a versatile and regioselective synthesis of acylated *N*-heterocycles through copper-catalyzed cascade reactions of saturated cyclic tertiary amines with 2-oxo-2-arylacetic acids. Interestingly, compared with iron,[5g] copper catalyst has unique capability to promote the decarboxylative decomposition of glyoxalic acid to give an acyl radical as a key intermediate and an acylation species. By using this novel protocol, a series of acyl heterocycles such as tetrahedropyridines, 1,4-oxazines, 1,4-thiazines, dihydropyrroles, pyrroles and azepines were prepared. Compared with literature methods, the protocol reported herein has notable features such as good efficiency, easily obtainable substrates, non-noble metal catalyst, and stable, non-corrosive and easy to handle acylation reagent.

EXPERIMENTAL SECTION

I. General methods. All the commercial reagents were used without further purification. Melting points were recorded with a micro melting point apparatus and uncorrected. The ^{1}H NMR spectra were recorded at 400 MHz or 600 MHz. The ^{13}C NMR spectra were recorded at 100 MHz or 150 MHz. Chemical shifts were expressed in parts per million (δ), and were reported as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), dd (doublet of doublet), m (multiplet), etc. The coupling constants J were given in Hz. High resolution mass spectra (HRMS) were obtained *via* ESI mode by using a MicrOTOF mass spectrometer. The conversion of starting materials was monitored by thin layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm), and components were visualized by observation under UV light (254 and 365 nm).

II. Experimental Procedures

1. Typical Procedure for the Synthesis of 3a

To a reaction tube equipped with a stir bar were added 1-phenylpiperidine (**1a**, 81 mg, 0.5 mmol), CH_3CN (3 mL), 2-oxo-2-phenylacetic acid (**2a**, 90 mg, 0.6 mmol), $CuBr_2$ (11 mg, 0.05 mmol) and TBP (183 μL, 1 mmol) with stirring. The mixture was stirred under air at 60 ℃ for 24 h. Afterwards, it was quenched with water (3 mL), and extracted with ethyl acetate (10 mL × 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (5:1) as the eluent to give **3a** in a yield of 75%. **3b-3t**, **5a-5j, 7a-7h**, **8a-8f** and **10a-10f** were obtained in a similar manner.

Phenyl(1-phenyl-1,4,5,6-tetrahydropyridin-3-yl)methanone (3a)

Yellow solid (99 mg, 75%), mp 119-120 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.06 (quint, J = 6.0 Hz, 2H), 2.60 (t, J = 6.0 Hz, 2H), 3.69 (t, J = 5.6 Hz, 2H), 6.96 (d, J = 8.0 Hz, 2H), 7.06 (t, J = 7.2 Hz, 1H), 7.28-7.32 (m, 2H), 7.38-7.43 (m, 3H), 7.53-7.56 (m, 3H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 20.0, 21.2, 47.0, 112.8, 118.1, 123.7, 128.1, 128.4, 129.5, 129.9, 140.5, 145.6, 147.0, 194.8. HRMS calcd for $C_{18}H_{18}NO$: 264.1383 $[M+H]^+$, found: 264.1383.

Phenyl(1-(*o*-tolyl)-1,4,5,6-tetrahydropyridin-3-yl)methanone (3b)

Yellow solid (91 mg, 66%), mp 93-94 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.05-2.09 (m, 2H), 2.25 (s, 3H), 2.63 (t, *J* = 6.0 Hz, 2H), 3.53 (t, *J* = 5.6 Hz, 2H), 7.03 (d, *J* = 6.8 Hz, 1H), 7.08 (s, 1H), 7.14-7.21 (m, 3H), 7.31-7.34 (m, 3H), 7.48 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 18.2, 19.9, 21.4, 49.5, 110.2, 125.7, 127.0, 127.1, 128.0, 128.2, 129.4, 131.6, 133.4, 140.9, 145.6, 151.0, 194.3. HRMS calcd for $C_{19}H_{19}NNaO$: 300.1359 $[M+Na]^+$, found: 300.1369.

Phenyl(1-(*m*-tolyl)-1,4,5,6-tetrahydropyridin-3-yl)methanone (3c)

Yellow solid (101 mg, 73%), mp 120-121 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.04 (quint, *J* = 6.0 Hz,, 2H), 2.31 (s, 3H), 2.60 (t, *J* = 6.6 Hz, 2H), 3.67 (t, *J* = 6.0 Hz, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.78 (s, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.37-7.41 (m, 3H), 7.53-7.55 (m, 3H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 20.1, 21.2, 21.6, 47.2, 112.5, 115.4, 119.1, 124.6, 128.1, 128.5, 129.3, 129.9, 139.5, 140.6, 145.7, 147.3, 194.7. HRMS calcd for $C_{19}H_{20}NO$: 278.1539 $[M+H]^+$, found: 278.1539.

(1-(3-Fluorophenyl)-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3d)

Yellow solid (87 mg, 62%), mp 109-110 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.06-2.10 (m, 2H), 2.60 (t, *J* = 6.0 Hz, 2H), 3.66 (t, *J* = 5.6 Hz, 2H), 6.66 (d, *J* = 10.8 Hz, 1H), 6.71-6.76 (m, 2H), 7.23 (t, *J* = 7.2 Hz,, 1H), 7.40-7.46 (m, 3H), 7.51 (s, 1H), 7.55 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 20.1, 21.2, 46.9, 105.1 (d, $^{2}J_{C\text{-}F}$ = 25.2 Hz), 110.0 (d, $^{2}J_{C\text{-}F}$ = 20.7 Hz), 113.1 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 113.8, 128.2, 128.4, 130.1, 130.7 (d, $^{3}J_{C\text{-}F}$ = 9.8 Hz), 140.3, 145.8, 147.1 (d, $^{3}J_{C\text{-}F}$ = 9.8 Hz), 163.5 (d, $^{1}J_{C\text{-}F}$ = 245.1 Hz), 194.9. HRMS calcd for $C_{18}H_{16}FNNaO$: 304.1108 $[M+Na]^+$, found: 304.1137.

(1-(3-Bromophenyl)-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3e)

Yellow solid (109 mg, 64%), mp 105-106 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.06 (quint, *J* = 6.0 Hz, 2H), 2.59 (t, *J* = 6.0 Hz, 2H), 3.65 (t, *J* = 5.6 Hz, 2H), 6.87 (d, *J* = 7.2 Hz, 1H), 7.12-7.18 (m, 3H), 7.40-7.45 (m, 3H), 7.48 (s, 1H), 7.55 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ:

20.1, 21.2, 47.0, 113.9, 116.4, 121.1, 123.3, 126.3, 128.2, 128.4, 130.2, 130.7, 140.2, 145.8, 146.8, 194.9. HRMS calcd for $C_{18}H_{17}BrNO$: 342.0488 $[M+H]^+$, found: 342.0490.

(1-(3-Nitrophenyl)-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3f)

Yellow solid (106 mg, 69%), mp 126-128 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.12 (quint, J = 6.0 Hz,, 2H), 2.62 (t, J = 6.4 Hz, 2H), 3.74 (t, J = 5.6 Hz, 2H), 7.24 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 7.42-7.48 (m, 4H), 7.56 (s, 1H), 7.58 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 2H), 7.82 (t, J = 2.0 Hz, 1H), 7.87 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 20.1, 21.1, 46.8, 112.1, 115.1, 117.5, 122.8, 128.3, 128.5, 130.4, 130.5, 139.9, 144.7, 146.3, 149.1, 195.0. HRMS calcd for $C_{18}H_{17}N_2O_3$: 309.1234 $[M+H]^+$, found: 309.1251.

(1-(4-Ethylphenyl)-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3g)

Yellow solid (109 mg, 75%), mp 75-76 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.18 (t, J = 7.6 Hz, 3H), 2.02 (quint, J = 6.0 Hz,, 2H), 2.54-2.61 (m, 4H), 3.65 (t, J = 5.6 Hz, 2H), 6.88 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 7.34-7.41 (m, 3H), 7.52-7.54 (m, 3H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 15.7, 20.0, 21.2, 28.1, 47.3, 112.2, 118.4, 128.1, 128.4, 128.9, 129.7, 140.0, 140.7, 143.6, 147.5, 194.5. HRMS calcd for $C_{20}H_{22}NO$: 292.1696 $[M+H]^+$, found: 292.1697.

(1-(4-Bromophenyl)-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3h)

Yellow solid (123 mg, 72%), mp 139-140 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.06 (quint, J = 6.0 Hz, 2H), 2.59 (t, J = 6.0 Hz, 2H), 3.65 (t, J = 5.6 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 7.39-7.44 (m, 5H), 7.47 (s, 1H), 7.53 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 20.0, 21.1, 47.0, 113.5, 116.3, 119.5, 128.1, 128.4, 130.0, 132.4, 140.3, 144.6, 146.1, 194.8. HRMS calcd for $C_{18}H_{17}BrNO$: 342.0488 $[M+H]^+$, found: 342.0480.

(1-(3,5-Dimethylphenyl)-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3i)

Yellow solid (105 mg, 72%), mp 98-99 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.93 (quint, J = 6.0 Hz,, 2H), 2.17 (s, 6H), 2.50 (t, J = 6.0 Hz, 2H), 3.56 (t, J = 5.6 Hz, 2H), 6.49 (s, 2H), 6.62 (s, 1H), 7.27-7.33 (m, 3H), 7.43 (s, 1H), 7.46 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 20.2, 21.3,

21.5, 47.3, 112.2, 116.4, 125.7, 128.0, 128.5, 129.8, 139.3, 140.7, 145.8, 147.5, 194.6. HRMS calcd for $C_{20}H_{21}NNaO$: 314.1515 $[M+Na]^+$, found: 314.1520.

(1-(3,4-Dimethoxyphenyl)-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3j)

Yellow solid (113 mg, 70%), mp 125-126 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.04 (quint, *J* = 6.0 Hz, 2H), 2.59 (t, *J* = 6.0 Hz, 2H), 3.66 (t, *J* = 5.6 Hz, 2H), 3.82 (s, 6H), 6.51-6.53 (m, 2H), 6.78 (d, *J* = 8.0 Hz, 1H), 7.35-7.40 (m, 3H), 7.45 (s, 1H), 7.53 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 19.9, 21.2, 47.7, 55.9, 56.2, 103.6, 110.9, 111.7, 111.9, 128.0, 128.3, 129.7, 139.9, 140.7, 146.1, 148.1, 149.6, 194.3. HRMS calcd for $C_{20}H_{22}NO_3$: 324.1594 $[M+H]^+$, found: 324.1590.

(1-Mesityl-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3k)

Yellow solid (102 mg, 67%), mp 82-83 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.07 (quint, *J* = 6.0 Hz, 2H), 2.17 (s, 6H), 2.25 (s, 3H), 2.64 (t, *J* = 6.0 Hz, 2H), 3.37 (t, *J* = 5.6 Hz, 2H), 6.87 (s, 2H), 6.91 (s, 1H), 7.26-7.34 (m, 3H), 7.45 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 17.8, 19.7, 20.8, 21.2, 48.4, 108.8, 127.9, 128.2, 129.2, 129.4, 135.5, 137.6, 141.1, 141.5, 151.9, 193.9. HRMS calcd for $C_{21}H_{24}NO$: 306.1852 $[M+H]^+$, found: 306.1851.

(1-(Naphthalen-1-yl)-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3l)

Yellow solid (94 mg, 60%), mp 95-96 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.18 (br s, 2H), 2.72 (br s, 2H), 3.71 (br s, 2H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.28-7.30 (m, 4H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.51-7.58 (m, 4H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.88 (t, *J* = 7.2 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 20.1, 21.6, 50.5, 110.8, 122.6, 122.8, 125.7, 126.7, 126.9, 127.5, 128.0, 128.3, 128.7, 129.2, 129.5, 134.7, 140.7, 143.4, 151.6, 194.4. HRMS calcd for $C_{22}H_{19}NNaO$: 336.1359 $[M+Na]^+$, found: 336.1358.

(3,4-Dihydro-2*H*-[1,2'-bipyridin]-5-yl)(phenyl)methanone (3m)

Yellow solid (91 mg, 69%), mp 115-116 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.06-2.07 (m, 2H), 2.61 (t, *J* = 6.0 Hz, 2H), 3.766-3.773 (m, 2H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.88 (t, *J* = 5.4 Hz, 1H), 7.41-7.47 (m, 3H), 7.57-7.61 (m, 3H), 8.227-8.232 (m, 1H), 8.30 (s, 1H). ^{13}C NMR (150 Hz,

$CDCl_3$) δ: 20.4, 21.1, 44.2, 108.9, 114.5, 117.7, 128.1, 128.7, 130.1, 138.3, 140.3, 143.4, 148.3, 154.4, 195.5. HRMS calcd for $C_{17}H_{17}N_2O$: 265.1335 $[M+H]^+$, found: 265.1334.

(1-Benzyl-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3n)

Yellow solid (71 mg, 51%), mp 102-103 ℃. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.86-1.90 (m, 2H), 2.51 (t, *J* = 6.0 Hz, 2H), 3.11 (t, *J* = 6.0 Hz, 2H), 4.26 (s, 2H), 7.15-7.20 (m, 3H), 7.31-7.38 (m, 6H), 7.47-7.49 (m, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 19.5, 21.0, 46.1, 60.2, 108.2, 127.3, 127.9, 128.1, 128.3, 128.9, 129.3, 136.2, 141.1, 152.4, 193.3. HRMS calcd for $C_{19}H_{20}NO$: 278.1539 $[M+H]^+$, found: 278.1529.

(1-Ethyl-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3o)

Yellow solid (31 mg, 29%), mp 97-98 ℃. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.14 (t, *J* = 7.6 Hz, 3H), 1.90 (quint, *J* = 6.0 Hz, 2H), 2.50 (t, *J* = 6.0 Hz, 2H), 3.12-3.20 (m, 4H), 7.03 (s, 1H), 7.34-7.39 (m, 3H), 7.44-7.47 (m, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 13.8, 19.6, 21.1, 45.9, 51.0, 107.6, 127.9, 128.3, 129.1, 141.4, 151.8, 192.9. HRMS calcd for $C_{14}H_{18}NO$: 216.1383 $[M+H]^+$, found: 216.1381.

(6-Methyl-1-phenyl-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3p)

Yellow solid (75 mg, 54%), mp 102-104 ℃. ^1H NMR (600 MHz, $CDCl_3$) δ: 1.29 (d, *J* = 6.6 Hz, 3H), 1.90-1.98 (m, 2H), 2.42-2.47 (m, 1H), 2.80-2.83 (m, 1H), 4.21 (s, 1H), 7.01 (d, *J* = 7.8 Hz, 2H), 7.07 (t, *J* = 7.8 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.38-7.42 (m, 3H), 7.47 (s, 1H), 7.54 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 16.2, 18.0, 26.8, 51.5, 112.2, 119.0, 123.9, 128.1, 128.4, 129.6, 129.8, 140.6, 144.9, 146.0, 194.8. HRMS calcd for $C_{19}H_{20}NO$: 278.1539 $[M+H]^+$, found: 278.1536.

(6-Ethyl-1-phenyl-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3q)

Syrup (64 mg, 44%). ^1H NMR (400 MHz, $CDCl_3$) δ: 0.95 (t, *J* = 7.6 Hz, 3H), 1.60-1.72 (m, 2H), 1.75-1.84 (m, 1H), 2.15-2.21 (m, 1H), 2.31-2.40 (m, 1H), 2.76-2.82 (m, 1H), 3.92-3.95 (m, 1H), 6.99 (d, *J* = 7.6 Hz, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 7.28-7.32 (m, 2H), 7.36-7.44 (m, 3H), 7.48 (s, 1H), 7.52-7.55 (m, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 10.3, 16.2, 22.7, 24.0, 57.5, 112.5, 119.2,

123.9, 128.1, 128.4, 129.6, 129.8, 140.7, 145.2, 146.2, 194.7. HRMS calcd for $C_{20}H_{21}NNaO$: 314.1515 $[M+Na]^+$, found: 314.1516.

(1,4-Diphenyl-1,4,5,6-tetrahydropyridin-3-yl)(phenyl)methanone (3r)

Yellow solid (100 mg, 59%), mp 85-86 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.09-2.14 (m, 1H), 2.17-2.25 (m, 1H), 3.44-3.51 (m, 1H), 3.58-3.61 (m, 1H), 4.44 (d, *J* = 3.6 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 2H), 7.08 (t, *J* = 7.6 Hz, 1H), 7.17-7.21 (m, 1H), 7.27-7.33 (m, 6H), 7.37-7.45 (m, 3H), 7.59 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 2H), 7.83 (s, 1H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 29.3, 35.0, 42.9, 113.9, 118.2, 123.9, 126.3, 127.8, 128.1, 128.4, 128.6, 129.6, 130.0, 140.6, 145.3, 145.5, 147.0, 193.9. HRMS calcd for $C_{24}H_{22}NO$: 340.1696 $[M+H]^+$, found: 340.1696.

(3-Bromophenyl)(1-phenyl-1,4,5,6-tetrahydropyridin-3-yl)methanone (3s)

Yellow solid (107 mg, 63%), mp 113-114 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.06 (quint, *J* = 6.0 Hz, 2H), 2.59 (t, *J* = 6.0 Hz, 2H), 3.70 (t, *J* = 5.6 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.09 (t, *J* = 7.2 Hz, 1H), 7.26 (t, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.44-7.46 (m, 1H), 7.50 (s, 1H), 7.55 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 7.69 (s, 1H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 19.9, 21.1, 47.2, 112.5, 118.4, 122.4, 124.1, 126.8, 129.60, 129.65, 131.4, 132.7, 142.5, 145.5, 147.4, 192.7. HRMS calcd for $C_{18}H_{17}BrNO$: 342.0488 $[M+H]^+$, found: 342.0498.

(4-Chlorophenyl)(1-phenyl-1,4,5,6-tetrahydropyridin-3-yl)methanone (3t)

Yellow solid (95 mg, 64%), mp 126-127 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.07 (quint, *J* = 6.0 Hz, 2H), 2.60 (t, *J* = 6.0 Hz, 2H), 3.71 (t, *J* = 5.6 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 2H), 7.50-7.51 (m, 3H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 20.0, 21.1, 47.1, 112.7, 118.2, 123.9, 128.4, 129.6, 129.8, 135.9, 138.9, 145.6, 146.9, 193.2. HRMS calcd for $C_{18}H_{16}ClNNaO$: 320.0813 $[M+Na]^+$, found: 320.0831.

(1-Phenyl-1,4,5,6-tetrahydropyridin-3-yl)(*p*-tolyl)methanone (3u)

Yellow solid (79 mg, 57%), mp 100-101 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.99 (quint, *J* = 6.0 Hz, 2H), 2.31 (s, 3H), 2.53 (t, *J* = 6.0 Hz, 2H), 3.62 (t, *J* = 5.6 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.99 (t, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 8.0 Hz, 2H), 7.24 (t, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 7.6 Hz, 2H),

7.50 (s, 1H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 19.1, 20.2, 20.4, 46.0, 111.9, 117.1, 122.4, 127.5, 127.7, 128.5, 136.7, 139.0, 144.7, 145.4, 193.6. HRMS calcd for $C_{19}H_{20}NO$: 278.1539 $[M+H]^+$, found: 278.1530.

Methyl 4-(1-phenyl-1,4,5,6-tetrahydropyridine-3-carbonyl)benzoate (3v)

Yellow solid (72 mg, 45%), mp 132-133 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.07 (quint, J = 6.4 Hz, 2H), 2.61 (t, J = 6.4 Hz, 2H), 3.71 (t, J = 5.6 Hz, 2H), 3.93 (s, 3H), 6.96 (d, J = 7.6 Hz, 2H), 7.08 (t, J = 7.6 Hz, 1H), 7.31 (t, J = 8.0 Hz, 2H), 7.47 (s, 1H), 7.59 (d, J = 8.4 Hz, 2H), 8.07 (d, J = 8.0 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 19.9, 21.1, 47.2, 52.3, 112.7, 118.3, 124.1, 128.3, 129.4, 129.6, 131.1, 144.8, 145.5, 147.6, 166.7, 193.6. HRMS calcd for $C_{20}H_{19}NNaO_3$: 344.1257 $[M+Na]^+$, found: 344.1263.

4-(1-Phenyl-1,4,5,6-tetrahydropyridine-3-carbonyl)benzonitrile (3w)

Yellow solid (73 mg, 51%), mp 127-129 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.07 (quint, J = 6.0 Hz, 2H), 2.60 (t, J = 6.0 Hz, 2H), 3.72 (t, J = 5.6 Hz, 2H), 6.97-6.99 (m, 2H), 7.11 (t, J = 7.2 Hz, 1H), 7.31-7.35 (m, 2H), 7.41 (s, 1H), 7.61 (dd, J_1 = 6.8 Hz, J_2 = 1.6 Hz, 2H), 7.69 (dd, J_1 = 6.8 Hz, J_2 = 1.6 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 19.8, 21.0, 47.4, 112.4, 113.3, 118.47, 118.53, 124.4, 128.9, 129.7, 132.1, 144.9, 145.4, 147.7, 192.2. HRMS calcd for $C_{19}H_{16}N_2NaO$: 311.1155 $[M+Na]^+$, found: 311.1161.

(1-Phenyl-1,4,5,6-tetrahydropyridin-3-yl)(thiophen-2-yl)methanone (3x)

Yellow solid (95 mg, 71%), mp 134-135 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.98 (quint, J = 6.4 Hz, 2H), 2.54 (t, J = 6.4 Hz, 2H), 3.63 (t, J = 5.6 Hz, 2H), 6.98-7.04 (m, 4H), 7.27 (td, J_1 = 7.6 Hz, J_2 = 2.0 Hz, 2H), 7.38 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.41 (dd, J_1 = 5.2 Hz, J_2 = 1.2 Hz, 1H), 7.91 (s, 1H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 20.5, 21.2, 47.0, 112.8, 118.2, 123.7, 127.0, 129.6, 129.8, 129.9, 144.3, 145.2, 145.7, 185.1. HRMS calcd for $C_{16}H_{16}NOS$: 270.0947 $[M+H]^+$, found: 270.0965.

1-(1-Phenyl-1,4,5,6-tetrahydropyridin-3-yl)ethanone (3y)

Syrup (23 mg, 23%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.89 (quint, *J* = 6.4 Hz, 2H), 2.17 (s, 3H), 2.33 (t, *J* = 6.4 Hz, 2H), 3.54 (t, *J* = 6.0 Hz, 2H), 7.00-7.04 (m, 3H), 7.27-7.31 (m, 2H), 7.69 (s, 1H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 19.8, 21.2, 24.3, 46.7, 113.5, 118.1, 123.5, 129.5, 142.8, 145.9, 195.0. HRMS calcd for $C_{13}H_{16}NO$: 202.1226 $[M+H]^+$, found: 202.1251.

Phenyl(4-phenyl-3,4-dihydro-2*H*-1,4-oxazin-6-yl)methanone (5a)

Yellow solid (86 mg, 65%), mp 112-113 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.80 (t, *J* = 4.0 Hz, 2H), 4.33 (t, *J* = 4.0 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 7.06 (t, *J* = 7.2 Hz, 1H), 7.27 (s, 1H), 7.34 (t, *J* = 8.0 Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 45.3, 63.4, 116.6, 123.2, 127.8, 128.2, 128.8, 129.7, 130.9, 135.2, 138.7, 143.9, 187.9. HRMS calcd for $C_{17}H_{16}NO_2$: 266.1176 $[M+H]^+$, found: 266.1177.

(4-(3-Fluorophenyl)-3,4-dihydro-2*H*-1,4-oxazin-6-yl)(phenyl)methanone (5b)

Yellow solid (88 mg, 62%), mp 100-101 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.76 (br s, 2H), 4.33 (br s, 2H), 6.65 (d, *J* = 10.8 Hz, 1H), 6.73-6.74 (m, 2H), 7.22 (s, 1H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.2 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.70 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 45.1, 63.4, 103.6 (d, $^{2}J_{C\text{-}F}$ = 25.1 Hz), 109.6 (d, $^{2}J_{C\text{-}F}$ = 21.8 Hz), 111.6 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 126.3, 128.2, 128.8, 131.0 (d, $^{3}J_{C\text{-}F}$ = 9.8 Hz), 131.2, 135.6, 138.4, 145.3 (d, $^{3}J_{C\text{-}F}$ = 9.9 Hz), 163.6 (d, $^{1}J_{C\text{-}F}$ = 245.1 Hz), 188.0. HRMS calcd for $C_{17}H_{15}FNO_2$: 284.1081 $[M+H]^+$, found: 284.1098.

Phenyl(4-(*p*-tolyl)-3,4-dihydro-2*H*-1,4-oxazin-6-yl)methanone (5c)

Yellow solid (71 mg, 51%), mp 93-94 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.30 (s, 3H), 3.78 (br s, 2H), 4.31 (br s, 2H), 6.87 (d, *J* = 7.2 Hz, 2H), 7.13 (d, *J* = 7.2 Hz, 2H), 7.23 (s, 1H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 20.6, 45.5, 63.3, 116.8, 128.1, 128.6, 128.8, 130.2, 130.8, 133.1, 134.8, 138.8, 141.7, 187.6. HRMS calcd for $C_{18}H_{18}NO_2$: 280.1332 $[M+H]^+$, found: 280.1332.

(3-Chlorophenyl)(4-phenyl-3,4-dihydro-2*H*-1,4-oxazin-6-yl)methanone (5d)

Yellow solid (88 mg, 59%), mp 111-112 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.80 (t, *J* = 4.4 Hz, 2H), 4.31 (t, *J* = 4.4 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 7.08 (t, *J* = 7.2 Hz, 1H), 7.28 (s, 1H), 7.33-7.37 (m, 3H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.69 (s, 1H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 45.4, 63.3, 116.8, 123.5, 126.9, 128.1, 128.9, 129.5, 129.8, 130.9, 134.3, 134.9, 140.3, 143.8, 185.9. HRMS calcd for $C_{17}H_{15}ClNO_2$: 300.0786 $[M+H]^+$, found: 300.0795.

(4-Phenyl-3,4-dihydro-2*H*-1,4-oxazin-6-yl)(*p*-tolyl)methanone (5e)

Yellow solid (95 mg, 68%), mp 133-135 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.29 (s, 3H), 3.67 (t, *J* = 4.0 Hz, 2H), 4.20 (t, *J* = 4.0 Hz, 2H), 6.86 (d, *J* = 8.0 Hz, 2H), 6.94 (t, *J* = 7.2 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 2H), 7.18 (s, 1H), 7.22 (t, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 20.5, 44.1, 62.3, 115.4, 121.9, 126.2, 127.76, 127.84, 128.6, 134.1, 134.8, 140.3, 142.8, 186.6. HRMS calcd for $C_{18}H_{18}NO_2$: 280.1332 $[M+H]^+$, found: 280.1342.

(4-Fluorophenyl)(4-phenyl-3,4-dihydro-2*H*-1,4-oxazin-6-yl)methanone (5f)

Yellow solid (82 mg, 58%), mp 76-77 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.74 (t, *J* = 4.0 Hz, 2H), 4.25 (t, *J* = 4.0 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.99-7.05 (m, 3H), 7.21 (s, 1H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.65-7.69 (m, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 45.3, 63.3, 115.2 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 116.5, 123.3, 127.3, 129.8, 131.2 (d, $^3J_{C\text{-}F}$ = 8.7 Hz), 134.8, 135.1, 143.9, 164.4 (d, $^1J_{C\text{-}F}$ = 250.2 Hz), 186.3. HRMS calcd for $C_{17}H_{15}FNO_2$: 284.1081 $[M+H]^+$, found: 284.1093.

(4-Chlorophenyl)(4-(*p*-tolyl)-3,4-dihydro-2*H*-1,4-oxazin-6-yl)methanone (5g)

Yellow solid (112 mg, 72%), mp 95-96 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.25 (s, 3H), 3.72 (t, *J* = 4.0 Hz, 2H), 4.24 (t, *J* = 4.0 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.16 (s, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 20.6, 45.6, 63.2, 116.8, 128.2, 128.4, 130.2, 130.3, 133.3, 134.7, 137.0, 137.1, 141.7, 186.1. HRMS calcd for $C_{18}H_{17}ClNO_2$: 314.0942 $[M+H]^+$, found: 314.0956.

Phenyl(4-phenyl-3,4-dihydro-2*H*-1,4-thiazin-6-yl)methanone (5h)

Yellow solid (87 mg, 62%), mp 144-145 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.13 (t, *J* = 4.8 Hz, 2H), 4.06 (t, *J* = 5.4 Hz, 2H), 7.00 (d, *J* = 7.8 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 7.33 (t, *J* = 7.2 Hz,

2H), 7.40 (t, *J* = 7.2 Hz, 2H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.57 (d, *J* = 7.2 Hz, 2H), 7.64 (s, 1H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 24.0, 48.7, 108.7, 119.7, 124.8, 128.3, 128.4, 129.7, 130.4, 139.1, 143.2, 146.0, 191.8. HRMS calcd for $C_{17}H_{16}NOS$: 282.0947 $[M+H]^+$, found: 282.0953.

(4-Phenyl-3,4-dihydro-2*H*-1,4-thiazin-6-yl)(*p*-tolyl)methanone (5i)

Yellow solid (75 mg, 51%), mp 103-104 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.31 (s, 3H), 3.05-3.06 (m, 2H), 3.98-3.99 (m, 2H), 6.93 (d, *J* = 7.8 Hz, 2H), 7.05 (t, *J* = 7.8 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 2H), 7.26 (t, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.60 (s, 1H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 21.5, 24.1, 48.6, 108.7, 119.7, 124.6, 128.6, 128.9, 129.7, 136.2, 140.8, 142.7, 146.1, 191.8. HRMS calcd for $C_{18}H_{18}NOS$: 296.1104 $[M+H]^+$, found: 296.1104.

(4-Bromophenyl)(4-phenyl-3,4-dihydro-2*H*-1,4-thiazin-6-yl)methanone (5j)

Yellow solid (93 mg, 52%), mp 112-113 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.13 (t, *J* = 4.8 Hz, 2H), 4.07 (t, *J* = 5.2 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 7.16 (t, *J* = 7.2 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.59 (s, 1H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 24.0, 48.8, 108.4, 119.8, 125.0, 125.1, 129.8, 130.1, 131.5, 137.8, 143.2, 145.9, 190.5. HRMS calcd for $C_{17}H_{15}BrNOS$: 360.0052 $[M+H]^+$, found: 360.0055.

Phenyl(1-phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)methanone (7a)

Syrup (85 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.17 (t, *J* = 10.0 Hz, 2H), 4.05 (t, *J* = 10.0 Hz, 2H), 6.91 (d, *J* = 7.6 Hz, 2H), 7.00 (t, *J* = 7.2 Hz, 1H), 7.29-7.33 (m, 2H), 7.42-7.49 (m, 3H), 7.53 (s, 1H), 7.64-7.66 (m, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 27.2, 49.9, 114.6, 118.3, 122.2, 128.0, 128.4, 129.7, 130.5, 140.9, 141.0, 146.2, 190.4. HRMS calcd for $C_{17}H_{15}NNaO$: 272.1046 $[M+Na]^+$, found: 272.1058.

(1-(4-Chlorophenyl)-4,5-dihydro-1*H*-pyrrol-3-yl)(phenyl)methanone (7b)

Yellow solid (95 mg, 67%), mp 144-145 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.07 (t, *J* = 9.6 Hz, 2H), 3.92 (t, *J* = 9.6 Hz, 2H), 6.72-6.74 (m, 2H), 7.16-7.18 (m, 2H), 7.35-7.37 (m, 3H), 7.40-7.42 (m, 1H), 7.56-7.57 (m, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 27.3, 50.0, 115.7, 118.9, 127.1, 127.9,

128.4, 129.6, 130.7, 139.6, 140.8, 145.4, 190.4. HRMS calcd for $C_{17}H_{15}ClNO$: 284.0837 $[M+H]^+$, found: 284.0837.

(1-(3,5-Dimethylphenyl)-4,5-dihydro-1*H*-pyrrol-3-yl)(phenyl)methanone (7c)

Yellow solid (84 mg, 61%), mp 88-89 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.29 (s, 6H), 3.14 (t, *J* = 10.0 Hz, 2H), 4.02 (t, *J* = 9.6 Hz, 2H), 6.53 (s, 2H), 6.65 (s, 1H), 7.44-7.50 (m, 4H), 7.66 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 21.5, 27.1, 50.0, 112.7, 117.9, 124.2, 128.0, 128.3, 130.4, 139.4, 140.9, 141.1, 146.5, 190.2. HRMS calcd for $C_{19}H_{20}NO$: 278.1539 $[M+H]^+$, found: 278.1545.

(1-Phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)(*m*-tolyl)methanone (7d)

Syrup (76 mg, 58%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.40 (s, 3H), 3.14 (t, *J* = 9.6 Hz, 2H), 4.02 (t, *J* = 9.6 Hz, 2H), 6.89 (d, *J* = 7.8 Hz, 2H), 6.99 (t, *J* = 7.2 Hz, 1H), 7.28-7.32 (m, 4H), 7.43 (d, *J* = 6.6 Hz, 1H), 7.47 (s, 1H), 7.51 (s, 1H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 21.5, 27.2, 49.9, 114.6, 118.3, 122.2, 125.1, 128.1, 128.6, 129.7, 131.3, 138.2, 140.9, 141.0, 146.2, 190.7. HRMS calcd for $C_{18}H_{18}NO$: 264.1383 $[M+H]^+$, found: 264.1382.

(3-Bromophenyl)(1-phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)methanone (7e)

Yellow solid (105 mg, 64%), mp 85-86 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.14 (t, *J* = 9.6 Hz, 2H), 4.05 (t, *J* = 9.6 Hz, 2H), 6.92 (d, *J* = 7.2 Hz, 2H), 7.02 (t, *J* = 7.2 Hz, 1H), 7.29-7.33 (m, 3H), 7.49 (s, 1H), 7.56 (d, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.78 (s, 1H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 27.1, 50.1, 114.9, 117.9, 122.6, 122.7, 126.5, 129.7, 130.0, 130.9, 133.4, 140.6, 142.8, 146.7, 188.3. HRMS calcd for $C_{17}H_{15}BrNO$: 328.0332 $[M+H]^+$, found: 328.0340.

(1-Phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)(*p*-tolyl)methanone (7f)

Syrup (82 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.42 (s, 3H), 3.16 (t, *J* = 10.0 Hz, 2H), 4.04 (t, *J* = 9.6 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 7.00 (t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 2H), 7.29-7.33 (m, 2H), 7.54(s, 1H), 7.57 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 21.5, 27.3, 49.8, 114.6, 118.3, 122.1, 128.1, 129.0, 129.6, 138.2, 140.9, 141.0, 145.9, 190.4. HRMS calcd for $C_{18}H_{18}NO$: 264.1383 $[M+H]^+$, found: 264.1386.

(4-Chlorophenyl)(1-phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)methanone (7g)

Syrup (82 mg, 58%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.14 (t, *J* = 9.6 Hz, 2H), 4.04 (t, *J* = 9.6 Hz, 2H), 6.91 (d, *J* = 7.2 Hz, 2H), 7.01 (t, *J* = 7.2 Hz, 1H), 7.31 (t, *J* = 7.2 Hz, 2H), 7.40 (d, *J* = 7.2 Hz, 2H), 7.49 (s, 1H), 7.59 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 27.1, 50.0, 114.8, 118.0, 122.5, 128.6, 129.4, 129.7, 136.6, 139.2, 140.7, 146.4, 188.8. HRMS calcd for $C_{17}H_{15}ClNO$: 284.0837 $[M+H]^+$, found: 284.0837.

(4-Bromophenyl)(1-phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)methanone (7h)

Syrup (98 mg, 60%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.13 (t, *J* = 9.6 Hz, 2H), 4.03 (t, *J* = 9.6 Hz, 2H), 6.91 (d, *J* = 7.8 Hz, 2H), 7.01 (t, *J* = 7.2 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.49 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.56 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 27.1, 49.9, 114.8, 118.0, 122.5, 124.9, 129.6, 129.7, 131.5, 139.7, 140.7, 146.2, 188.9. HRMS calcd for $C_{17}H_{15}BrNO$: 328.0332 $[M+H]^+$, found: 328.0331.

(1-Benzyl-1*H*-pyrrol-3-yl)(phenyl)methanone (8a)[14]

Syrup (70 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.06 (s, 2H), 6.68 (t, *J* = 2.8 Hz, 1H), 6.72 (t, *J* = 2.8 Hz, 1H), 7.12-7.14 (m, 2H), 7.26-7.35 (m, 4H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.48-7.51 (m, 1H), 7.80-7.82 (m, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 53.9, 111.4, 122.8, 124.8, 127.3, 128.2, 128.4, 128.9, 129.0, 131.4, 136.6, 140.1, 190.7. HRMS calcd for $C_{18}H_{15}NNaO$: 284.1046 $[M+Na]^+$, found: 284.1048.

(1-Benzyl-1*H*-pyrrol-3-yl)(3-(trifluoromethyl)phenyl)methanone (8b)

Syrup (77 mg, 47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.11 (s, 2H), 6.68-6.70 (m, 1H), 6.72-6.74 (m, 1H), 7.16-7.18 (m, 2H), 7.26-7.27 (m, 1H), 7.32-7.38 (m, 3H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 7.2 Hz, 1H), 8.07 (s, 1H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 54.0, 111.4, 123.1, 123.9 (q, $^{1}J_{C\text{-}F}$ = 270.1 Hz), 124.2, 125.7 (q, $^{3}J_{C\text{-}F}$ = 4.3 Hz), 127.4, 127.8 (q, $^{3}J_{C\text{-}F}$ = 3.6 Hz), 128.3, 128.4, 128.8, 129.1, 130.7 (q, $^{2}J_{C\text{-}F}$ = 32.7 Hz), 132.1, 136.2, 140.6, 189.0. HRMS calcd for $C_{19}H_{15}F_3NO$: 330.1100 $[M+H]^+$, found: 330.1113.

(1-Benzyl-1*H*-pyrrol-3-yl)(4-chlorophenyl)methanone (8c)

Syrup (75 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.09 (s, 2H), 6.68-6.71 (m, 2H), 7.15-7.17 (m, 2H), 7.26-7.27 (m, 1H), 7.32-7.38 (m, 3H), 7.40-7.43 (m, 2H), 7.75-7.79 (m, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 54.0, 111.4, 122.9, 124.5, 127.3, 128.1, 128.3, 128.5, 129.0, 130.3, 136.4, 137.6, 138.3, 189.3. HRMS calcd for $C_{18}H_{15}ClNO$: 296.0837 $[M+H]^+$, found: 296.0852.

4-((3-Benzoyl-1*H*-pyrrol-1-yl)methyl)benzonitrile (8d)

Yellow solid (81 mg, 57%), mp 103-104 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 5.17 (s, 2H), 6.69 (s, 1H), 6.75 (s, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.27 (s, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 2H), 7.82 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 53.3, 112.0, 112.2, 118.4, 122.8, 125.3, 127.5, 128.2, 128.3, 128.9, 131.6, 132.8, 139.7, 142.0, 190.6. HRMS calcd for $C_{19}H_{14}N_2NaO$: 309.0998 $[M+Na]^+$, found: 309.1004.

(1-Methyl-1*H*-pyrrol-3-yl)(phenyl)methanone (8e)[3b]

Yellow solid (55 mg, 59%), mp 88-89 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.67 (s, 3H), 6.62 (s, 1H), 6.67 (s, 1H), 7.16 (s, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 36.7, 111.1, 123.4, 124.6, 128.2, 128.8, 129.1, 131.3, 140.1, 190.7. HRMS calcd for $C_{12}H_{11}NNaO$: 208.0733 $[M+Na]^+$, found: 208.0730.

(4-Bromophenyl)(1-methyl-1*H*-pyrrol-3-yl)methanone (8f)

Syrup (79 mg, 60%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.70 (s, 3H), 6.64 (s, 2H), 7.16 (s, 1H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 36.7, 111.1, 123.5, 124.3, 126.0, 128.9, 130.5, 131.4, 138.8, 189.3. HRMS calcd for $C_{12}H_{10}BrNNaO$: 285.9838 $[M+Na]^+$, found: 285.9842.

3-(3-Benzoyl-1H-pyrrol-1-yl)propanenitrile (8g)[15]

Syrup (53 mg, 47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.71 (t, *J* = 6.8 Hz, 2H), 4.09 (t, *J* = 6.4 Hz, 2H), 6.60-6.62 (m, 1H), 6.65-6.66 (m, 1H), 7.18-7.19 (m, 1H), 7.33-7.37 (m, 2H), 7.41-7.45 (m, 1H), 7.70-7.72 (m, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 20.6, 45.5, 111.9, 117.0, 122.1, 125.3, 127.8, 128.3, 128.9, 131.7, 139.7, 190.6. HRMS calcd for $C_{14}H_{12}N_2NaO$: 247.0842 $[M+Na]^+$, found: 247.0849.

Phenyl(1-phenyl-4,5,6,7-tetrahydro-1*H*-azepin-3-yl)methanone (10a)

Syrup (91 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.93-2.00 (m, 4H), 2.84 (t, *J* = 6.4 Hz, 2H), 4.03 (t, *J* = 6.0 Hz, 2H), 6.96 (d, *J* = 8.0 Hz, 2H), 7.04 (t, *J* = 7.2 Hz, 1H), 7.25-7.29 (m, 3H), 7.33-7.39 (m, 3H), 7.52 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 23.5, 25.3, 27.5, 50.6, 119.1, 119.4, 123.7, 128.0, 128.5, 129.5, 129.8, 141.2, 146.5, 152.9, 197.1. HRMS calcd for $C_{19}H_{20}NO$: 278.1539 $[M+H]^+$, found: 278.1539.

(1-(4-Methoxyphenyl)-4,5,6,7-tetrahydro-1*H*-azepin-3-yl)(phenyl)methanone (10b)

Syrup (109 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.93-1.97 (m, 4H), 2.84 (t, *J* = 6.0 Hz, 2H), 3.75 (s, 3H), 3.96 (t, *J* = 5.6 Hz, 2H), 6.78-6.82 (m, 2H), 6.90-6.94 (m, 2H), 7.19 (s, 1H), 7.33-7.36 (m, 3H), 7.48-7.50 (m, 2H). ^{13}C NMR (100 Hz, $CDCl_3$) δ: 23.4, 25.6, 27.7, 51.7, 55.6, 114.6, 117.4, 121.9, 127.9, 128.5, 129.6, 140.6, 141.5, 154.1, 156.6, 196.8. HRMS calcd for $C_{20}H_{22}NO_2$: 308.1645 $[M+H]^+$, found: 308.1647.

(1-(4-Bromophenyl)-4,5,6,7-tetrahydro-1*H*-azepin-3-yl)(phenyl)methanone (10c)

Syrup (115 mg, 65%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.95-1.96 (m, 4H), 2.82-2.83 (m, 2H), 3.97 (br s, 2H), 6.81 (d, *J* = 7.8 Hz, 2H), 7.21 (s, 1H), 7.35-7.40 (m, 5H), 7.51 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 23.8, 25.1, 27.4, 50.6, 116.2, 120.2, 120.6, 128.0, 128.5, 130.1, 132.4, 140.9, 145.5, 151.8, 197.2. HRMS calcd for $C_{19}H_{19}BrNO$: 356.0645 $[M+H]^+$, found: 356.0646.

(1-Phenyl-4,5,6,7-tetrahydro-1*H*-azepin-3-yl)(*p*-tolyl)methanone (10d)

Yellow solid (92 mg, 63%), mp 80-81 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.96-1.98 (m, 4H), 2.35 (s, 3H), 2.83-2.84 (m, 2H), 4.00-4.02 (m, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 7.03 (t, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 7.6 Hz, 2H), 7.26-7.30 (m, 3H), 7.44 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 21.4, 23.7, 25.3, 27.5, 50.5, 119.28, 119.33, 123.5, 128.7, 128.8, 129.5, 138.3, 140.2, 146.5, 152.3, 197.0. HRMS calcd for $C_{20}H_{22}NO$: 292.1696 $[M+H]^+$, found: 292.1678.

(3-Bromophenyl)(1-phenyl-4,5,6,7-tetrahydro-1*H*-azepin-3-yl)methanone (10e)

Syrup (105 mg, 59%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.94-2.01 (m, 4H), 2.82-2.83 (m, 2H), 4.01-4.04 (m, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 7.08 (t, *J* = 7.2 Hz, 1H), 7.20-7.26 (m, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.51 (dd, J_1 = 7.6 Hz, J_2 = 0.8 Hz, 1H), 7.66 (d, *J* = 1.2 Hz, 1H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 23.5, 25.3, 27.5, 50.9, 118.5, 119.8, 122.2, 124.2, 127.0, 129.57, 129.59, 131.4, 132.7, 143.3, 146.6, 153.4, 195.1. HRMS calcd for $C_{19}H_{19}BrNO$: 356.0645 $[M+H]^+$, found: 356.0649.

(4-Chlorophenyl)(1-phenyl-4,5,6,7-tetrahydro-1*H*-azepin-3-yl)methanone (10f)

Yellow solid (95 mg, 61%), mp 121-122 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.97-1.98 (m, 4H), 2.82-2.83 (m, 2H), 4.02 (br s, 2H), 6.96 (d, *J* = 7.2 Hz, 2H), 7.07 (t, *J* = 6.6 Hz, 1H), 7.24 (s, 1H), 7.28 (t, *J* = 6.6 Hz, 2H), 7.32 (d, *J* = 7.8 Hz, 2H), 7.46 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR (150 Hz, $CDCl_3$) δ: 23.6, 25.3, 27.5, 50.9, 118.7, 119.6, 124.1, 128.2, 129.6, 130.0, 135.9, 139.6, 146.6, 152.9, 195.5. HRMS calcd for $C_{19}H_{19}ClNO$: 312.1150 $[M+H]^+$, found: 312.1149.

2. Scale-up Synthesis of 3a.

To a reaction tube equipped with a stir bar were added 1-phenylpiperidine (**1a**, 5 mmol), CH_3CN (20 mL), 2-oxo-2-phenylacetic acid (**2a**, 6 mmol), $CuBr_2$ (0.5 mmol) and TBP (10 mmol) with stirring. The mixture was stirred under air at 60 ℃ for 24 h. Then, it was quenched with water (20 mL), and extracted with ethyl acetate (60 mL × 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (5:1) as the eluent to give **3a** (0.71 g, 54%).

Supporting Information. Copies of ^{1}H and ^{13}C NMR spectra of all products and the X-ray crystal structure and data of **3a**. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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