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Cascade Oxidative Coupling/Cyclization: A Gateway to 3-Amino Polysubstituted Five-Membered Heterocycles

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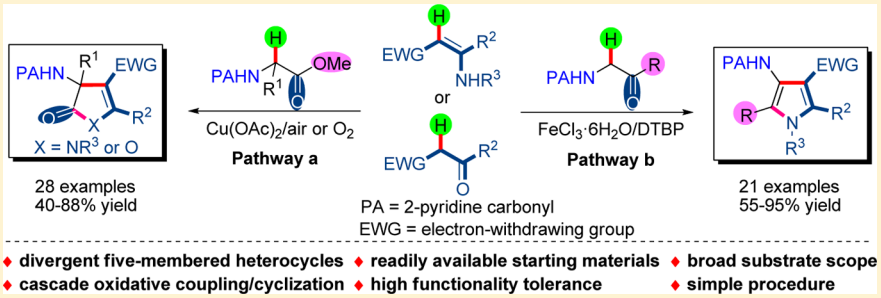
Supporting Information



ABSTRACT: Taking advantage of the coordinating activation strategy, we have developed the cascade oxidative coupling/cyclization of α-C(sp^3)−H bonds of amines with enamines or β-keto esters for the synthesis of three types of five-membered heterocycles. α-Amino acids as the substrate lead to 3-amino 1,3-dihydro-2*H*-pyrrol-2-ones and furan-2(3*H*)-ones by using air or dioxygen as the sole clean oxidant, respectively. α-Amino ketones give a range of 3-amino 1*H*-pyrroles by using di-*tert*-butyl peroxide as the oxidant. A three-component, one-pot reaction from readily available amine, β-keto ester, and α-amino ketone enhances the practicality of the modular construction of 1*H*-pyrrole scaffolds. This programmed protocol features simple reaction conditions, readily available starting materials, broad substrate scope, and high functional group tolerance.

INTRODUCTION

Domino reactions, which enable the formation of two or more chemical bonds in sequence in a one-pot reaction without the need for time-consuming protection/deprotection and isolation of intermediates, are a powerful and ideal strategy for the efficient and rapid synthesis of complex molecular structures.[1,2] With minimal waste generation and a green chemical transformation method, a vast variety of complex heterocyclic architectures can be easily accessed in the least amount of steps.[2] Generally, these cascade transformations require functionalized reaction partners. In principle, this inherent problem could be smoothly solved by using a transition-metal-catalyzed oxidative coupling reaction of abundant and accessible starting materials because it efficiently avoids the prefunctionalization of substrates. Despite an appealing strategy, the design and development of novel domino reactions involving transition-metal-catalyzed oxidative C-(sp^3)−H bond transformations is still a challenging puzzle.[3] The serious inadequacy of successful examples may be explained by the following issues. First, the transition-metal-catalyzed oxidative coupling reaction of C(sp^3)−H bonds is still in its infancy,[4,5] rendering logical and strategic bond disconnections involving an oxidative coupling reaction difficult. Second, harsh oxidation conditions are usually unavoidable, resulting from incompatibility with reactive functionalities, which are necessary for sequential transformations.

3-Amino polysubstituted five-membered heterocycles as important structural motifs and synthetically important precursors in drug discovery and natural product synthesis have attracted great interest from organic chemists (Figure 1).[6] Despite its great importance, however, methods to obtain such scaffolds are relatively rare and are often limited by multistep synthesis, low yield, prefunctionalized starting materials, reaction scope, and/or functional group tolerance, which restrict the structural diversity and practicability.[2,6−8] Thus, a simple, general, and straightforward procedure for their preparation is in high demand. Following our continuous interest in C(sp^3)−H functionalizations,[3h,9] we now disclose the divergent synthesis of 3-amino polysubstituted five-membered heterocycles through the cascade reactions between α-C(sp^3)−H bonds of amines and enamines containing an electron-withdrawing group (EWG) or β-keto esters.

As illustrated in Scheme 1, our retrosynthetic analysis for targeted 3-amino polysubstituted five-membered heterocycles begins with an intermolecular oxidative coupling of α-C(sp^3)−H bonds of amines with enamines or β-keto esters, followed by a cyclization. However, the practical implementation of the disconnection strategy faces the following two obstacles. First, enamines as the nucleophile in oxidative coupling reactions have not yet been demonstrated so far, which may be ascribed

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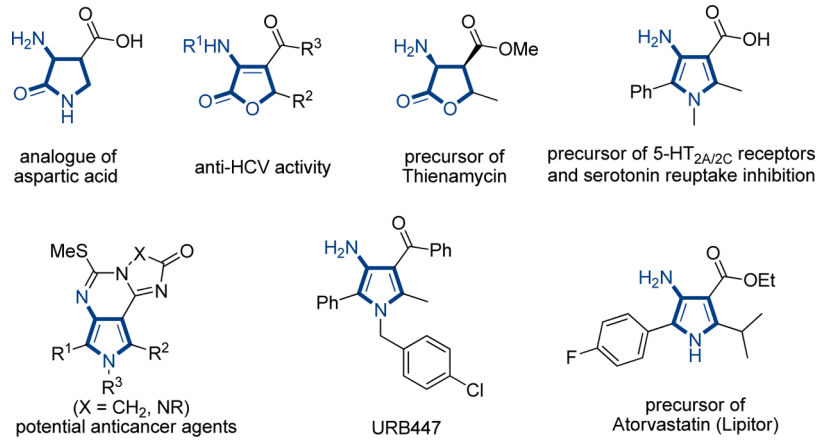
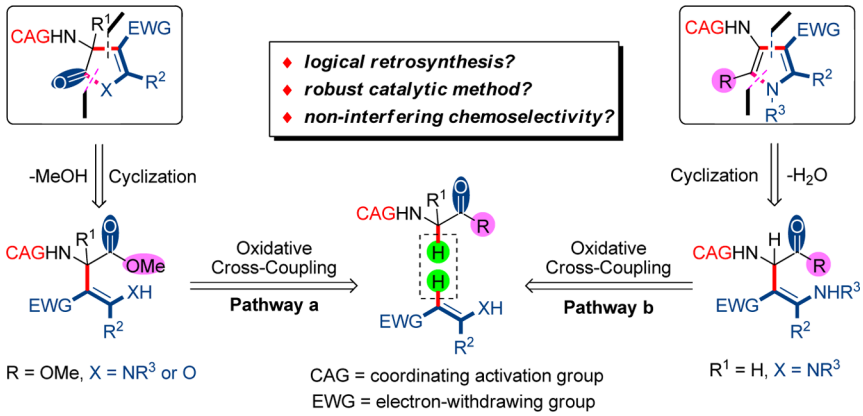


Figure 1. Selected biological and pharmaceutical molecules containing 3-amino polysubstituted five-membered heterocycles.

Scheme 1. Retrosynthetic Analysis for 3-Amino Five-Membered Heterocycles



to the difficult compatibility and stability of reactive enamines in the existing methods. Thus, one of the bottlenecks of this protocol would be the establishment of an efficient method to allow the oxidative couple of α-C(sp^3)−H bonds of amines such as α-amino acid and α-amino ketone substrates with enamines or β-keto esters. Second, it is difficult to find a catalytic reaction condition suitable for both the intermolecular oxidative coupling and subsequent cyclization in one pot. Recently, we developed a coordinating activation strategy for activating α-C(sp^3)−H bonds of amines by tethering the coordinating 2-pyridine carbonyl group at the nitrogen atom, in which the coordination of a metal center toward the coordinating group could activate amine substrates.[9b,e] In the current work, we envisioned that such a coordinating activation strategy in association with a simple metal salt such as copper or iron salt, which serves not only as the catalyst for oxidative coupling process but also as Lewis acid for cyclization, would smoothly promote this cascade oxidative coupling/cyclization process under mild conditions. Thus, a combination of readily available substrates with a metal salt as the catalyst would offer an attractive and practical gateway to rapidly assemble a library of 3-amino five-membered heterocycles.

RESULTS AND DISCUSSION

Among the coordinating groups developed by us, the 2-pyridine carbonyl group has proved to be an ideal candidate for illuminating the coordinating activation strategy.[9b,e] Consequently, we focused on the oxidative coupling/cyclization reaction of easily available methyl 2-phenyl-2-(picolinamido)-acetate (**1a**) with ethyl (*Z*)-3-(*p*-tolylamino)but-2-enoate (**2a**) as a model reaction under air atmosphere (Table 1). First, a range of catalysts such as iron, nickel, and copper salts were investigated (Table 1, entries 1−6 and 8). Fortunately, copper salts displayed the catalytic activity, and 20 mol % of $Cu(OAc)_2$ gave the fully substituted 3-amino 1,3-dihydro-2*H*-pyrrol-2-one **3a** in a good yield in dioxane at 110 °C for 24 h (Table 1, entry 5). In the absence of metal catalyst, no desired product **3a** was observed (Table 1, entry 7). However, other N-protecting groups such as benzoyl and tosyl failed to produce the targeted compound under the standard reaction conditions. Interestingly, when 20 mol % of $FeCl_3{\cdot}6H_2O$ was employed in combination with di-*tert*-butyl peroxide (DTBP) as the oxidant in 1,2-dichloroethylene (1,2-DCE) at 110 °C for 24 h under air atmosphere, the desired product **3a** could also be obtained in 73% yield (Table 1, entry 20). After various parameters such as solvent, reaction time, and temperature were screened, 3-amino polysubstituted 1,3-dihydro-2*H*-pyrrol-2-one was obtained in 76% yield in the presence of $Cu(OAc)_2$ (20 mol %) in dioxane under air atmosphere (Table 1, entry 5). It is worth noting that no additional oxidant is required in the copper catalytic system, and accordingly, dioxygen from air as the sole oxidant makes this procedure simple and green.

With the optimized reaction conditions in hand, we investigated the enamine scope of the cascade oxidative coupling/cyclization reaction (Table 2). To our delight, a relatively broad range of enamines could couple with 2-phenyl-2-(picolinamido)acetate (**1a**). For instance, both *N*-aryl- and *N*-

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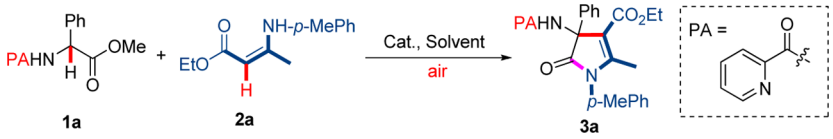
Table 1. Optimization of the Oxidative Coupling/Cyclization of Methyl 2-Phenyl-2-(picolinamido)acetate 1a with Ethyl 3-(*p*-Tolylamino)but-2-enoate 2a[a]



entry	cat.	solvent	temp (°C)	yield (%)[b]
1	$FeCl_3·6H_2O$	dioxane	110	ND
2	$Ni(acac)_2$	dioxane	110	ND
3	CuBr	dioxane	110	11
4	$CuCl_2$	dioxane	110	ND
5	**$Cu(OAc)_2$**	**dioxane**	**110**	**76**
6[c]	$Cu(OAc)_2$	dioxane	110	43
7		dioxane	110	ND
8	$Cu(OAc)_2·H_2O$	dioxane	110	59
9	$Cu(OAc)_2$	THF	110	ND
10	$Cu(OAc)_2$	toluene	110	48
11	$Cu(OAc)_2$	1,2-DCE	110	46
12	$Cu(OAc)_2$	CH_3CN	110	58
13[d]	$Cu(OAc)_2$	dioxane	110	54
14[e]	$Cu(OAc)_2$	dioxane	110	49
15[f]	$Cu(OAc)_2$	dioxane	110	61
16[g]	$Cu(OAc)_2$	dioxane	110	ND
17[h]	$Cu(OAc)_2$	dioxane	110	51
18	$Cu(OAc)_2$	dioxane	120	73
19	$Cu(OAc)_2$	dioxane	100	46
20[i]	**$FeCl_3·6H_2O$**	**1,2-DCE**	**110**	**73**

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (2.0 equiv), solvent (1.0 mL), and cat. (20 mol %) at indicated temperature for 24 h under air. [b]Isolated yield after chromatographic purification. [c]10 mol % of $Cu(OAc)_2$ was used. [d]The reaction was performed under O_2. [e]The reaction was performed for 18 h. [f]DTBP (2.0 equiv) was used as the oxidant under N_2 atmosphere. [g]$K_2S_2O_8$ (2.0 equiv) was used as the oxidant under N_2 atmosphere. [h]Ag_2CO_3 (2.0 equiv) was used as the oxidant under N_2 atmosphere. [i]DTBP (3.0 equiv) and 1,2-DCE (2.0 mL) were used. PA = 2-pyridine carbonyl.

alkyl-substituted *β*-enamino esters **2** allowed access to 3-amino 1,3-dihydro-2*H*-pyrrol-2-ones (Table 2, **3a**−**3g**). *β*-Enamino esters **2** could be ethyl, methyl, and benzyl esters and smoothly reacted with **1a** to afford the desired products in good yields (Table 2, **3a**, **3h**, and **3i**). Fortunately, N-unsubstituted *β*-enamino esters **2** were tolerated well (Table 2, **3k** and **3l**).[10] It is notable that 1,3-dihydro-2*H*-pyrrol-2-ones with a variety of substituents on the C5-position, such as alkyl, aryl, heteroaryl, and even hydrogen, could be synthesized in good yields. In addition to various *β*-enamino esters, other types of enamines such as *β*-enamino ketone, *β*-enamino sulfone, and *β*-enamino nitrile also smoothly coupled with **1a** to afford 3-amino 1,3-dihydro-2*H*-pyrrol-2-ones in synthetically useful yields (Table 2, **3u**−**3w**). Furthermore, other *α*-amino acid substrates such as phenylalanine and thienylalanine derivatives could undergo the oxidative coupling/cyclization with *β*-enamino esters in good yields using the Fe(III)/DTBP catalytic system (Table 2, **3x** and **3y**). Interestingly, when dienamine was used as a reaction partner, the desired di-1,3-dihydro-2*H*-pyrrol-2-one **3m** was obtained in 60% yield. More importantly, this methodology was very tolerant of synthetically valuable functional groups on enamines (e.g., halide, nitrile, ester, ketone, sulfone, and alkoxy groups, etc.), which would offer an opportunity for further transformation.

To extend the application scope of the catalytic system, *β*-keto esters as the reaction partner were investigated. To our delight, these reactions smoothly proceeded to furnish 3-amino furan-2(3*H*)-ones in synthetically useful yields under slightly modified reaction conditions (Table 3, **4a**−**4c**).[10]

To further demonstrate the substrate-controlled strategy for the synthesis of diverse molecules, we next sought to identify substrates that could form other kinds of heterocycles (Table 4). Fortunately, when *α*-amino ketones were used instead of *α*-amino acid esters, 3-amino 1*H*-pyrroles were smoothly furnished. Amazingly, a wide range of enamine substrates could undergo the oxidative coupling/cyclization with *α*-amino ketones, leading to various 3-amino 1*H*-pyrroles in good yields under the Fe(III)/DTBP catalytic system (Table 4, **5a**−**5t**).[10] Lewis acids such as $AlCl_3$, $ZnCl_2$, or $Zn(OTf)_2$ could not catalyze this transformation. Furthermore, the reaction could proceed well in the presence of $FeCl_3$ as the catalyst under both air and N_2 atmosphere, giving **5a** in 76 and 77% yields, respectively. This protocol was compatible with the functional groups such as alkyl, aryl, halide, nitrile, ester, ketone, and alkoxy groups. N-Unsubstituted enamines **2** could be tolerated to give free (NH)-3-amino pyrroles. Notably, $Cu(OAc)_2$ (20 mol %) could also be used as the catalyst, affording **5b** in 44% yield in dioxane at room temperature under air for 12 h.

Subsequently, a three-component, one-pot reaction for the preparation of 3-amino 1*H*-pyrroles was investigated (Table 5). In the presence of $FeCl_3·6H_2O$ (20 mol %), *β*-enamino esters were easily formed by the condensation of amine and *β*-keto ester at room temperature. Then, in situ formed *β*-enamino ester underwent sequential oxidative coupling/cyclization with *α*-amino ketone under the standard conditions, affording 3-amino 1*H*-pyrroles in moderate to good yields. This modular one-pot synthesis of 3-amino polysubstituted 1*H*-pyrroles from three simple and easily available starting materials enhances the

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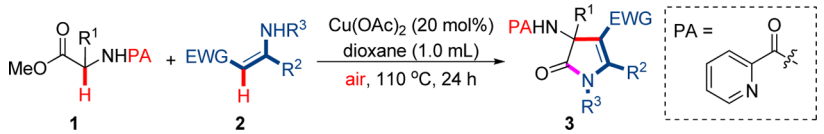
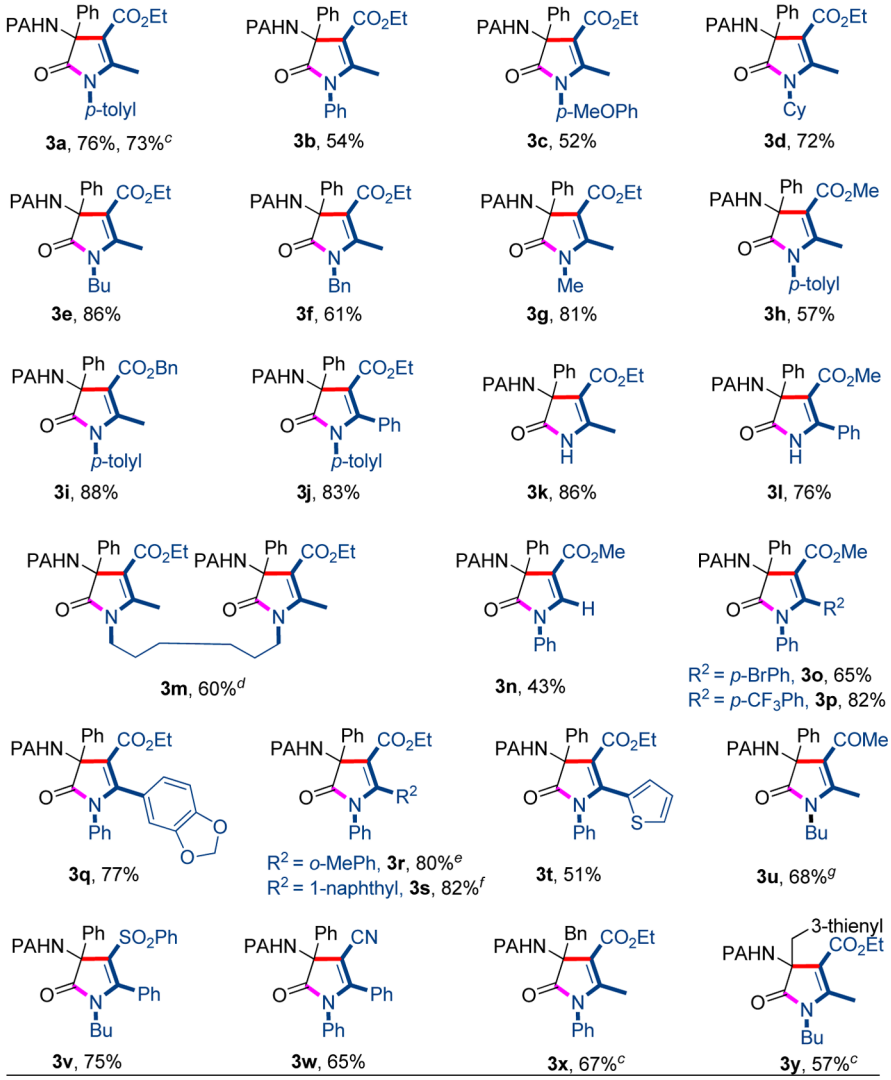
Table 2. Scope of 3-Amino Polysubstituted 1,3-Dihydro-2*H*-pyrrol-2-ones[a,b]





[a]Reaction conditions: **1** (0.25 mmol), **2** (0.50 mmol, 2.0 equiv), $Cu(OAc)_2$ (20 mol %), and dioxane (1.0 mL) at 110 °C for 24 h under air. [b]Isolated yields. [c]$FeCl_3·6H_2O$ (20 mol %), DTBP (0.75 mmol, 3.0 equiv), and DCE (2.0 mL) at 110 °C for 24 h under air. [d]**1** (0.75 mmol), **2** (0.25 mmol), $Cu(OAc)_2$ (40 mol %), and dioxane (2 mL) for 36 h. [e]Diastereomeric ratio = 1.2:1 (^{1}H NMR analysis) attributed to the atropisomers because of hindered rotation. [f]Diastereomeric ratio = 2.0:1 (^{1}H NMR analysis) attributed to the atropisomers because of hindered rotation. [g]30 mol % of $Cu(OAc)_2$ was used. PA = 2-pyridine carbonyl.

practicality. Finally, the coordinating auxiliary 2-pyridine carbonyl group could be easily removed in good yield by treatment with $BF_3·Et_2O$ in enthanol at 140 °C for 12 h (Scheme 2).

To gain insight into the possible mechanism of this oxidative coupling/cyclization process, the following competition experiments were performed in the $Cu(OAc)_2$/air catalytic system. First, a radical trapping reagent (e.g., 2,2,6,6-tetramethylpiperidine oxide (TEMPO) and 2,6-di-*tert*-butyl-4-methylphenol (BHT)) could not suppress the reaction of **1a** with **2a** (Scheme 3A), implying that a free radical intermediate was not involved in this reaction. Second, when the reaction was performed with 20 mol % of $Cu(OAc)_2$ under N_2 atmosphere, only the desired product **3a** was obtained in 13% yield, except for the remaining starting materials, suggesting that the oxidative coupling step precedes the C−N bond-forming step. In addition, **3a** was obtained in 68% yield with a stoichiometric amount of $Cu(OAc)_2$ under the standard conditions, which indicated that dioxygen as the terminal oxidant was only involved in the reoxidation of copper(I) (Scheme 3B).[11] In the formation of 3-amino 1*H*-pyrrole, TEMPO could dramatically diminish the reaction efficiency of **1d** with **2b**, indicating that a free radical intermediate might be involved in the $FeCl_3·6H_2O$/DTBP catalytic system (Scheme 3C).[12]

Based on the above control experiments, the plausible mechanisms for these oxidative coupling/cyclization processes

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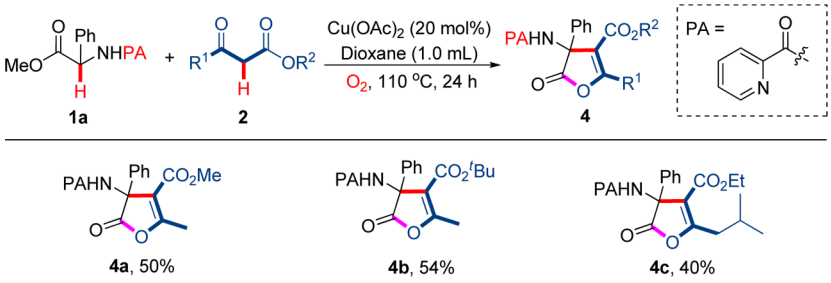
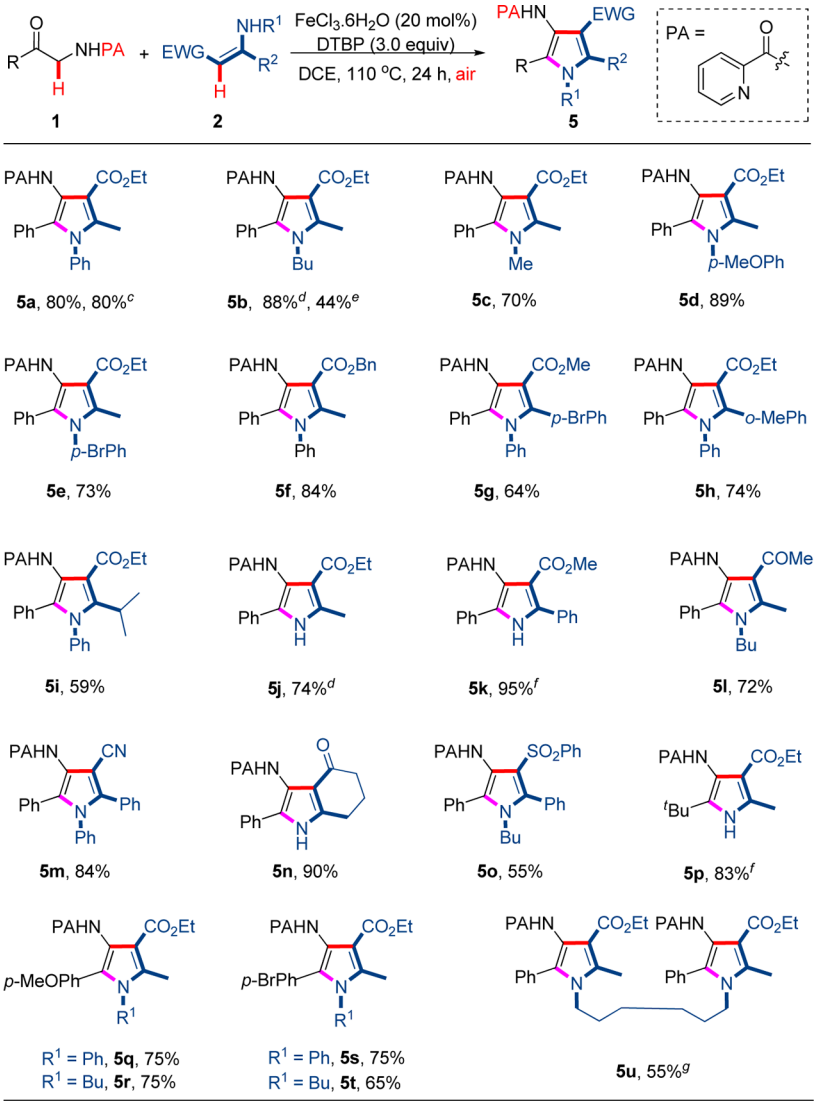
Table 3. Synthesis of 3-Amino Polysubstituted Furan-2(3*H*)-ones[a,b]



[a]Reaction conditions: **1a** (0.25 mmol), **2** (1.0 mmol, 4.0 equiv), $Cu(OAc)_2$ (20 mol %), and dioxane (1.0 mL) at 110 °C for 24 h under O_2. [b]Isolated yields. PA = 2-pyridine carbonyl.

Table 4. Scope of 3-Amino Polysubstituted 1*H*-Pyrroles[a,b]



[a]Reaction conditions: **1** (0.25 mmol), **2** (0.50 mmol, 2.0 equiv), $FeCl_3{\cdot}6H_2O$ (20 mol %), DTBP (0.75 mmol, 3.0 equiv), and DCE (2.0 mL) at 110 °C for 24 h under air. [b]Isolated yields. [c]The reaction was performed under N_2. [d]18 h. [e]$Cu(OAc)_2$ (20 mol %) and dioxane (1.0 mL) at room temperature for 12 h under air. [f]10 mol % of $FeCl_3{\cdot}6H_2O$ and 2.0 equiv of DTBP were used. [g]0.25 mmol of **2**, 0.75 mmol of **1**, $FeCl_3{\cdot}6H_2O$ (40 mol %), DTBP (6.0 equiv), and 1,2-DCE (4.0 mL) were used. PA = 2-pyridine carbonyl.

are proposed in Scheme 4. Initially, 2-pyridine carbonyl α-amino acid ester or α-amino ketone coordinates with a metal catalyst ($Cu(OAc)_2$ or $FeCl_3{\cdot}6H_2O$) to generate the intermediate **IM1** or **IM4**.[9b] Next, for the $Cu(OAc)_2$/air catalytic system (pathway a), the ketimine intermediate **IM2** is formed through oxidation by copper(II),[11,13] followed by the reaction with the nucleophile (enamine or β-keto ester). For the $FeCl_3{\cdot}6H_2O$/DTBP catalytic system (pathway b), the

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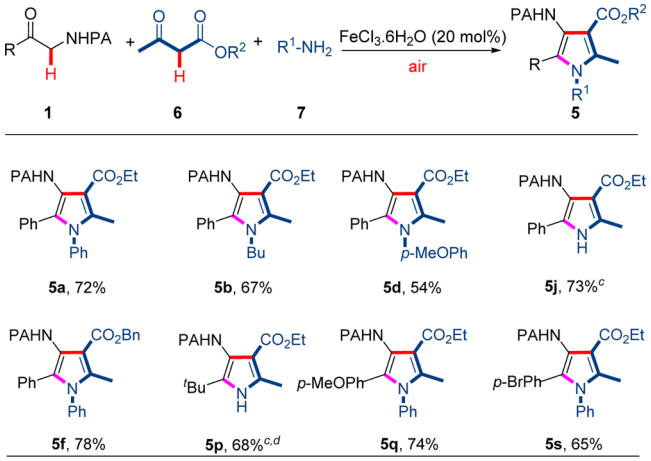
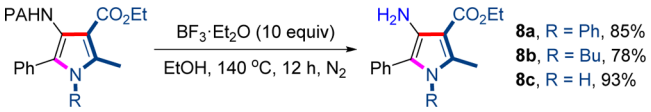
Table 5. One-Pot Synthesis of 3-Amino Polysubstituted 1*H*-Pyrroles[a,b]

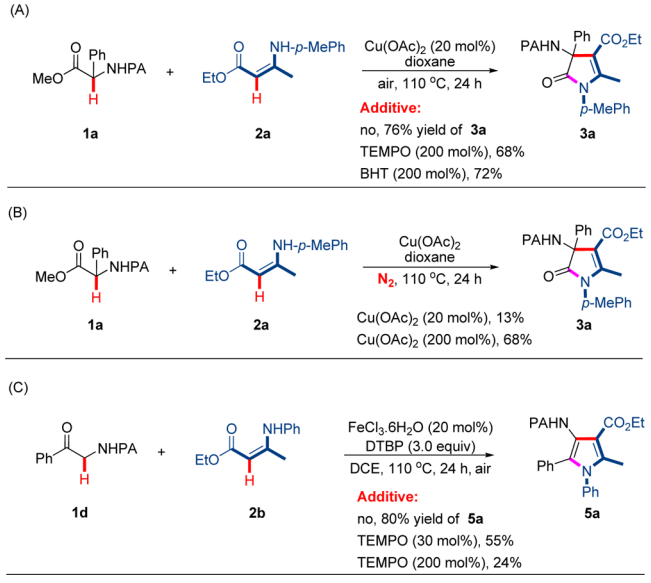


[a]Reaction conditions: **6** (0.50 mmol), **7** (0.50 mmol), $FeCl_3·6H_2O$ (20 mol %), and 1,2-DCE (2.0 mL) at 25 °C for 6 h under air. Then **1** (0.25 mmol) and DTBP (0.75 mmol, 3.0 equiv) were added and stirred at 110 °C for 24 h. [b]Isolated yields. [c]NH_4OAc (2.0 equiv) was used as the ammonia source. [d]DTBP (2.0 equiv) was used. PA = 2-pyridine carbonyl.

Scheme 2. Removal of the Auxiliary Group



Scheme 3. Investigation of the Reaction Mechanism



radical intermediate **IM5** is formed by abstracting the α-hydrogen atom of **IM4** by the *tert*-butoxy radical, followed by an intramolecular single-electron transfer to lead to the imine intermediate **IM6**. The coupled product **IM3-1** is formed through the Mannich-type reaction, which can tautomerize to the intermediate **IM3-2**. Subsequently, the cyclization process affords a 3-amino five-membered heterocycle. The released low-valent metal cataylst Cu(I) or Fe(II) is reoxidized by O_2 and DTBP, respectively.

CONCLUSION

In conclusion, we have developed divergent oxidative coupling/cyclization processes of α-amino acids/α-amino ketones with enamines or β-keto esters through Cu(II) or Fe(III) catalysis to produce 3-amino polysubstituted five-membered heterocycles including 3-amino 1,3-dihydro-2*H*-pyrrol-2-ones, 3-amino furan-2(3*H*)-ones, and 3-amino pyrroles. A three-component, one-pot reaction from simple and easily available amine, β-keto ester, and α-amino ketone enhances the practicality of the modular construction of 3-amino 1*H*-pyrrole scaffolds. This programmed protocol features simple reaction conditions, readily available starting materials, broad substrate scope, and high functional group tolerance. The coordinating activation strategy for activating α-C(sp^3)−H bonds has exhibited a potential in the concise synthesis of complex heterocycles.

EXPERIMENTAL SECTION

General Information. The ^1H NMR (400 MHz) chemical shifts were measured relative to $CDCl_3$ or TMS as the internal reference ($CDCl_3$, δ = 7.26 ppm; TMS, δ = 0.00 ppm). The ^{13}C NMR (100 MHz) chemical shifts were given using $CDCl_3$ as the internal standard ($CDCl_3$, δ = 77.16 ppm). High-resolution mass spectra (HR-MS) were obtained with a Q-TOF (ESI).

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. α-Amino acid derivatives and α-amino ketone derivatives **1** were prepared according to the literature procedure,[9b,14a] and enamine derivatives **2** were prepared according to the literature procedure.[14b−d] All solvents were purified and dried according to standard methods prior to use.

General Procedure for the Cascade Oxidative Coupling/Cyclization of α-Amino Acid Esters with Enamines or β-Keto Esters. A Schlenk tube with a magnetic stir bar was charged with α-amino acid derivatives **1** (0.25 mmol, 1.0 equiv), enamines **2** (0.50 mmol, 2.0 equiv) or β-keto esters **2** (1.0 mmol, 4.0 equiv), and $Cu(OAc)_2$ (9.1 mg, 0.05 mmol, 0.2 equiv) under air or O_2 atmosphere. The tube was sealed with a Teflon-coated cap, and the mixture was stirred at 110 °C for 24 h. After being cooled to ambient temperature, the solution was diluted with 20 mL of CH_2Cl_2, filtered through a Celite pad, and washed with 10−20 mL of CH_2Cl_2. The combined organic phases were concentrated, and the residue was purified by column chromatography on silica gel to provide the desired product.

General Procedure for the Cascade Oxidative Coupling/Cyclization of α-Amino Ketones with Enamines. A Schlenk tube with a magnetic stir bar was charged with α-amino ketone derivatives **1** (0.25 mmol, 1.0 equiv), enamines **2** (0.50 mmol, 2.0 equiv), $FeCl_3·6H_2O$ (13.6 mg, 0.05 mmol, 0.2 equiv), and DCE (2.0 mL) under an air atmosphere. The reaction mixture was stirred at room temperature for several minutes, and DTBP (137.0 μL, 0.75 mmol, 3.0 equiv) was then added. The tube was sealed with a Teflon-coated cap, and the mixture was stirred at 110 °C for 24 h. After being cooled to ambient temperature, the solution was diluted with 20 mL of CH_2Cl_2, filtered through a Celite pad, and washed with 10−20 mL of CH_2Cl_2. The combined organic phases were concentrated, and the residue was purified by column chromatography on silica gel to provide the desired product.

General Procedure for the Three-Component, One-Pot Synthesis of Polysubstituted 1*H*-Pyrroles. A Schlenk tube with a magnetic stir bar was charged with β-keto esters **6** (0.50 mmol, 2.0 equiv), amines **7** (0.50 mmol, 2.0 equiv), $FeCl_3·6H_2O$ (13.6 mg, 0.05 mmol, 0.2 equiv), and DCE (2.0 mL) under an air atmosphere. The reaction mixture was stirred at 25 °C for 6 h, and then α-amino ketone derivatives **1** (0.25 mmol, 1.0 equiv) and DTBP (137.0 μL, 0.75 mmol, 3.0 equiv) were added. The tube was sealed with a Teflon-coated cap, and the mixture was stirred at 110 °C for 24 h. After being cooled to ambient temperature, the solution was diluted with 20 mL of CH_2Cl_2, filtered through a Celite pad, and washed with 10−20 mL of CH_2Cl_2. The combined organic phases were concentrated, and the residue was

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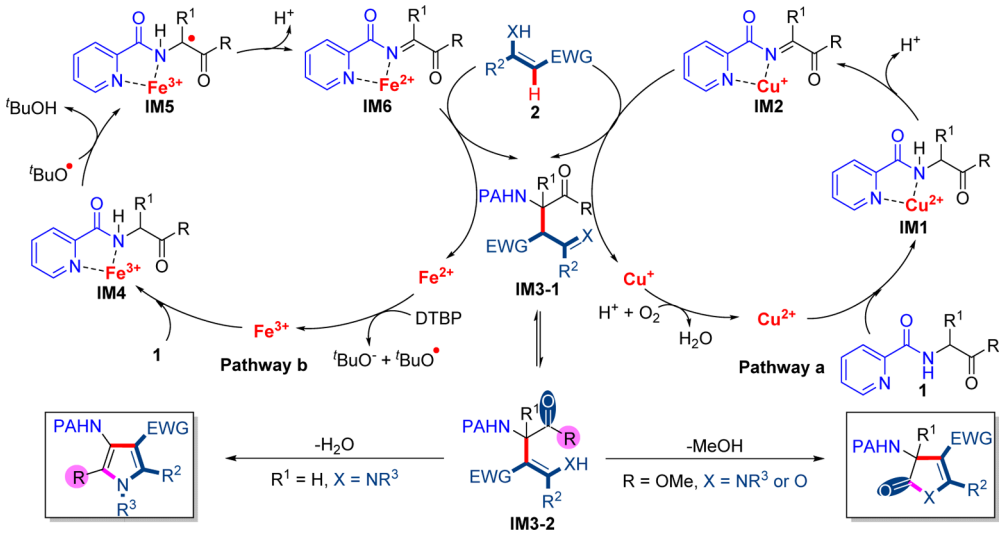
Scheme 4. Proposed Mechanism



purified by column chromatography on silica gel to provide the desired product.

*Methyl 2-Phenyl-2-(picolinamido)acetate (**1a**).*[9b] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.77 (s, 3H), 5.77 (d, J = 7.6 Hz, 1H), 7.32−7.40 (m, 3H), 7.42−7.49 (m, 3H), 7.83 (t, J = 7.6 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 8.59 (d, J = 4.4 Hz, 1H), 8.95 (d, J = 6.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.9, 56.7, 122.4, 126.5, 127.5, 128.7, 129.1, 136.6, 137.4, 148.3, 149.3, 163.8, 171.2 ppm.

*Methyl 3-Phenyl-2-(picolinamido)propanoate (**1b**).*[9b] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.19−3.29 (m, 2H), 3.73 (s, 3H), 5.05−5.10 (m, 1H), 7.18 (d, J = 7.6 Hz, 2H), 7.22−7.30 (m, 3H), 7.40−7.43 (m, 1H), 7.83 (t, J = 7.6 Hz, 1H), 8.16 (d, J = 7.6 Hz, 1H), 8.49 (d, J = 7.6 Hz, 1H), 8.55 (d, J = 4.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.4, 52.4, 53.6, 122.4, 126.5, 127.2, 128.7, 129.4, 136.1, 137.4, 148.4, 149.4, 164.1, 171.9 ppm.

*Methyl 2-(Picolinamido)-3-(thiophen-3-yl)propanoate (**1c**).*[9b] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.30 (d, J = 5.6 Hz, 2H), 3.75 (s, 3H), 5.04−5.09 (m, 1H), 6.93 (d, J = 4.4 Hz, 1H), 7.05 (s, 1H), 7.25−7.27 (m, 1H), 7.42−7.44 (m, 1H), 7.84 (t, J = 6.8 Hz, 1H), 8.17 (d, J = 7.6 Hz, 1H), 8.52 (d, J = 7.2 Hz, 1H), 8.56 (d, J = 4.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.8, 52.5, 53.0, 122.4, 122.9, 126.1, 126.5, 128.4, 136.2, 137.4, 148.4, 149.4, 164.1, 171.8 ppm.

*N-(2-Oxo-2-phenylethyl)picolinamide (**1d**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.97 (d, J = 4.8 Hz, 2H), 7.44 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.49−7.53 (m, 2H), 7.60−7.64 (m, 1H), 7.85 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.02−8.04 (m, 2H), 8.20 (d, J = 8.0 Hz, 1H), 8.62−8.63 (m, 1H), 8.95 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.5, 122.3, 126.5, 128.1, 129.0, 134.1, 134.7, 137.3, 148.5, 149.7, 164.7, 194.0 ppm. HRMS (ESI$^+$): calcd for $C_{14}H_{13}N_2O_2$ [M + H]$^+$ 241.0972, found 241.0967.

*N-(3,3-Dimethyl-2-oxobutyl)picolinamide (**1e**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (s, 9H), 4.48 (d, J = 4.8 Hz, 2H), 7.43 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.83 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 8.59 (dq, J = 4.8 Hz, 0.8 Hz, 1H), 8.70 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.5, 43.3, 44.8, 122.2, 126.4, 137.3, 148.5, 149.7, 164.7, 210.3 ppm. HRMS (ESI$^+$): calcd for $C_{12}H_{17}N_2O_2$ [M + H]$^+$ 221.1285, found 221.1287.

*N-(2-(4-Methoxyphenyl)-2-oxoethyl)picolinamide (**1f**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.89 (s, 3H), 4.92 (d, J = 4.8 Hz, 2H), 6.97−6.99 (m, 2H), 7.45 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.85 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.00−8.04 (m, 2H), 8.20 (d, J = 7.6 Hz, 1H), 8.63−8.64 (m, 1H), 8.97 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.1, 55.7, 114.2, 122.3, 126.4, 127.7, 130.4, 137.3, 148.5, 149.7, 164.3, 164.7, 192.3 ppm. HRMS (ESI$^+$): calcd for $C_{15}H_{14}N_2NaO_3$ [M + Na]$^+$ 293.0897, found 293.0910.

*N-(2-(4-Bromophenyl)-2-oxoethyl)picolinamide (**1g**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.93 (d, J = 4.8 Hz, 2H), 7.45 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.64−7.67 (m, 2H), 7.85 (td, J = 7.6 Hz, 1.6 Hz, 1H), 7.88−7.91 (m, 2H), 8.19 (d, J = 7.6 Hz, 1H), 8.62 (dq, J = 4.8 Hz, 0.8 Hz, 1H), 8.91 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.4, 122.4, 126.6, 129.4, 129.6, 132.4, 133.4, 137.4, 148.6, 149.5, 164.8, 193.1 ppm. HRMS (ESI$^+$): calcd for $C_{14}H_{11}BrN_2NaO_2$ [M + Na]$^+$ 340.9896, found 340.9899.

*Ethyl 2-Methyl-5-oxo-4-phenyl-4-(picolinamido)-1-p-tolyl-4,5-dihydro-1H-pyrrole-3-carboxylate (**3a**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.24) afforded **3a** as a pale yellow solid (86.8 mg, 76% yield). Mp: 136−138 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (t, J = 6.8 Hz, 3H), 2.38 (s, 3H), 2.42 (s, 3H), 4.01−4.15 (m, 2H), 7.26 (m, 4H), 7.38−7.48 (m, 4H), 7.67 (d, J = 6.8 Hz, 2H), 7.84 (t, J = 6.8 Hz, 1H), 8.18 (d, J = 7.6 Hz, 1H), 8.56 (m, 1H), 8.94 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 14.3, 21.3, 59.7, 65.1, 107.2, 122.3, 126.3, 126.5, 128.4, 128.9, 129.1, 130.1, 131.6, 137.29, 137.34, 138.9, 148.4, 149.4, 158.2, 163.8, 163.9, 175.1 ppm. IR (KBr): 3382, 2986, 1754, 1692, 1633, 1506, 1250, 1096 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{27}H_{25}N_3NaO_4$ [M + Na]$^+$ 478.1737, found 478.1742.

*Ethyl 2-Methyl-5-oxo-1,4-diphenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3b**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.22) afforded **3b** as a pale yellow solid (60.2 mg, 54% yield). Mp: 124−126 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (t, J = 6.8 Hz, 3H), 2.43 (s, 3H), 4.01−4.17 (m, 2H), 7.38−7.48 (m, 9H), 7.68 (d, J = 7.2 Hz, 2H), 7.83 (t, J = 7.6 Hz, 1H), 8.17 (d, J = 8.0 Hz, 1H), 8.55−8.56 (m, 1H), 8.95 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 14.3, 59.7, 65.1, 107.3, 122.3, 126.2, 126.5, 128.6, 128.9, 129.1, 129.5, 134.2, 137.2, 137.3, 148.4, 149.3, 157.9, 163.8, 163.9, 175.0 ppm. IR (KBr): 3385, 2983, 1753, 1700, 1682, 1630, 1495, 1241, 1092 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{26}H_{23}N_3NaO_4$ [M + Na]$^+$ 464.1581, found 464.1592.

*Ethyl 1-(4-Methoxyphenyl)-2-methyl-5-oxo-4-phenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3c**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.26) afforded **3c** as a pale yellow solid (60.8 mg, 52% yield). Mp: 176−178 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (t, J = 7.2 Hz, 3H), 2.41 (s, 3H), 3.81 (s, 3H), 4.00−4.17 (m, 2H), 6.96 (d, J = 9.2 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.36−7.44 (m, 4H), 7.66−7.68 (m, 2H), 7.83 (td, J = 8.0 Hz, 1.6 Hz, 1H), 8.16 (d, J = 7.6 Hz, 1H), 8.55−8.56 (m, 1H), 8.94 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.3, 55.6, 59.6, 65.0, 107.0, 114.7, 122.3, 126.2, 126.5, 126.8, 128.9, 129.1, 129.8, 137.2, 137.3, 148.4, 149.3, 158.4, 159.8, 163.8, 163.9, 175.3 ppm. IR (KBr): 3378, 2928, 1753, 1691, 1633, 1512, 1250, 1096 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{27}H_{25}N_3NaO_5$ [M + Na]$^+$ 494.1686, found 494.1692.

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*Ethyl 1-Cyclohexyl-2-methyl-5-oxo-4-phenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3d**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.28) afforded **3d** as a pale yellow solid (80.7 mg, 72% yield). Mp: 110−112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00 (t, J = 7.2 Hz, 3H), 1.15−1.32 (m, 3H), 1.62−1.71 (m, 2H), 1.78−1.94 (m, 3H), 2.08−2.27 (m, 2H), 2.68 (s, 3H), 3.68−3.75 (m, 1H), 3.92−4.09 (m, 2H), 7.31−7.41 (m, 4H), 7.53−7.55 (m, 2H), 7.79 (t, J = 7.6 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.52−8.53 (m, 1H), 8.83 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.2, 14.2, 25.3, 26.2, 26.3, 29.9, 30.0, 54.4, 59.4, 64.9, 107.1, 122.3, 125.8, 126.4, 128.6, 129.0, 137.2, 137.7, 148.3, 149.4, 158.6, 163.5, 163.7, 175.6 ppm. IR (KBr): 3390, 2931, 2857, 1740, 1690, 1626, 1500, 1219, 1094 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{26}H_{29}N_3NaO_4$ [M + Na]$^+$ 470.2050, found 470.2048.

*Ethyl 1-Butyl-2-methyl-5-oxo-4-phenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3e**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.26) afforded **3e** as a pale yellow solid (91.1 mg, 86% yield). Mp: 116−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, J = 7.2 Hz, 3H), 1.03 (t, J = 7.2 Hz, 3H), 1.25−1.38 (m, 2H), 1.50−1.75 (m, 2H), 2.66 (s, 3H), 3.50−3.65 (m, 2H), 3.95−4.12 (m, 2H), 7.33−7.43 (m, 4H), 7.56−7.58 (m, 2H), 7.81 (t, J = 7.6 Hz, 1H), 8.12 (d, J = 7.6 Hz, 1H), 8.53−8.54 (m, 1H), 8.84 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.6, 13.8, 14.3, 20.1, 31.1, 40.5, 59.5, 64.9, 106.9, 122.3, 126.0, 126.4, 128.8, 129.1, 137.3, 137.5, 148.3, 149.4, 157.9, 163.66, 163.74, 175.5 ppm. IR (KBr): 3383, 2965, 2872, 1736, 1689, 1627, 1337, 1069 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{24}H_{27}N_3NaO_4$ [M + Na]$^+$ 444.1894, found 444.1897.

*Ethyl 1-Benzyl-2-methyl-5-oxo-4-phenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3f**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.22) afforded **3f** as a pale yellow solid (69.6 mg, 61% yield). Mp: 120−122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03 (t, J = 7.2 Hz, 3H), 2.50 (s, 3H), 3.95−4.12 (m, 2H), 4.77 (d, J = 16.4 Hz, 1H), 4.95 (d, J = 16.0 Hz, 1H), 7.24−7.30 (m, 5H), 7.39−7.42 (m, 4H), 7.63 (d, J = 7.2 Hz, 2H), 7.83 (t, J = 7.6 Hz, 1H), 8.17 (d, J = 8.0 Hz, 1H), 8.55−8.56 (m, 1H), 8.90 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.0, 14.2, 44.0, 59.6, 65.1, 107.3, 122.3, 126.1, 126.5, 126.9, 127.6, 128.88, 128.92, 129.2, 136.7, 137.3, 137.4, 148.3, 149.3, 157.6, 163.6, 163.7, 175.6 ppm. IR (KBr): 3365, 2948, 1754, 1693, 1627, 1502, 1435, 1094, 697 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{27}H_{25}N_3NaO_4$ [M + Na]$^+$ 478.1737, found 478.1740.

*Ethyl 1,2-Dimethyl-5-oxo-4-phenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3g**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.21) afforded **3g** as a yellow solid (77.1 mg, 81% yield). Mp: 138−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (t, J = 7.2 Hz, 3H), 2.64 (s, 3H), 3.17 (s, 3H), 3.97−4.13 (m, 2H), 7.33−7.43 (m, 4H), 7.57−7.59 (m, 2H), 7.82 (td, J = 7.6 Hz, 1.2 Hz, 1H), 8.10 (d, J = 7.6 Hz, 1H), 8.53−8.55 (m, 1H), 8.85 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.7, 14.2, 26.9, 59.5, 64.9, 106.7, 122.2, 126.1, 126.5, 128.8, 129.0, 137.2, 137.3, 148.3, 149.2, 157.9, 163.6, 163.7, 175.6 ppm. IR (KBr): 3384, 2975, 1744, 1690, 1626, 1502, 1174, 1051 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{21}H_{21}N_3NaO_4$ [M + Na]$^+$ 402.1424, found 402.1433.

*Methyl 2-methyl-5-oxo-4-phenyl-4-(picolinamido)-1-p-tolyl-4,5-dihydro-1H-pyrrole-3-carboxylate (**3h**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.21) afforded **3h** as a brown solid (62.9 mg, 57% yield). Mp: 192−194 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3H), 2.42 (s, 3H), 3.63 (s, 3H), 7.26 (m, 4H), 7.39−7.43 (m, 4H), 7.67 (d, J = 7.2 Hz, 2H), 7.83 (t, J = 7.2 Hz, 1H), 8.17 (d, J = 7.6 Hz, 1H), 8.56−8.57 (m, 1H), 8.95 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 21.3, 51.0, 65.1, 106.9, 122.3, 126.3, 126.5, 128.4, 128.9, 129.2, 130.1, 131.6, 137.2, 137.3, 139.0, 148.4, 149.4, 158.4, 163.9, 164.3, 175.1 ppm. IR (KBr): 3380, 2952, 1750, 1696, 1634, 1505, 1245, 1096 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{26}H_{23}N_3NaO_4$ [M + Na]$^+$ 464.1581, found 464.1585.

*Benzyl 2-Methyl-5-oxo-4-phenyl-4-(picolinamido)-1-p-tolyl-4,5-dihydro-1H-pyrrole-3-carboxylate (**3i**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.25) afforded **3i** as a pale yellow solid (113.6 mg, 88% yield). Mp: 114−116 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3H), 2.43 (s, 3H), 5.01 (d, J = 12.8 Hz, 1H), 5.17 (d, J = 12.4 Hz, 1H), 7.04−7.06 (m, 2H), 7.11 (t, J = 7.2 Hz, 2H), 7.17 (t, J = 6.8 Hz, 1H), 7.26 (m, 4H), 7.37−7.42 (m, 4H), 7.66 (d, J = 7.2 Hz, 2H), 7.83 (t, J = 7.6 Hz, 1H), 8.16 (d, J = 7.6 Hz, 1H), 8.48−8.49 (m, 1H), 8.96 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 21.3, 65.1, 65.4, 106.9, 122.3, 126.2, 126.4, 127.7, 127.8, 128.3, 128.4, 128.9, 129.2, 130.2, 131.5, 136.3, 137.2, 137.3, 139.0, 148.4, 149.3, 159.1, 163.6, 163.8, 175.0 ppm. IR (KBr): 3376, 2934, 1753, 1689, 1629, 1496, 1243, 1092 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{32}H_{27}N_3NaO_4$ [M + Na]$^+$ 540.1894, found 540.1902.

*Ethyl 5-Oxo-2,4-diphenyl-4-(picolinamido)-1-p-tolyl-4,5-dihydro-1H-pyrrole-3-carboxylate (**3j**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.38) afforded **3j** as a white solid (108.3 mg, 83% yield). Mp: 178−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.2 Hz, 3H), 2.23 (s, 3H), 3.86−4.02 (m, 2H), 7.00−7.07 (m, 4H), 7.27−7.34 (m, 3H), 7.37−7.40 (m, 2H), 7.42−7.50 (m, 4H), 7.79−7.81 (m, 2H), 7.85 (t, J = 7.6 Hz, 1H), 8.22 (d, J = 7.6 Hz, 1H), 8.57−8.59 (m, 1H), 9.04−9.05 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 21.2, 59.7, 65.5, 108.6, 122.4, 126.2, 126.5, 127.7, 128.1, 129.0, 129.3, 129.45, 129.50, 129.6, 129.9, 131.9, 137.2, 137.3, 137.7, 148.4, 149.4, 158.1, 162.8, 164.0, 175.1 ppm. IR (KBr): 3348, 2982, 1749, 1694, 1623, 1499, 1338, 1125 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{32}H_{27}N_3NaO_4$ [M + Na]$^+$ 540.1894, found 540.1902.

*Ethyl 2-Methyl-5-oxo-4-phenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3k**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/1, v/v, R_f = 0.26) afforded **3k** as a pale yellow solid (78.9 mg, 86% yield). Mp: 214−216 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (t, J = 7.2 Hz, 3H), 2.52 (s, 3H), 3.97−4.13 (m, 2H), 7.34−7.44 (m, 4H), 7.59−7.62 (m, 2H), 7.82 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.11 (d, J = 7.6 Hz, 1H), 8.55−8.56 (m, 1H), 8.80 (s, 1H), 8.92 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 14.3, 59.6, 65.8, 107.1, 122.3, 126.2, 126.6, 128.9, 129.1, 137.1, 137.4, 148.5, 149.2, 156.3, 163.7, 176.4 ppm. IR (KBr): 3374, 3257, 2989, 1755, 1694, 1670, 1633, 1513, 1082 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{20}H_{19}N_3NaO_4$ [M + Na]$^+$ 388.1268, found 388.1275.

*Methyl 5-Oxo-2,4-diphenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3l**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.21) afforded **3l** as a white solid (79.5 mg, 76% yield). Mp: 220−222 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.48 (s, 3H), 7.38−7.44 (m, 7H), 7.67−7.69 (m, 4H), 7.81 (t, J = 8.0 Hz, 1H), 8.06 (d, J = 7.6 Hz, 1H), 8.11 (br s, 1H), 8.56−8.57 (m, 1H), 8.94 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.0, 66.5, 107.1, 122.5, 126.1, 126.5, 128.3, 129.0, 129.1, 129.3, 129.8, 130.8, 137.0, 137.4, 148.4, 149.3, 154.9, 163.3, 163.9, 176.1 ppm. IR (KBr): 3386, 3361, 2982, 2932, 1741, 1691, 1630, 1500, 1214, 1100 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{24}H_{19}N_3NaO_4$ [M + Na]$^+$ 436.1268, found 436.1267.

*Diethyl 1,1′-(Hexane-1,6-diyl)bis(2-methyl-5-oxo-4-phenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate) (**3m**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 2/1, v/v, R_f = 0.24) afforded **3m** as a pale yellow solid (120.6 mg, 60% yield). Mp: 156−158 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03 (t, J = 7.2 Hz, 6H), 1.23−1.28 (m, 4H), 1.51−1.54 (m, 2H), 1.60−1.67 (m, 2H), 2.61 (s, 6H), 3.43−3.61 (m, 4H), 3.95−4.12 (m, 4H), 7.27−7.33 (m, 1H), 7.34−7.42 (m, 7H), 7.55−7.57 (m, 4H), 7.77−7.82 (m, 2H), 8.09−8.11 (m, 2H), 8.53−8.54 (m, 2H), 8.82 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.7, 14.3, 26.1, 26.2, 28.8, 28.9, 40.3, 40.4, 59.5, 64.9, 106.90, 106.94, 122.3, 126.1, 126.4, 128.79, 128.81, 129.09, 129.11, 137.3, 137.51, 137.53, 148.3, 149.4, 157.8, 163.6, 163.7, 175.51, 175.54 ppm. IR (KBr): 3401, 2932, 1742, 1690, 1626, 1501, 1063 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{46}H_{48}N_6NaO_8$ [M + Na]$^+$ 835.3426, found 835.3437.

*Methyl 5-Oxo-1,4-diphenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3n**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.32) afforded

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3n as a pale yellow solid (44.3 mg, 43% yield). Mp: 202−204 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.71 (s, 3H), 7.29 (t, J = 7.2 Hz, 1H), 7.40−7.48 (m, 6H), 7.52−7.54 (m, 2H), 7.68−7.70 (m, 2H), 7.82 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.13 (d, J = 7.6 Hz, 1H), 8.16 (s, 1H), 8.56−8.57 (m, 1H), 8.98 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.5, 65.6, 112.0, 122.4, 122.7, 126.3, 126.7, 127.2, 129.36, 129.44, 136.0, 136.1, 137.4, 145.4, 148.5, 149.0, 162.8, 164.1, 174.2 ppm. IR (KBr): 3434, 2943, 1757, 1706, 1680, 1626, 1497, 1243, 1132 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{24}H_{20}N_3O_4$ [M + H]$^+$ 414.1448, found 414.1449.

*Methyl 2-(4-Bromophenyl)-5-oxo-1,4-diphenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3o**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.37) afforded **3o** as a pale yellow solid (94.9 mg, 65% yield). Mp: 240−242 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.49 (s, 3H), 7.15 (d, J = 7.6 Hz, 2H), 7.18−7.26 (m, 5H), 7.42−7.50 (m, 6H), 7.76 (d, J = 7.6 Hz, 2H), 7.86 (t, J = 7.6 Hz, 1H), 8.20 (d, J = 7.6 Hz, 1H), 8.58−8.59 (m, 1H), 9.04 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.3, 65.5, 108.7, 122.5, 124.3, 126.2, 126.6, 128.2, 128.3, 128.6, 129.1, 129.2, 129.4, 131.17, 131.24, 134.3, 136.9, 137.4, 148.5, 149.3, 157.0, 163.2, 164.2, 174.8 ppm. IR (KBr): 3354, 2948, 1752, 1705, 1682, 1634, 1494, 1240, 1120 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{30}H_{23}BrN_3O_4$ [M + H]$^+$ 568.0866, found 568.0871.

*Ethyl 5-Oxo-1,4-diphenyl-4-(picolinamido)-2-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3p**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.43) afforded **3p** as a pale yellow solid (116.7 mg, 82% yield). Mp: 142−144 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.2 Hz, 3H), 3.88−4.03 (m, 2H), 7.17−7.27 (m, 5H), 7.42−7.57 (m, 8H), 7.79−7.81 (m, 2H), 7.85 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 8.58−8.59 (m, 1H), 9.07 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 60.0, 65.5, 109.5, 122.4, 123.8 (d, J = 271.0 Hz), 124.8 (q, J = 4.0 Hz), 126.1, 126.6, 128.2, 128.3, 129.0, 129.2, 129.4, 130.1, 131.4 (q, J = 32.0 Hz), 133.6, 134.2, 136.7, 137.4, 148.5, 149.2, 156.3, 162.4, 164.2, 174.8 ppm. IR (KBr): 3374, 2988, 1754, 1701, 1640, 1495, 1327, 1124 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{32}H_{25}F_3N_3O_4$ [M + H]$^+$ 572.1792, found 572.1799.

*Ethyl 2-(Benzo[d][1,3]dioxol-5-yl)-5-oxo-1,4-diphenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3q**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.27) afforded **3q** as a pale yellow solid (105.4 mg, 77% yield). Mp: 188−190 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.2 Hz, 3H), 3.90−4.05 (m, 2H), 5.92 (s, 2H) 6.70−6.72 (m, 1H), 6.85−6.87 (m, 2H), 7.18−7.22 (m, 3H), 7.25−7.29 (m, 2H), 7.39−7.49 (m, 4H), 7.76−7.78 (m, 2H), 7.84 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.21 (d, J = 7.6 Hz, 1H), 8.57−8.58 (m, 1H), 9.03 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 59.8, 65.6, 101.4, 107.9, 108.7, 110.2, 122.4, 122.9, 124.2, 126.1, 126.5, 127.9, 128.3, 128.9, 129.0, 129.3, 134.7, 137.2, 137.3, 147.2, 148.4, 148.7, 149.4, 157.6, 162.7, 164.0, 174.9 ppm. IR (KBr): 3368, 2984, 2901, 1751, 1684, 1498, 1242, 1033 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{32}H_{25}N_3NaO_6$ [M + Na]$^+$ 570.1636, found 570.1647.

*Ethyl 5-Oxo-1,4-diphenyl-4-(picolinamido)-2-o-tolyl-4,5-dihydro-1H-pyrrole-3-carboxylate (**3r**).* The ratio of the two diastereoisomers is 1.2:1. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.26) afforded **3r** as a white solid (103.8 mg, 80% yield). Mp: 122−124 °C. ^{1}H NMR (400 MHz, $CDCl_3$, a mixture of two isomers): δ = 0.81−0.86 (m, $CO_2CH_2C\underline{H}_3$, major + minor isomer), 2.31 (s, $C\underline{H}_3$, major isomer), 2.45 (s, $C\underline{H}_3$, minor isomer), 3.84−4.00 (m, $CO_2C\underline{H}_2CH_3$, major + minor isomer), 7.06−7.24 (m), 7.33 (dd, J = 7.6 Hz, 1.6 Hz), 7.41−7.51 (m), 7.81−7.88 (m), 8.22−8.25 (m), 8.57−8.59 (m), 9.03 (s, PAN$\underline{H}$, major + minor isomer) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, a mixture of two isomers): δ = 13.80, 13.83, 19.9, 20.3, 59.7, 65.4, 65.5, 109.1, 109.5, 122.4, 122.5, 125.1, 125.5, 126.2, 126.5, 127.8, 127.95, 127.99, 128.6, 128.7, 129.06, 129.11, 129.2, 129.3, 129.4, 129.5, 129.6, 129.7, 130.1, 130.2, 130.4, 134.4, 134.5, 135.8, 137.2, 137.26, 137.28, 137.3, 137.4, 148.5, 149.5, 149.6, 158.2, 158.3, 162.66, 162.71, 163.9, 164.1, 174.8, 175.2 ppm. IR (KBr): 3367, 2973, 2926, 1748, 1701, 1628, 1497, 1240, 1106 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{32}H_{27}N_3NaO_4$ [M + Na]$^+$ 540.1894, found 540.1909.

*Ethyl 2-(Naphthalen-1-yl)-5-oxo-1,4-diphenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3s**).* The ratio of the two diastereoisomers is 2.0:1. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.24) afforded **3s** as a white solid (114.0 mg, 82% yield). Mp: 180−182 °C. ^{1}H NMR (400 MHz, $CDCl_3$, a mixture of two isomers): δ = 0.49−0.56 (m, $CO_2CH_2C\underline{H}_3$, major + minor isomer), 3.67−3.83 (m, $CO_2C\underline{H}_2CH_3$, major + minor isomer), 6.97−7.08 (m), 7.16−7.17 (m), 7.32−7.58 (m), 7.74−7.85 (m), 7.87−7.91 (m), 7.94−7.96 (m), 8.05−8.07 (m), 8.27 (d, J = 8.0 Hz), 8.35 (d, J = 7.6 Hz), 8.41−8.43 (m), 8.58−8.61 (m), 9.10−9.13 (m) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, a mixture of two isomers): δ = 13.37, 13.42, 59.6, 65.56, 65.57, 65.67, 65.69, 110.50, 110.51, 110.83, 110.85, 122.4, 122.6, 124.4, 124.8, 124.9, 126.1, 126.25, 126.31, 126.6, 126.7, 127.0, 127.2, 127.5, 127.9, 127.96, 128.00, 128.1, 128.5, 128.6, 128.7, 129.1, 129.2, 129.4, 129.7, 129.9, 131.3, 131.5, 133.01, 133.03, 134.4, 134.6, 137.1, 137.3, 137.4, 148.5, 149.4, 149.5, 157.0, 157.1, 162.5, 162.6, 164.1, 164.2, 175.0, 175.4 ppm. IR (KBr): 3361, 2978, 1749, 1697, 1630, 1498, 1333, 1093 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{35}H_{28}N_3O_4$ [M + H]$^+$ 554.2074, found 554.2078.

*Ethyl 5-Oxo-1,4-diphenyl-4-(picolinamido)-2-(thiophen-2-yl)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3t**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.20) afforded **3q** as yellow solid (66.1 mg, 51% yield). Mp: 168−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, J = 7.2 Hz, 3H), 3.93−4.09 (m, 2H), 6.94 (dd, J = 4.8 Hz, 3.6 Hz, 1H), 7.21−7.32 (m, 6H), 7.40−7.49 (m, 5H), 7.75−7.77 (m, 2H), 7.85 (td, J = 8.0 Hz, 1.6 Hz, 1H), 8.21 (d, J = 8.0 Hz, 1H), 8.58−8.59 (m, 1H), 9.03 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 60.0, 65.8, 110.4, 122.5, 126.1, 126.5, 126.6, 128.3, 128.5, 128.6, 129.0, 129.1, 129.3, 129.4, 132.3, 134.9, 137.1, 137.4, 148.4, 149.4, 150.8, 162.6, 164.0, 174.6 ppm. IR (KBr): 3354, 1751, 1687, 1619, 1494, 1114, 753, 696 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{29}H_{23}N_3NaO_4S$ [M + Na]$^+$ 532.1301, found 532.1315.

*N-(4-Acetyl-1-butyl-5-methyl-2-oxo-3-phenyl-2,3-dihydro-1H-pyrrol-3-yl)picolinamide (**3u**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.15) afforded **3u** as a brown solid (66.9 mg, 68% yield). Mp: 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, J = 7.2 Hz, 3H), 1.27−1.37 (m, 2H), 1.49−1.72 (m, 2H), 2.06 (s, 3H), 2.69 (s, 3H), 3.52−3.65 (m, 2H), 7.36−7.46 (m, 4H), 7.57−7.59 (m, 2H), 7.83 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.11 (d, J = 7.6 Hz, 1H), 8.55−8.56 (m, 1H), 8.95 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.4, 13.7, 20.1, 30.3, 31.0, 40.4, 65.1, 116.1, 122.4, 126.0, 126.7, 129.2, 129.6, 137.0, 137.5, 148.5, 149.1, 157.9, 163.4, 175.3, 192.7 ppm. IR (KBr): 3403, 2957, 2869, 1734, 1680, 1622, 1595, 1499, 1357, 1069 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{23}H_{25}N_3NaO_3$ [M + Na]$^+$ 414.1788, found 414.1797.

*N-(1-Butyl-2-oxo-3,5-diphenyl-4-(phenylsulfonyl)-2,3-dihydro-1H-pyrrol-3-yl)picolinamide (**3v**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.24) afforded **3v** as yellow oil (104.1 mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.64 (t, J = 7.2 Hz, 3H), 0.94−1.06 (m, 2H), 1.18−1.41 (m, 2H), 3.09−3.16 (m, 1H), 3.40−3.47 (m, 1H), 6.85 (t, J = 7.2 Hz, 2H), 7.11−7.19 (m, 4H), 7.42−7.61 (m, 7H), 7.76 (d, J = 6.0 Hz, 1H), 7.81 (t, J = 7.6 Hz, 1H), 7.90−7.91 (m, 3H), 8.63 (m, 1H), 9.05 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.4, 19.6, 30.5, 41.2, 66.9, 115.3, 122.2, 126.3, 126.7, 127.3, 127.6, 128.0, 128.3, 128.4, 128.6, 129.35, 129.38, 130.6, 130.8, 132.3, 136.3, 137.3, 142.5, 148.5, 149.0, 158.4, 163.5, 174.4 ppm. IR (KBr): 3382, 3061, 2960, 2870, 1744, 1683, 1619, 1588, 1496, 1150, 1071 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{32}H_{30}N_3O_4S$ [M + H]$^+$ 552.1952, found 552.1954.

*N-(4-Cyano-2-oxo-1,3,5-triphenyl-2,3-dihydro-1H-pyrrol-3-yl)-picolinamide (**3w**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.26) afforded **3w** as a brown solid (75.7 mg, 65% yield). Mp: 100−102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19−7.21 (m, 2H), 7.25−7.36 (m, 5H), 7.39−7.57 (m, 7H), 7.84−7.88 (m, 3H), 8.18 (d, J = 7.6 Hz, 1H),

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8.56−8.57 (m, 1H), 8.95 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 65.6, 90.8, 115.8, 122.5, 126.5, 127.0, 127.5, 127.8, 128.3, 128.7, 129.0, 129.2, 129.9, 130.0, 131.2, 134.4, 135.0, 137.5, 148.5, 148.6, 159.6, 164.2, 174.2 ppm. IR (KBr): 3353, 2213, 1758, 1696, 1631, 1593, 1493, 1370, 1335, 1144 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{29}H_{20}N_4NaO_2$ $[M + Na]^+$ 479.1478, found 479.1479.

*Ethyl 4-Benzyl-2-methyl-5-oxo-1-phenyl-4-(picolinamido)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3x**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.19) afforded **3x** as a brown solid (76.5 mg, 67% yield). Mp: 118−120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (t, J = 7.2 Hz, 3H), 1.94 (s, 3H), 3.36 (d, J = 12.0 Hz, 1H), 3.75 (d, J = 11.6 Hz, 1H), 4.21−4.35 (m, 2H), 6.85 (br s, 2H), 7.16−7.17 (m, 2H), 7.26−7.31 (m, 3H), 7.33−7.40 (m, 3H), 7.42−7.45 (m, 1H), 7.82 (t, J = 8.0 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.59−8.60 (m, 1H), 8.68 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.3, 14.6, 41.7, 59.8, 63.8, 105.9, 122.3, 126.5, 127.5, 128.0, 128.3, 128.9, 129.4, 130.5, 133.5, 133.8, 137.3, 148.3, 149.2, 156.3, 163.3, 163.9, 175.8 ppm. IR (KBr): 3383, 2982, 1749, 1684, 1628, 1507, 1380, 1104 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{27}H_{25}N_3NaO_4$ $[M + Na]^+$ 478.1737, found 478.1748.

*Ethyl 1-Butyl-2-methyl-5-oxo-4-(picolinamido)-4-(thiophen-3-ylmethyl)-4,5-dihydro-1H-pyrrole-3-carboxylate (**3y**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.22) afforded **3y** as pale yellow oil (63.2 mg, 57% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, J = 7.2 Hz, 3H), 1.15−1.34 (m, 7H), 2.25 (s, 3H), 3.24−3.34 (m, 1H), 3.32 (d, J = 12.4 Hz, 1H), 3.41−3.48 (m, 1H), 3.67 (d, J = 12.4 Hz, 1H), 4.16−4.25 (m, 2H), 6.79 (d, J = 4.8 Hz, 1H), 6.96 (d, J = 2.8 Hz, 1H), 7.12 (dd, J = 4.8 Hz, 3.2 Hz, 1H), 7.39−7.42 (m, 1H), 7.78 (t, J = 7.6 Hz, 1H), 8.05 (dd, J = 7.6 Hz, 0.8 Hz, 1H), 8.51 (s, 1H), 8.55−8.56 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.3, 13.8, 14.6, 20.2, 30.8, 36.3, 40.1, 59.6, 62.9, 105.6, 122.3, 124.2, 124.6, 126.4, 129.3, 133.7, 137.3, 148.3, 149.3, 156.8, 163.0, 163.8, 176.5 ppm. IR (KBr): 3386, 2960, 2930, 2870, 1737, 1688, 1624, 1510, 1070, 774 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{23}H_{28}N_3O_4S$ $[M + H]^+$ 442.1795, found 442.1798.

*Methyl 2-Methyl-5-oxo-4-phenyl-4-(picolinamido)-4,5-dihydrofuran-3-carboxylate (**4a**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.25) afforded **4a** as a pale yellow solid (44.0 mg, 50% yield). Mp: 168−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.62 (s, 3H), 3.66 (s, 3H), 7.43−7.45 (m, 4H), 7.57−7.59 (m, 2H), 7.85 (t, J = 7.6 Hz, 1H), 8.14 (d, J = 7.6 Hz, 1H), 8.56−8.57 (m, 1H), 8.86 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6, 51.6, 64.0, 109.0, 122.5, 126.3, 126.9, 129.4, 129.6, 135.7, 137.5, 148.6, 163.2, 164.3, 166.6, 171.5 ppm. IR (KBr): 3378, 2953, 1820, 1716, 1679, 1498, 1434, 1149, 1035 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{19}H_{16}N_2NaO_5$ $[M + Na]^+$ 375.0951, found 375.0956.

*tert-Butyl 2-Methyl-5-oxo-4-phenyl-4-(picolinamido)-4,5-dihydrofuran-3-carboxylate (**4b**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/4, v/v, R_f = 0.36) afforded **4b** as a pale yellow solid (53.8 mg, 54% yield). Mp: 186−188 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 9H), 2.58 (s, 3H), 7.40−7.48 (m, 4H), 7.56−7.58 (m, 2H), 7.86 (t, J = 7.6 Hz, 1H), 8.15 (d, J = 7.6 Hz, 1H), 8.55−8.56 (m, 1H), 8.80 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 28.1, 64.0, 81.5, 110.5, 122.5, 126.2, 126.9, 129.3, 129.5, 136.1, 137.6, 148.5, 148.7, 161.9, 164.2, 165.8, 171.6 ppm. IR (KBr): 3394, 2978, 2931, 1822, 1705, 1681, 1496, 1431, 1149, 1033 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{22}H_{22}N_2NaO_5$ $[M + Na]^+$ 417.1421, found 417.1430.

*Ethyl 2-Isobutyl-5-oxo-4-phenyl-4-(picolinamido)-4,5-dihydrofuran-3-carboxylate (**4c**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/4, v/v, R_f = 0.40) afforded **4c** as a pale yellow solid (40.6 mg, 40% yield). Mp: 156−158 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.09−1.13 (m, 9H), 2.21−2.27 (m, 1H), 2.88−2.98 (m, 2H), 4.04−4.18 (m, 2H), 7.43−7.44 (m, 4H), 7.58−7.60 (m, 2H), 7.84 (t, J = 7.6 Hz, 1H), 8.15 (d, J = 7.6 Hz, 1H), 8.55 (m, 1H), 8.83 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.6, 22.7, 27.2, 36.7, 60.4, 64.0, 109.8, 122.6, 126.3, 126.9, 129.4, 129.5, 136.0, 137.5, 148.5, 148.8, 162.7, 164.1, 169.2, 171.7 ppm. IR (KBr): 3388, 2962, 2872, 1824, 1711, 1676, 1499, 1431, 1154, 1032 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{23}H_{25}N_2O_5$ $[M + H]^+$ 409.1758, found 409.1766.

*Ethyl 2-Methyl-1,5-diphenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5a**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.18) afforded **5a** as an offwhite solid (84.9 mg, 80% yield). Mp: 146−148 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (t, J = 7.2 Hz, 3H), 2.39 (s, 3H), 4.26 (q, J = 7.2 Hz, 2H), 7.07−7.13 (m, 7H), 7.32−7.35 (m, 3H), 7.40 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.79 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.15 (d, J = 7.6 Hz, 1H), 8.60−8.61 (m, 1H), 10.03 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.1, 14.3, 59.8, 108.1, 118.4, 122.6, 126.1, 127.0, 127.9, 128.3, 128.9, 129.0, 129.1, 129.7, 131.4, 136.3, 137.3, 137.6, 148.2, 150.3, 163.0, 165.3 ppm. IR (KBr): 3334, 2984, 1689, 1500, 1278, 1093, 699 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{26}H_{24}N_3O_3$ $[M + H]^+$ 426.1812, found 426.1822.

*Ethyl 1-Butyl-2-methyl-5-phenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5b**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.20) afforded **5b** as a pale yellow solid (89.2 mg, 88% yield). Mp: 102−104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.76 (t, J = 7.2 Hz, 3H), 1.16 (t, J = 7.2 Hz, 3H), 1.10−1.20 (m (overlap), 2H), 1.46−1.54 (m, 2H), 2.60 (s, 3H), 3.79 (t, J = 7.6 Hz, 2H), 4.20 (q, J = 7.2 Hz, 2H), 7.27−7.31 (m, 1H), 7.34−7.40 (m, 5H), 7.75 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 8.54−8.55 (m, 1H), 9.84 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.9, 13.6, 14.3, 19.8, 32.7, 44.1, 59.5, 107.1, 117.9, 122.4, 125.9, 127.8, 128.35, 128.42, 130.5, 131.9, 134.8, 137.2, 148.1, 150.3, 162.8, 165.3 ppm. IR (KBr): 3370, 2963, 2933, 2869, 1688, 1506, 1271, 1099, 702 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{24}H_{28}N_3O_3$ $[M + H]^+$ 406.2125, found 406.2130.

*Ethyl 1,2-Dimethyl-5-phenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5c**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.12) afforded **5c** as yellow oil (63.3 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (t, J = 7.2 Hz, 3H), 2.60 (s, 3H), 3.43 (s, 3H), 4.20 (q, J = 7.2 Hz, 2H), 7.28−7.31 (m, 1H), 7.35−7.41 (m, 5H), 7.78 (td, J = 8.0 Hz, 1.6 Hz, 1H), 8.12 (d, J = 7.6 Hz, 1H), 8.56−8.58 (m, 1H), 9.83 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.0, 14.3, 32.0, 59.6, 107.1, 117.7, 122.6, 126.1, 127.8, 128.5, 128.9, 130.2, 131.5, 135.6, 137.3, 148.1, 150.3, 163.2, 165.2 ppm. IR (KBr): 3328, 2979, 1686, 1611, 1513, 1280, 1091, 699 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{21}H_{22}N_3O_3$ $[M + H]^+$ 364.1656, found 364.1662.

*Ethyl 1-(4-Methoxyphenyl)-2-methyl-5-phenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5d**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.11) afforded **5d** as a dark brown solid (101.2 mg, 89% yield). Mp: 150−152 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (t, J = 7.2 Hz, 3H), 2.37 (s, 3H), 3.79 (s, 3H), 4.25 (q, J = 7.2 Hz, 2H), 6.82−6.85 (m, 2H), 7.01−7.05 (m, 2H), 7.07−7.12 (m, 5H), 7.40 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.79 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.14 (d, J = 7.6 Hz, 1H), 8.60−8.61 (m, 1H), 10.02 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.0, 14.3, 55.5, 59.7, 107.8, 114.2, 118.2, 122.6, 126.1, 126.9, 127.9, 129.1, 129.75, 129.82, 130.3, 131.6, 136.6, 137.3, 148.2, 150.3, 159.2, 162.9, 165.3 ppm. IR (KBr): 3324, 2988, 1699, 1692, 1513, 1246, 1081, 686 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{27}H_{26}N_3O_4$ $[M + H]^+$ 456.1918, found 456.1926.

*Ethyl 1-(4-Bromophenyl)-2-methyl-5-phenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5e**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.19) afforded **5e** as a pale yellow solid (92.1 mg, 73% yield). Mp: 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (t, J = 7.2 Hz, 3H), 2.39 (s, 3H), 4.26 (q, J = 7.2 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 7.08−7.16 (m, 5H), 7.41 (dd, J = 7.2 Hz, 4.8 Hz, 1H), 7.47 (d, J = 8.8 Hz, 2H), 7.80 (td, J = 7.6 Hz, 1.2 Hz, 1H), 8.14 (d, J = 8.0 Hz, 1H), 8.60−8.61 (m, 1H), 10.02 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.1, 14.3, 59.9, 108.5, 118.8, 122.3, 122.6, 126.2, 127.2, 128.1, 128.9, 129.8, 130.4, 131.2, 132.4, 136.1, 136.7, 137.3, 148.2, 150.2, 163.0, 165.1 ppm. IR (KBr): 3338, 2984, 1707, 1694, 1507, 1491, 1270, 1080, 697 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{26}H_{23}BrN_3O_3$ $[M + H]^+$ 504.0917, found 504.0929.

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*Benzyl 2-Methyl-1,5-diphenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5f**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.20) afforded **5f** as a pale yellow solid (102.2 mg, 84% yield). Mp: 102−104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.40 (s, 3H), 5.26 (s, 2H), 7.08−7.13 (m, 7H), 7.19−7.21 (m, 3H), 7.29−7.38 (m, 6H), 7.76 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.08 (d, J = 7.6 Hz, 1H), 8.47−8.48 (m, 1H), 9.92 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.3, 65.8, 108.0, 118.4, 122.6, 126.0, 127.1, 127.89, 127.93, 128.3, 128.4, 128.9, 129.1, 129.3, 129.8, 131.3, 136.5, 136.7, 137.2, 137.6, 148.2, 150.1, 163.2, 165.0 ppm. IR (KBr): 3343, 2925, 1691, 1515, 1496, 1419, 1090, 699 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{31}H_{26}N_3O_3$ [M + H]$^+$ 488.1969, found 488.1964.

*Methyl 2-(4-Bromophenyl)-1,5-diphenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5g**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.17) afforded **5g** as a pale yellow solid (88.5 mg, 64% yield). Mp: 182−184 °C. H NMR (400 MHz, $CDCl_3$): δ = 3.62 (s, 3H), 6.88 (d, J = 6.8 Hz, 2H), 7.07−7.14 (m, 10H), 7.33 (d, J = 8.0 Hz, 2H), 7.41−7.44 (m, 1H), 7.81 (t, J = 7.6 Hz, 1H), 8.15 (d, J = 7.6 Hz, 1H), 8.63−8.64 (m, 1H), 10.15 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.2, 109.5, 119.4, 122.5, 122.7, 126.3, 127.4, 127.9, 128.0, 128.7, 129.2, 130.0, 130.2, 130.5, 130.6, 131.1, 133.2, 136.4, 137.3, 137.4, 148.4, 150.2, 163.0, 164.9 ppm. IR (KBr): 3334, 2949, 1703, 1503, 1474, 1166, 1077, 697 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{30}H_{23}BrN_3O_3$ [M + H]$^+$ 552.0917, found 552.0923.

*Ethyl 1,5-Diphenyl-4-(picolinamido)-2-o-tolyl-1H-pyrrole-3-carboxylate (**5h**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.22) afforded **5h** as a pale yellow solid (92.9 mg, 74% yield). Mp: 92−94 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, J = 7.2 Hz, 3H), 2.14 (s, 3H), 3.98−4.13 (m, 2H), 6.89−6.90 (m, 2H), 7.01−7.08 (m, 5H), 7.11−7.19 (m, 7H), 7.42 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.80 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.15 (d, J = 7.6 Hz, 1H), 8.64−8.65 (m, 1H), 10.35 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 20.4, 59.7, 109.3, 119.3, 122.6, 124.8, 126.1, 127.1, 127.6, 127.9, 128.4, 128.5, 128.7, 129.0, 129.3, 129.8, 131.67, 131.71, 132.0, 137.3, 137.7, 137.9, 138.5, 148.4, 150.4, 162.6, 164.6 ppm. IR (KBr): 3342, 2975, 1700, 1501, 1262, 1168, 1077, 699 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{32}H_{28}N_3O_3$ [M + H]$^+$ 502.2125, found 502.2137.

*Ethyl 2-Isopropyl-1,5-diphenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5i**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.27) afforded **5i** as a pale yellow solid (66.4 mg, 59% yield). Mp: 112−1114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.2 Hz, 3H), 1.30 (d, J = 6.8 Hz, 3H), 3.10−3.17 (m, 1H), 4.28 (q, J = 7.2 Hz, 2H), 7.05−7.09 (m, 5H), 7.14−7.16 (m, 2H), 7.32−7.33 (m, 3H), 7.39 (dd, J = 7.6 Hz, 4.8 Hz, 1H), 7.78 (t, J = 8.0 Hz, 1H), 8.10 (d, J = 7.6 Hz, 1H), 8.59−8.60 (m, 1H), 10.13 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 20.9, 27.1, 60.0, 107.4, 118.8, 122.6, 126.1, 126.9, 127.8, 128.4, 128.6, 128.9, 129.4, 129.9, 131.8, 137.3, 138.2, 144.6, 148.2, 150.4, 162.4, 165.1 ppm. IR (KBr): 3365, 2974, 1695, 1503, 1264, 1175, 1069, 701 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{28}H_{28}N_3O_3$ [M + H]$^+$ 454.2125, found 454.2124.

*Ethyl 2-Methyl-5-phenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5j**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.17) afforded **5j** as a yellow solid (64.5 mg, 74% yield). Mp: 112−114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.2 Hz, 3H), 2.30 (s, 3H), 4.26 (q, J = 7.2 Hz, 2H), 7.09−7.17 (m, 3H), 7.28−7.31 (m, 2H), 7.45 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.82 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.17 (d, J = 7.6 Hz, 1H), 8.65−8.67 (m, 1H), 9.42 (s, 1H), 10.33 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 14.5, 59.6, 107.8, 117.2, 122.7, 124.1, 125.5, 126.3, 126.6, 128.5, 132.2, 135.9, 137.4, 148.4, 150.2, 162.7, 165.4 ppm. IR (KBr): 3351, 3285, 2977, 1697, 1669, 1518, 1087, 690 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{20}H_{19}N_3NaO_3$ [M + Na]$^+$ 372.1319, found 372.1326.

*Methyl 2,5-Diphenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5k**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.23) afforded **5k** as a yellow solid (94.4 mg, 95% yield). Mp: 116−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.69 (s, 3H), 7.19 (t, J = 7.2 Hz, 1H), 7.25−7.28 (m, 2H), 7.32−7.39 (m, 3H), 7.42−7.52 (m, 5H), 7.79 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.04 (dd, J = 8.0 Hz, 0.8 Hz, 1H), 8.67−8.68 (m, 1H), 8.94 (br s, 1H), 10.53 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.2, 107.8, 118.9, 122.8, 126.0, 126.1, 126.3, 127.3, 128.2, 128.5, 128.6, 129.3, 132.1, 136.4, 137.4, 148.5, 150.1, 162.4, 165.3 ppm. IR (KBr): 3262, 2948, 1679, 1522, 1463, 1258, 1068, 694 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{24}H_{19}N_3NaO_3$ [M + Na]$^+$ 420.1319, found 420.1324.

*N-(4-Acetyl-1-butyl-5-methyl-2-phenyl-1H-pyrrol-3-yl)-picolinamide (**5l**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.10) afforded **5l** as a dark brown solid (67.3 mg, 72% yield). Mp: 98−100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.76 (t, J = 7.2 Hz, 3H), 1.10−1.19 (m, 2H), 1.47−1.55 (m, 2H), 2.38 (s, 3H), 2.59 (s, 3H), 3.77 (t, J = 8.0 Hz, 2H), 7.27−7.39 (m, 6H), 7.77 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 8.51−8.52 (m, 1H), 9.65 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.7, 13.6, 19.9, 30.3, 32.8, 44.1, 117.1, 118.1, 122.6, 126.3, 128.1, 128.5, 129.4, 130.5, 131.1, 134.3, 137.4, 148.3, 149.8, 164.0, 195.1 ppm. IR (KBr): 3356, 2962, 2930, 1869, 1674, 1647, 1504, 1421, 703 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{23}H_{25}N_3NaO_2$ [M + Na]$^+$ 398.1839, found 398.1841.

*N-(4-Cyano-1,2,5-triphenyl-1H-pyrrol-3-yl)picolinamide (**5m**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.17) afforded **5m** as a yellow solid (92.6 mg, 84% yield). Mp: 108−110 °C. H NMR (400 MHz, $CDCl_3$): δ = 6.93−6.96 (m, 2H), 7.10−7.13 (m, 2H), 7.15−7.21 (m, 5H), 7.22−7.27 (m, 6H), 7.44 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.85 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.28 (d, J = 7.6 Hz, 1H), 8.52−8.53 (m, 1H), 9.57 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 93.0, 115.6, 120.6, 122.9, 126.7, 128.1, 128.31, 128.33, 128.4, 128.6, 128.7, 129.0, 129.1, 129.2, 129.9, 130.2, 130.3, 137.0, 137.5, 139.9, 148.2, 149.2, 163.9 ppm. IR (KBr): 3358, 2924, 2225, 1696, 1583, 1568, 1499, 697 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{29}H_{21}N_4O$ [M + H]$^+$ 441.1710, found 441.1714.

*N-(4-Oxo-2-phenyl-4,5,6,7-tetrahydro-1H-indol-3-yl)-picolinamide (**5n**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 2/1, v/v, R_f = 0.12) afforded **5n** as a gray solid (75.0 mg, 90% yield). Mp: 80−82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.96−2.03 (m, 2H), 2.39 (t, J = 6.4 Hz, 2H), 2.49 (t, J = 6.4 Hz, 2H), 7.09−7.16 (m, 3H), 7.27−7.30 (m, 2H), 7.44 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.81 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.14 (d, J = 8.0 Hz, 1H), 8.66−8.68 (m, 1H), 9.80 (s, 1H), 10.54 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.4, 23.8, 38.2, 115.3, 115.4, 122.6, 124.7, 125.8, 126.4, 126.7, 128.4, 132.2, 137.4, 143.1, 148.7, 149.9, 162.7, 195.1 ppm. IR (KBr): 3324, 3256, 2938, 1670, 1637, 1530, 1484, 692 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{20}H_{18}N_3O_2$ [M + H]$^+$ 332.1394, found 332.1389.

*N-(1-Butyl-2,5-diphenyl-4-(phenylsulfonyl)-1H-pyrrol-3-yl)-picolinamide (**5o**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.12) afforded **5o** as a pale yellow solid (73.5 mg, 55% yield). Mp: 168−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.50 (t, J = 7.2 Hz, 3H), 0.79−0.88 (m, 2H), 1.13−1.21 (m, 2H), 3.65 (t, J = 7.6 Hz, 2H), 7,15−7.19 (m, 2H), 7.30−7.51 (m, 14H), 7.78 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 8.65−8.67 (m, 1H), 9.95 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.3, 19.5, 32.5, 45.1, 116.4, 117.1, 122.5, 126.3, 127.1, 128.1, 128.4, 128.57, 128.63, 129.3, 129.96, 130.02, 130.2, 131.0, 131.5, 132.3, 135.9, 137.2, 143.2, 148.5, 149.9, 162.7 ppm. IR (KBr): 3437, 2959, 2930, 2869, 1693, 1509, 1316, 1150, 696, 606 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{32}H_{30}N_3O_3S$ [M + H]$^+$ 536.2002, found 536.2007.

*Ethyl 5-tert-Butyl-2-methyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5p**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/2, v/v, R_f = 0.13) afforded **5p** as a yellow solid (68.4 mg, 83% yield). Mp: 126−128 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (t, J = 7.2 Hz, 3H), 1.32 (s, 9H), 2.44 (s, 3H), 4.07 (q, J = 7.2 Hz, 2H), 7.44 (dd, J = 7.6 Hz, 4.8 Hz, 1H), 7.86 (td, J = 7.6 Hz, 1.2 Hz, 1H), 8.26 (d, J = 8.0 Hz, 1H), 8.34 (br s, 1H), 8.61−

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8.63 (m, 1H), 9.31 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 14.1, 29.8, 32.0, 59.2, 108.8, 114.5, 122.6, 126.2, 132.8, 134.2, 137.4, 148.3, 150.3, 164.9, 165.0 ppm. IR (KBr): 3302, 2954, 1674, 1505, 1274, 1115, 744 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{18}H_{23}N_3NaO_3$ $[M + Na]^+$ 352.1632, found 352.1640.

*Ethyl 5-(4-Methoxyphenyl)-2-methyl-1-phenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5q**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.10) afforded **5q** as a yellow solid (89.9 mg, 75% yield). Mp: 126−128 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (t, J = 7.2 Hz, 3H), 2.38 (s, 3H), 3.66 (s, 3H), 4.25 (q, J = 7.2 Hz, 2H), 6.61−6.65 (m, 2H), 7.01−7.04 (m, 2H), 7.09−7.12 (m, 2H), 7.31−7.36 (m, 3H), 7.40 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.79 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 8.59−8.60 (m, 1H), 9.95 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.0, 14.3, 55.0, 59.7, 108.0, 113.4, 117.9, 122.6, 123.8, 126.1, 128.2, 128.9, 129.0, 129.1, 131.0, 136.0, 137.3, 137.7, 148.2, 150.3, 158.4, 163.0, 165.3 ppm. IR (KBr): 3348, 2980, 2932, 2838, 1693, 1672, 1518, 1245, 1091, 696 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{27}H_{25}N_3NaO_4$ $[M + Na]^+$ 478.1737, found 478.1744.

*Ethyl 1-Butyl-5-(4-methoxyphenyl)-2-methyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5r**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.12) afforded **5r** as a pale yellow solid (86.1 mg, 75% yield). Mp: 118−120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79 (t, J = 7.2 Hz, 3H), 1.15 (t, J = 7.2 Hz, 3H), 1.12−1.21 (m (overlap), 2H), 1.47−1.54 (m, 2H), 2.59 (s, 3H), 3.76 (t, J = 7.6 Hz, 2H), 3.79 (s, 3H), 4.20 (q, J = 7.2 Hz, 2H), 6.88−6.91 (m, 2H), 7.29−7.32 (m, 2H), 7.37 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.77 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 8.55−8.56 (m, 1H), 9.78 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.9, 13.7, 14.3, 19.9, 32.8, 44.1, 55.2, 59.5, 107.0, 113.9, 117.8, 122.5, 124.1, 126.0, 128.4, 131.8, 134.6, 137.2, 148.1, 150.4, 159.2, 162.9, 165.4 ppm. IR (KBr): 3354, 2961, 2933, 2870, 1692, 1682, 1522, 1248, 1095 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{25}H_{29}N_3NaO_4$ $[M + Na]^+$ 458.2050, found 458.2051.

*Ethyl 5-(4-Bromophenyl)-2-methyl-1-phenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5s**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.24) afforded **5s** as a brown solid (95.2 mg, 75% yield). Mp: 170−172 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.2 Hz, 3H), 2.38 (s, 3H), 4.27 (q, J = 7.2 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 7.08−7.13 (m, 2H), 7.21 (d, J = 8.4 Hz, 2H), 7.34−7.39 (m, 3H), 7.41−7.44 (m, 1H), 7.81 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.62−8.63 (m, 1H), 10.14 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.1, 14.4, 59.9, 108.0, 119.0, 121.1, 122.6, 126.3, 127.5, 128.6, 128.8, 129.3, 130.7, 131.2, 136.7, 137.37, 137.39, 148.3, 150.1, 162.7, 165.2 ppm. IR (KBr): 3350, 2930, 1678, 1518, 1421, 1165, 1090, 698 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{26}H_{22}BrN_3NaO_3$ $[M + Na]^+$ 526.0737, found 526.0739.

*Ethyl 5-(4-Bromophenyl)-1-butyl-2-methyl-4-(picolinamido)-1H-pyrrole-3-carboxylate (**5t**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v, R_f = 0.25) afforded **5t** as a yellow solid (78.6 mg, 65% yield). Mp: 98−100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, J = 7.2 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H), 1.14−1.21 (m (overlap), 2H), 1.45−1.53 (m, 2H), 2.59 (s, 3H), 3.77 (t, J = 7.6 Hz, 2H), 4.22 (q, J = 7.2 Hz, 2H), 7.24−7.28 (m, 2H), 7.39 (ddd, J = 7.6 Hz, 4.8 Hz, 1.2 Hz, 1H), 7.47−7.50 (m, 2H), 7.78 (td, J = 7.6 Hz, 1.6 Hz, 1H), 8.08 (d, J = 7.6 Hz, 1H), 8.56−8.58 (m, 1H), 9.95 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.9, 13.6, 14.3, 19.8, 32.7, 44.1, 59.6, 107.0, 118.4, 122.0, 122.4, 126.1, 126.8, 131.1, 131.6, 132.0, 135.1, 137.2, 148.1, 150.1, 162.5, 165.1 ppm. IR (KBr): 3286, 2961, 2867, 1689, 1541, 1422, 1095 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{24}H_{26}BrN_3NaO_3$ $[M + Na]^+$ 506.1050, found 506.1057.

*Diethyl 1,1′-(Hexane-1,6-diyl)bis(2-methyl-5-phenyl-4-(picolinamido)-1H-pyrrole-3-carboxylate) (**5u**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 2/1, v/v, R_f = 0.30) afforded **5u** as a yellow solid (106.7 mg, 55% yield). Mp: 200−202 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (m, 4H), 1.16 (t, J = 7.2 Hz, 6H), 1.39 (m, 4H), 2.56 (s, 6H), 3.72 (t, J = 7.6 Hz, 4H), 4.21 (q, J = 7.2 Hz, 4H), 7.28−7.39 (m, 12H), 7.77 (td, J = 7.6 Hz, 1.6 Hz, 2H), 8.09 (d, J = 8.0 Hz, 2H), 8.56−8.57 (m, 2H), 9.84 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.0, 14.3, 26.0, 30.4, 44.0, 59.6, 107.2, 118.0, 122.5, 126.0, 127.9, 128.4, 128.5, 130.4, 131.9, 134.8, 137.2, 148.1, 150.3, 162.8, 165.3 ppm. IR (KBr): 3352, 2958, 2932, 2866, 1692, 1514, 1258, 1104, 703 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{46}H_{48}N_6NaO_6$ $[M + Na]^+$ 803.3528, found 803.3532.

*Ethyl 4-Amino-2-methyl-1,5-diphenyl-1H-pyrrole-3-carboxylate (**8a**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v, R_f = 0.48) afforded **8a** as a white solid (68.0 mg, 85% yield). Mp: 100−102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (t, J = 7.2 Hz, 3H), 2.36 (s, 3H), 4.32 (br s, 2H), 4.35 (q, J = 7.2 Hz, 2H), 7.03−7.10 (m, 5H), 7.15−7.19 (m, 2H), 7.27−7.35 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.2, 14.8, 59.5, 103.2, 116.1, 125.7, 127.9, 128.4, 128.6, 128.9, 129.1, 131.8, 132.1, 135.1, 138.1, 166.5 ppm. IR (KBr): 3444, 2983, 1677, 1597, 1267, 1117, 703 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{20}H_{21}N_2O_2$ $[M + H]^+$ 321.1598, found 321.1600.

*Ethyl 4-Amino-1-butyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylate (**8b**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v, R_f = 0.45) afforded **8b** as brown oil (58.7 mg, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.74 (t, J = 7.2 Hz, 3H), 1.06−1.16 (m, 2H), 1.36 (t, J = 7.2 Hz, 3H), 1.39−1.45 (m, 2H), 2.53 (s, 3H), 3.76 (t, J = 7.6 Hz, 2H), 4.02 (br s, 2H), 4.31 (q, J = 7.2 Hz, 2H), 7.28−7.33 (m, 3H), 7.41−7.44 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.1, 13.7, 14.7, 19.8, 32.7, 43.7, 59.2, 102.0, 115.4, 127.0, 129.0, 130.2, 131.2, 131.9, 133.4, 166.4 ppm. IR (KBr): 3386, 2961, 2933, 2871, 1682, 1531, 1213, 701 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{18}H_{24}N_2NaO_2$ $[M + Na]^+$ 323.1730, found 323.1728.

*Ethyl 4-Amino-2-methyl-5-phenyl-1H-pyrrole-3-carboxylate (**8c**).* Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/5, v/v, R_f = 0.32) afforded **8c** as a brown solid (57.1 mg, 93% yield). Mp: 164−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (t, J = 6.8 Hz, 3H), 2.45 (s, 3H), 4.28 (q, J = 6.8 Hz, 2H), 4.41 (br s, 2H), 7.12 (t, J = 6.8 Hz, 1H), 7.32−7.39 (m, 4H), 8.44 (br s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 14.6, 59.2, 103.3, 112.1, 124.0, 124.9, 129.2, 131.5, 132.7, 134.0, 166.6 ppm. IR (KBr): 3404, 3307, 2979, 1668, 1575, 1289, 1094, 698 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{14}H_{17}N_2O_2$ $[M + H]^+$ 245.1285, found 245.1285.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02838.

Copies of ^{1}H NMR and ^{13}C NMR spectra of the products (PDF)
X-ray data of **3l** (CIF)
X-ray data of **4a** (CIF)
X-ray crystal data of **5a** (CIF)

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Notes

The authors declare no competing financial interest.

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