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Synthesis of Multisubstituted Pyrroles from Doubly Activated Cyclopropanes Using an Iron-Mediated Oxidation Domino Reaction

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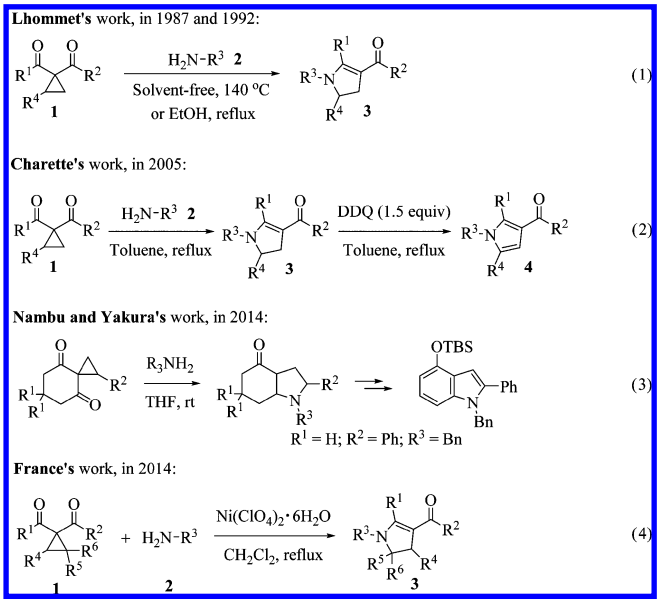
Supporting Information

ABSTRACT: An alternative route has been developed for the construction of multisubstituted pyrrole derivatives from readily available, doubly activated cyclopropanes and anilines using an iron-mediated oxidation domino reaction (i.e., sequential ring-opening, cyclization, and dehydrogenation reactions). This reaction uses readily available reactants and is tolerant of a broad range of substrates, with the desired products being formed in good to excellent yields.

Pyrroles[1] are one of the most important types of heterocyclic compound in organic chemistry, and compounds belonging to this structural class are frequently used as the core scaffold in natural products,[2] pharmaceuticals,[3] dyes,[4] agrochemicals,[5] and functional materials.[6] In light of their numerous applications, considerable research efforts have been devoted to the development of novel synthetic methods for the efficient construction of pyrroles.[7] Traditionally, pyrroles have been synthesized using a variety of different methods, including the Knorr,[8] Paal–Knorr,[9] and Hantzsch reactions,[10] which have been used for more than a century.[11] However, the synthesis of the highly functionalized pyrroles remains challenging, with regioselectivity being one of the biggest issues, and this problem is invariably complicated by the poor chemical stability of many pyrrole derivatives, which can lead to their degradation under harsh reaction conditions.[12] In this study, we have developed an iron-mediated oxidation domino[13] reaction for the synthesis of multisubstituted pyrrole derivatives from doubly activated cyclopropanes with a simultaneous oxidative–dehydrogenation reaction (Scheme 1).

Cyclopropanes are extremely versatile building blocks in organic syntheses because of the ease with which they can be synthesized and their high level of reactivity.[14] Several studies on cyclopropanes have focused on the ring-opening reactions of doubly activated donor–acceptor cyclopropanes (D–A cyclopropanes)[14d,15] **1** with nucleophilic amines **2** as a strategy for the synthesis of 2,3-dihydropyrroles (including their conversion to pyrroles).[16] In 1987 and 1992, Lhommet et al.[17] reported two convenient methods for the synthesis of 1,2,5-trisubstituted 4,5-dihydro-3-pyrrolecarboxylates **3** in modest to good yields by heating a mixture of doubly activated D–A cyclopropane **1** and amine **2** at 140 °C in the absence of a solvent or heating the same compounds in a sealed tube in methanol (Scheme 1, eq 1). In 2005, Charette et al.[18] developed a stepwise procedure for the preparation of 4-nitro- and 4-cyano-pyrroles **4**. This reaction involved the sequential ring-opening/cyclization reaction of **1** with an amine **2** to give the corresponding 4-cyano-2,3-dihydropyrrole **3**, which was oxidized with DDQ in refluxing toluene to give the corresponding pyrrole **4** (Scheme 1, eq 2). More recently, Nambu and Yakura et al.[19] reported the development of an efficient ring-opening reaction for the cyclization of cyclohexane-1,3-dione-2-spirocyclopropanes with primary amines at room temperature. Notably, this reaction did not require the addition of an additive, and the 2-substituted tetrahydroindol-4-one products could be readily converted to

Scheme 1. Sequential Ring-Opening/Cyclization Reactions of Cyclopropanes 1 with Amines 2



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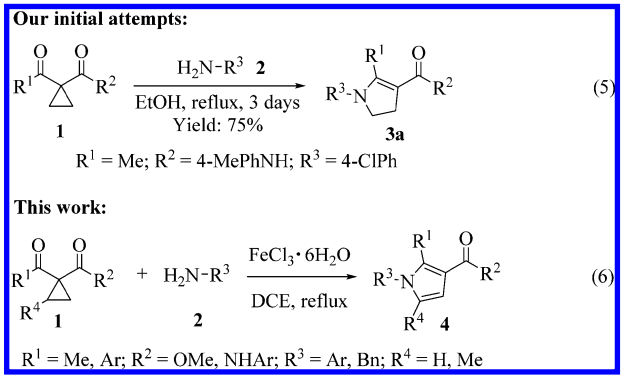
the corresponding 2-substituted 4-hydroxyindole derivatives in good yields via a multistep derivatization reaction (Scheme 1, eq 3). In 2014, France et al.[20] reported their work toward the development of a sequential ring-opening/cyclization reaction between cyclopropanes and amines. In this particular case, $Ni(ClO_4)_2·6H_2O$ was used as a mild catalyst to facilitate the synthesis of 4-carboxy-dihydropyrroles **3** via the ring-opening/cyclization reaction of **1** with a primary amine **2** (Scheme 1, eq 4). Despite these advances, there is still an urgent need to develop a facile procedure for the synthesis of pyrroles via the sequential ring-opening/cyclization/dehydrogenation reaction of doubly activated cyclopropanes and amines.

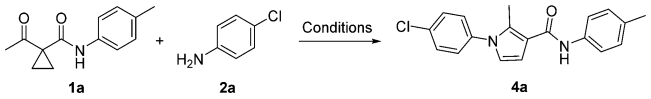
Iron salts have been used on numerous occasions in organic synthesis as effective, reusable, operationally simple, and environmentally benign catalysts,[21] and several studies have been reported in the literature concerning the iron-catalyzed ring-opening reaction of cyclopropanes.[22] Iron-catalyzed oxidation[21a,23] has been applied to a wide range of synthetic transformations, including olefin epoxidation reactions[23] and the chemistry of Fe-porphyrins.[24] Iron catalysts have also been used in various C−H oxidation reactions,[25] including the Gif reaction,[26] Fenton chemistry,[27] and nonheme mimicking systems.[28] Several iron-catalyzed reactions[29] have been reported by our group during the past decade, as well as numerous ring-opening reactions involving cyclopropanes.[30] Very recently, we developed two one-pot protocols for the direct formation of structurally sophisticated α-formyl pyrrole[29e] and γ-amino ketone derivatives[31] from 2,3-dihydro-1*H*-pyrroles **3**. While preparing these substrates using Lhommet's method,[17a] it was observed that the reactions of 1-acyl-1-arylaminoformyl cyclopropane derivatives **1** generally required several days to reach completion (Scheme 2, eq 5, **3a** as an example). It was later envisaged that the addition of an appropriate green catalyst such as an iron salt would accelerate the reaction and provide the desired product over a much shorter reaction time. Subsequent experimental work revealed that cyclopropane **1a** reacted with 4-chloroaniline in EtOH in the presence of $FeCl_3·6H_2O$ to give pyrrole **4a** and its transesterification derivative ethyl 1-(4-chlorophenyl)-2-methyl-1*H*-pyrrole-3-carboxylate in yields of 16% and 72%, respectively, where the desired product **3a** was simultaneously oxidized (Table 1, entry 6). These findings indicated that it could be possible to develop a new approach for the direct synthesis of multisubstituted pyrroles **4** from doubly activated cyclopropanes **1** (Scheme 2, eq 6).

Scheme 2. Our Initial Attempts



Based on these preliminary results, 1-acetyl-1-*N*-(4-methylphenyl) carbamyl cyclopropane (**1a**) and 4-chloroaniline (**2a**) were selected as model substrates to explore the optimal conditions for the ring-opening/cyclization/oxidation sequence. Some of the key results of these optimization experiments are summarized in Table 1. Pleasingly, the results of these screening reactions not only indicated that the reaction time could be dramatically reduced but also showed that the Lhommet product **3a** could be oxidized *in situ* to give 1-(4-chlorophenyl)-2-methyl-*N*-(*p*-tolyl)-1*H*-pyrrole-3-carboxamide (**4a**) in 68% yield when a mixture of **1a** and **2a** in 1,2-dichloroethane (DCE) was heated at reflux in the presence of $FeCl_3·6H_2O$ (0.5 equiv) for 21 h in air (Table 1, entry 3). When the reaction was conducted in the presence of 0.2 equiv of $FeCl_3·6H_2O$, compound **4a** was obtained in 50% yield after 9.0 h, together with recovered **1a** (30%), and the yield of **4a** could not be further increased by prolonging the reaction times (Table 1, entry 2). When the reaction was conducted in the absence of or with increasing amounts of $FeCl_3·6H_2O$, the yield of **4a** decreased dramatically (Table 1, entries 1 and 4). Furthermore, the use of a pure oxygen atmosphere was not necessary to achieve a high conversion (Table 1, entry 5). Several other solvents were also screened against the reaction, including EtOH, CH_3CN, THF, DMSO, 1,4-dioxane, and toluene,[18] and all six of these solvents were found to be much less efficient than DCE for the desired conversion process (Table 1, entries 6−11). Several other iron salts were also screened against this intermolecular domino reaction, including $Fe_2(SO_4)_3·xH_2O$, Fe_2O_3, $Fe(OTf)_2$, $Fe(acac)_3$, and anhydrous $FeCl_3$, and $Fe_2(SO_4)_3·xH_2O$, Fe_2O_3, $Fe(OTf)_2$, and $Fe(acac)_3$ showed much lower levels of catalytic activity than $FeCl_3·6H_2O$ (Table 1, entries 12−15). In contrast, the use of anhydrous $FeCl_3$ afforded **4a** in 70% yield (Table 1, entry 16), but its

Table 1. Survey of the Reaction Conditions[a]



entry	cat. (equiv)	solvent	time/h	yield/%
1	$FeCl_3·6H_2O$ (0)	DCE	24	30[b]
2	$FeCl_3·6H_2O$ (0.2)	DCE	9	50[c]
3	$FeCl_3·6H_2O$ (0.5)	DCE	21	68
4	$FeCl_3·6H_2O$ (1.2)	DCE	21	35[b]
5	$FeCl_3·6H_2O$ (0.5)	DCE	21	63[d]
6	$FeCl_3·6H_2O$ (0.5)	EtOH	48	16[e]
7	$FeCl_3·6H_2O$ (0.5)	CH_3CN	48	0[b]
8	$FeCl_3·6H_2O$ (0.5)	THF	48	trace[b]
9	$FeCl_3·6H_2O$ (0.5)	DMSO	48	trace[f]
10	$FeCl_3·6H_2O$ (0.5)	1,4-dioxane	48	20[b]
11	$FeCl_3·6H_2O$ (0.5)	toluene	48	38[g]
12	$Fe_2(SO_4)_3·xH_2O$ (0.5)	DCE	48	45[h]
13	Fe_2O_3 (0.5)	DCE	48	15[i]
14	$Fe(OTf)_2$ (0.5)	DCE	30	55[b]
15	$Fe(acac)_3$ (0.5)	DCE	48	NR
16	$FeCl_3$ (0.5)	DCE	20	70

[a]Unless otherwise indicated, all of the reactions were carried out with **1a** (217 mg, 1.0 mmol) and **2a** (1.2 mmol) in solvent (4.0 mL) at reflux in air. [b]Along with a complex mixture. [c]30% **1a** was recovered. [d]Reaction was performed under an atmosphere of O_2. [e]72% ethyl 1-(4-chlorophenyl)-2-methyl-1*H*-pyrrole-3-carboxylate was obtained. [f]Reaction was performed at 100 °C, and 90% **1a** was recovered. [g]Reaction was performed at 100 °C, and 29% **1a** was recovered. [h]15% **1a** was recovered. [i]50% **1a** was recovered.

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Table 2. Extension of the Reaction Scope[a]

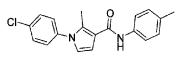
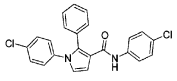
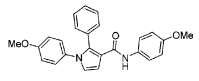
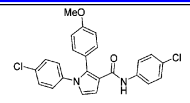
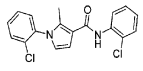
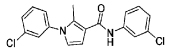
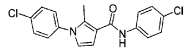
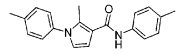
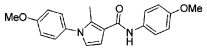
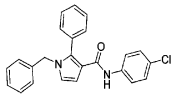
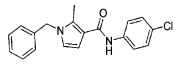
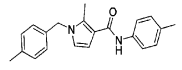
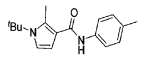
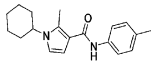
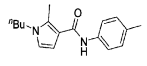
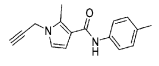
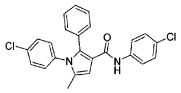
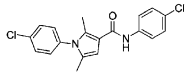
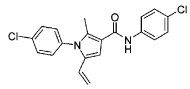
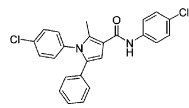
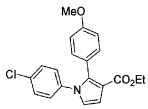
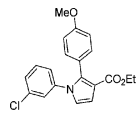
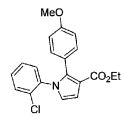
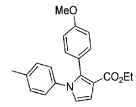
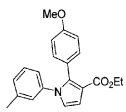
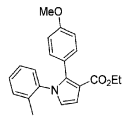
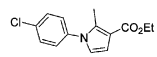
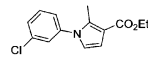
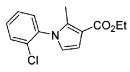
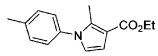
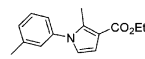
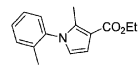
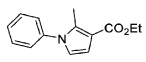
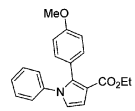
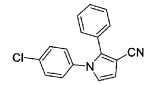
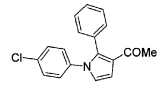
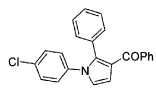
 **4a**, 21 h, 68%	 **4b**, 32 h, 85%	 **4c**, 35 h, 80%[b]	 **4d**, 38 h, 86%
 **4e**, 18 h, 61%	 **4f**, 25 h, 66%	 **4g**, 21 h, 68%	 **4h**, 24 h, 63%
 **4i**, 48 h, 65%[b]	 **4j**, 48 h, 81%[b]	 **4k**, 48 h, 61%[c]	 **4l**, 48 h, 64%[c]
 **4m**, 48 h, 0%[d]	 **4n**, 25 h, 21%[e]	 **4o**, 21 h, 31%[f]	 **4p**, 48 h, 0%[g]
 **4q**, 28 h, 78%	 **4r**, 18 h, 70%	 **4s**, 21 h, 0%[h]	 **4t**, 25 h, trace%[i]
 **4u**, 28 h, 71%	 **4v**, 28 h, 68%	 **4w**, 36 h, 51%	 **4x**, 21 h, 78%
 **4y**, 28 h, 67%	 **4z**, 28 h, 58%	 **4a'**, 24 h, 72%	 **4b'**, 23 h, 68%
 **4c'**, 23 h, 56%	 **4d'**, 24 h, 72%	 **4e'**, 24 h, 77%	 **4f'**, 28 h, 62%
 **4g'**, 24 h, 73%	 **4h'**, 21 h, 74%	 **4i'**, 48 h, 0%[j]	 **4j'**, 48 h, 0%[k]
 **4k'**, 48 h, 0%[l]			

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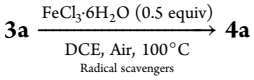
Table 2. continued

[a]Unless otherwise indicated, all of the reactions were carried out with **1** (1.0 mmol), **2** (1.2 mmol), and $FeCl_3·6H_2O$ (0.5 equiv) in DCE (4.0 mL) at 100 °C in air. [b]3.0 equiv of amine were used. [c]2.0 equiv of amine were used. [d]91% **1a** was recovered, and 86% starting material was recovered after 48 h when the reaction was performed in the absence of $FeCl_3·6H_2O$. [e]42% starting material was recovered, and the yield of **4n** could not be increased by prolonging the reaction times. [f]26% 1-butyl-3-(*p*-tolyl)urea was also obtained. [g]23% starting material was recovered together with 21% 1-(prop-2-yn-1-yl)-3-(*p*-tolyl)urea. [h]33% *N*,1-bis(4-chlorophenyl)-2-methyl-5-vinyl-4,5-dihydro-1*H*-pyrrole-3-carboxamide (**3s**) was obtained together with some unidentified complex mixture. [i]29% *N*,1-bis(4-chlorophenyl)-2-methyl-5-phenyl-4,5-dihydro-1*H*-pyrrole-3-carboxamide (**3t**) was obtained together with some unidentified complex mixture. [j]51% starting material was recovered together with some unidentified complex mixture. [k]40% starting material was recovered together with some unidentified complex mixture. [l]35% starting material was recovered together with some unidentified complex mixture.

Table 3. Radical Trapping Experiments



		TEMPO		diphenylethylene		duroquinone	
radical scavengers	no scavenger	1 equiv, 8 h	10 equiv, 2 h	1 equiv, 21 h	10 equiv, 8 h	1 equiv, 21 h	10 equiv, 6 h
recovered **3a**	0	trace	0	23	22	32	27
4a	68	25	21	32	28	20	19

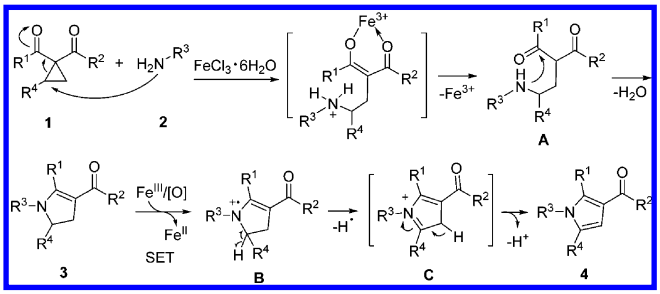
hygroscopic properties and higher price precluded its use over $FeCl_3·6H_2O$.

With the optimized conditions in hand (Table 1, entry 3), we proceeded to investigate the scope of this new domino reaction using a series of different doubly activated cyclopropanes **1** and amines **2**. As shown in Table 2, doubly activated arylaminoformyl cyclopropane substrates **1b**−**i** bearing electron-withdrawing groups (EWG) or electron-donating groups (EDG) on the phenyl ring of their R^2 groups reacted with arylamines **2** with EWG or EDG on their phenyl ring to afford the corresponding multisubstituted pyrroles **4b**−**i** in 61−86% yields. Interestingly, the use of benzylamines instead of anilines was well tolerated with the desired annulation products **4j**−**l** being formed in 61−81% yields. It is noteworthy, however, that these reactions required more than 2 equiv of the benzylamine, which could be readily oxidized under the reaction conditions. Starting materials bearing an acetyl group at their 1-position (i.e., R^1 = Me) gave lower yields than those bearing an aryl formyl group at their 1-position (i.e., R^1 = Ar) (e.g., **4g** vs **4b** and **4d**, **4i** vs **4c**, **4k** vs **4j**). Unfortunately, the aliphatic amine *tert*-butylamine did not perform well in the reaction and afforded none of the desired compound **4m**. To determine whether the failure of this reaction was caused by the steric hindrance of the *tert*-butyl group, several less sterically hindered amines were investigated, including cyclohexylamine, *n*-butylamine, and propargylamine. Notably, **4n** and **4o** were obtained in yields of 21% and 31%, respectively, whereas the propargylamine only afforded the 1-(prop-2-yn-1-yl)-3-(*p*-tolyl)urea in 21% yield together with recovered **1a** (23%) instead of the desired compound **4p**.[32] Interestingly, compounds **1q** and **1r** (R^4 = −Me) reacted with 4-chloroaniline to form the corresponding highly substituted pyrroles **4q** and **4r** in yields of 78% and 70%, respectively, without any of the 3-methyl isomers being formed.[33] However, compounds **1s** and **1t** (R^4 = −CH═CH_2 or −Ph) only afforded 2,3-dihydro-1*H*-pyrroles **3s** and **3t** in 33% and 29% yields, respectively. Several 1-acyl-1-ethoxylcarbonyl cyclopropanes **1u**−**h′** were also reacted under the optimized conditions and gave the corresponding 3-ester substituted pyrroles **4u**−**h′** in 51−78% yields. In these cases, the yields roughly decreased according to the position of the substituent on the phenyl ring of **2** (i.e., *para*- > *meta*- > *ortho*-substituted anilines), regardless of the electronic nature of the substituent pattern of **1**. Starting materials **1i′**−**k′** with a −CN, −COPh, and −COMe group at their 1-position did not give the desired compounds **4i′**−**k′**, and some of the starting materials were recovered along with some unidentified complex mixture.

Several radical trapping experiments were conducted using three different kinds of radical scavenger, including 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), diphenylethylene, and 2,3,5,6-tetramethylbenzo-1,4-quinone (duroquinone), to determine whether a radical process was involved in the transformation of **3** to **4**. The results of these experiments revealed that the reactions were significantly inhibited by the radical scavengers, which resulted in the formation of complex mixtures containing unidentified materials (Table 3). These results suggested that a radical process could be involved in this transformation.[34]

A mechanism was proposed for the current reaction, which is shown in Scheme 3. Briefly, the aniline **2** would initially attack

Scheme 3. Proposed Mechanism



the more electrophilic carbon of the doubly activated cyclopropane **1** in an S_N2-like reaction to afford the corresponding 2,3-dihydro-1*H*-pyrrole **3** via the γ-amino ketone intermediate **A**.[17a,19,30a,c] The subsequent single electron-transfer (SET) oxidation of **3** by Fe^{3+} and O_2 would generate the radical species **B**,[35] which would give the 1*H*-pyrrole **4** through sequential radical dehydrogenation and deprotonation reactions.[36] It is also possible, however, that amine **2** could react with the carbonyl to form an imine, which could undergo a Cloke-type rearrangement to give the five-membered 2,3-dihydro-1*H*-pyrrole **3**.[19,37]

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In conclusion, we have developed a straightforward and efficient domino reaction for the synthesis of multisubstituted pyrrole derivatives **4** in moderate to good yields (51−86%) via the reaction of readily available doubly activated cyclopropanes **1** with anilines **2** in the presence of air and Fe(III). This method offers a complementary approach to highly substituted pyrrole compounds with advantages that include a variety of cheap and readily available reactants and a wide range of substrates with dense or flexible substitution patterns.

EXPERIMENTAL SECTION

General Information. All reagents were purchased from commercial sources and used without further treatment. All reactions were carried out under an air atmosphere. ^{1}H NMR and ^{13}C{^{1}H} NMR spectra were recorded on a 400 MHz NMR spectrometer (^{1}H: 400 MHz, ^{13}C{^{1}H}: 100 MHz at 25 °C), and TMS was the internal standard. Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, m = multiplet), coupling constants in hertz (Hz). All high-resolution mass spectra (HRMS) were measured on a mass spectrometer by using electrospray ionization (ESI-oa-TOF), and the purity of all samples used for HRMS (>95%) were confirmed by ^{1}H and ^{13}C{^{1}H} NMR spectroscopic analysis. Melting points were measured on a melting point apparatus equipped with a thermometer and were uncorrected. All reactions were monitored by TLC with GF254 silica gel coated plates. Flash chromatography was carried out on SiO_2 (silica gel 200−300 mesh).

Typical Experimental Procedure for the Synthesis of 4 (4a as an Example). To a round-bottom flask (25 mL) equipped with a spherical condenser (20 cm length) were added 1-acetyl-*N*-(*p*-tolyl)cyclopropane-1-carboxamide **1a** (217 mg, 1.0 mmol), 4-chloroaniline **2a** (154 mg, 1.2 mmol), $FeCl_3{\cdot}6H_2O$ (135 mg, 0.5 mmol), and DCE (4.0 mL). Then the mixture was well stirred at 100 °C in air until **1a** was completely consumed (TLC monitor). After cooling off, the mixture was filtered through a pad of Celite, eluting with CH_2Cl_2 (6 mL × 3). The volatiles were removed under reduced pressure, and the residue was purified by short flash silica gel column chromatography to give compound **4a** (221 mg, 68%) (eluent: petroleum ether/ethyl acetate = 10/1).

1-(4-Chlorophenyl)-2-methyl-*N*-(*p*-tolyl)-1*H*-pyrrole-3-carboxamide (4a). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (221 mg, 68%). Mp 180−182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.4 Hz, 3H), 7.47−7.44 (m, 2H), 7.23 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 3.2 Hz, 1H), 6.48 (d, J = 3.2 Hz, 1H), 2.48 (s, 3H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.9, 137.7, 136.0, 134.8, 134.1, 133.5, 129.7, 129.6, 127.6, 121.3, 120.2, 116.7, 107.1, 22.0, 12.2. HRMS (ESI), m/z calcd for $C_{19}H_{17}ClN_2O$ ([M + H]$^+$) 325.1102; found, 325.1131.

***N*,1-Bis(4-chlorophenyl)-2-phenyl-1*H*-pyrrole-3-carboxamide (4b).** The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 15/2) as a white solid (346 mg, 85%). Mp 190−192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.39 (m, 3H), 7.32−7.30 (m, 2H), 7.24 (d, J = 8.8 Hz, 2H), 7.18−7.10 (m, 5H), 7.01 (d, J = 8.4 Hz, 2H), 6.93 (dd, J = 9.6, 3.2 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.6, 137.8, 137.0, 133.5, 133.4, 131.5, 130.7, 129.5, 129.3, 129.2, 128.9, 128.4, 127.3, 123.2, 120.4, 119.7, 111.1. HRMS (ESI), m/z calcd for $C_{23}H_{16}Cl_2N_2O$ ([M + Na]$^+$) 429.0532; found, 429.0544.

***N*,1-Bis(4-methoxyphenyl)-2-phenyl-1*H*-pyrrole-3-carboxamide (4c).** The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate =15/2) as a white solid (318 mg, 80%). Mp 155−158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.36 (m, 3H), 7.33−7.31 (m, 2H), 7.13 (d, J = 8.8 Hz, 2H), 7.06 (s, 1H), 7.00 (d, J = 8.8 Hz, 2H), 6.91 (d, J = 3.2 Hz, 1H), 6.88 (d, J = 3.2 Hz, 1H), 6.78−6.74 (m, 4H), 3.76 (s, 3H), 3.73 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.8, 158.7, 155.9, 133.4, 132.4, 131.8, 131.6, 131.2, 129.0, 128.9, 127.4, 123.3, 121.0, 119.3, 114.2, 114.1, 110.4, 55.53, 55.50. HRMS (ESI), m/z calcd for $C_{25}H_{22}N_2O_3$ ([M + H]$^+$) 399.1703; found, 399.1708.

***N*,1-Bis(4-chlorophenyl)-2-(4-methoxyphenyl)-1*H*-pyrrole-3-carboxamide (4d).** The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 15/2) as a white solid (376 mg, 86%). Mp 150−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 1H), 7.24−7.13 (m, 8H), 6.99 (d, J = 8.4 Hz, 2H), 6.92−6.90 (m, 3H), 6.87 (d, J = 2.8 Hz, 1H), 3.82 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.7, 160.2, 137.8, 137.0, 133.5, 133.2, 132.7, 129.2, 128.8, 128.2, 127.2, 122.8, 122.3, 120.5, 119.2, 114.5, 110.8, 55.4. HRMS (ESI), m/z calcd for $C_{24}H_{18}Cl_2N_2O_2$ ([M + H]$^+$) 437.0818; found, 437.0818.

***N*,1-Bis(2-chlorophenyl)-2-methyl-1*H*-pyrrole-3-carboxamide (4e).** The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (210 mg, 61%). Mp 128−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.19 (s, 1H), 7.57−7.55 (m, 1H), 7.43−7.37 (m, 3H), 7.34−7.29 (m, 2H), 7.04−6.99 (m, 1H), 6.66 (d, J = 3.2 Hz, 1H), 6.59 (d, J = 3.2 Hz, 1H), 2.40 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.6, 136.6, 136.4, 135.5, 132.8, 130.5, 130.4, 129.7, 129.0, 127.8, 127.8, 123.8, 122.5, 121.5, 121.3, 115.7, 107.0, 11.7. HRMS (ESI), m/z calcd for $C_{18}H_{14}Cl_2N_2O$ ([M + Na]$^+$) 367.0375; found, 367.0385.

***N*,1-Bis(3-chlorophenyl)-2-phenyl-1*H*-pyrrole-3-carboxamide (4f).** The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (228 mg, 66%). Mp 175−178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 8.19 (s, 1H), 7.65 (s, 1H), 7.43−7.40 (m, 3H), 7.30 (s, 1H), 7.25−7.21 (m, 1H), 7.19−7.17 (m, 1H), 7.05 (d, J = 3.2 Hz, 1H), 6.71 (d, J = 3.2 Hz, 1H), 6.50 (d, J = 3.2 Hz, 1H), 2.49 (s, 3H) . ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.9, 130.5, 130.0, 128.5, 126.6, 124.6, 123.8, 121.5, 120.1, 118.0, 107.2, 12.3. HRMS (ESI), m/z calcd for $C_{18}H_{14}Cl_2N_2O$ ([M + H]$^+$) 345.0556; found, 345.0567.

***N*,1-Bis(4-chlorophenyl)-2-methyl-1*H*-pyrrole-3-carboxamide (4g).** The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (235 mg, 68%). Mp 184−186 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.4 Hz, 3H), 7.46 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 6.70 (s, 1H), 6.48 (s, 1H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.9, 137.6, 137.2, 135.3, 134.2, 129.7, 129.1, 128.8, 127.6, 121.5, 121.3, 116.2, 107.1, 12.2. HRMS (ESI), m/z calcd for $C_{18}H_{14}Cl_2N_2O$ ([M + Na]$^+$) 367.0375; found, 367.0399.

2-Methyl-*N*,1-di-*p*-tolyl-1*H*-pyrrole-3-carboxamide (4h). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (192 mg, 63%). Mp 158−160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56−7.51 (m, 3H), 7.29 (d, J = 8.8 Hz, 2H), 7.17 (t, J = 8.0 Hz, 4H), 6.72 (d, J = 3.2 Hz, 1H), 6.48 (d, J = 3.2 Hz, 1H), 2.50 (s, 3H), 2.44 (s, 3H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.1, 138.1, 136.7, 136.1, 135.1, 130.0, 129.6, 126.2, 121.5, 120.2, 116.1, 106.6, 21.2, 21.0, 12.2. HRMS (ESI), m/z calcd for $C_{20}H_{20}N_2O$ ([M + Na]$^+$) 327.1468; found, 327.1466.

***N*,1-Bis(4-methoxyphenyl)-2-methyl-1*H*-pyrrole-3-carboxamide (4i).** The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (218 mg, 65%). Mp 161−163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.51 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 8.8 Hz, 2H), 6.96 (d, J = 9.2 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 6.66 (d, J = 3.2 Hz, 1H), 6.47 (d, J = 2.8 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.1, 159.1, 156.0, 135.0, 132.0, 131.7, 127.5, 122.0, 121.5, 115.8, 114.4, 114.1, 106.5, 55.6, 55.5, 12.1. HRMS (ESI), m/z calcd for $C_{20}H_{20}N_2O_3$ ([M + H]$^+$) 337.1547; found, 337.1553.

1-Benzyl-*N*-(4-chlorophenyl)-2-phenyl-1*H*-pyrrole-3-carboxamide (4j). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 15/2) as a white solid (313 mg, 81%). Mp 137−139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.48 (m, 3H), 7.39−7.36 (m, 2H), 7.29−7.26 (m, 2H),7.15−7.06 (m, 5H), 6.94−6.92 (m, 2H), 6.88 (d, J = 2.8 Hz, 1H), 6.77 (d, J = 3.2 Hz, 1H), 4.92 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.6, 137.4, 137.2, 134.1, 131.2, 131.0, 129.9, 129.4, 128.8, 128.1, 127.8, 126.8,

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122.1, 120.2, 118.4, 110.3, 51.0. HRMS (ESI), *m/z* calcd for $C_{24}H_{19}ClN_2O$ ([M + H]$^+$) 387.1259; found, 387.1267.

1-Benzyl-*N*-(4-chlorophenyl)-2-methyl-1*H*-pyrrole-3-carboxamide (4k). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (198 mg, 61%). Mp 120−122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 7.6 Hz, 3H), 7.35−7.28 (m, 5H), 7.01 (d, J = 7.2 Hz, 2H), 6.61 (s, 1H), 6.39 (s, 1H), 5.06 (s, 2H), 2.50 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.1, 137.3, 136.9, 135.3, 129.0, 129.0, 128.6, 127.9, 126.5, 121.3, 121.0, 115.4, 106.2, 100.1, 50.6, 11.1. HRMS (ESI), *m/z* calcd for $C_{19}H_{17}ClN_2O$ ([M + H]$^+$) 325.1102; found, 325.1124.

2-Methyl-1-(4-methylbenzyl)-*N*-(*p*-tolyl)-1*H*-pyrrole-3-carboxamide (4l). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (204 mg, 64%). Mp 122−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.0 Hz, 3H), 7.14 (d, J = 8.0 Hz, 4H), 6.92 (d, J = 7.6 Hz, 2H), 6.59 (d, J = 2.8 Hz, 1H), 6.39 (d, J = 3.2 Hz, 1H), 5.02 (s, 2H), 2.52 (s, 3H), 2.34 (s, 3H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.1, 137.6, 136.1, 134.8, 134.0, 133.2, 129.6, 129.5, 126.5, 120.7, 120.1, 115.7, 106.1, 50.3, 21.2, 21.0, 11.0. HRMS (ESI), *m/z* calcd for $C_{21}H_{22}N_2O$ ([M + Na]$^+$) 341.1624; found, 341.1624.

1-Cyclohexyl-2-methyl-*N*-(*p*-tolyl)-1*H*-pyrrole-3-carboxamide (4n). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (62 mg, 21%). Mp 121−123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.0 Hz, 2H), 7.41 (s, 1H), 7.12 (d, J = 8.0 Hz, 2H), 6.66 (d, J = 3.2 Hz, 1H), 6.34 (d, J = 3.2 Hz, 1H), 3.90−3.84 (m, 1H), 2.59 (s, 3H), 2.31 (s, 3H), 1.99−1.89 (m, 4H), 1.76 (d, J = 12.8 Hz, 1H), 1.64−1.54 (m, 2H), 1.47−1.37 (m, 2H), 1.29−1.21 (m, 1H).^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.2, 136.0, 133.7, 133.0, 129.3, 119.9, 115.9, 114.7, 105.6, 55.0, 33.9, 25.8, 25.3, 20.8, 10.7. HRMS (ESI), *m/z* calcd for $C_{19}H_{24}N_2O$ ([M + H]$^+$) 297.1961; found, 297.1964.

1-Butyl-2-methyl-*N*-(*p*-tolyl)-1*H*-pyrrole-3-carboxamide (4o). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (83.7 mg, 31%). Mp 115−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 2H), 7.41 (s, 1H), 7.13 (d, J = 8.4 Hz, 2H), 6.54 (d, J = 2.8 Hz, 1H), 6.31 (d, J = 2.8 Hz, 1H), 3.82 (t, J = 7.2 Hz, 2H), 2.57 (s, 3H), 2.31 (s, 3H), 1.73−1.65 (m, 2H), 1.39−1.29 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.0, 136.0, 134.1, 133.0, 129.3, 119.8, 114.9, 105.4, 46.4, 32.9, 20.8, 19.8, 13.6, 10.8. HRMS (ESI), *m/z* calcd for $C_{17}H_{22}N_2O$ ([M + H]$^+$) 271.1805; found, 271.1809.

***N*,1-Bis(4-chlorophenyl)-5-methyl-2-phenyl-1*H*-pyrrole-3-carboxamide (4q).** The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (328 mg, 78%). Mp 254−256 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.34 (m, 2H), 7.29−7.24 (m, 5H), 7.16−7.13 (m, 4H), 7.05−7.00 (m, 3H), 6.64 (s, 1H), 2.10 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.8, 134.2, 131.6, 129.8, 129.4, 129.2, 129.0, 128.9, 120.4, 108.9, 13.0. HRMS (ESI), *m/z* calcd for $C_{24}H_{18}Cl_2N_2O$ ([M + H]$^+$) 421.0869; found, 421.0868.

***N*,1-Bis(4-chlorophenyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxamide (4r).** The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (251 mg, 70%). Mp 175−178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.8 Hz, 2H), 7.51−7.47 (m, 3H), 7.28 (d, J = 8.8 Hz, 2H), 7.14 (d, J = 8.8 Hz, 2H), 6.18 (s, 1H), 2.33 (s, 3H), 2.00 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.0, 137.3, 136.1, 135.4, 134.8, 129.9, 129.6, 129.1, 129.0, 128.5, 121.1, 114.4, 104.6, 12.9, 12.4. HRMS (ESI), *m/z* calcd for $C_{19}H_{16}Cl_2N_2O$ ([M + H]$^+$) 359.0712; found, 359.0712.

Ethyl 1-(4-Chlorophenyl)-2-(4-methoxyphenyl)-1*H*-pyrrole-3-carboxylate (4u). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 15/1) as a white solid (252 mg, 71%). Mp 152−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 8.8 Hz, 2H), 7.12 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 6.82 (s, 2H), 6.79 (d, J = 8.8 Hz, 2H), 4.21−4.16 (m, 2H), 3.79 (s, 3H), 1.22 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.8, 159.4, 138.2, 137.9, 133.0, 132.5, 129.2, 127.3, 123.2, 122.4, 114.9, 113.2, 111.5, 59.7, 55.2, 14.4. HRMS (ESI), *m/z* calcd for $C_{20}H_{18}ClNO_3$ ([M + H]$^+$) 356.1048; found, 356.1042.

Ethyl 1-(3-Chlorophenyl)-2-(4-methoxyphenyl)-1*H*-pyrrole-3-carboxylate (4v). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 15/1) as a white solid (241 mg, 68%). Mp 140−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (s, 1H), 7.24−7.14 (m, 5H), 6.89−6.80 (m, 4H), 4.22−4.17 (m, 2H), 3.80 (s, 3H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.8, 159.5, 140.8, 138.0, 134.7, 132.6, 130.0, 127.5, 126.3, 124.6, 123.2, 122.4, 115.1, 113.3, 111.6, 59.8, 55.3, 14.4. HRMS (ESI), *m/z* calcd for $C_{20}H_{18}ClNO_3$ ([M + H]$^+$) 356.1048; found, 356.1048.

Ethyl 1-(2-Chlorophenyl)-2-(4-methoxyphenyl)-1*H*-pyrrole-3-carboxylate (4w). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 15/1) as a white solid (181 mg, 51%). Mp 112−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, J = 8.0, 1.6 Hz, 1H), 7.25−7.21 (m, 1H), 7.19−7.11 (m, 4H), 6.84 (d, J = 2.8 Hz, 1H), 3.80 (s, 3H), 6.74−6.72(m, 3H), 1.22 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.8, 159.3, 139.1, 137.3, 132.4, 132.2, 130.3, 130.2, 129.6, 127.3, 123.2, 122.8, 114.0, 112.9, 111.0, 59.6, 55.2, 14.4. HRMS (ESI), *m/z* calcd for $C_{20}H_{18}ClNO_3$ ([M + H]$^+$) 356.1048; found, 356.1046.

Ethyl 2-(4-Methoxyphenyl)-1-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (4x). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/1) as a white solid (261 mg, 78%). Mp 103−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 8.8 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 6.94 (d, J = 8.4 Hz, 2H), 6.82 6 (d, J = 1.6 Hz, 2H), 6.78 (d, J = 8.8 Hz, 2H), 4.23−4.17 (m, 2H), 3.77 (s, 3H), 2.31 (s, 3H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.9, 159.2, 137.9, 137.2, 137.0, 132.5, 129.5, 125.9, 123.6, 122.6, 114.3, 113.0, 110.9, 59.5, 55.1, 21.0, 14.4. HRMS (ESI), *m/z* calcd for $C_{21}H_{21}NO_3$ ([M + H]$^+$) 336.1594; found, 336.1593.

Ethyl 2-(4-Methoxyphenyl)-1-(*m*-tolyl)-1*H*-pyrrole-3-carboxylate (4y). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (224 mg, 67%). Mp 138−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.16−7.13 (m, 2H), 7.10 (d, J = 7.6 Hz, 1H), 7.03 (d, J = 7.6 Hz, 1H), 6.93 (s, 1H), 6.84(d, J = 3.2 Hz, 2H), 6.82−6.77 (m, 4H), 4.22−4.17 (m, 2H), 3.77 (s, 3H), 2.28 (s, 3H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.9, 159.2, 139.6, 139.0, 137.9, 132.5, 128.7, 127.9, 126.7, 123.6, 123.3, 122.6, 114.4, 113.0, 111.0, 59.6, 55.2, 21.3, 14.4. HRMS (ESI), *m/z* calcd for $C_{21}H_{21}NO_3$ ([M + H]$^+$) 336.1594; found, 336.1594.

Ethyl 2-(4-Methoxyphenyl)-1-(*o*-tolyl)-1*H*-pyrrole-3-carboxylate (4z). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (194 mg, 58%). Mp 100−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21−7.20 (m, 1H), 7.14−7.12 (m, 5H), 6.84 (d, J = 2.8 Hz, 1H), 6.71 (d, J = 8.8 Hz, 2H), 6.68 (d, J = 2.8 Hz, 1H), 4.23−4.18 (m, 2H), 3.73 (s, 3H), 1.93 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.0, 159.1, 138.9, 138.7, 135.5, 132.1, 130.8, 128.5, 128.5, 126.4, 123.4, 122.6, 113.5, 112.9, 110.9, 59.6, 55.1, 17.6, 14.4. HRMS (ESI), *m/z* calcd for $C_{21}H_{21}NO_3$ ([M + H]$^+$) 336.1594; found, 336.1593.

Ethyl 1-(4-Chlorophenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (4a′). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 15/1) as a white solid (189 mg, 72%). Mp 58−60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.43 (m, 2H), 7.23−7.19 (m, 2H), 6.65 (dd, J = 12.0, 3.2 Hz, 2H), 4.29 (q, J = 7.2 Hz, 2H), 2.43 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.5, 137.7, 136.0, 133.9, 129.6, 127.6, 121.2, 113.7, 110.5, 59.6, 14.6, 12.3. HRMS (ESI), *m/z* calcd for $C_{14}H_{14}ClNO_2$ ([M + Na]$^+$) 286.0605; found, 286.0584.

Ethyl 1-(3-Chlorophenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (4b′). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate =15/1) as a yellow oil liquid (179 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.40 (m, 2H), 7.30−7.29 (m, 1H), 7.19−7.17 (m, 1H), 6.67−6.65 (m, 2H), 4.33−4.27 (m, 2H), 2.45 (s, 3H), 1.36 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.6, 140.4, 136.0, 135.1, 130.4, 128.4, 126.7, 124.7, 121.3, 114.0, 110.8, 59.7, 29.9, 14.7, 12.3. HRMS (ESI), *m/z* calcd for $C_{14}H_{14}ClNO_2$ ([M + Na]$^+$) 286.0605; found, 286.0592.

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Ethyl 1-(2-Chlorophenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (4c′). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 15/1) as a yellow oil liquid (147 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, J = 8.0, 1.6 Hz, 1H), 7.44−7.36 (m, 2H), 7.30 (dd, J = 7.6, 1.6 Hz, 1H), 6.70 (d, J = 3.2 Hz, 1H), 2.43 (d, J = 3.2 Hz, 1H), 4.33−4.28 (m, 2H), 2.31 (s, 3H), 1.36 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.7, 137.1, 137.0, 132.9, 130.5, 130.2, 129.8, 127.8, 121.2, 113.1, 110.4, 59.6, 29.8, 14.7, 11.7. HRMS (ESI), m/z calcd for $C_{14}H_{14}ClNO_2$ ([M + H]$^+$) 264.0786; found, 264.0783.

Ethyl 2-Methyl-1-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (4d′). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 15/2) as a white solid (175 mg, 72%). Mp 43−45 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 6.66−6.64 (m, 2H), 4.33−4.27 (m, 2H), 2.43 (s, 3H), 4.42 (s, 3H), 1.36 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.8, 138.1, 136.8, 136.2, 129.9, 126.2, 121.5, 113.2, 110.1, 59.5, 21.2, 14.7, 12.3. HRMS (ESI), m/z calcd for $C_{15}H_{17}NO_2$ ([M + H]$^+$) 244.1332; found, 244.1321.

Ethyl 2-Methyl-1-(*m*-tolyl)-1*H*-pyrrole-3-carboxylate (4e′). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate =15/2) as a yellow oil liquid (187 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 7.6 Hz, 1H), 6.65 (s, 2H), 4.33−4.27 (m, 2H), 2.44 (s, 3H), 4.41 (s, 3H), 1.36 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.8, 139.5, 139.3, 136.2, 129.1, 128.8, 127.0, 123.4, 121.4, 113.3, 110.1, 59.5, 21.4, 14.7, 12.3. HRMS (ESI), m/z calcd for $C_{15}H_{17}NO_2$ ([M + H]$^+$) 244.1322; found, 244.1332.

Ethyl 2-Methyl-1-(*o*-tolyl)-1*H*-pyrrole-3-carboxylate (4f′). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 15/2) as a yellow oil liquid (151 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.28 (m, 3H), 7.15 (d, J = 8.0 Hz, 1H), 6.68 (d, J = 2.8 Hz, 1H), 6.52 (d, J = 3.2 Hz, 1H), 4.33−4.27 (m, 2H), 2.25 (s, 3H), 2.01 (s, 3H), 1.37 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.8, 138.3, 136.6, 136.1, 131.0, 129.0, 128.0, 126.8, 121.0, 112.6, 110.0, 59.5, 17.3, 14.7, 11.7. HRMS (ESI), m/z calcd for $C_{15}H_{17}NO_2$ ([M + H]$^+$) 244.1332; found, 244.1312.

Ethyl 2-Methyl-1-phenyl-1*H*-pyrrole-3-carboxylate (4g′). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 15/2) as a yellow oil liquid (167 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.6 Hz, 2H), 7.41 (d, J = 7.2 Hz, 1H), 7.27 (d, J = 7.6 Hz, 2H), 6.67 (s, 2H), 4.33−4.28 (m, 2H), 2.45 (s, 3H), 1.37 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.7, 139.3, 136.1, 129.4, 128.1, 126.4, 121.4, 113.4, 110.3, 59.5, 14.7, 12.3. HRMS (ESI), m/z calcd for $C_{14}H_{15}NO_2$ ([M + H]$^+$) 230.1176; found, 230.1150.

Ethyl 2-(4-Methoxyphenyl)-1-phenyl-1*H*-pyrrole-3-carboxylate (4h′). The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/1) as a white solid (238 mg, 74%). Mp 95−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.23 (m, 3H), 7.15 (d, J = 8.8 Hz, 2H), 7.07−7.05 (m, 2H), 6.87−6.83 (m, 2H), 4.78 (d, J = 8.8 Hz, 2H), 4.02 (m, 2H), 3.77 (s, 3H),1.23 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.9, 159.2, 139.6, 137.9, 132.5, 129.0, 127.2, 126.1, 123.5, 122.5, 114.5, 113.0, 111.1, 59.6, 55.2, 14.4. HRMS (ESI), m/z calcd for $C_{20}H_{19}NO_3$ ([M + H]$^+$) 322.1438; found, 322.1439.

***N*,1-Bis(4-chlorophenyl)-2-methyl-5-vinyl-4,5-dihydro-1*H*-pyrrole-3-carboxamide (3s).** The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a white solid (123 mg, 33%). Mp 171−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.49 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.24 (s, 1H), 6.98 (d, J = 8.4 Hz, 2H), 6.78 (s, 1H), 5.84 (dt, 1H), 5.13−5.06 (q, 2H), 4.56−4.50 (t, J = 8.4 Hz, 1H), 3.15 (t, J = 11.2 Hz, 1H), 2.71 (t, J = 9.6 Hz, 1H), 2.22 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.9, 158.0, 139.6, 137.6, 137.5, 131.4, 129.3, 128.8, 128.1, 127.6, 121.0, 118.2, 100.9, 68.3, 35.3, 14.3. HRMS (ESI), m/z calcd for $C_{20}H_{18}Cl_2N_2O$ ([M + H]$^+$) 373.0869; found, 373.0848.

***N*,1-Bis(4-chlorophenyl)-2-methyl-5-phenyl-4,5-dihydro-1*H*-pyrrole-3-carboxamide (3t).** The product was isolated by flash chromatography (eluent: petroleum ether/ethyl acetate = 10/2) as a yellow oil (123 mg, 29%). ^{1}H NMR (400 MHz, DMSO) δ 8.63 (s, 1H), 7.70 (d, J = 8.8 Hz, 2H), 7.33 (s, 2H), 7.30 (d, J = 2.8 Hz, 2H), 7.28 (s, 1H), 7.13 (d, J = 8.8 Hz, 2H), 7.00 (d, J = 8.8 Hz, 2H), 6.54 (d, J = 8.8 Hz, 2H), 5.44 (t, J = 9.2 Hz, 1H), 3.47 (t, J = 12.8 Hz, 1H), 2.89−2.73 (m, 1H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 165.1, 156.4, 148.1, 143.1, 140.5, 139.5, 129.3, 129.1, 128.9, 128.6, 127.1, 126.9, 121.8, 115.6, 102.1, 67.5, 38.8, 14.3. HRMS (ESI), m/z calcd for $C_{24}H_{20}Cl_2N_2O$ ([M + H]$^+$) 423.1025; found, 423.1014.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR and ^{13}C{^{1}H} NMR spectra of compound **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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