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Graphical Abstract

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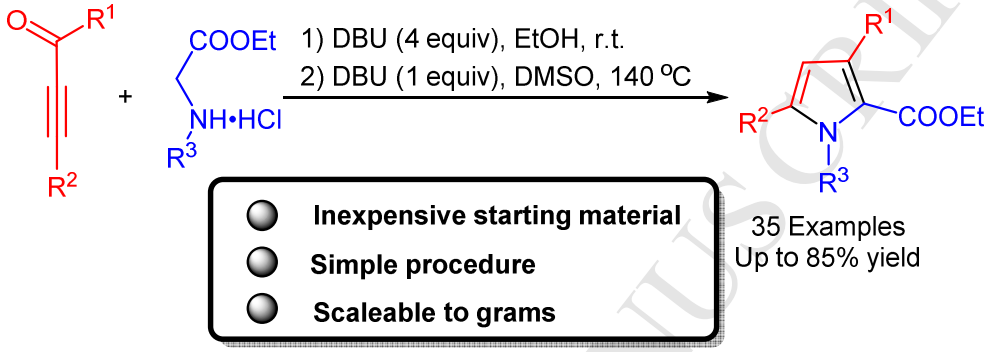

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DBU-Promoted Tandem Michael-addition/Cyclization for the Synthesis of Polysubstituted Pyrroles

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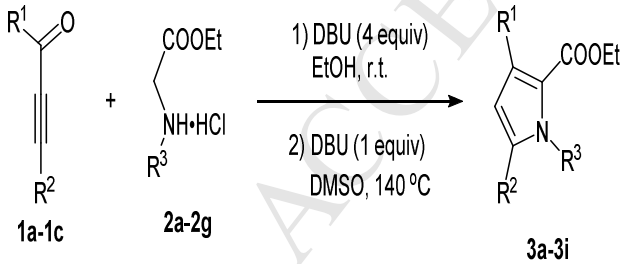
ABSTRACT

An efficient and transition-metal-free method for the synthesis of the structurally diversified pyrroles is described. Various *α,β*-unsaturated ynones reacted with *N*-substituted ethyl glycine ethyl ester hydrochlorides in the presence of DBU to form the corresponding products in good yields. This protocol has the advantages of readily available starting materials, mild reaction conditions and a wide scope of substrates, which provides a practical route for the synthesis of polysubstituted pyrroles.

1. Introduction

Pyrroles represent an important class of nitrogen-containing heterocycles, which show diverse pharmacological properties such as anti-HIV-1,[1] antitumor,[2] antifungel[3] and other bioactivities.[4] For examples, Atorvastatin, Lamellarin Q and Porphobilinogen are prevalent pyrrole-derived clinical drugs (Scheme 1).



Scheme 1 Selected biological and pharmaceutical molecules bearing highly substituted pyrrole

Pyrrole cores also appear frequently in natural products[5] and functional materials such as conducting materials.[6] Due to their wide applications, the development of new and more efficient method for construction of pyrroles has long been an active topic in synthetic chemistry. The traditional methods for synthesis of pyrroles are the Paal-Knorr[7] or Hantazsch[8] reactions. Transition-metal-catalyzed methodologies are other important and efficient approaches for construction of pyrrole derivatives in recent years.[9]

On the other hand, *α,β*-unsaturated ynones are important building blocks in the synthesis of heterocycles because of their easy preparation and commercial availability.[10] Till now, *α,β*-unsaturated ynones have been successfully used in the synthesis of pyridines,[11] furfurans,[12] and other heterocycles.[13] As versatile building blocks, they could also be applied for construction of pyrrole derivatives. For instance, Cu-assisted cycloisomerisation reactions of *α,β*-unsaturated ynone-derived alkynyl imines were reported to provide pyrrole derivatives in good yields.[14] One-pot reactions of ynones with benzylamines could afford pyrrole derivatives under metal free conditions, but amino acid esters failed to give the corresponding pyrrole derivatives under the same conditions.[15] Meanwhile, there is an ester group at 2-position of pyrrole ring of Lamellarin Q. In our research works, we found that the reaction of ynones and amino acid esters produced the ester group-containing pyrrole derivatives in good yields when the reaction was performed in a two-step way in the presence of DBU. Herein, we would like to disclose a practical DBU-mediated synthesis of ester group-containing

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polysubstituted pyrroles from the reaction of amino acid esters and ynones.

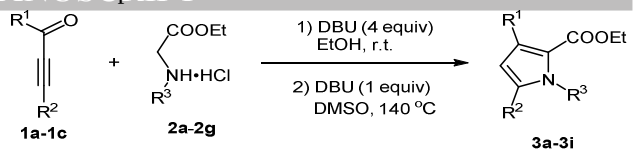
2. Results and discussion

We initiated our study with the reaction of 1,3-diphenylprop-2-yn-1-one **1a** (1 equiv), glycine ethyl ester hydrochloride **2a** (1 equiv) and DBU (1 equiv) in DMSO at room temperature. After 12 h, the reaction mixture was then heated at 140 °C for another 4 h. The desired product **3a** was obtained in 25% yield with another compound **4a** being formed in 32% yield (Table 1, entry 1). We envisioned that enaminone **4a** would be the intermediate for the desired product **3a**. Based on literature reports about the formation of enaminones, alcoholic solvent was beneficial to generate the compound **4a**.[16] Thus, the mixture of 1,3-diphenylprop-2-yn-1-one **1a** (1 equiv), glycine ethyl ester hydrochloride **2a** (1 equiv) and DBU (1 equiv) were firstly stirred in ethanol at room temperature for 12 h to form the compound **4a**, and then the ethanol was replaced by DMSO. The reaction mixture was heated at 140 °C for another 4 h to afford the product **3a** in 48% yield, but the compound **4a** was still obtained in 19% yield (Table 1, entry 2). When both two steps were carried out in ethanol, there was no product **3a** formed, and only enaminone **4a** was obtained in 45% yield (Table 1, entry 3). Meanwhile, the toluene and 1,4-dioxane were used as the solvents for the second step, the desired product **3a** was not formed in both of the solvents. When DMF was used, the **3a** was obtained in 35% yield with the compound **4a** being formed in 13% yield (Table 1, entry 4−6). The result indicated that DMSO is the suitable solvent for the second step. When the reaction temperature in the second step was decreased, the yield of the desired product **3a** decreased (Table 1, entries 7−10). Further studies showed that the yield of product **3a** reached to 85% when 4 equiv of glycine ethyl ester hydrochloride **2a** and 4 equiv of DBU in step one were used (Table 1, entry 17). The other bases such as KOH, NaOH, K_3PO_4, Na_3PO_4, K_2CO_3, Cs_2CO_3, Et_3N, and DABCO were also examined, but DBU gave the best result. Thus, the best reaction conditions were the treatment of 1 equiv of 1,3-diphenylprop-2-yn-1-one with 4 equiv of glycine ethyl ester hydrochloride and 4 equiv of DBU in ethanol at room temperature for 12 h, and then the ethanol was vaporized. The residue was redissolved in DMSO, and another 1 equiv of DBU was added. The mixture was heated at 140 °C for another 4 h. The target product **3a** was then obtained.

With the optimal reaction conditions in hand, the scope of the reaction was investigated. First, glycine ethyl ester hydrochloride and its *N*-substituted derivatives **2a−2g** were reacted with ynones **1a−1c**. As shown in Table 2, the substituents on nitrogen atom of glycine ethyl ester had great influence on the reaction. When *N*-phenyl glycine ethyl ester was used in the reaction, no product **3b** was obtained (Table 2, entry 2). When *N*-Boc glycine ethyl ester was applied in the reaction, the deprotected product **3a** was formed instead of Boc-protected product **3c** (Table 2, entry 3). *N*-Alkyl glycine ethyl ester could also be applied in the reaction to afford the corresponding products (Table 2, entries 5−9), but the yields were lower. When the bulky *t*-butyl group was attached to the nitrogen atom, no product was formed (Table 2, entry 8). These results indicated that the electronic properties and steric hindrance at the N atom disfavored this reaction.

Afterward, various ynones **1b−1aa** were investigated in the reaction. As shown in Table 3. Both electrodonating and electrowithdrawing groups on phenyl rings of 1,3-diarylynones were well tolerated and provided the corresponding products in good yields (Table 3, entries 1−14). Further observation showed that the steric hindrance on phenyl rings of aromatic ynones did not influence the transformation obviously. For instance, when the substituents on aromatic ring of R^1 group were methyl or chlorine group, the *para*-, *ortho*- and *meta*-substituted products **3j−3n** were obtained in almost the same yields (Table 3, entries 1−5). Meanwhile, the electronic properties of the substituents on phenyl rings of aromatic ynones had influence on the product yields. For examples, when both substituents on aromatic rings of R^1 and R^2 groups were methyl group, the yield of **3u** was 67% (Table 3, entry 12). However, when the substituent on aromatic rings of R^1 group was chlorine and the substituent on aromatic rings of R^2 group was methyl group, the yield of **3v** decreased to 49% (Table 3, entry 13). When the R^1 or/and R^2 groups were aliphatic substituents, the corresponding products were produced in low yields (Table 3, entries 15−26). Especially, no product

Table 1 Optimization of Reaction Conditions[a]



Entry	1a/2a	Step 1 DBU	Step 2 DBU	Temp (°C)	Yield (%)[b] 3a/4a
1[c]	1:1	1 equiv.	/	140	25/32
2	1:1	1 equiv.	/	140	48/19
3[d]	1:1	1 equiv.	/	reflux	0/45
4[e]	1:1	1 equiv.	/	reflux	0/27
5[f]	1:1	1 equiv.	/	reflux	0/36
6[g]	1:1	1 equiv.	/	140	35/13
7	1:1	1 equiv.	/	120	37/21
8	1:1	1 equiv.	/	100	28/30
9	1:1	1 equiv.	/	50	23/25
10	1:1	1 equiv.	/	r.t.	10/43
11	1:1	1 equiv.	1 equiv.	140	54/15
12	1:1	2 equiv.	1 equiv.	140	58/12
13	1:1	3 equiv.	1 equiv.	140	60/8
14	1:1	4 equiv.	1 equiv.	140	69/0
15	1:2	4 equiv.	1 equiv.	140	71/0
16	1:3	4 equiv.	1 equiv.	140	82/0
17	1:4	4 equiv.	1 equiv.	140	85/0
18	1:4	4 equiv.	1.5 equiv.	140	76/0

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (1.0−4.0 equiv) and DBU (1.0−4.0 equiv) were mixed in EtOH (5 mL), and stirred at r.t. for 12 h. EtOH was vaporized, and then another portion of DBU (0−1.5 equiv) and DMSO (5 mL) was added. The mixture was stirred at 140 °C for 4 h. [b] Isolated yields. [c] Step 1: using DMSO as solvent. [d] Step 2: using EtOH as solvent. [e] Step 2: using toluene as solvent. [f] Step 2: using 1,4-dioxane as solvent. [g] Step 2: using DMF as solvent.

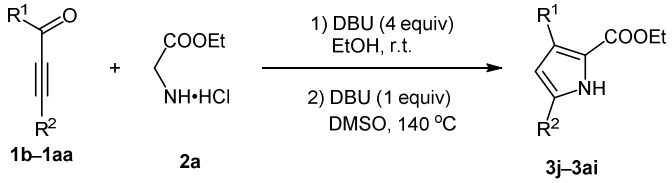
Table 2 Reaction of *N*-Substituted Glycine Ethyl Ester Hydrochlorides **2a−2g** with Ynones **1a−1c**[a]

Entry	R^1	R^2	R^3	Product	Yield (%)[b]
1	C_6H_5 (**1a**)	C_6H_5 (**1a**)	H (**2a**)	**3a**	85
2	C_6H_5 (**1a**)	C_6H_5 (**1a**)	C_6H_5 (**2b**)	**3b**	0
3	C_6H_5 (**1a**)	C_6H_5 (**1a**)	Boc (**2c**)	**3c**	0 (62[c])
4	C_6H_5 (**1a**)	C_6H_5 (**1a**)	Benzyl (**2d**)	**3d**	65
5	C_6H_5 (**1a**)	C_6H_5 (**1a**)	Methyl (**2e**)	**3e**	76
6	4-$CH_3C_6H_4$ (**1b**)	C_6H_5 (**1b**)	Methyl (**2e**)	**3f**	57
7	4-ClC_6H_4 (**1c**)	C_6H_5 (**1c**)	Methyl (**2e**)	**3g**	65
8	C_6H_5 (**1a**)	C_6H_5 (**1a**)	*t*-Butyl (**2f**)	**3h**	0
9	C_6H_5 (**1a**)	C_6H_5 (**1a**)	*n*-Butyl (**2g**)	**3i**	37

[a]Reaction conditions: **1a−1c** (0.5 mmol, 1 equiv), **2a−2g** (4.0 equiv) and DBU (4.0 equiv) were mixed in EtOH (5 mL) and then stirred at r.t. for 12 h, EtOH was vaporized, and then another portion of DBU (1.0 equiv) and DMSO (5 mL) was added. The mixture was stirred at 140 °C for 4 h. [b]Isolated yields. [c]Yield of **3a**.

was formed if R^1 was *t*-butyl group (Table 3, entry 18). When R^1 was trifluoromethyl group, only intermediate **4ai** was obtained instead of the corresponding pyrrole in the yield of 92% (Table 3, entry 26).

Table 3 Reaction of Glycine Ethyl Ester Hydrochlorides **2a** with Various Ynones **1b**−**1aa**[a]

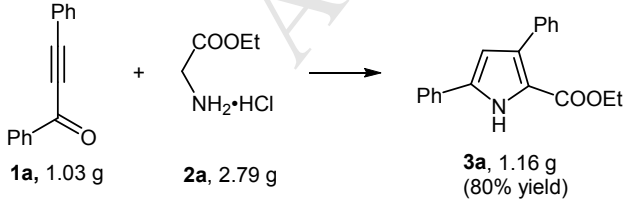


1b–1aa **2a** **3j–3ai**

Entry	R^1	R^2	Product	Yield (%)[b]
1	4-$CH_3C_6H_4$ (**1b**)	C_6H_5 (**1b**)	**3j**	74
2	4-ClC_6H_4 (**1c**)	C_6H_5 (**1c**)	**3k**	76
3	2-$CH_3C_6H_4$ (**1d**)	C_6H_5 (**1d**)	**3l**	67
4	3-ClC_6H_4 (**1e**)	C_6H_5 (**1e**)	**3m**	73
5	2-ClC_6H_4 (**1f**)	C_6H_5 (**1f**)	**3n**	64
6	4-$CH_3OC_6H_4$ (**1g**)	C_6H_5 (**1g**)	**3o**	72
7	4-FC_6H_4 (**1h**)	C_6H_5 (**1h**)	**3p**	69
8	4-$CF_3C_6H_4$ (**1i**)	C_6H_5 (**1i**)	**3q**	75
9	3,5-$Cl_2C_6H_3$ (**1j**)	C_6H_5 (**1j**)	**3r**	84
10	2-Naphthyl (**1k**)	C_6H_5 (**1k**)	**3s**	70
11	1-Naphthyl (**1l**)	C_6H_5 (**1l**)	**3t**	65
12	4-$CH_3C_6H_4$ (**1m**)	4-$CH_3C_6H_4$ (**1m**)	**3u**	67
13	4-ClC_6H_5 (**1n**)	4-$CH_3C_6H_4$ (**1n**)	**3v**	49
14	3,5-$Cl_2C_6H_3$ (**1o**)	4-$CH_3C_6H_4$ (**1o**)	**3w**	78
15	Benzyl (**1p**)	C_6H_5 (**1p**)	**3x**	64
16	Methyl (**1q**)	C_6H_5 (**1q**)	**3y**	38
17	*i*-Propyl (**1r**)	C_6H_5 (**1r**)	**3z**	30
18	*t*-Butyl (**1s**)	C_6H_5 (**1s**)	**3aa**	0
19	Cyclohexyl (**1t**)	C_6H_5 (**1t**)	**3ab**	13
20	Cinnamyl (**1u**)	C_6H_5 (**1u**)	**3ac**	58
21	4-$CH_3C_6H_4$ (**1v**)	Cyclopropyl (**1v**)	**3ad**	45
22	3,5-$Cl_2C_6H_3$ (**1w**)	Cyclopropyl (**1w**)	**3ae**	60
23	C_6H_5 (**1x**)	*t*-Butyl (**1x**)	**3af**	10
24	C_6H_5 (**1y**)	Cyclohexyl (**1y**)	**3ag**	15
25	Methyl (**1z**)	H (**1z**)	**3ah**	19
26	Trifluoromethyl (**1aa**)	C_6H_5 (**1aa**)	**3ai** (**4ai**)	0 (92[c])

[a] Reaction conditions: **1b**−**1aa** (0.5 mmol), **2a** (4.0 equiv), DBU (4.0 equiv) were mixed in EtOH (5 mL), and then stirred at r.t. for 12 h, EtOH was vaporized, and then another portion of DBU (1.0 equiv) and DMSO (5 mL) was added. The mixture was stirred at 140 °C for 4 h. [b] Isolated yields. [c] Yield of **4ai**.

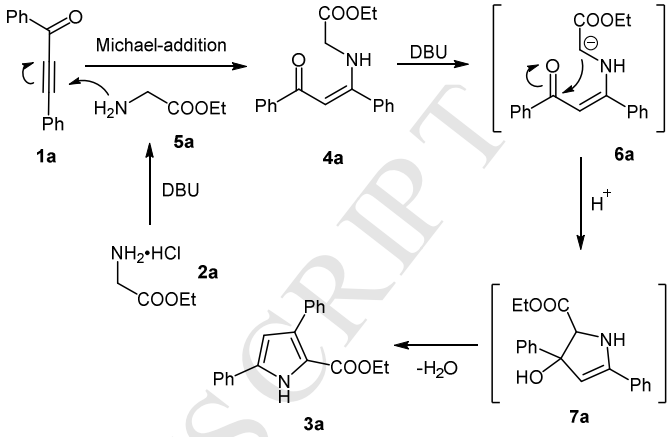
In order to further demonstrate the utilities of this process in synthesis of pyrrole derivatives, a gram-scale experiment was conducted (Scheme 2). When 1.03 gram of 1,3-diphenylprop-2-yn-1-one **1a** reacted with 2.79 gram of glycine ethyl ester hydrochloride **2a** under the standard reaction conditions. The product **3a** was obtained in 80% yield. This result showed this process was an efficient and practical method to prepare pyrrole derivatives



1a, 1.03 g **2a**, 2.79 g **3a**, 1.16 g (80% yield)

Scheme 2 Gram-scale synthesis of ethyl 3,5-diphenyl-1*H*-pyrrole-2-carboxylate **3a**

On the basis of the literature,[12a,16] and our experimental results, a tentative mechanism for the reaction was proposed, which was depicted in Scheme 3. First, glycine ethyl ester hydrochloride **2a** was neutralized by DBU to give glycine ethyl ester **5a**, which performed 1,4-addition reaction with ynone **1a** to provide the enaminone **4a**. Deprotonation of the enaminone **4a** by DBU generated the anion intermediate **6a**, which conducted 1,2-addition to carbonyl group to generate intermediate **7a**. Dehydration of **7a** gave the product **3a**.



Scheme 3 Proposed mechanism

3. Conclusions

In summary, we have developed an effective and practical tandem Michael addition/cyclization of *α,β*-unsaturated ynones with *N*-substituted glycine ethyl ester hydrochlorides for the synthesis of polysubstituted pyrroles under transition-metal-free conditions. A series of polysubstituted pyrroles were obtained in good yields. This protocol overcomes some literature limitations, and makes the glycine ethyl ester hydrochlorides applicable for the preparation of polysubstituted pyrroles.

4. Experimental Section

All of the commercially available reagents and solvents were used without further purification. *α,β*-unsaturated ynones and compounds **2f** and **2g** were prepared according to the literature procedure.[10e,17] Flash chromatography was performed using silica gel 60 (230-400 mesh). Analytical thin layer chromatography (TLC) was conducted using silica gel GF254. TLC plates were analysed by an exposure to ultraviolet (UV) light and/or submersion in a phosphomolybdic acid solution or in iodine vapour. ^{1}H NMR spectra were measured on 600 MHz and 400 MHz spectrometers. Chemical shifts were recorded as follows: chemical shift in parts per million from internal tetramethylsilane on the δ scale, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), coupling constant (hertz), integration, and assignment. ^{13}C NMR spectra were measured on 150 MHz and 100 MHz spectrometers. Chemical shifts were recorded in parts per million from the solvent resonance employed as the internal standard (deuterochloroform at 77.0 ppm).

*4.1. General experimental procedure for the synthesis of compounds **3***

α,β-Unsaturated ynones (1; 0.5 mmol, 1 equiv), *N*-substituted glycine ethyl ester hydrochlorides (2; 2.0 mmol, 4 equiv) and DBU (2.0 mmol, 4 equiv) were mixed in ethanol (5 mL) and stirred at room temperature for 12 h. When TLC showed intermediate **4** was generated, ethanol was evaporated. DBU (0.5 mmol, 1 equiv) and DMSO (5 mL) were then added, the mixture was stirred at 140 °C for 4 h. After completion of the reaction, the

mixture was diluted with ethyl acetate (3 × 10 mL) and washed with brine (3 × 10 mL). The organic phase was dried over anhydrous Na_2SO_4 and filtered. The solvents were vaporized, and the residue was purified by silica gel column chromatography with EtOAc/petroleum ether (1 : 5−1 : 3) as the eluent to afford the products **3**.

*4.2. Ethyl 3,5-diphenyl-1H-pyrrole-2-carboxylate[18] (**3a**)*

Yellow oil (85%, 123.6 mg); R_f = 0.5 (EA/ PE = 1/5). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.66 (s, 1H), 7.61 (d, *J* = 7.8 Hz, 2H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.41−7.36 (m, 4H), 7.31 (d, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 7.2 Hz, 1H), 6.61 (d, *J* = 3.0 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 1.22 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.4, 135.5, 135.2, 133.4, 131.1, 129.5, 128.9, 127.8, 127.6, 127.0, 124.8, 118.6, 109.9, 60.4, 14.1.

*4.3. Ethyl 1-benzyl-3,5-diphenyl-1H-pyrrole-2-carboxylate (**3d**).*

Yellow oil (65%, 123.8 mg); R_f = 0.4 (EA/ PE = 1/5). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.46 (d, *J* = 7.2 Hz, 2H), 7.35−7.33 (m, 7H), 7.28 (t, *J* = 7.2 Hz, 1H), 7.24 (t, *J* = 8.4 Hz, 2H), 7.17 (t, *J* = 7.8 Hz, 1H), 6.92 (t, *J* = 7.2 Hz, 2H), 6.34 (d, *J* = 2.4 Hz, 1H), 5.60 (s, 2H), 4.00 (q, *J* = 7.2 Hz, 2H), 0.93 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.7, 140.5, 139.4, 136.6, 134.0, 132.0, 129.5, 129.4, 128.5, 128.4, 128.2, 127.5, 126.7, 126.6, 125.7, 119.7, 112.0, 59.8, 49.6, 13.6. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{26}H_{23}NO_2Na$: 404.1621; found 404.1621.

*4.4. Ethyl 1-methyl-3,5-diphenyl-1H-pyrrole-2-carboxylate (**3e**).*

Pale yellow oil (76%, 116.0 mg); R_f = 0.6 (EA/ PE = 1/5). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.43−7.40 (m, 6H), 7.38−7.32 (m, 3H), 7.27 (t, *J* = 7.2 Hz, 1H), 6.24 (d, *J* = 1.8 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 1.06 (t, *J* = 7.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.0, 140.2, 136.7, 133.4, 131.9, 129.5, 129.3, 128.4, 128.0, 127.4, 126.5, 120.3, 111.3, 59.7, 35.0, 13.8. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{19}NO_2Na$: 328.1308; found 328.1313.

*4.5. Ethyl 1-methyl-5-phenyl-3-(p-tolyl)-1H-pyrrole-2-carboxylate (**3f**).*

Pale yellow oil (57%, 91.0 mg); R_f = 0.6 (EA/ PE = 1/5). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.41−7.37 (m, 4H), 7.34−7.32 (m, 3H), 7.14 (d, *J* = 7.8 Hz, 2H), 6.22 (d, *J* = 1.2 Hz, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 2.35 (s, 3H), 1.10 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.0, 140.1, 136.0, 133.6, 133.3, 131.9, 129.3, 129.3, 128.4, 128.1, 127.9, 120.2, 111.3, 59.7, 34.9, 21.1, 13.8. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{21}H_{21}NO_2Na$: 342.1465; found 342.1469.

*4.6. Ethyl 3-(4-chlorophenyl)-1-methyl-5-phenyl-1H-pyrrole-2-carboxylate (**3g**).*

Dark yellow oil (65%, 55.1 mg); R_f = 0.5 (EA/ PE = 1/5).^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.43−7.40 (m, 4H), 7.38−7.34 (m, 3H), 7.30 (d, *J* = 8.4 Hz, 2H), 6.20 (d, *J* = 1.8 Hz, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 1.10 (t, *J* = 7.2 Hz, 3H).^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.0, 140.3, 135.2, 132.4, 132.0, 131.7, 130.8, 129.3, 128.5, 128.1, 127.5, 120.2, 111.2, 60.0, 35.0, 14.0. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{18}ClNO_2Na$: 362.0918; found 362.0910.

*4.7. Ethyl 1-butyl-3,5-diphenyl-1H-pyrrole-2-carboxylate (**3i**).*

Dark yellow oil (37%, 64.2 mg); R_f = 0.5 (EA/ PE = 1/10).^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.42−7.41 (m, 6H), 7.39−7.36 (m, 1H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 1H), 6.19 (d, *J* = 1.8 Hz, 1H), 4.33 (t, *J* = 6.0 Hz, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 1.64−1.59 (m, 2H), 1.18−1.11 (m, 2H), 1.05(t, *J* = 7.2 Hz, 3H), 0.77 (t, *J* = 7.2 Hz, 3H).^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.0, 140.0, 137.0, 133.7, 132.5, 129.6, 129.4, 128.4, 128.0, 127.4, 126.4, 119.1, 111.7, 59.8, 46.0, 33.9, 19.7, 13.7, 13.6.HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{23}H_{26}NO_2$: 348.1958; found 348.1954.

*4.8. Ethyl 5-phenyl-3-(p-tolyl)-1H-pyrrole-2-carboxylate[18] (**3j**)*

White solid (74%, 112.8 mg); m. p. 169−170°C; R_f = 0.5 (EA/ PE = 1/5). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.40 (s, 1H), 7.60 (d, *J* = 7.2 Hz, 2H), 7.50 (d, *J* = 7.8 Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 2H), 6.61 (d, *J* = 3.0 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 2.39 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.2, 136.8, 135.3, 133.5, 132.1, 131.1, 129.4, 129.0, 128.4, 127.9, 124.8, 118.5, 109.9, 60.3, 21.2, 14.3.

*4.9. Ethyl 3-(4-chlorophenyl)-5-phenyl-1H-pyrrole-2-carboxylate[19] (**3k**).*

White solid (76%, 123.8 mg); m. p. 184−185 °C; R_f = 0.4 (EA/ PE = 1/5). ^{1}H NMR (600 MHz, DMSO-d_6) δ = 12.0 (s, 1H), 7.90 (d, *J* = 7.8 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.43−7.40 (m, 4H), 7.30 (t, *J* = 7.2 Hz, 1H), 6.77 (d, *J* = 2.4 Hz, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ = 165.3, 140.8, 139.1, 136.3, 136.0, 135.9, 135.8, 133.6, 132.4, 132.4, 130.4, 123.6, 114.7, 64.6, 19.1.

*4.10. Ethyl 5-phenyl-3-(o-tolyl)-1H-pyrrole-2-carboxylate (**3l**).*

White solid (67%, 102.2 mg); m. p. 157−158 °C; R_f = 0.5 (EA/ PE = 1/5). H NMR (600 MHz, $CDCl_3$) δ = 9.54 (br, 1H), 7.61 (d, *J* = 7.8 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.25−7.23 (m, 3H), 7.20−7.17 (m, 1H), 6.49 (d, *J* = 3.0 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.24 (s, 3H), 1.07 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.3, 136.6, 135.6, 135.3, 132.6, 131.2, 130.1, 129.4, 129.0, 127.8, 127.2, 124.9, 124.7, 120.0, 110.2, 60.1, 20.3, 14.0. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{20}NO_2$: 306.1489; found 306.1486.

*4.11. Ethyl 3-(3-chlorophenyl)-5-phenyl-1H-pyrrole-2-carboxylate (**3m**).*

White solid (73%, 119 mg); m. p. 178−179 °C; R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.71 (s, 1H), 7.62−7.60 (m, 3H), 7.46−7.39 (m, 3H), 7.34−7.29 (m, 3H), 6.60 (d, *J* = 2.4 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.25 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.3, 137.0, 135.7, 133.4, 131.7, 130.9, 129.7, 129.0, 128.8, 128.0, 127.7, 127.0, 124.9, 118.8, 109.7, 60.6, 14.1. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{17}ClNO_2$: 326.0942; found 326.0938.

*4.12. Ethyl 3-(2-chlorophenyl)-5-phenyl-1H-pyrrole-2-carboxylate (**3n**).*

White solid (64%, 104.4 mg); m. p. 184−185 °C; R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.93 (br, 1H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.45−7.38 (m, 4H), 7.31−7.24 (m, 3H), 6.57 (d, *J* = 2.8, 1H), 4.16 (q, *J* = 7.2, 2H), 1.07 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.4, 135.5, 135.0, 133.9, 131.8, 131.1, 129.7, 129.0, 128.9, 128.3, 127.8, 125.9, 124.9, 120.4, 110.2, 60.4, 13.9. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{17}ClNO_2$: 326.0942; found 326.0937.

*4.13. Ethyl 3-(4-methoxyphenyl)-5-phenyl-1H-pyrrole-2-carboxylate[18] (**3o**).*

White solid (72%, 115.6 mg); m.p. 133−134 °C; R_f = 0.5 (EA/ PE = 1/5). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.46 (br, 1H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.54 (d, *J* = 8.8 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 6.93 (t, *J* = 8.8 Hz, 2H), 6.59 (d, *J* =

3.2 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.2, 158.9, 135.4, 133.3, 131.1, 130.6, 129.0, 127.8, 127.5, 124.8, 118.3, 113.1, 109.8, 60.3, 55.3, 14.3.

*4.14. Ethyl 3-(4-fluorophenyl)-5-phenyl-1H-pyrrole-2-carboxylate (**3p**).*

Yellow oil (69%, 106.6 mg); R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.56 (s, 1H), 7.61−7.53 (m, 4H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 8.8 Hz, 2H), 6.58 (d, *J* = 3.2 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.24 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.1 (d, *J* = 247.5 Hz), 161.2, 135.5, 132.4, 131.1, 131.1 (d, *J* = 9.0 Hz), 131.0, 129.0, 128.0, 124.8, 118.6, 114.5 (d, *J* = 21.0 Hz), 109.8, 60.5, 14.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ = −61.25. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{19}H_{17}FNO_2$: 310.1238; found 310.1234.

*4.15. Ethyl 5-phenyl-3-(4-(trifluoromethyl) phenyl)-1H-pyrrole-2-carboxylate (**3q**).*

Yellow oil (75%, 134.6 mg); R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (600 MHz, DMSO-d_6) δ = 12.12 (s, 1H), 7.90 (d, *J* = 7.8 Hz, 2H), 7.75, (d, *J* = 8.4 Hz ,2H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.8 Hz, 1H), 6.82 (d, *J* = 3.0 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 1.17 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ = 160.4, 139.7, 136.1, 131.0, 130.8, 130.1, 128.7, 127.7, 127.2 (q, J_{C-F} = 31.5 Hz), 125.6, 124.6 (q, J_{C-F} = 270.0 Hz), 124.4 (q, J_{C-F} = 4.5 Hz,), 119.1, 109.9, 59.9, 14.1. ^{19}F NMR (376 MHz, DMSO-d_6) δ = −61.25. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{17}F_3NO_2$: 360.1206; found 360.1201.

*4.16. Ethyl 3-(3,5-dichlorophenyl)-5-phenyl-1H-pyrrole-2-carboxylate (**3r**).*

Yellow oil (84%, 151.2 mg); R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.91 (s, 1H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.35 (d, *J* = 1.8 Hz, 2H), 7.28 (t, *J* = 7.8 Hz, 2H), 7.22−7.18 (m, 2H), 6.45 (d, *J* = 3.0 Hz, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 1.14 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.3, 138.1, 136.1, 133.9, 130.7, 130.1, 128.9, 128.0, 128.0, 126.7, 125.0, 119.0, 109.6, 60.8, 14.0. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{16}Cl_2NO_2$: 360.0553; found 360.0549.

*4.17. Ethyl 3-(naphthalen-2-yl)-5-phenyl-1H-pyrrole-2-carboxylate (**3s**).*

White solid (70%, 119.4 mg); m. p. 174−176 °C; R_f = 0.5 (EA/ PE = 1/5). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.65 (s, 1H), 8.05 (s, 1H), 7.86−7.82 (m, 3H), 7.74−7.71 (m, 1H), 7.63 (d, *J* = 7.2 Hz, 2H), 7.48−7.39 (m, 4H), 7.31 (t, *J* = 10.8 Hz, 1H), 6.72 (d, *J* = 3.2 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.20 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.4, 135.6, 133.3, 133.2, 132.7, 132.6, 131.1, 129.0, 128.2, 128.1, 128.0, 127.9, 127.6, 126.9, 125.9, 125.7, 124.8, 118.9, 110.2, 60.5, 14.2. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{23}H_{20}NO_2$: 342.1489; found 342.1482.

*4.18. Ethyl 3-(naphthalen-1-yl)-5-phenyl-1H-pyrrole-2-carboxylate (**3t**).*

White solid (65%, 110.8 mg); m. p. 178−179 °C; R_f = 0.5 (EA/ PE = 1/5). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.69 (br, 1H), 7.91−7.83 (m, 3H), 7.65 (d, *J* = 7.2 Hz, 2H), 7.50 (d, *J* = 4.8 Hz, 2H), 7.47−7.38 (m, 4H), 7.32 (t, *J* = 7.2 Hz, 1H), 6.67 (d, *J* = 3.0 Hz, 1H), 3.97 (q, *J* = 7.2 Hz, 2H), 0.70 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.5, 135.5, 133.8, 133.4, 132.6, 131.2, 130.9, 129.0, 128.0, 127.9, 127.5, 127.4, 126.4, 125.6, 125.4, 124.9, 124.8, 120.8, 111.2, 60.1, 13.5. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{23}H_{20}NO_2$: 342.1489; found 342.1485.

*4.19. Ethyl 3,5-di-p-tolyl-1H-pyrrole-2-carboxylate (**3u**).*

White solid (67%, 106.8 mg); m. p. 173−175 °C; R_f = 0.6 (EA/ PE = 1/5). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.46(br, 1H), 7.40 (d, *J* = 7.2 Hz, 4H), 7.10 (d, *J* = 8.4 Hz, 4H), 6.45 (d, *J* = 3.6 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 2.28 (s, 3H), 2.26 (s, 3H), 1.15 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.3, 137.7, 136.6, 135.6, 133.5, 132.2, 129.6, 129.4, 128.3, 124.7, 124.6, 118.1, 109.5, 60.3, 21.2, 21.1, 14.2. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{22}NO_2$: 320.1645; found 320.1648.

*4.20. Ethyl 5-(4-chlorophenyl)-3-(p-tolyl)-1H-pyrrole-2-carboxylate (**3v**).*

White solid (49%, 83.2 mg); m. p. 176−177 °C; R_f = 0.4 (EA/ PE = 1/5). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.44 (s, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 6.49 (d, *J* = 3.0 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.31 (s, 3H), 1.17 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.3, 136.9, 134.2, 133.6, 133.5, 131.9, 129.7, 129.3, 129.2, 128.4, 126.0, 118.8, 110.2, 60.5, 21.2, 14.2. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{19}ClNO_2$: 340.1099; found 340.1096.

*4.21. Ethyl 3-(3,5-dichlorophenyl)-5-(p-tolyl)-1H-pyrrole-2-carboxylate (**3w**).*

White solid (78%, 158.4 mg); m. p. 182−183 °C; R_f = 0.4 (EA/ PE = 1/5). ^{1}H NMR (600 MHz, DMSO-d_6) δ = 12.04 (s, 1H), 7.79 (d, *J* = 6.0 Hz, 2H), 7.58 (s, 2H), 7.48 (s, 1H), 7.21 (d, *J* = 6.0 Hz, 2H), 6.81 (s, 1H), 4.21 (q, *J* = 6.0 Hz, 2H), 2.31 (s, 3H), 1.21 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ = 160.7, 139.3, 137.4, 136.7, 133.6, 129.6, 129.5, 128.5, 128.4, 126.4, 125.9, 119.1, 109.9, 60.2, 21.2, 14.4. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{18}Cl_2NO_2$: 374.0709; found 374.0711.

*4.22. Ethyl 3-benzyl-5-phenyl-1H-pyrrole-2-carboxylate (**3x**).*

White solid (64%, 97.6 mg); m. p. 165−166 °C; R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.15 (s, 1H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.29−7.25 (m, 5H), 7.21−7.18 (m, 1H), 6.31 (d, *J* = 3.0 Hz, 1H), 4.35 (q, *J* = 6.6 Hz, 2H), 4.19 (s, 2H), 1.35 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.6, 141.2, 135.3, 131.2, 129.5, 128.9, 128.8, 128.7, 128.3, 127.7, 125.9, 124.6, 109.7, 60.2, 33.2, 14.5. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{20}NO_2$: 306.1489; found 306.1485.

*4.23. Ethyl 3-methyl-5-phenyl-1H-pyrrole-2-carboxylate (**3y**).*

Yellow oil (38%, 43.5 mg); R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.41 (s, 1H), 7.55 (d, *J* = 7.8 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 1H), 6.37 (d, *J* = 3.0 Hz, 1H), 4.32 (q, *J* = 7.2 Hz, 2H), 2.38 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.0, 135.3, 131.4, 129.3, 128.8, 127.5, 124.7, 119.9, 110.2, 60.1, 14.5, 13.0.HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{14}H_{15}NO_2Na$: 252.0995; found 252.1000.

*4.24. Ethyl 3-isopropyl-5-phenyl-1H-pyrrole-2-carboxylate (**3z**).*

Pale yellow oil (38%, 48.8 mg); R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.56 (s, 1H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 7.2 Hz, 1H), 6.48 (d, *J* = 3.2 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 3.59−3.52 (m, 1H), 1.35 (t, *J* = 6.8 Hz, 3H), 1.27 (d, *J* = 7.2 Hz, 6H). ^{13}C NMR (150

MHz, $CDCl_3$) δ = 161.8, 141.3, 135.5, 131.5, 128.8, 127.4, 124.7, 118.5, 105.9, 60.0, 25.7, 23.7, 14.4. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{16}H_{19}NO_2Na$: 280.1308; found 280.1310.

*4.25. Ethyl 3-cyclohexyl-5-phenyl-1H-pyrrole-2-carboxylate (**3ab**).*

Pale yellow oil (13%, 19.3 mg); R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.30 (s, 1H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 8.4 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 1H), 6.46 (d, *J* = 3.0 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 3.20−3.15 (m, 1H), 1.95 (d, *J* = 9.6 Hz, 2H), 1.83 (d, *J* = 12.0 Hz, 2H), 1.75 (d, *J* = 14.4 Hz, 1H), 1.43−1.40 (m, 4H), 1.37 (t, *J* = 6.6 Hz, 3H), 1.29−1.25 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.7, 140.6, 135.3, 131.5, 128.8, 127.4, 124.7, 118.5, 106.4, 60.0, 35.9, 34.2, 26.9, 26.3, 14.4. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{19}H_{23}NO_2Na$: 320.1621; found 320.1624.

*4.26. Ethyl 5-phenyl-3-styryl-1H-pyrrole-2-carboxylate (**3ac**).*

Yellow oil (58%, 91.9 mg); R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (600 MHz, DMSO-d_6) δ = 11.85 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 2H), 7.79 (d, *J* = 16.2 Hz, 1H), 7.52 (d, *J* = 7.2 Hz, 2H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.2 Hz, 1H) ,7.25 (d, *J* = 7.8 Hz, 1H), 7.15 (d, *J* = 16.2 Hz, 1H), 7.12 (d, *J* = 1.8 Hz, 1H), 4.36 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ = 160.8, 137.6, 136.6, 131.1, 129.3, 128.8, 128.6, 128.6, 127.5, 127.3, 126.0, 125.5, 121.3, 120.1, 104.9, 59.8, 14.5. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{20}NO_2$: 318.1489; found 318.1485.

*4.27. Ethyl 5-cyclopropyl-3-(p-tolyl)-1H-pyrrole-2-carboxylate (**3ad**).*

Yellow oil (45%, 60.5 mg); R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.89 (s, 1H), 7.43 (d, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 5.95 (d, *J* = 3.0 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 2.36 (s, 3H), 1.87−1.82 (m, 1H), 1.25 (t, *J* = 7.2 Hz, 3H), 0.96−0.93 (m, 2H), 0.74−0.72 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 160.9, 139.0, 136.5, 132.8, 132.3, 129.3, 128.3, 116.1, 108.2, 60.0, 21.2, 14.3, 8.4, 7.4. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{17}H_{20}NO_2$: 270.1489; found 270.1487.

*4.28. Ethyl 5-cyclopropyl-3-(3,5-dichlorophenyl)-1H-pyrrole-2 carboxy-late (**3ae**).*

Yellow oil (60%, 96.9 mg); R_f = 0.5 (EA/ PE = 1/4). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.20 (br, 1H), 7.34 (d, *J* = 2.4 Hz, 2H), 7.19 (t, *J* = 1.8 Hz, 1H), 5.86 (d, *J* = 3.0 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 1.80−1.76 (m, 1H), 1.20 (t, *J* = 6.6 Hz, 3H), 0.90−0.87 (m, 2H), 0.66 (q, *J* = 6.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 160.9, 139.6, 138.4, 133.9, 129.4, 128.0, 126.6, 116.7, 108.8, 60.4, 14.1, 8.4, 7.6. HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{16}H_{16}Cl_2NO_2$: 324.0553; found 324.0555.

*4.29. Ethyl 5-(tert-butyl)-3-phenyl-1H-pyrrole-2-carboxylate (**3af**).*

Pale yellow oil (10%, 13.6 mg); R_f = 0.4 (EA/ PE = 1/4). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.86 (br, 1H), 7.55 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.27 (t, *J* = 10.2 Hz, 1H), 6.10 (d, *J* = 3.0 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 1.35 (s, 9H), 1.23 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.4, 146.1, 135.5, 132.3, 129.5, 127.5, 126.8, 116.2, 108.0, 60.1, 31.6, 30.2, 14.3. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{17}H_{21}NO_2Na$: 294.1465; found 294.1462.

*4.30. Ethyl 5-cyclohexyl-3-phenyl-1H-pyrrole-2-carboxylate (**3ag**).*

Pale yellow oil (15%, 11.1 mg); R_f = 0.4 (EA/ PE = 1/5). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.29 (br, 1H), 7.55 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.26 (t, *J* =7.8 Hz, 1H), 6.07 (d, *J* = 3.0 Hz, 1H), 4.23 (q, *J* = 6.6 Hz, 2H), 2.63−2.59 (m, 1H), 2.02 (d, *J* = 15.0 Hz, 2H), 1.82 (d, *J* = 13.2 Hz, 2H), 1.73−1.70 (m, 1H), 1.45−1.32 (m, 4H), 1.28−1.24 (m, 1H) 1.22 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.5, 142.7, 135.7, 132.4, 129.5, 127.4, 126.7, 116.1, 108.3, 60.0, 36.8, 32.7, 26.1, 26.0, 14.2. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{19}H_{23}NO_2Na$: 320.1621; found 320.1630.

*4.31. Ethyl 3-methyl-1H-pyrrole-2-carboxylate (**3ah**).*

Pale yellow oil (19%, 14.5 mg); R_f = 0.3 (EA/ PE = 1/3). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.47 (br, 1H), 6.82 (t, *J* = 4.2 Hz, 1H), 5.94(t, *J* = 4.2 Hz, 1H), 4.31 (q, *J* = 10.2 Hz, 2H), 2.31 (s, 3H), 1.35 (t, *J* = 10.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.4, 133.9, 121.3, 116.0, 108.8, 60.0, 14.5, 13.1. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_8H_{11}NO_2Na$: 176.0682; found 176.0686.

*4.32. Ethyl (3-oxo-1,3-diphenylprop-1-en-1-yl) carbamate[20] (**4a**)*

Yellow solid (92%, 142 mg); R_f = 0.3 (EA/ PE = 1/5); m. p. 79−80 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.43 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 2H), 7.43−7.37 (m, 8H), 5.87 (s, 1H), 4.17 (q, *J* = 6.0 Hz, 2H), 3.95 (d, *J* = 6.6 Hz, 2H), 1.23 (t, *J* = 8.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 190.0, 169.2, 165.7, 139.8, 135.0, 130.7, 129.5, 128.5, 128.0, 127.5, 127.0, 94.5, 61.3, 46.2, 13.9.

*4.33. Ethyl 4,4,4-trifluoro-3-oxo-1-phenylbut-1-en-1-yl glycinate (**4ai**).*

Pale yellow oil (92%, 138.4 mg); R_f = 0.3 (EA/ PE = 1/3). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 11.10 (s, 1H), 7.43−7.37 (m, 3H), 7.28 (d, *J* = 6.6 Hz, 2H), 5.41 (s, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 3.95 (d, *J* = 6.0 Hz, 2H), 1.16 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 177.0 (q, $J_{C\text{-}F}$ = 33.0 Hz), 170.2, 168.3, 133.4,130.6, 129.0, 127.2, 117.3 (q, $J_{C\text{-}F}$ = 288.0 Hz), 91.0, 61.8, 46.6, 14.0.^{19}F NMR (376 MHz, $CDCl_3$) δ = −77.11. HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{14}H_{14}F_3NO_3Na$: 324.0818; found 324.0817.

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