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MICROWAVE-ASSISTED ONE POT SYNTHESIS OF *N*-SUBSTITUED 2-METHYL-1*H*-PYRROLE-3-CARBOXYLATE DERIVATIVES WITHOUT CATALYST AND SOLVENT

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Abstract – An efficient one-pot synthetic method for the *N*-substituted 2-methyl-1*H*-pyrrole-3-carboxylate derivatives has been accomplished via a microwave irradiation MCRs of various α-bromoacetophenone, amines, and ethyl acetoacetate without any solvent and catalyst. This approach provides a convenient one pot method for the synthesis of *N*-substituted 2-methyl-1*H*-pyrrole-3-carboxylate derivatives.

Green chemistry has come to the forefront of current chemical research to exploit efficient, sustainable, and environmentally benign synthetic methodologies and inexpensive and environmentally friendly reagents.[1,2] Growing environmental concern in green chemistry has turned the great interest into multicomponent reactions (MCRs) as the new direction in organic chemistry,[3] multicomponent reactions have been widely utilized in medicinal synthesis and combinatorial chemistry because of their simplicity, advanced selectivity, high efficiency and good yield over conventional chemical reactions.[4] Beside these, microwave assisted organic synthesis (MAOS)[5] is particularly welcome in the chemical and organic synthesis by reducing reaction times, heightening product yields and increasing product purities.

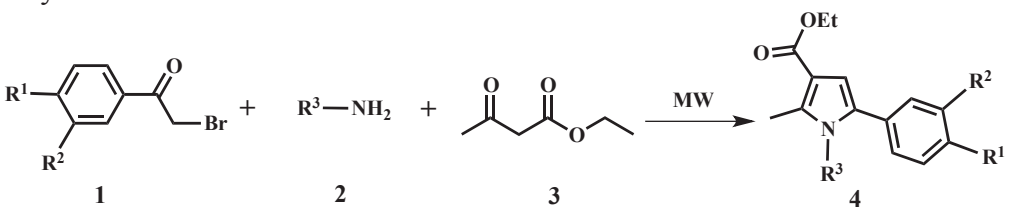
The last decade has witnessed the synthesis of heterocycles continuing to attract the attentions in medicinal chemistry and in organic synthesis, considerable efforts have been devoted to the synthesis of this type of compounds.[6] With a privileged heterocyclic entity, pyrrole derivatives have displayed an important role in composition of biologically active compounds,[7] functional materials,[8] and medicinal chemistry.[9] Also, there are varieties of approaches to the substituted pyrrole derivatives, including the classical Knorr, Paal–Knorr and Hantzsch reactions. Accordingly, many of diversities of pyrroles have been reported. For example, 1,2-diaryl(heteroaryl)pyrroles and -3-methylpyrroles derivatives were prepared in a two-step procedure from *N*-allylbenzotriazoles via intramolecular oxidative cyclization in

the presence of Pd(II) catalyst;[10] Simple synthesis of substituted pyrroles using iodine-catalyst had been accomplished with excellent yields by Banik.[11] Recently, Nikhil developed a three-component system to synthesize pyrrole derivatives from corresponding amines and nitrostyrenes using (diacetoxyiodo)benzene in ethanol.[12]

However, there are some flaws in the existing synthetic methodologies for the substituted pyrrole derivatives. Traditional multistep synthesis is not straightforward and the overall yields remained lower; although few MCRs strategies had been applied in the synthesis of pyrrole derivatives recently,[13] complicated and metal catalysts were over-used in most of these methods which could lead to the environment problems to some extent; the preparation of *N*-substituted pyrroles still suffered from limitations.

In the context of our current research into MCRs based on the use of β-dicarbonyl building blocks for the synthesis of heterocycles, a new multicomponent strategy by Hantzsch synthesis of pyrroles were considered, which could overcome some shortcomings as a general synthetic method. We also wished to describe a new more simple protocol for an environment-friendly, rapid, and convenient synthesis. Therefore, the way of microwave irradiation was introduced in order to improve efficiency.

Table 1. Optimization of reaction condition for the synthesis of ethyl 2-methyl-1,5-diphenyl-1*H*-pyrrole-3-carboxylate **4a**



1 2 3 4

Entry	Molar Ratio (α-bromoacetophenone /aniline/ ethyl acetoacetate)	Solvent	Time	Power (W)	Yield[a] (%)
1	1.0 : 1.0 : 1.0	acetic acid	48 h	— [b]	20
2	1.0 : 1.0 : 1.0	acetic acid	45 min	150	62
3	1.0 : 1.0 : 1.0	acetic acid	30 min	300	65
4	1.0 : 1.0 : 1.0	acetic acid	15 min	500	76
5	1.0 : 1.0 : 2.0	acetic acid	15 min	500	81
6	1.0 : 1.0 : 2.5	acetic acid	15 min	500	85
7	1.0 : 1.0 : 2.5	acetic acid	15 min	600	77
8	1.0 : 1.0 : 2.5	— [c]	15 min	500	87

[a] Isolated yield.
[b] Refluxing reaction
[c] Without solvent

With this goal in mind, the studies were initiated by the reaction of a one-pot three component condensation reaction of α-bromoacetophenone, aniline, and ethyl acetoacetate with conventional way in refluxing acetic acid. After 48 hours of operation at refluxing, a new spot was observed by TLC though both aniline and α-bromoacetophenone were not completely consumed. We managed to separate and

obtain the ethyl 2-methyl-1,5-diphenyl-1*H*-pyrrole-3-carboxylate by the flash column chromatography with the yield of 20% (Table 1, entry 1). Although the reaction yield was quite lower, we were so glad to see that multi-substituted pyrrole, namely ethyl 2-methyl-1,5-diphenyl-1*H*-pyrrole-3-carboxylate, was also accessible by employing commercially available 2-α-bromoacetophenone, aniline, and ethyl acetoacetate as starting materials without any catalyst. This exciting result encouraged us to carry out more efficient pattern into this reaction. Then the microwave irradiation was applied. Only after 15 min of operation at frequency of 300 W, the 2-bromo-1-phenylethanone was completely consumed and the yield was raised to 65% (Table 1, entry 3).

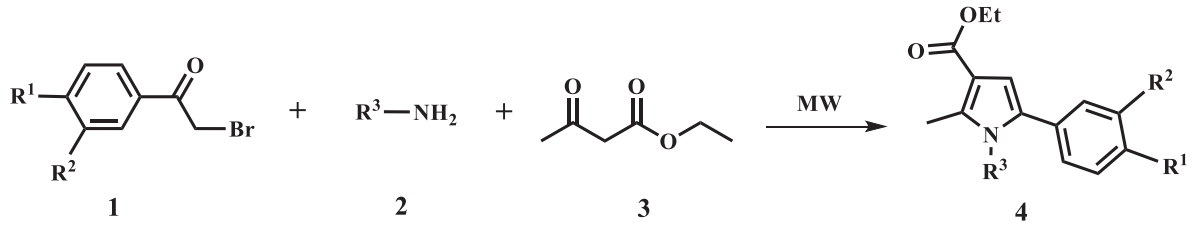
In search for an optimization of reaction conditions, the one-pot reaction for the three components of α-bromoacetophenone, aniline, and ethyl acetoacetate as model reaction were studied and the results are summarized in Table 1. According to our experience in using the ethyl acetoacetate,[14] the amount of ethyl acetoacetate should be slightly excessive in microwave reaction, which was verified by controlling the amounts (Table 1, entries 4–6) to set the molar ratio for completion of the reaction. It was found that 2.5 equivalents of ethyl acetoacetate in presence of one equivalent of α-bromoacetophenone and one equivalent of aniline offered short reaction time (15 min) and the better yields (76%, Table 1, entry 6).

Besides, the effect of different microwave power was evaluated by settings such as 150, 300, 500, and 600 W. It was observed that the lower the power, the longer the reaction time. If the microwave power ran up to 600 W, the reaction mixture quickly became black hard lump which could prevent the reaction further development and led to the lower yield. The result showed that the irradiation at 500 W gives better result. Subsequently, we attempted to complete this reaction with the condition of free solvent. Under the same reaction time, the yields of the products were found to be constant. Through these experiments, a power at 500 W and a time of 15 min without solvent were the optimal conditions to complete the reaction (Table 1, entry 8). Under these conditions, ethyl 2-methyl-1,5-diphenyl-1*H*-pyrrole-3-carboxylate was obtained with good yields.

After optimizing the conditions, the scope and generality of this method were investigated by the reaction of substituted α-bromoacetophenone, various types of amines and ethyl acetoacetate under microwave-irradiation with free solvent. As shown in Table 2, our method could be adapted to the preparation of pyrroles bearing the following types of substituents at nitrogen: aryl (compounds **4a**–**4l**), alkyl (compounds **4m**–**4o**) and heterocyclic methyl (compounds **4p**–**4r**). Especially, the compounds **4p**–**4r** modified by furan moiety did not affect the stability of this type of pyrrole derivatives and we got the clear spectrum for their characterizations. Furthermore, the scope of α-bromoacetophenone in this Hantzsch reaction was much broader than the one described in the previous literature. According to the literature,[15] we prepared two substituted α-bromoacetophenone, namely 4-methyl-α-bromoacetophenone and 3-bromo-4-methoxy-α-bromoacetophenone, respectively. We carried out similar reaction with

various α-bromoacetophenone containing electron-withdrawing (Br) and electron-donating (Me) functional groups but it did not show any remarkable differences in the yields of products and reaction times. These successful results clearly indicate that the present protocol is also extendable to a wide variety of substrates for both α-bromoacetophenones and amines. All structures of the products were characterized and determined by the IR, ^{1}H NMR, ^{13}C NMR and elementary analysis. We could not get the single-crystal for these *N*-substituted 2-methyl-1*H*-pyrrole-3-carboxylate derivatives because of their lower melting points.

Table 2. Synthesized *N*-substituted 2-methyl-1*H*-pyrrole-3-carboxylate derivatives by a one-pot three component condensation reaction [a]



1 **2** **3** **4**

Entry	R^1	R^2	R^3	Product	Yield [b] (%)
1	H	H	C_6H_5	**4a**	87
2	H	H	4-ClC_6H_4	**4b**	80
3	H	H	4-MeC_6H_4	**4c**	85
4	H	H	4-$MeOC_6H_4$	**4d**	85
5	Me	H	C_6H_5	**4e**	82
6	Me	H	4-ClC_6H_4	**4f**	81
7	Me	H	4-MeC_6H_4	**4g**	81
8	Me	H	4-$MeOC_6H_4$	**4h**	82
9	MeO	Br	C_6H_5	**4i**	83
10	MeO	Br	4-ClC_6H_4	**4j**	76
11	MeO	Br	4-MeC_6H_4	**4k**	88
12	MeO	Br	4-$MeOC_6H_4$	**4l**	79
13	H	H	n-Bu	**4m**	84
14	Me	H	n-Bu	**4n**	82
15	MeO	Br	n-Bu	**4o**	80
16	H	H	C_4H_3O-2-CH_2	**4p**	79
17	Me	H	C_4H_3O-2-CH_2	**4q**	81
18	MeO	Br	C_4H_3O-2-CH_2	**4r**	83

[a] All reactions were carried out using α-bromoacetophenone (1.0 mmol), amine (1.0 mmol) and ethyl acetoacetate (2.5 mmol) at 450 W under microwave irradiation without solvent.
[b] Isolated yield based on α-bromoacetophenone

EXPERIMENTAL

All melting points were estimated using a X4 melting apparatus in open capillaries. and are uncorrected. IR spectra were determined as KBr disks with a Perkin-Elmer Spectrum one FT-IR. The ^{1}H NMR spectra were recorded using a Bruker AV400MHz spectrometer using $CDCl_3$ as solvent and TMS as an internal standard. The ^{13}C NMR spectra were determined using TMS as an internal reference with a Bruker

AV400MHz spectrometer operating at 100 MHz. Elemental analyses were performed on a Perkin-Elmer 240 microanalyser. TLC was carried out on a Merck Kieselgel GF254. Column chromatography was performed using Merck Kieselgel 60 (0.075-0.15 mm). All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

Starting Materials. 4-Methyl-α-bromoacetophenone and 3-bromo-4-methoxy-α-bromoacetophenone were prepared according to the literature.[15] All other chemicals used in this study were commercially available.

Typical Procedure for the Preparation of Products 4a-4r. A mixture of various α-bromoacetophenones **1** (1 mmol), amines **2** (1 mmol), and ethyl acetoacetate **3** (2.5 mmol) was placed in a pressurized microwave vial with snap on cap. The reaction mixture was subjected to microwave irradiation for appropriate time at 500 W. After the completion of the reaction (as indicated by TLC) and cooling to room temperature, the oil crude products were obtained and then purified by column chromatography on silica gel using EtOAc/*n*-hexane to afford the pure compounds **4a-4r** for analysis.

Ethyl 2-methyl-1,5-diphenyl-1*H*-pyrrole-3-carboxylate (4a): Yellow solid, 87% yield. IR (KBr) *υ*: 3092, 2980, 2927, 1685, 1380, 1281, 1202 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ*: 7.40–7.37 (m, 3H, ArH), 7.14–7.11 (m, 5H, ArH), 7.04–6.99 (m, 2H, ArH), 6.80 (s, 1H, ArH), 4.33 (q, *J* = 5.2 Hz, 2H, CH_2), 2.41 (s, 3H, CH_3), 1.38 (t, 3H, *J* = 5.0 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 165.6, 138.1, 138.1, 133.9, 132.4, 129.2, 128.5, 128.2, 128.1, 128.0, 126.5, 112.8, 110.0, 59.5, 14.6, 12.5; Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59%. Found: C, 78.50; H, 6.41; N, 4.68%.

Ethyl 1-(4-chlorophenyl)-2-methyl-5-phenyl-1*H*-pyrrole-3-carboxylate (4b): 80% yield. IR (KBr) *υ*: 3370, 2920, 1682, 1587, 1445, 1252, 1170, 1029 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ*: 7.35–7.31 (m, 2H, ArH), 7.06–7.04 (m, 3H, ArH), 7.04 (d, *J* = 7.5 Hz, 2H, ArH), 7.02 (d, *J* = 7.5 Hz, 2H, ArH), 6.78 (s, 1H, ArH), 4.32 (q, *J* = 5.0 Hz, 2H, CH_2), 2.39 (s, 3H, CH_3), 1.37 (t, *J* = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 165.4, 137.8, 136.6, 134.1, 133.8, 132.0, 129.7, 129.4, 128.2, 128.1, 126.7, 113.2, 110.2, 59.5, 14.5, 12.4; Anal. Calcd for $C_{20}H_{18}ClNO_2$: C, 70.69; H, 5.34; N, 4.12%. Found: C, 70.52; H, 5.23; N, 4.19%.

Ethyl 2-methyl-5-phenyl-1-*p*-tolyl-1*H*-pyrrole-3-carboxylate (4c): 85% yield. IR (KBr) *υ*: 3372, 2923, 1682, 1589, 1441, 1320, 1249, 1170, 1019 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ*: 7.18 (m, 2H, ArH), 7.16 (m, 3H, ArH), 7.06 (d, 2H, *J* = 7.5 Hz, ArH), 7.02 (d, 2H, *J* = 7.5 Hz, ArH), 6.79 (s, 1H, ArH), 4.32 (q, *J* = 5.0 Hz, 2H, CH_2), 2.42 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 1.37 (t, 3 H, *J* = 5.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 165.6, 138.2, 138.1, 135.5, 133.9, 132.5, 130.1, 129.9, 129.8, 129.3, 128.2, 128.1, 127.9, 127.5,

126.3, 126.2, 126.1, 120.9, 112.7, 109.9, 59.5, 21.1, 14.05, 12.60; Anal. Calcd for $C_{21}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39%. Found: C, 79.10; H, 6.53; N, 4.56%.

Ethyl 1-(4-methoxyphenyl)-2-methyl-5-phenyl-1*H*-pyrrole-3-carboxylate (4d): 85% yield. IR (KBr) υ: 3375, 2925, 1680, 1600, 1443, 1325, 1250, 1170, 1024 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.16–7.12 (m, 3H, ArH), 7.06–7.04 (m, 4H, ArH), 6.93 (d, J = 7.5 Hz, 2H, ArH), 6.78 (s, 1H, ArH), 4.31 (q, J = 5.0 Hz, 2H, CH_2), 3.83 (s, 3H, OCH_3), 2.39 (s, 3H, CH_3), 1.38 (t, J = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.6, 159.2, 138.3, 136.9, 135.6, 134.0, 132.5, 131.9, 130.8, 129.4, 129.2, 128.1, 128.0, 127.5, 126.4, 126.3, 126.2, 121.10, 112.6, 109.7, 59.4, 55.4, 14.6, 12.5; Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18%. Found: C, 75.36; H, 6.18; N, 4.34%.

Ethyl 2-methyl-1-phenyl-5-*p*-tolyl-1*H*-pyrrole-3-carboxylate (4e): 82% yield. IR (KBr) υ: 3075, 2925, 1691, 1488, 1310, 1194, 848, 791 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.39–7.36 (m, 3H, ArH), 7.14–7.11 (m, 2H, ArH), 6.88 (d, J = 7.5 Hz, 4H, ArH), 6.73 (s, 1H, ArH), 4.33 (q, 2H, J = 5.0 Hz, CH_2), 3.83 (s, 3H, OCH_3), 2.39 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 1.37 (t, J = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.6, 138.2, 138.1, 135.4, 133.8, 132.4, 130.1, 129.8, 129.7, 129.2, 128.1, 128.0, 127.9, 127.5, 126.3, 126.1, 126.1, 120.8, 112.6, 109.8, 59.4, 22.6, 14.5, 12.6; Anal. Calcd for $C_{21}H_{21}NO_2$: C, 78.97; H, 6.63; N, 4.39%. Found: C, 78.92; H, 6.57; N, 4.50%.

Ethyl 1-(4-chlorophenyl)-2-methyl-5-*p*-tolyl-1*H*-pyrrole-3-carboxylate (4f): 81% yield. IR (KBr) υ: 3377, 2927, 1682, 1600, 1449, 1327, 1252, 1175, 1029 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.37 (d, J = 7.2 Hz, 2H, ArH), 7.08 (d, J = 7.2 Hz, 2H, ArH), 6.98 (d, J = 7.2 Hz, 2H, ArH), 6.93 (d, J = 7.2 Hz, 2H, ArH), 6.78 (s, 1H, ArH), 4.31 (q, J = 5.0 Hz, 2H, CH_2), 2.39 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 1.37 (t, J = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.5, 136.3, 133.4, 133.1, 129.3, 128.8, 128.3, 127.40, 111.8, 109.7, 59.2, 29.6, 14.5, 12.5; Anal. Calcd for $C_{21}H_{20}ClNO_2$: C, 71.28; H, 5.70; N, 3.96%. Found: C, 71.45; H, 5.65; N, 4.04%.

Ethyl 2-methyl-1,5-di-*p*-tolyl-1*H*-pyrrole-3-carboxylate (4g): 81% yield. IR (KBr) υ: 3371, 2922, 1680, 1600, 1447, 1325, 1250, 1173, 1027cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.17 (d, J = 7.2 Hz, 2H, ArH), 7.01 (d, J = 7.2 Hz, 2H, ArH), 6.94 (d, J = 7.2 Hz, 4H, ArH), 6.74 (s, 1H, ArH), 4.32 (q, J = 5.0 Hz, 2H, CH_2), 2.42 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 1.37 (t, 3 H, J = 5.0 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.6, 138.0, 137.9, 136.0, 135.5, 133.9, 129.8, 129.7, 129.6, 129.0, 128.7, 128.2, 128.1, 127.9, 126.1, 112.5, 109.3, 59.4, 21.1, 21.0, 14.5, 12.4; Anal. Calcd for $C_{22}H_{23}NO_2$: C, 79.25; H, 6.95; N, 4.20%. Found: C, 79.41; H, 6.79; N, 4.34%.

Ethyl 1-(4-methoxyphenyl)-2-methyl-5-*p*-tolyl-1*H*-pyrrole-3-carboxylate (4h): 82% yield. IR (KBr) υ: 3377, 2927, 1682, 1600, 1449, 1327, 1252, 1175, 1029 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.04 (d, J = 7.2 Hz, 2H, ArH), 6.94 (d, J = 7.2 Hz, 4H, ArH), 6.88 (d, J = 7.2 Hz, 2H, ArH), 6.72 (s, 1H, ArH), 4.31

(q, J = 5.0 Hz, 2H, CH_2), 3.81 (s, 3H, OCH_3), 2.36 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 1.36 (t, J = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.6, 138.2, 137.8, 136.2, 134.0, 126.5, 129.4, 129.32, 129.1, 129.1, 128.7, 128.5, 128.3, 128.2, 128.0, 127.9, 126.3, 112.7, 109.5, 59.5, 21.1, 14.6, 12.5; Anal. Calcd for $C_{22}H_{23}NO_3$: C, 75.62; H, 6.63; N, 4.01%. Found: C, 75.77; H, 6.49; N, 4.12%.

Ethyl 5-(3-bromo-4-methoxyphenyl)-2-methyl-1-phenyl-1*H*-pyrrole-3-carboxylate (4i): 83% yield. IR (KBr) υ: 2918, 1680, 1601, 1445, 1325, 1249, 1175, 1021 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41–7.39 (m, 3H, ArH), 7.28 (s, 1H, ArH), 7.12 (d, J = 7.2 Hz, 2H, ArH), 6.85 (d, J = 7.2 Hz, 1H, ArH), 6.72 (s, 1H, ArH), 6.63 (d, J = 7.2 Hz, 1H, ArH), 4.31 (q, J = 5.0 Hz, 2H, CH_2), 3.81 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3), 1.36 (t, J = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.5, 154.5, 138.0, 137.8, 133.0, 132.1, 129.3, 129.3, 128.5, 128.4, 128.1, 126.4, 126.3, 112.8, 111.3, 111.1, 109.7, 59.5, 56.1, 14.2, 12.5; Anal. Calcd for $C_{21}H_{20}BrNO_3$: C, 60.88; H, 4.87; N, 3.38%. Found: C, 60.76; H, 5.01; N, 3.29%.

Ethyl 5-(3-bromo-4-methoxyphenyl)-1-(4-chlorophenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (4j): 76% yield. IR (KBr) υ: 3367, 2926, 1680, 1598, 1324, 1250, 1172, 1027 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37 (d, J = 7.2 Hz, 2H, ArH), 7.32 (s, 1H, ArH), 7.05 (d, J = 7.2 Hz, 2H, ArH), 6.79 (d, J = 7.2 Hz, 1H, ArH), 6.71 (s, 1H, ArH), 6.65 (d, J = 7.2 Hz, 1H, ArH), 4.30 (q, J = 5.0 Hz, 2H, CH_2), 3.82 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3), 1.36 (t, J = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.9 ,149.1, 134.9, 133.4, 131.1, 129.6, 129.4, 127.8, 127.5, 120.8, 120.7, 112.7, 106.8, 110.3, 60.9, 55.1, 14.1, 12.5; Anal. Calcd for $C_{21}H_{19}BrClNO_3S$: C, 56.21; H, 4.27; N, 3.12%. Found: C, 56.39; H, 4.20; N, 3.21%.

Ethyl 5-(3-bromo-4-methoxyphenyl)-2-methyl-1-*p*-tolyl-1*H*-pyrrole-3-carboxylate (4k): 85% yield. IR (KBr) υ: 3370, 2925, 1680, 1600, 1447, 1325, 1250, 1173, 1027 cm^{-1}. ^{1}H NMR (400 MHz, CDCl,) δ: 7.43 (d, J = 7.2 Hz, 2H, ArH), 7.34 (s, 1H, ArH), 7.01 (d, J = 7.2 Hz, 2H, ArH), 6.86 (d, J = 7.2 Hz, 1H, ArH), 6.71 (s, 1H, ArH), 6.65 (d, J = 7.2 Hz, 1H, ArH), 4.31 (q, J = 5.0 Hz, 2H, CH_2), 3.82 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 1.36 (t, J = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.5, 138.1, 138.0, 136.2, 135.1, 133.0, 129.2, 128.0, 124.6, 120.8, 112.6, 111.0, 110.5, 109.5, 59.4, 56.1, 21.0, 14.2, 12.4; Anal. Calcd for $C_{22}H_{22}BrNO_3$: C, 61.69; H, 5.18; N, 3.27%. Found: C, 61.80; H, 5.11; N, 3.15%.

Ethyl 5-(3-bromo-4-methoxyphenyl)-1-(4-methoxyphenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (4l): 79% yield. IR (KBr) υ: 3370, 2920, 1675, 1593, 1442, 1320, 1247, 1168, 1022 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41 (d, J = 7.2 Hz, 2H, ArH), 7.30 (s, 1H, ArH), 7.10 (d, J = 7.2 Hz, 2H, ArH), 6.93 (d, J = 7.2 Hz, 1H, ArH), 6.73 (s, 1H, ArH), 6.69 (d, J = 7.2 Hz, 1H, ArH), 4.31 (q, J = 5.0 Hz, 2H, CH_2), 3.84 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.37 (s, 3H, CH_3), 1.36 (t, J = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz,

$CDCl_3$) δ: 165.6, 138.2, 137.2, 134.1, 132.2, 130.5, 129.2, 128.0, 127.5, 126.5, 124.5, 121.0, 114.7, 114.4, 112.5, 110.5, 109.4, 59.4, 56.1, 55.4, 14.2, 12.4; Anal. Calcd for $C_{22}H_{22}NO_4$: C, 59.47; H, 4.99; N, 3.15%. Found: C, 59.60; H, 5.09; N, 3.11%.

Ethyl 1-butyl-2-methyl-5-phenyl-1*H*-pyrrole-3-carboxylate (4m): 84% yield. IR (KBr) υ: 2980, 2927, 1685, 1380, 1281, 1202, 757cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39 (d, J = 7.2 Hz, 2H, ArH), 7.28 (t, J = 7.2 Hz, 3H, ArH), 6.53 (s, 1H, ArH), 4.26 (q, J = 5.0 Hz, 2H, CH_2), 3.86–3.83 (m, 2H, CH_2), 2.59 (s, 3H, CH_3), 1.51–1.46 (m, 2H, CH_2), 1.33 (t, J = 5.0 Hz, 3H, CH_3), 1.17–1.11(m, 2H, CH_2), 0.77 (t, J = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.5, 136.3, 133.4, 133.1, 129.3, 128.8, 128.3, 127.4, 111.8, 109.7, 59.2, 43.8, 32.7, 19.6, 14.5, 13.4, 11.5; Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91%. Found: C, 75.90; H, 8.27; N, 4.76%.

Ethyl 1-butyl-2-methyl-5-*p*-tolyl-1*H*-pyrrole-3-carboxylate (4n): 82% yield. IR (KBr) υ: 2983, 2924, 1685, 1380, 1280, 1200, 757cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.26–7.18 (m, 4H, ArH), 6.49 (s, 1H, ArH), 4.26 (q, J = 5.0 Hz, 2H, CH_2), 3.86–3.83 (m, 2H, CH_2), 2.58 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 1.52–1.48 (m, 2H, CH_2), 1.33 (t, J = 5.0 Hz, 3H, CH_3), 1.18–1.12 (m, 2H, CH_2), 0.80 (t, J = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.5, 136.3, 133.4, 133.1, 129.3, 128.8, 128.3, 127.4, 111.8, 109.7, 59.2, 43.8, 32.7, 19.6, 14.5, 13.4, 11.5; Anal. Calcd for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42; N, 4.68%. Found: C, 76.08; H, 8.39; N, 4.76%.

Ethyl 5-(3-bromo-4-methoxyphenyl)-1-butyl-2-methyl-1*H*-pyrrole-3-carboxylate (4o): 80% yield. IR (KBr) υ: 2984, 2930, 1687, 1384, 1285, 1207, 757cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32 (s, 1H, ArH), 6.96 (d, J = 7.2 Hz, 1H, ArH), 6.73 (s, 1H, ArH), 6.69 (d, J = 7.2 Hz, 1H, ArH), 4.27 (q, J = 5.0 Hz, 2H, CH_2), 3.87–3.84 (m, 2H, CH_2), 3.82 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3), 1.52–1.48 (m, 2H, CH_2), 1.33 (t, J = 5.0 Hz, 3H, CH_3), 1.18–1.12 (m, 2H, CH_2), 0.80 (t, 3H, J = 5.0 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.5, 155.3, 136.3, 134.1, 131.6, 129.5, 127.0, 111.8, 111.6, 111.3, 109.8, 60.3, 59.3, 56.3, 43.8, 32.7, 19.7, 14.5, 13.8, 11.5; Anal. Calcd for $C_{19}H_{24}BrNO_3$: C, 57.88; H, 6.14; N, 3.55%. Found: C, 57.79; H, 6.23; N, 3.47%.

Ethyl 1-(furan-2-yl)-2-methyl-5-phenyl-1*H*-pyrrole-3-carboxylate (4p): 79% yield. IR (KBr) υ: 3010, 2976, 2890, 1725, 1496, 1317, 1182, 850, 791cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35 (d, J = 7.2 Hz, 1H, ArH), 7.34–7.25 (m, 5H, ArH), 6.60 (s, 1H, ArH), 6.28 (t, J = 5.2 Hz, 1H, ArH), 5.92 (d, J = 5.2 Hz, 1H, ArH), 4.29 (q, J = 5.0 Hz, 2H, CH_2), 2.60 (s, 3H, CH_3), 1.34 (t, 3H, J = 5.0 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.7, 157.3, 147.6, 140.9, 137.6, 136.6, 133.4, 132.9, 128.8, 128.6, 128.1, 127.9, 113.5, 107.8, 51.8, 45.2, 21.5; Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74%. Found: C, 73.14; H, 5.85; N, 4.80%.

Ethyl 1-(furan-2-yl)-2-methyl-5-*p*-tolyl-1*H*-pyrrole-3-carboxylate (4q): 81% yield. IR (KBr) *υ*: 3071, 2994, 2928, 1724, 1495, 1316, 1181, 848, 792cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.33 (d, *J* = 7.2 Hz, 1H, ArH), 7.25 (d, *J* = 7.2 Hz, 2H, ArH), 7.18 (d, *J* = 7.2 Hz, 2H, ArH), 6.56 (s, 1H, ArH), 6.28 (t, *J* = 5.2 Hz, 1H, ArH), 5.93 (d, *J* = 5.2 Hz, 1H, ArH), 4.29 (q, *J* = 5.0 Hz, 2H, CH_2), 2.59 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 1.34 (t, *J* = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 165.5, 150.5, 142.2, 137.4, 136.8, 133.9, 130.8, 129.5, 129.3, 129.1, 128.8, 128.6, 112.3, 110.3, 109.4, 107.4, 59.3, 41.6, 21.1, 14.5, 11.4; Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53%. Found: C, 73.90; H, 6.03; N, 4.46%.

Ethyl 1-(furan-2-yl)-2-methyl-5-phenyl-1*H*-pyrrole-3-carboxylate (4r): 83% yield. IR (KBr) *υ*: 3059, 2994, 2928, 1723, 1494, 1315, 1180, 848, 791cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.55 (s, 1H, ArH), 7.35 (d, *J* = 7.2 Hz, 1H, ArH), 7.26 (d, *J* = 7.2 Hz, 1H, ArH), 6.89 (d, *J* = 7.2 Hz, 1H, ArH), 6.55 (s, 1H, ArH), 6.30 (t, *J* = 5.2 Hz, 1H, ArH), 5.97 (d, *J* = 5.2 Hz, 1H, ArH), 4.29 (q, *J* = 5.0 Hz, 2H, CH_2), 3.92 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 1.34 (t, *J* = 5.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 165.4, 155.5, 150.2, 142.4, 137.0, 134.4, 132.1, 129.6, 126.3, 112.4, 111.5, 110.4, 109.9, 107.7, 59.4, 56.3, 41.6, 14.5, 11.5; Anal. Calcd for $C_{19}H_{18}BrNO_4$: C, 56.45; H, 4.49; N, 3.46%. Found: C, 56.39; H, 4.54; N, 3.61%.

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