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ORIGINAL PAPER

Sonochemically assisted synthesis of N-substituted pyrroles catalyzed by ZnO nanoparticles under solvent-free conditions

Ashraf S Shahvelayati[1] · Maryam Sabbaghan[2] · Solmaz Banihashem[1]

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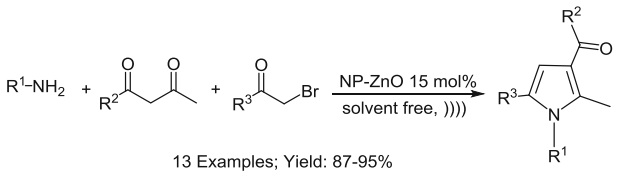
Abstract An efficient and rapid synthesis of 1,2,3,5-tetrasubstituted pyrrole derivatives from a one-pot multicomponent reaction of amines, 1,3-dicarbonyl compounds, and α-haloketones in the presence of ZnO nanoparticles catalyst under ultrasonic irradiation and solvent-free conditions is described.
Graphical abstract



Keywords Tetrasubstituted pyrrole derivatives · Multicomponent reaction · ZnO nanoparticles · Ultrasonic irradiation · 1,3-Dicarbonyl compounds

Introduction

Pyrroles are considered as an important class of compounds with different biological activities [1, 2]. The pyrrole moiety is found in many naturally occurring compounds such as heme, chlorophyll, and vitamin B_{12}. Pyrroles also exist in various bioactive drugs such as antioxidant, anti-inflammatory, antiviral, and antitumor agents [3–5].

Many methods have been developed for preparation of pyrroles [6–9]. Despite these new developments, the classical Hantzsch reaction remains the most attractive method for the synthesis of pyrroles [10]. Facile and green synthetic procedures establish an important goal in organic synthesis. Elimination of hazardous solvents, reduction of reaction time, and using catalyst are among the most important principles of the green chemistry [11–14]. The development of multicomponent reactions (MCRs) in the presence of nano-metal oxides such as ZnO nanostructures, used not only as an environmentally benign reaction media, but also as an efficient and reusable catalyst, is a new technique that meets the requirements of green chemistry [15–17]. Moreover, ultrasound has increasingly been used in organic synthesis in the last decades and a large number of organic reactions can be carried out in higher yields, shorter reaction time and milder conditions under it [18, 19].

As part of our current studies on the development of new routes in heterocyclic synthesis [20–22], we report an efficient ultrasonic-assisted one-pot synthesis of functionalized pyrroles **4a–4m** in good yields by a three-component reaction between amines **1**, β-dicarbonyls **2**, and α-bromoketones **3** under solvent-free condition (Scheme 1). Herein, ZnO nanoparticles (NPs) exhibited high activity and products are produced in high yield in the presence of them.

Results and discussion

Structure and morphology of the ZnO-NPs

In general, a nanoparticle is considered to be more reactive because it offers higher surface area and low coordinating

✉ Ashraf S Shahvelayati
avelayati@yahoo.com

[1] Department of Chemistry, Yadegar-e-Imam Khomeini (RAH) Shahre-rey Branch, Islamic Azad University, Tehran, Iran

[2] Chemistry Department, Faculty of Sciences, Shahid Rajaee Teacher Training University, Tehran, Iran

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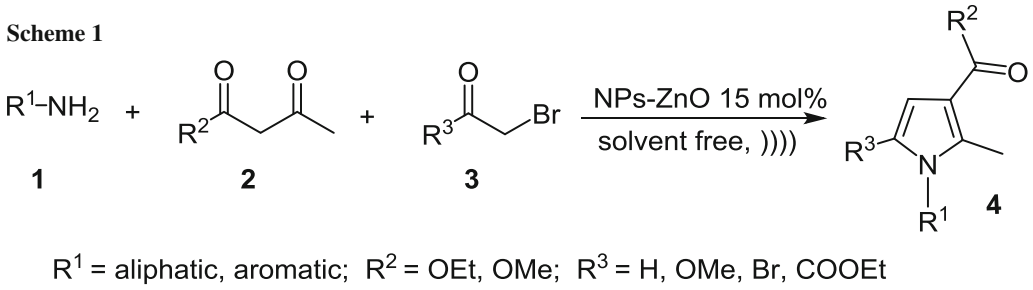
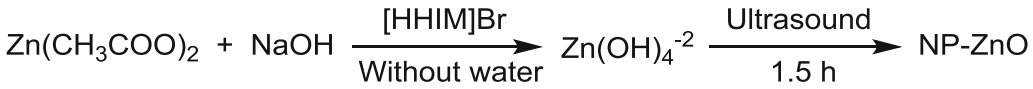
Scheme 1



Scheme 2



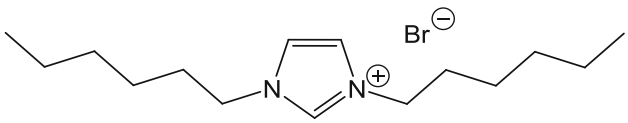


Fig. 1 Structure of dihexylimidazolium bromide

sites. The surface area of the catalyst increases tremendously when the size decreases to nano levels, which is responsible for the higher catalytic activity. Thus, we used ZnO-NPs in preparation of tetrasubstituted pyrroles as an efficient catalyst. The ZnO-NPs were obtained from zinc acetate dihydrate as a zinc source, and the chemical reaction can be formulated as shown in Scheme 2.

With using IL as a template, ZnO-NPs with smaller crystallite size were obtained [23–27]. The structure of the IL [HHIM]Br, used in this study, is shown in Fig. 1. The characteristic results revealed that using ionic liquids in water prevents a drastic increase in the crystallite size. Without IL, the shielding effect of excess OH^- on the growth rate of various faces becomes slow. The structure of these ZnO-NPs was studied using SEM and XRD (Figs. 2, 3). The figures indicate that the catalyst is consisted of pure phases and no characteristic peaks is observed for other impurities, such as $Zn(OH)_2$.

Catalytic activity of ZnO-NPs in the synthesis of polysubstituted pyrroles

The reaction of aromatic and aliphatic amines **1**, β-carbonyls **2**, and α-bromoketones **3** under solvent-free condition and ultrasonic irradiation was investigated to produce pyrroles **4** in good yields and then, it was compared with the reaction without catalyst under reflux in

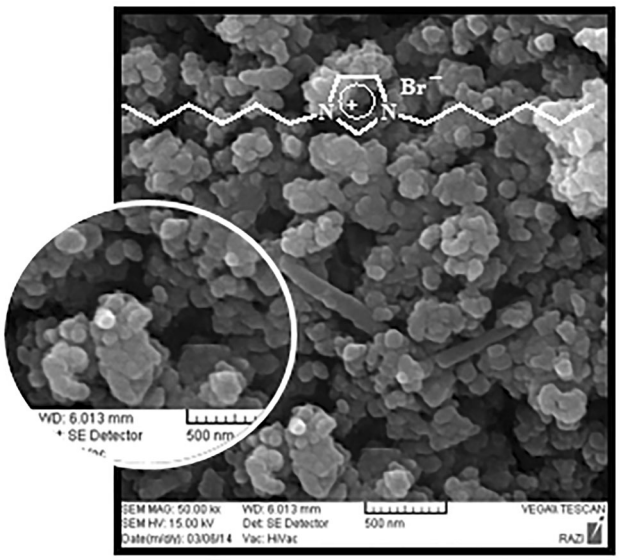


Fig. 2 SEM image of ZnO-NPs

ethanol (Table 1) [28]. The structures of compounds **4a–4m** were deduced from their elemental analyses and their IR, ^{1}H NMR, and ^{13}C NMR. The mass spectra of these compounds displayed molecular ion peaks at appropriate *m/z* values. The compounds **4d** [29–31] and **4e**, **4k** [14] have been reported before in the literatures. The ^{1}H NMR spectrum of **4m** in $CDCl_3$ showed three singlets in $\delta = 2.06$, 2.27, 2.42 ppm for methyl groups, together with one triplet and one quartet (1.18, 4.14 ppm, respectively) for the ethoxy group, one singlet signal (7.11 ppm) for CH-pyrrole and two doublets (6.99, 7.13 ppm) for the aromatic protons. The ^{13}C NMR spectrum of **4m** showed 15 signals in agreement with the proposed structure. Partial assignments of these resonances are given in spectral data section

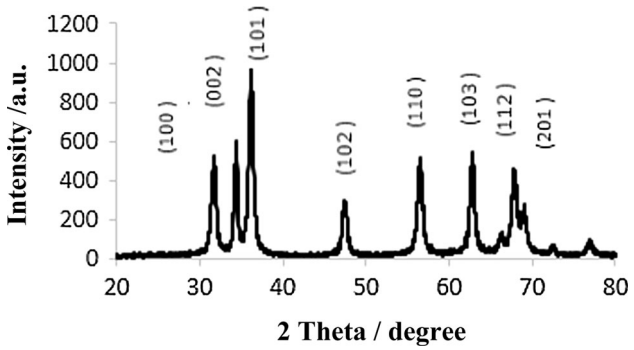


Fig. 3 XRD of ZnO-NPs

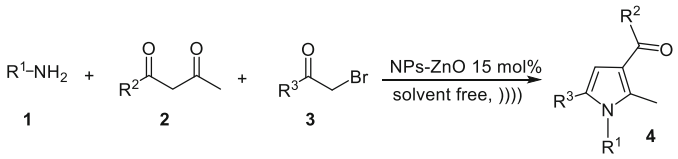
(**4m** product). The ^{1}H and ^{13}C NMR spectra of the other products are similar to those of **4m** except for the alkyl and aryl substituents, which exhibit characteristic signals in the appropriate regions of the NMR spectra.

The catalyst can be reused two times without significant loss of activity. The reusability of the catalyst was checked for the synthesis of ethyl 4-acetyl-5-methyl-1-(*p*-tolyl)-1*H*-pyrrole-2-carboxylate (Table 1, entry 13). After filtering and washing out the catalyst in each run, it was dried at room temperature for 24 h and used for the next catalytic cycle.

The influence of various reaction parameters such as solvent, catalyst loading, and time was examined. Initially we have screened various solvents such as ethanol, acetonitrile, *n*-hexane, and dichloromethane for **4a** product formation under reflux in the absence of catalyst (Table 2). It was observed that the reaction proceeded very slowly and the product yield was very low. The best result was obtained under ultrasonic irradiation and solvent-free conditions in the presence of ZnO-NPs at 40 °C (Table 2, entry 6). The reaction was also studied under catalyst in the absence of sonication, which resulted in lower product yield at higher temperature for a longer time (Table 2, entry 5).

The catalyst loading was optimized by increasing the amount of ZnO-NPs from 0.5 to 15% for 1 mmol scale reaction (Table 3). The yield increased with the increase of catalyst; however, there was a very marginal increase when the catalyst loading increased to 20%. Therefore, 15% catalyst was chosen as an optimal amount.

Table 1 Reaction conditions for formation of pyrroles **4a–4m**: amine (1 mmol), 1,3-dicarbonyl (1 mmol), α-bromoketone (1 mmol)



Entry	R^1	R^2	R^3	Product	Yield[a]/%	Yield[b]/%
1	Et	Me	C_6H_5	**4a**	74	90
2	Et	OEt	C_6H_5	**4b**	71	88
3	Et	Me	4-MeO-C_6H_4	**4c**	70	87
4	$C_6H_5CH_2$	OEt	C_6H_5	**4d**	72	89
5	$C_6H_5CH_2$	Me	C_6H_5	**4e**	77	94
6	C_6H_5	Me	4-Br-C_6H_4	**4f**	Trace	93
7	C_6H_5	Me	4-MeO-C_6H_4	**4g**	Trace	87
8	C_6H_5	OEt	CO_2Et	**4h**	Trace	92
9	C_6H_5	Me	CO_2Et	**4i**	Trace	89
10	4-MeC_6H_4	Me	4-Br-C_6H_4	**4j**	Trace	95
11	4-MeC_6H_4	Me	C_6H_5	**4k**	Trace	94
12	4-MeC_6H_4	OEt	CO_2Et	**4l**	Trace	90
13	4-MeC_6H_4	Me	CO_2Et	**4m**	Trace	92[c]

[a] Yield obtained after 3 days (no catalyst, reflux under ethanol)

[b] Yield obtained after 30 min at 40 °C (ZnO-NPs as catalyst, solvent- free, ultrasonic irradiation)

[c] **4m**, yield 92% under ZnO-NPs for the first time, 90% in the second run, and 89% in the third run with recycled catalyst

Table 2 Effect of solvent and catalyst on the synthesis of pyrrole **4a**

Entry	Solvent/catalyst	Time/h	Temperature	Yield/%
1	Ethanol/none/reflux	72	Reflux	77
2	CH_3CN/none/reflux	72	Reflux	70
3	*n*-Hexane/none/reflux	72	Reflux	60
4	CH_2Cl_2/none/reflux	72	Reflux	45
5	Solvent-free/ZnO-NPs	6–9	80 °C	74[a]
6	Solvent-free/ZnO-NPs/ Ultrasonic irradiation	0.5	40 °C	90[a]

[a] ZnO-NPs are prepared according to the experimental section

Table 3 Effect of catalyst loading on the synthesis of pyrrole **4h** under ultrasonic irradiation

Entry	ZnO/mol%	Yield/%
1	No catalyst	Trace
2	5	43
3	10	75
4	15	92
5	20	93

A tentative mechanism for this transformation is proposed in Scheme 3. Presumably, enaminone **5**, formed by the initial reaction of amine **1** and 1,3-dicarbonyl **2**, which attacks α-bromoketones **3** and undergoes HBr elimination to produce **6**, which is in equilibrium with the enamine tautomer **7**. Cyclization of this intermediate followed dehydration, affords products **4**. ZnO-NPs have Lewis acid sites (Zn^{2+}) and Lewis basic sites (O^{2-}). In this reaction, the Zn^{2+} sites are interacting with carbonyl groups in 1,3-dicarbonyl compound and α-bromoketone and O^{2-} site of ZnO-NPs taking up a proton of **7** to generate **8** [32, 33].

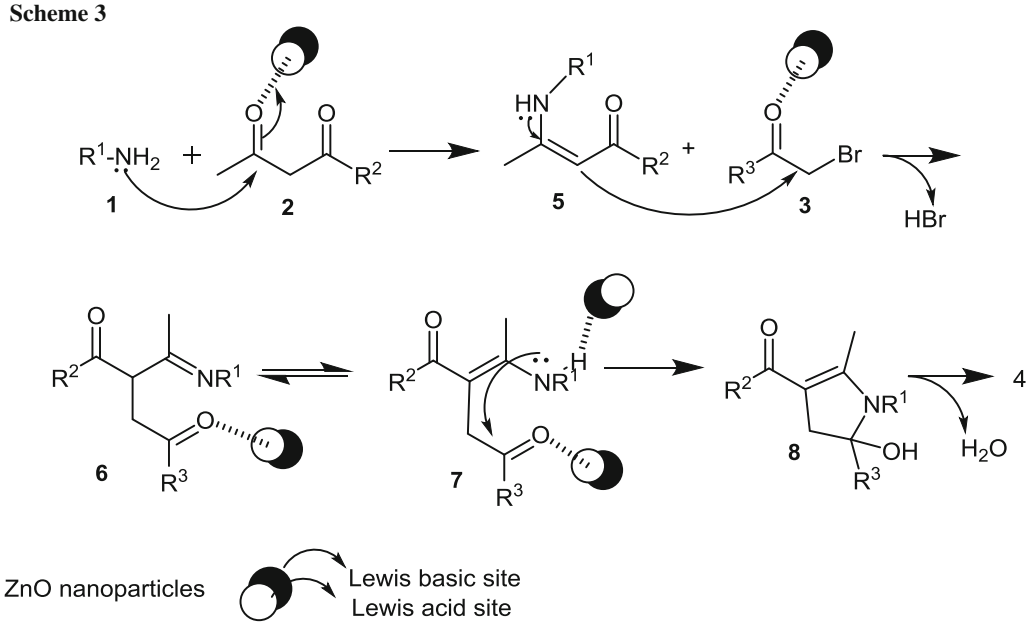
In summary, we have efficiently synthesized some tetrasubstituted pyrrole derivatives from the one-pot three-component reactions of amine, 1,3-diketones, and α-bromoketones in the presence of ZnO-NPs by ultrasonic irradiation and under solvent-free conditions. Zinc oxide nanoparticles satisfactorily catalyzed these reactions as a green, mild, and effective catalyst. Surprisingly, synthesis of *N*-arylpyrroles only proceeded in the presence of this catalyst under ultrasonic and solvent-free conditions, which is among the fastest reported procedure in the literature. We have concluded, however, that primary aromatic amines such as aniline do not react with diketones and α-bromoketones significantly in the absence of catalyst. The catalyst was recyclable and has been reused for three successive runs with little loss of the catalytic activity.

Experimental

All chemicals were obtained from Fluka or Merck and were used without further purification. The IL used in this study was 1,3-dihexylimidazolium bromide ([HHIM]Br) synthesized according to the procedure reported in the literature [34]; its structure was confirmed by ^{1}H NMR and FT-IR spectra.

IR spectra were obtained using Shimadzu FTIR-460 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were

Scheme 3



recorded with a Bruker DRX-300 AVANCE instrument in $CDCl_3$ at 300.1 and 75.4 MHz, respectively (δ in ppm, J in Hz). Mass spectra were obtained on a Finnigan MAT-8430 at 70 eV. Elemental analyses (C, H, N) were performed with a Heraeus CHN-O-Rapid analyzer.

All reactions were carried out under ultrasonic irradiation. Sonication was performed in a LBS2-10 FALC ultrasonic instrument clearer with a frequency of 60 kHz and an intensity of 285 W. The reaction flask was located in the water bath of the ultrasonic cleaner, and the temperature of the water bath was controlled at 40 °C.

Sonochemical synthesis of ZnO-NPs

Zinc acetate was employed as a zinc source. In a typical experiment, 0.3 g $Zn(AcO)_2{\cdot}2H_2O$ (1 mmol) was added to the template, 1.5 g dihexylimidazolium bromide, and then 0.2 g NaOH (5 mmol) was added to them. The mixture was stirred at room temperature; then was irradiated with ultrasound (40 kHz, 70 W) for 1.5 h under ambient condition. During the irradiation, the temperature of the reaction mixture rose to 70 °C. After irradiation, the precipitate was washed by distilled water and ethanol (96%) several times. Finally, the ZnO sample was dried in the air at room temperature during 24 h.

The morphology of ZnO-NPs was determined using scanning electron microscopy (SEM) with a Holland Philips XL30 microscope. X-ray diffraction (XRD) analysis was carried out at room temperature using a Holland Philips Xpert X-ray powder diffractometer with Cu Ka radiation ($\lambda = 0.15406$ nm), over the 2θ collection range of 20°–80°.

General procedure for the synthesis of pyrrole derivatives 4a–4m

A mixture of β-dicarbonyl compound (1 mmol), aliphatic and aromatic amines (1 mmol), and α-haloketone (1 mmol) and ZnO-NPs (15% mmol) was irradiated under ultrasound at 40 °C for the appropriate time. After completion of the reaction as indicated by TLC, the residue was purified by column chromatography (silica gel 230–240 mesh; Merck) using ethyl acetate/*n*-hexane (1:9) as eluent to afford the pure products. All products gave satisfactory spectral data in accordance with the assigned structures.

1-(1-Ethyl-2-methyl-5-phenyl-1H-pyrrole-3-yl)ethanone (**4a**, $C_{15}H_{17}NO$)
Pale yellow oil; IR (KBr): $\bar{\nu} = 1706$, 1512, 1273, 1222, 688 cm^{-1}; ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.05$ (t, 3H, $J = 7.2$ Hz, CH_3), 2.27 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 3.77 (q, 2H, $J = 7.2$ Hz, CH_2N), 6.32 (s, 1H, CH), 7.20–7.29 (m, 5H, 5 CH) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 11.90$, 15.95, 28.54, 38.71, 110.33, 120.92, 127.66, 128.50, 129.40, 132.89, 132.96, 135.61, 195.06 ppm; MS: $m/z = 227$ (M^+, 24), 211 (75), 198 (100), 77 (12).

Ethyl 1-ethyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylate (**4b**, $C_{16}H_{19}NO_2$)
Pale yellow oil; IR (KBr): $\bar{\nu} = 1709$, 1515, 1455, 1375, 690 cm^{-1}; ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.21$ (t, 3H, $J = 7.1$ Hz, CH_3), 2.42 (s, 3H, CH_3), 2.65 (t, 3H, $J = 7.2$ Hz, Me), 3.92 (q, 2H, $J = 7.1$ Hz, CH_2N), 4.29 (q, 2H, $J = 7.2$ Hz, CH_2O), 6.48 (s, 1H, CH), 7.32-7.38 (m, 5H, 5 CH) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 10.51$, 15.40, 17.36, 30.38, 60.91, 104.78, 108.03, 127.54, 129.81, 129.29, 132.71, 133.16, 142.10, 166.00 ppm; MS: $m/z = 257$ (M^+, 16), 228 (83), 211 (100), 185 (23), 77 (12).

1-[1-Ethyl-5-(4-methoxyphenyl)-2-methyl-1H-pyrrole-3-yl]ethanone (**4c**, $C_{16}H_{19}NO_2$)
Pale yellow oil; IR (KBr): $\bar{\nu} = 1713$, 1520, 1450, 1376, 1172, 850, 690 cm^{-1}; ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.03$ (t, 3H, $J = 7.2$ Hz, CH_3), 2.26 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 3.72 (q, 2H, $J = 7.2$ Hz, CH_2N), 6.27 (s, 1H, CH), 6.79 (d, 2H, $J = 8.2$ Hz, 2 CH), 7.13 (d, 2H, $J = 8.2$ Hz, 2 CH) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 11.79$, 16.30, 28.28, 37.41, 55.93, 112.79, 119.27, 122.84, 126.15, 129.20, 134.88, 137.26, 156.90, 198.63 ppm; MS: $m/z = 257$ (M^+, 21), 241 (80), 228 (100), 107 (18).

Ethyl 1-benzyl-2-methyl-5-phenyl-1H-pyrrole-3-carboxylate (**4d**) [29–31]
Yellow oil; IR (KBr): $\bar{\nu} = 1715$, 1457, 1375, 761 cm^{-1}; ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.10$ (t, 3H, $J = 7.1$ Hz, CH_3), 2.05 (s, 3H, CH_3), 4.02 (q, 2H, $J = 7.1$ Hz, CH_2O), 4.81 (s, 2H, CH_2N), 6.27 (s, 1H, CH), 6.69 (d, 2H, $J = 8.2$ Hz, 2 CH), 6.87–6.93 (m, 3H, 3 CH), 7.05-7.45 (m, 5H, 5 CH) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 12.06$, 14.11, 43.72, 60.94, 107.82, 121.67, 126.15, 126.55, 128.48, 129.27, 129.91, 133.14, 132.72, 133.13, 136.29, 142.13, 166.05 ppm; MS: $m/z = 319$ (M^+, 19), 273 (76), 228 (76), 91 (29).

1-(1-Benzyl-2-methyl-5-phenyl-1H-pyrrole-3-yl)ethanone (**4e**)
Yellow oil; IR (KBr): $\bar{\nu} = 1716$, 1459, 1374, 761 cm^{-1}; ^1H NMR spectrum was found to agree with the one described in Murthy et al. [14].

1-[5-(4-Bromophenyl)-2-methyl-1-phenyl-1H-pyrrole-3-yl]ethanone (**4f**, $C_{19}H_{16}BrNO$)
Pale yellow oil; IR (KBr): $\bar{\nu} = 1711$, 1504, 1409, 1228, 696 cm^{-1}; ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 2.43$ (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 6.73 (s, 1H, CH), 7.04 (d, 2H, $J = 7.8$ Hz, 2 CH), 7.13–7.17 (m, 5H, 5 CH) 7.40 (d, 2H,

$J = 8.2$ Hz, 2 CH) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 13.84, 30.60, 117.23, 125.34, 126.81, 127.96, 128.72, 129.73, 130.40, 131.65, 131.85, 132.24, 133.81, 137.63, 199.12$ ppm; MS: $m/z = 355$ (M^++2, 56), 353 (M^+, 52), 339 (100), 337 (97), 312 (23), 310 (21).

1-[5-(4-Methoxyphenyl)-2-methyl-1-phenyl-1H-pyrrole-3-yl]ethanone (**4g**, $C_{20}H_{19}NO_2$)
Pale yellow oil; IR (KBr): $\bar{\nu} = 1712, 1524, 1405, 1179, 763, 695$ cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.08$ (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 3.85 (s, 3H, CH_3O), 6.54 (s, 1H, CH), 6.94 (d, 2H, $J = 8.1$ Hz, CH_2O), 7.48 (d, 2H, $J = 8.1$ Hz, 2 CH), 7.26–7.52 (m, 5H, 5 CH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 12.95, 31.06, 55.27, 113.71, 120.40, 122.58, 125.89, 126.22, 128.03, 128.32, 129.31, 130.39, 135.19, 138.79, 158.68, 197.68$ ppm; MS: $m/z = 305$ (M^+, 49), 289 (100), 262 (28), 107 (14).

Diethyl 5-methyl-1-phenyl-1H-pyrrole-2,4-dicarboxylate (**4h**, $C_{17}H_{19}NO_4$)
Pale yellow oil; IR (KBr): $\bar{\nu} = 1713, 1559, 1418, 1354, 1249, 727$ cm^{-1}; ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.32$ (t, 3H, $J = 7.2$ Hz, CH_3), 1.36 (t, 3H, $J = 7.2$ Hz, CH_3), 2.30 (s, 3H, CH_3), 4.31 (q, 2H, $J = 7.2$ Hz, CH_2O), 4.32 (q, 2H, $J = 7.2$ Hz, CH_2O), 7.24 (s, 1H, CH), 7.26–7.50 (m, 5H, 5 CH) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 11.85, 14.26, 14.30, 60.18, 60.37, 113.96, 116.03, 126.17, 126.57, 128.58, 129.45, 135.22, 138.21, 164.05, 165.29$ ppm; MS: $m/z = 301$ (M^+, 57), 286 (9), 256 (100), 228 (45), 77 (16).

Ethyl 4-acetyl-5-methyl-1-phenyl-1H-pyrrole-2-carboxylate (**4i**, $C_{16}H_{17}NO_3$)
Pale yellow oil; IR (KBr): $\bar{\nu} = 730, 1502, 1403, 1245, 1028, 695$ cm^{-1}; ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.18$ (t, 3H, $J = 7.1$ Hz, CH_3), 2.08 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 4.14 (q, 2H, $J = 7.1$ Hz, CH_2O), 7.15 (s, 1H, CH), 7.17–7.32 (m, 3H, 3 CH), 7.33 (2H, d, $J = 7.5$ Hz, 2 CH) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 12.11, 14.30, 31.51, 60.24, 114.99, 123.70, 126.18, 127.56, 128.70, 129.50, 134.72, 138.11, 164.13, 198.95$ ppm; MS: $m/z = 271$ (M^+, 61), 256 (30), 228 (72), 225 (100), 77 (18).

1-[5-(4-Bromophenyl)-2-methyl-1-(p-tolyl)-1H-pyrrole-3-yl]ethanone (**4j**, $C_{20}H_{18}BrNO$)
White powder; m.p.: 58–60 °C; IR (KBr): $\bar{\nu} = 1721, 1508, 1418, 823, 660$ cm^{-1}; ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 2.24$ (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.71 (s, 3H, CH_3), 6.56 (s, 1H, CH), 6.76 (2H, d, $J = 8.2$ Hz, 2 CH), 6.84 (d, 2H, $J = 8.2$ Hz, 2 CH), 7.05 (d, 2H, $J = 8.2$ Hz, 2 CH), 7.13 (d, 2H, $J = 8.2$ Hz, 2 CH) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 14.11, 22.69, 29.36, 110.53, 126.61, 128.03, 128.91, 129.52, 130.01, 131.25, 131.42, 131.94, 132.50, 134.60, 138.37, 198.18$ ppm; MS: $m/z = 369$ (M^++2, 58), 367 (M^+, 57), 353 (100), 351 (98), 326 (19), 324 (18), 91 (24).

1-[2-Methyl-5-phenyl-1-(p-tolyl)-1H-pyrrole-3-yl]ethanone (**4k**)
White powder; m.p.: 57–58 °C; IR (KBr): $\bar{\nu} = 1641, 1354, 1122, 686$ cm^{-1}; ^1H NMR spectrum was found to agree with the one described in Murthy et al. [14].

Diethyl 5-methyl-1-(p-tolyl)-1H-pyrrole-2,4-dicarboxylate (**4l**, $C_{18}H_{21}NO_4$)
White powder; m.p.: 60–62 °C; IR (KBr): $\bar{\nu} = 1710, 1525, 1431, 819, 760$ cm^{-1}; ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.32$ (t, 3H, $J = 7.1$ Hz, CH_3), 1.36 (t, 3H, $J = 7.1$ Hz, CH_3), 2.28 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 4.28 (q, 2H, $J = 7.1$ Hz, CH_2O), 4.34 (q, 2H, $J = 7.1$ Hz, CH_2O), 7.13 (d, 2H, $J = 8.2$ Hz, 2 CH), 7.21 (s, 1H, CH), 7.27 (d, 2H, $J = 8.2$ Hz, 2 CH) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 11.83, 14.28, 14.32, 21.09, 60.17, 60.34, 113.78, 115.88, 125.98, 126.68, 130.01, 135.38, 135.71, 138.68, 164.14, 165.35$ ppm; MS: $m/z = 315$ (M^+, 46), 300 (19), 270 (100), 242 (65), 91 (25).

Ethyl 4-acetyl-5-methyl-1-(p-tolyl)-1H-pyrrole-2-carboxylate (**4m**, $C_{17}H_{19}NO_3$)
White powder; m.p.: 63–64 °C; IR (KBr): $\bar{\nu} = 1699, 1396, 1164, 824, 630$ cm^{-1}; ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.18$ (t, 3H, $J = 7.1$ Hz, CH_3), 2.06 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 4.14 (q, 2H, $J = 7.1$ Hz, CH_2O), 6.99 (d, 2H, $J = 8.2$ Hz, 2 CH), 7.11 (s, 1H, CH), 7.13 (d, 2H, $J = 8.2$ Hz, 2 CH) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 12.09, 14.31, 21.11, 31.51, 60.21, 114.79, 123.54, 125.96, 127.66, 130.04, 134.89, 135.55, 138.79, 164.19, 198.97$ ppm; MS: m/z (%) = 285 (M^+, 63), 270 (24), 242 (75), 239 (100), 91 (22).

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