Ultrasonics Sonochemistry 18 (2011) 917–922

Contents lists available at ScienceDirect

Ultrasonics Sonochemistry

journal homepage: www.elsevier.com/locate/ultsonch

Short Communication

# Ultrasound-assisted synthesis of 2,5-dimethyl-N-substituted pyrroles catalyzed by uranyl nitrate hexahydrate

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ARTICLE INFO

*Article history:*
Received 15 December 2010
Received in revised form 4 February 2011
Accepted 6 February 2011
Available online 27 February 2011

*Keywords:*
2,5-Dimethyl-N-substituted pyrroles
$UO_2(NO_3)_2.6H_2O$
Ultrasonic irradiation
Soft conditions

ABSTRACT

An efficient synthesis of different novel 2,5-dimethyl-N-substituted pyrrole derivatives by the Paal–Knorr condensation has been accomplished using uranyl nitrate hexahydrate as catalyst under soft conditions and ultrasonic irradiation. The synthesized compounds were confirmed through spectral characterization using IR, $^1$H NMR, $^{13}$C NMR and mass spectra.



## 1. Introduction

The pyrrole scaffold is an useful structural pattern for exhibiting chemical functionality in biologically active molecules [1]. It has established broad application in drug development for the treatment as antibacterial, anti-inflammatory, antiviral, antitumoral, and antioxidant agent [2]. The pyrrole ring system is one of the most important substructures for biologically active compounds such as indolizidine alkaloids, unsaturated g-lactams and bicyclic lactams [3]. These structural units are found in a wide array of natural products, synthetic materials and bioactive molecules such as vitamin B12, heme and cytochromes [1,4]. Therefore, preparation of pyrroles has attracted considerable attention of chemists in recent years. There are several methods for the synthesis of pyrrole in the literature [5] from classical Hantzsch procedure [6], 1,3-dipolar cycloaddition reaction [7], aza-Wittig reaction [8], reductive coupling [9], titanium catalyzed hydroamination of diynes [10] and other multistep operations [11]. The most widely used method is the Paal–Knorr synthesis, which involves the cyclocondensation reaction of 1,4-dicarbonyl compounds with primary amines to produce substituted pyrroles. Several catalysts have been used in this reaction including HCl [12], p-TSA [13], HOAc [14], $H_2SO_4$ [15], $I_2$ [16], different metal complexes [17–30], and montmorillonite [16,31–32]. In addition, the above cyclocondensation process could proceed in ionic liquid [33], microwave irradiation [34] or ultrasound irradiation using $ZrCl_4$ as catalyst [35]. However, some of the synthetic protocols for the synthesis of 2,5-dimethyl-N-substituted pyrroles reported above suffer from one or more disadvantages, such as harsh reaction conditions, poor yields, prolonged reaction time period as well as use of corrosive, expensive reagents, limiting these methods. Thus, simple, efficient and flexible protocols for the synthesis of 2,5-dimethyl-N-substituted pyrroles are still the need as there is scope for further improvement towards milder reaction conditions, development of simple and inexpensive reagents convenient procedures and higher product yields.

Ultrasonic-assisted organic synthesis as a green synthetic approach is a powerful technique that is being used more and more to accelerate organic reactions [36,37]. A large number of organic reactions can be carried out in higher yields, shorter reaction time or milder conditions under ultrasound irradiation and considered a processing aid in terms of energy conservation and waste minimization which compared with traditional methods.

Uranyl nitrate is usually used as an electron dense stain for transmission electron microscopy. However, it has also found application as 0.01% aqueous solution as a local catalyst in the polymerization of methacrylates [38].

We report herein, a simple, mild and expeditious synthesis of 2,5-dimethyl-N-substituted pyrroles in high yields by reacting 1,4-dicarbonyl compound with substituted primary amines using uranyl nitrate hexahydrate [$UO_2(NO_3)_2.6H_2O$] (Scheme 1) as catalyst under soft conditions and ultrasonic irradiation.

## 2. Results and discussion

2,5-Dimethyl-N-substituted pyrroles **(3a–k)** were synthesized by the cyclocondensation of commercially available 2,5-hexanedione with different substituted primary amines using uranyl nitrate

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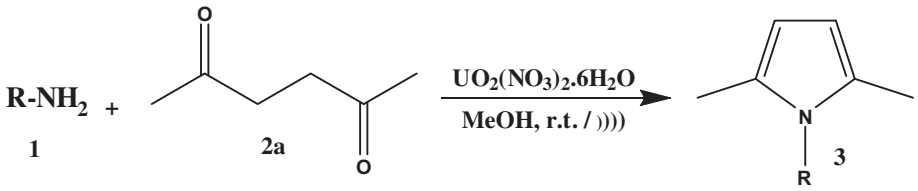
doi:10.1016/j.ultsonch.2011.02.007




**Scheme 1.** Synthesis of 2,5-dimethyl-N-substituted pyrroles catalyzed by uranyl nitrate hexahydrate.

hexahydrate [$UO_2(NO_3)_2.6H_2O$] (Scheme 1) as catalyst under soft conditions and ultrasonic irradiation. To optimize the reaction conditions, the reaction between 2,5-hexanedione and aniline was used as a model reaction. The results shown in Table 1 clearly indicate the scope and generality of the reaction with respect to various catalytic systems. In comparison with other catalysts such as $Bi(NO_3)_2.5H_2O$, [BMIm]I and $RuCl_3$ which have been recently reported in the synthesis of 2,5-dimethyl-N-substituted pyrroles, $UO_2(NO_3)_2.6H_2O$ employed here shows a more effective catalytic activity than the others in terms of amount of catalyst, yield and reaction time (Table 1, entry 8–10).The influence of other catalysts such as $Sr(NO_3)_2$, $Mg(NO_3)_2.6H_2O$ were also examined. It is notable that strontium nitrate was found to give quite high yields for this transformation compared with magnesium nitrate hexahydrate (Table 1, entry 6 & 7). However, in the absence of catalyst, the reaction yielded only 22% of product after 24 h of reaction.

Before taking up the reaction using ultrasonic irradiation, it was tried out using different solvents such as methanol, ethanol, acetonitrile, dichloromethane and chloroform as well as solvent free system under normal reaction conditions with 10 mol% of $UO_2(NO_3)_2.6H_2O$ as the catalyst (Table 2). However, it was noticed that the highest yield and shorter reaction duration was achievable with methanol while the others took longer duration to yield lesser product. Hence the ultrasonic irradiation which required only 5 min duration to complete reaction of aniline with 2,5-hexanedione and the product yield was 96% is compared to the normal reaction conditions, stirring at room temperature which have taken 30 min for reaction to completion and yield was slightly less (94%) with methanol as solvent (Table 2, entry 5). It was clear that the ultrasound could accelerate the reaction of amine and 2,5-hexancedione.

The following is expected to be plausible reason for the higher yield and lesser reaction time during ultrasonic irradiation:

Cavitation is a process of formation of bubbles having dynamic life during ultrasonic irradiation. These bubbles can be filled with gas or vapour and occur in organic solvents used in the ultrasonic irradiation. When these bubbles burst, it results in high temperature and high pressure which facilitate the intermolecular reaction.

**Table 1**
Comparison of effect of catalysts in the formation of 2,5-dimethyl-N-phenyl pyrrole[a] (**3a**) at room temperature.

| Entry | Catalyst | Mole % | Time (h) | Yield[b] (%) |
|---|---|---|---|---|
| 1 | No Catalyst | – | 24 | 22 |
| 2 | $UO_2(NO_3)_2.6H_2O$ | 1 | 2 | 57 |
| 3 | $UO_2(NO_3)_2.6H_2O$ | 2.5 | 2 | 69 |
| 4 | $UO_2(NO_3)_2.6H_2O$ | 5 | 1 | 88 |
| 5 | $UO_2(NO_3)_2.6H_2O$ | 10 | 0.5/5[c] | 94/96[c] |
| 6 | $Sr(NO_3)_2$ | 20 | 4 | 73 |
| 7 | $Mg(NO_3)_2.6H_2O$ | 20 | 4 | 55 |
| 8 | $Bi(NO_3)_2.5H_2O$ | 100 | 10 | 96[19] |
| 9 | [BMIm]I | 1.5 g | 3 | 96[33] |
| 10 | $RuCl_3$ | 5 | 0.5 | 94[30] |

[a] Aniline: 2,5-Hexanedione (1 mmol: 1.1 mmol).
[b] Isolated yield.
[c] At room temperature (h)/ultrasonic irradiation (min).

**Table 2**
Synthesis of 2,5-dimethyl-N-phenyl pyrrole[a] (**3a**) using 10 mol% of $UO_2(NO_3)_2.6H_2O$ in different solvent systems.

| Entry | Solvent | Time (min) | Yield[b] (%) |
|---|---|---|---|
| 1 | Acetonitrile | 120 | 79 |
| 2 | $CH_2Cl_2$ | 300 | 57 |
| 3 | $CHCl_3$ | 300 | 61 |
| 4 | Ethanol | 60 | 88 |
| 5 | Methanol | 30/5[c] | 94/96[c] |
| 6 | Solvent free | 60 | 83 |

[a] Aniline: 2,5-Hexanedione (1 mmol: 1.1 mmol).
[b] Isolated yield.
[c] At room temperature/Ultrasonic irradiation.

Apart from this, the shock wave produced by the bubble collapse can disrupt the solvent structure which can influence the reactivity by altering solvation of the reactive species present in the reaction mixture. Sonochemical rate enhancement is a known phenomenon in organic reactions [39]. It can be attributed that by the same mechanism, the yield of 2,5-dimethyl-N-substituted pyrroles is higher in ultrasound than in normal chemical reaction.

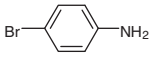
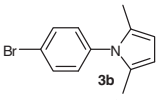
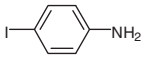
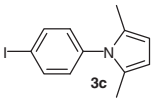
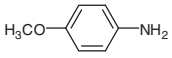
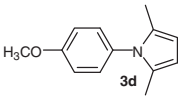
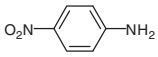
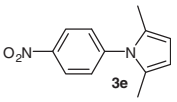
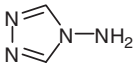
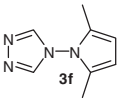
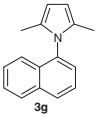
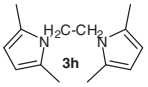
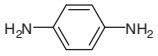
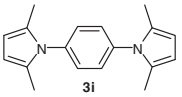
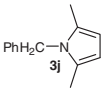
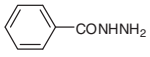
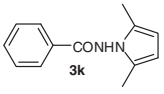
In order to evaluate the generality of the process, several diversified examples illustrating the present method for the synthesis of 2,5-dimethyl-N-substituted pyrroles (**3a–k**) was studied (Table 3). The reaction of 2,5-hexanedione (**2a**) with various aromatic/aliphatic substituted primary amines bearing electron donating groups, electron withdrawing groups and several heterocyclic moieties was carried out in the presence of $UO_2(NO_3)_2.6H_2O$ as catalyst under soft conditions and ultrasonic irradiation. The yields obtained were good to excellent without formation of any side products and these results are illustrated in Table 3. From these experiments, it is clearly demonstrated that the uranyl nitrate hexahydrate [$UO_2(NO_3)_2.6H_2O$] is indeed an effective catalyst and is undoubtedly superior to other catalysts, procedures with respect to reaction time, availability of catalyst, work-up procedure and yields. The compounds **IVa–e** were synthesized by refluxing different substituted acetohydrazides (**IIIa–e)** and 2,5-hexanedione in the presence of $UO_2(NO_3)_2.6H_2O$. The reaction time and yields of the compounds **IVa–e** are depicted in Table 4. The compounds **IIIa–e** were synthesized by refluxing the mixture of ethyl(substituted)mono/diacetate (**IIa–e**) and hydrazine hydrate in ethanol. The compounds **IIa–e** were synthesized by the reaction of ethyl chloroacetate with different mono and dihydroxy substituted aromatic compounds in the presence of $K_2CO_3$ as catalyst (Scheme 2) [40]. Structure of new derivatives of 2,5-dimethyl-N-substituted pyrroles (**3b–c**, **3k** and **IVa–e**) properly characterized by their IR, $^1H$ NMR, $^{13}C$ NMR and mass spectra, while the known compounds were identified by comparison of their spectroscopic data and melting points with the reported values in literature.

## 3. Experimental

### 3.1. General

All reagents purchased from Aldrich, Hi Media and Qualigens were used without further purification. $UO_2(NO_3)_2.6H_2O$

**Table 3**
Synthesis of 2,5-dimethyl-N-substituted pyrroles (**3a-k**) catalyzed by uranyl nitrate hexahydrate.

| Entry | Amine | Product | Time (min)[a] | Yield (%)[b] | M.P. (°C) |
|---|---|---|---|---|---|
| 1 | Ph-$NH_2$ |  **3a** | 30/5 | 94/96 | 48–50 |
| 2 |  |  **3b** | 60/6 | 89/90 | 56–58 |
| 3 |  |  **3c** | 60/6 | 86/88 | 62–64 |
| 4 |  |  **3d** | 45/6 | 86/84 | 60–62 |
| 5 |  |  **3e** | 60/5 | 87/90 | 144–146 |
| 6 |  |  **3f** | 120/8 | 76/72 | 140–142 |
| 7 |  |  **3g** | 120/10 | 83/81 | 120–122 |
| 8 | $NH_2(CH_2)_2NH_2$ |  **3h** | 180/15 | 87/85 | 134–136 |
| 9 |  |  **3i** | 180/15 | 90/87 | 248–250 |
| 10 | $PhCH_2NH_2$ |  **3j** | 90/6 | 88/86 | 40–42 |
| 11 |  |  **3k** | 300/16 | 81/83 | 156–158 |

[a] Under reflux conditions/Ultrasonic irradiation.
[b] Isolated yield.

purchased from LOBA Chemie and used as received. Infrared (IR) spectra were recorded at room temperature from 4000 $cm^{-1}$ to 400 $cm^{-1}$ with KBr pellets at a resolution of 4 $cm^{-1}$, using Avatar 330 equipped with DTGS detector. Most of the obtained vibrational bands of the IR spectrum were identified and compared with those values available in literature. The $^1H$ NMR was recorded on a Bruker AMX-400 (400, 500 MHz) instrument at room temperature using the X-WIN NMR version X-WIN NMR 1.3 cn drx software. Approximately 0.03 M solutions in $CDCl_3$ or DMSO-$d_6$ using TMS as internal reference were used for recording $^1H$ NMR spectra. The accuracy of the $^1H$ shifts considered as 0.02 ppm. The coupling constants $J$ are in Hz. $^{13}C$ NMR spectra were recorded on Bruker Avance III (125.75 MHz) spectrometer. Mass spectra were obtained using JEOL GC MATE II HRMS (EI) mass spectrometry. Sonication was performed in a SONICS, Vibra Cell, VC 130, ultrasonic processor equipped with a 3 mm wide and 140 mm long probe, which was immersed directly into the reaction mixture. The operating frequency was 20 kHz and the output power was 0–130 Watt through manual adjustment. Melting points were determined in open capillaries and are uncorrected.

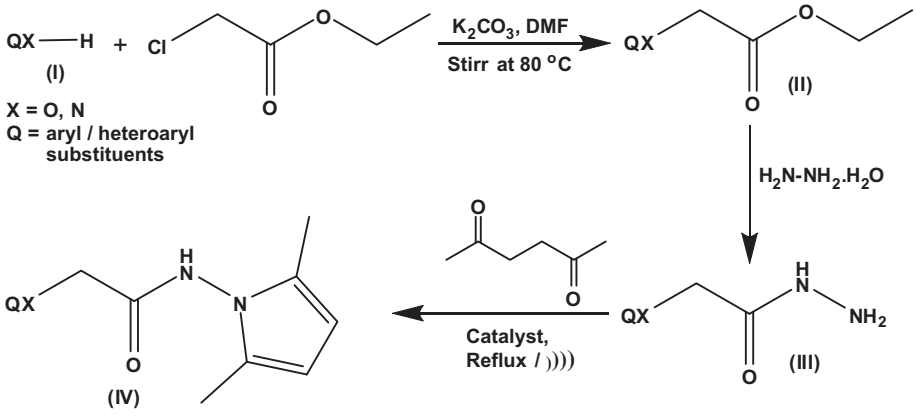
### *3.2. Procedure for the synthesis of 2,5-dimethyl-N-substituted pyrroles (**3a–k**)*

#### *3.2.1. Method A*

To a solution of the amine **1** (1 mmol) and 2,5-hexanedione **2a** (1.1 mmol) in methanol (2 mL) at room temperature, uranyl nitrate hexahydrate (10 mol%) was added. The mixture was stirred at room temperature for a period specified in Table 3. The progress of reaction was monitored by TLC. After completion of reaction the resulting mixture was filtered, washed with a 5% HCl solution to remove the excess amine and washed with a small amount of cold water. The crude product was weighed and recrystallized from 10% aqueous methanol. The reaction mixture was cooled in ice and the product was collected and dried.

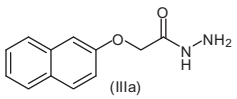
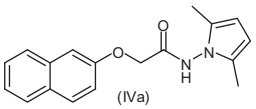
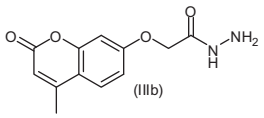
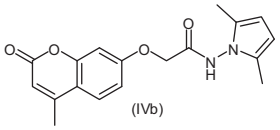
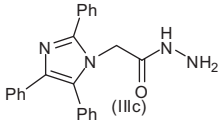
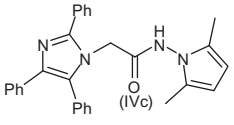
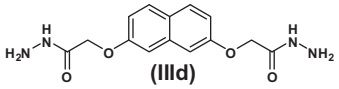
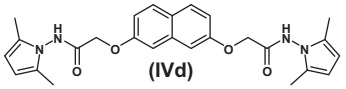
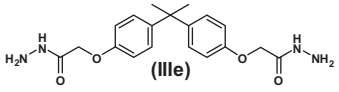
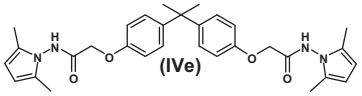
#### *3.2.2. Method B*

To a solution of the amine **1** (1 mmol) and 2,5-hexanedione **2a** (1.1 mmol) in methanol (2 mL) at room temperature, uranyl nitrate hexahydrate (10 mol%) was added and the resulting reaction mixture was subjected to ultrasonic irradiation using ultrasonic processor equipped with a 3 mm wide and 140 mm long probe, which was immersed directly into the reaction mixture for a period as shown in Table 3. The operating frequency was 16 kHz and the output power was 104 Watt through manual adjustment. The progress of reaction was monitored by TLC. After completion of




**Scheme 2.** Synthetic protocol of compounds **IVa–e**.

**Table 4**
Synthesis of compounds (**IVa–e**) using uranyl nitrate hexahydrate as catalyst.

| Entry | Reactant | Product | Time (h/min)[a] | Yield (%)[a,b] | M.P (°C) |
|---|---|---|---|---|---|
| 1 |  (IIIa) |  (IVa) | 2/16 | 87/84 | 204–206 |
| 2 |  (IIIb) |  (IVb) | 4/20 | 79/73 | 214–216 |
| 3 |  (IIIc) |  (IVc) | 4/20 | 82/75 | 240–242 |
| 4 |  (IIId) |  (IVd) | 6/25 | 76/71 | 224–226 |
| 5 |  (IIIe) |  (IVe) | 6/25 | 71/68 | 170–172 |

[a] Under reflux conditions/Ultrasonic irradiation.
[b] Isolated yield.

reaction the resulting mixture was filtered, washed with a 5% HCl solution to remove the excess amine and washed with a small amount of cold water. The separated product was filtered, washed with ice cold water, recrystallized from 10% aqueous methanol and dried at room temperature.

### 3.3. 1-(4-phenyl)-2,5-dimethyl-1H-pyrrole (**3a**)

mp 48–50 °C. IR (KBr, $\nu_{max}$, $cm^{-1}$): 3053, 2922, 1596, 1491, 1400, 1316, 1218, 1037, 999, 747. $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$: 7.49 (m, 2H, *m,m'*-ArH), 7.43 (m, 1H, *p*-ArH), 7.25 (m, 2H, *o,o'*-ArH) 5.94 (s, 2H, pyrrole), 2.07 (s, 6H, $2CH_3$). $^{13}$C NMR (125.75 MHz, $CDCl_3$) $\delta_C$: 139.02, 129.05, 128.82, 128.27, 127.63, 105.63, 13.02. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{12}H_{13}N$: 171.10; found: 171.1059.

### 3.4. 1-(4-Bromophenyl)-2,5-dimethyl-1H-pyrrole (**3b**)

mp 56–58 °C. IR (KBr, $\nu_{max}$, $cm^{-1}$): 3078, 2917, 1519, 1484, 1435, 1402, 1320, 1065, 998, 840, 760. $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.01 (s, 6H, $2CH_3$), 5.79 (s, 2H, pyrrole), 7.08 (d, 2H, $J$ = 8.4 Hz, *o,o'*-ArH), 7.57 (d, 2H, $J$ = 8.4 Hz, *m,m'*-ArH). $^{13}$C NMR (125.75 MHz, $CDCl_3$) $\delta_C$: 12.97, 106.13, 121.53, 128.67, 129.88, 132.32, 138.07. HRMS (EI): *m/z* $[M+H]^+$ calcd for $C_{12}H_{12}BrN$: 249.0153; found: 250.1000.

### 3.5. 1-(4-Iodophenyl)-2,5-dimethyl-1H-pyrrole (**3c**)

mp 62–64 °C. IR (KBr, $\nu_{max}$, $cm^{-1}$): 3073, 2916, 1583, 1484, 1434, 1403, 1321, 1053, 997, 838, 760. $^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$: 2.06 (s, 6H, $2CH_3$), 5.94 (s, 2H, pyrrole), 7.01 (d, 2H, $J$ = 8.5 Hz, *o,o'*-ArH), 7.83 (d, 2H, $J$ = 8.5 Hz, *m,m'*-ArH). $^{13}$C NMR (125.75 MHz, $CDCl_3$) $\delta_C$: 13.06, 92.98, 106.18, 128.66, 130.17, 138.34, 138.74. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{12}H_{12}IN$: 297.0014; found: 297.1000.

### 3.6. N-(2,5-dimethyl-1H-pyrrol-1-yl)benzamide (**3k**)

mp 156–158 °C. IR (KBr, $\nu_{max}$, $cm^{-1}$): 3263, 3062, 2934, 1664, 1602, 1537, 1488, 1282, 748. $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 2.13 (s, 6H, $CH_3$ on pyrrole), 5.77 (s, 2H, CH on pyrrole), 7.49 (m, 3H, ArH), 7.86 (d, 2H, $J$ = 7.2 Hz, ArH), 8.15 (s, 1H, CONH). $^{13}$C NMR (125.75 MHz, $CDCl_3$) $\delta_C$: 11.47, 103.61, 127.39, 127.50, 127.96, 128.12, 128.71, 128.76, 129.20, 131.51, 131.75, 132.39, 132.78, 166.28. ESI-MS: *m/z* calcd for $C_{13}H_{14}N_2O$: 214.11; found: 214.51 $[M]^+$. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_{14}N_2O$: 214.1106; found: 214.1200.

### 3.7. Procedure for the synthesis of compounds (**IVa–e**)

#### 3.7.1. Method A

To a suspensions of different substituted acetohydrazides **IIIa–e** (0.001 mol) in methanol/chloroform (1:1) mixture (20 mL) were added acetonyl acetone (0.002 mol) and uranyl nitrate hexahydrate (10 mol%) and the reaction mixture was refluxed for a period specified in Table 4. The reaction mixture was concentrated to half of the original volume and poured into crushed ice. The separated solid was filtered, washed with water and dried.

#### 3.7.2. Method B

To a suspensions of different substituted acetohydrazides **IIIa–e** (0.001 mol) in methanol/chloroform (1:1) mixture (20 mL) were added acetonyl acetone (0.002 mol) and uranyl nitrate hexahydrate (10 mol%) and the resulting reaction mixture was subjected to ultrasonic irradiation using ultrasonic processor equipped with a 3 mm wide and 140 mm long probe, which was immersed directly into the reaction mixture for a period as shown in Table 3. The operating frequency was 16 kHz and the output power was 104 Watt through manual adjustment. The progress of reaction was monitored by TLC. After completion of reaction the resulting mixture was poured into crushed ice. The separated product was filtered, washed with ice cold water and dried at room temperature.

*3.8. N-(2,5-dimethyl-1H-pyrrol-1-yl)-2-(naphthalen-2-yloxy)acetamide (**IVa**)*

mp 204–206 °C. IR (KBr, $\nu_{max}$, $cm^{-1}$): 3216, 3060, 2923, 1688, 1629, 1511, 1465, 1432, 1391, 1256, 1219, 1184, 1122, 1068, 963, 844, 754. $^1H$ NMR (400 MHz, $CDCl_3$) $\delta_H$: 1.61 (s, 3H, $CH_3$ on pyrrole), 2.02–2.41 (m, 3H, $CH_3$ on pyrrole), 4.60 (s, 1H, OCH), 4.83–4.91 (m, 1H, OCH), 6.85 (s, 2H, CH on pyrrole), 7.00–7.14 (m, 4H, ArH), 7.57–7.82 (m, 3H, ArH), 8.26 (s, 1H, CONH). $^{13}C$ NMR (125.75 MHz, $CDCl_3$) $\delta_C$: 11.41, 66.59, 103.60, 107.73, 119.20, 124.46, 127.06, 127.14, 127.36, 128.04, 129.32, 129.88, 134.41, 155.90, 167.85. ESI-MS: *m/z* calcd for $C_{18}H_{18}N_2O_2$: 294.14; found: 295.34 $[M+H]^+$. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{18}H_{18}N_2O_2$: 294.1368; found: 294.3500.

*3.9. N-(2,5-dimethyl-1H-pyrrol-1-yl)-2-(4-methyl-2-oxo-2H-chromen-7-yloxy)acetamide (**IVb**)*

mp 214–216 °C. IR (KBr, $\nu_{max}$, $cm^{-1}$): 3258, 3087, 2921, 1716, 1687, 1616, 1504, 1427, 1390, 1295, 1202, 1156, 1079, 846, 776. $^1H$ NMR (400 MHz, $CDCl_3$) $\delta_H$: 1.52 (s, 3H, $CH_3$ on coumarin), 2.07 (s, 6H, $2CH_3$ on pyrrole), 4.89 (s, 2H, $OCH_2$), 5.90 (s, 2H, CH on pyrrole), 7.23 (s, 1H, CH on coumarin), 7.42 & 7.49 (2d, 1H, $J$ = 6.8 & 7.6 Hz, ArH), 7.75–7.84 (m, 2H, ArH), 8.62 (s, 1H, CONH). $^{13}C$ NMR (125.75 MHz, $CDCl_3$) $\delta_C$: 11.39, 18.60, 66.75, 102.27, 103.65, 112.06, 112.99, 114.29, 127.03, 127.31, 153.82, 154.95, 160.48, 160.92, 167.32. ESI-MS: *m/z* calcd for $C_{18}H_{18}N_2O_4$: 326.13; found: 327.36 $[M+H]^+$. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{18}H_{18}N_2O_4$: 326.1267; found: 326.5646.

*3.10. N-(2,5-dimethyl-1H-pyrrol-1-yl)-2-(2,4,5-triphenyl-1H-imidazol-1-yl)acetamide (**IVc**)*

mp 240–242 °C. IR (KBr, $\nu_{max}$, $cm^{-1}$): 3251, 3056, 2923, 1685, 1213 $cm^{-1}$. $^1H$ NMR (500 MHz, DMSO-$d_6$) $\delta_H$: 1.80 (s, 6H, $C_{2,5}$–$CH_3$ on pyrrole ring), 4.65 (s, 2H, N-$CH_2$-CO), 5.63 (s, 2H, $C_{3,4}$–H on pyrrole ring), 7.15 & 7.22 (2t, 3H, $J$ = 7.75 Hz, *p*-ArH of 2,4,5-phenyl rings), 7.39–7.44 (m, 4H, *o,o′*-ArH of 4,5-phenyl rings), 7.52–7.54 (m, 6H, *m,m′*-ArH of 2,4,5-phenyl rings), 7.66–7.68 (m, 2H, *o,o′*-ArH of 2-phenyl ring), 10.88 (s, 1H, CONH). $^{13}C$ NMR (125.75 MHz, $CDCl_3$) $\delta_C$: 10.39, 10.75, 45.90, 104.00, 105.24, 126.49, 126.70, 126.83, 127.11, 127.33, 127.92, 128.07, 128.12, 128.57, 128.74, 128.96, 129.07, 129.15, 129.18, 129.25, 129.42, 129.89, 130.13, 130.21, 130.30, 130.66, 130.87, 131.19, 134.04, 137.66, 148.37, 148.48, 171.07. LC-MS: *m/z* calcd for $C_{29}H_{26}N_4O$: 446.21; found: 447.2 $[M+H]^+$. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{29}H_{26}N_4O$: 446.2107; found: 446.5400.

*3.11. 2,2′-(Naphthalene-2,7-diylbis(oxy))bis(N-(2,5-dimethyl-1H-pyrrol-1-yl)acetamide) (**IVd**)*

mp 224–226 °C. IR (KBr, $\nu_{max}$, $cm^{-1}$): 3324, 2920, 1707, 1631, 1514, 1435, 1389, 1252, 1209, 1162, 1062, 835, 754. $^1H$ NMR (400 MHz, $CDCl_3$) $\delta_H$: 2.05 (s, 12H, $CH_3$ on pyrrole), 4.84 (s, 4H, $OCH_2$), 5.82 (s, 4H, CH on pyrrole), 7.12 (s, 2H, ArH on C1 & C8 of naphthalene ring), 7.13 (d, 2H, $J$ = 8.2 Hz, ArH on C3 & C6 of naphthalene ring), 7.78 (d, 2H, $J$ = 8.6 Hz, ArH on C4 & C5 of naphthalene ring), 8.74 (s, 2H, CONH). $^{13}C$ NMR (100.6 MHz, $CDCl_3$) $\delta_C$: 10.81, 11.15, 66.99, 103.95, 104.46, 107.20, 116.23, 125.72, 127.74, 130.04, 135.32, 155.68, 167.01. ESI-MS: *m/z* calcd for $C_{26}H_{28}N_4O_4$: 460.21; found: 460.50 $[M]^+$. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{26}H_{28}N_4O_4$: 460.2111; found: 460.5200.

*3.12. 2,2′-(4,4′-(propane-2,2-diyl)bis(4,1-phenylene)) bis(oxy)bis(N-(2,5-dimethyl-1H-pyrrol-1-yl)acetamide) (**IVe**)*

mp 170–172 °C. IR (KBr, $\nu_{max}$, $cm^{-1}$): 3237, 2971, 1689, 1506, 1435, 1246, 1210, 1182, 1068, 831, 753, 580. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 1.57–1.65 (m, 6H, $CH_3$ on bisphenol), 2.05 (s, 12H, $CH_3$ on pyrrole), 4.75 (s, 4H, $OCH_2$), 5.80 (s, 2H, CONH), 6.89 (d, 4H, $J$ = 8.4 Hz, ArH), 7.19 (d, 4H, $J$ = 8.4 Hz, ArH), 8.57 (s, 2H, CONH). $^{13}C$ NMR (125.75 MHz, $CDCl_3$) $\delta_C$: 11.36, 31.19, 41.80, 66.61, 103.55, 114.74, 127.34, 127.89, 144.00, 155.79, 168.03. ESI-MS: *m/z* calcd for $C_{31}H_{36}N_4O_4$: 528.27; found: 529.52 $[M+H]^+$. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{31}H_{36}N_4O_4$: 528.2737; found: 528.1000.

## 4. Conclusion

It may be reasonably concluded that the present procedure for the synthesis of 2,5-dimethyl-N-substituted pyrroles through a one pot condensation of 1,4-dicarbonyl compounds and substituted primary amines establishes the potential of uranyl nitrate hexahydrate $[UO_2(NO_3)_2.6H_2O]$ as a good catalyst under soft conditions/ultrasonic irradiation for such condensation reactions and gives hope for further useful applications in organic synthesis. Moreover, this methodology offers substantial advantages with respect to simplicity of operation, yield of products, reaction times, availability of catalyst, choice of substituents on the pyrrole ring, easy work-up procedure under mild reaction conditions. Pyrroles with different N-substituted heterocyclic moieties (**IVa–e)** were prepared by using uranyl nitrate hexahydrate as catalyst under reflux conditions and ultrasonic irradiation.

## Acknowledgment

Authors, express thanks to the Administration of VIT University, Vellore for providing required facilities to support this work.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ultsonch.2011.02.007.

## References

[1] R.A. Jones, G.P. Bean, The Chemistry of Pyrroles, Academic, London, 1977.
[2] A. Furstner, A catalytic approach to (*R*)-(+)-Muscopyridine with integrated "Self-Clearance", Angew. Chem, Int. Ed. 42 (2003) 3528–3532.
[3] (a) R. Ragno, G.R. Marshall, R.D. Santo, R. Costi, S. Massa, R. Rompei, M. Artico, Antimycobacterial pyrroles: synthesis, Anti- *Mycobacterium tuberculosis* activity and QSAR studies, Bioorg. Med. Chem. 8 (2000) 1423–1432;
(b) C. Franc, F. Denone, C. Cuisiner, L. Ghosez, A general synthesis of 2-formyl-3-arylpyrroles, Tetrahedron Lett. 40 (1999) 4555–4558;
(c) J.-H. Liu, Q.-C. Yang, T.C.W. Mak, H.N.C. Wong, Highly regioselective synthesis of 2 3 4-trisubstituted 1 *H* -pyrroles: A formal total synthesis of Lukianol A, J. Org. Chem. 65 (2000) 3587–3595;
(d) R.K. Dieter, H. Yu, A facile synthesis of polysubstituted pyrroles, Org. Lett. 2 (2000) 2283–2286;
(e) C.W. Jefford, K. Sienkiewicz, S.R. Thuruton, Short, Enantiospecific Syntheses of Indolizidines 209B and 209D, and Piclavine A from diethyl-L-glutamate, Helv. Chim. Acta 78 (1995) 1511–1524;
(f) R.I.J. Amos, B.S. Gourlay, P.P. Molesworth, J.A. Smith, O.R. Sprod, Annulation of pyrrole: application to the synthesis of indolizidine alkaloids, Tetrahedron 61 (2005) 8226–8230.
[4] [a] J.A. Joule, K. Mills, Heterocyclic Chemistry, fourth ed., Blackwell, Science, Oxford, 2000;
[b] F. Bellina, R. Rossi, Synthesis and biological activity of pyrrole, pyrroline and pyrrolidine derivatives with two aryl groups on adjacent positions, Tetrahedron 62 (2006) 7213–7256;
[c] M.S. Butler, The role of natural product chemistry in drug discovery, J. Nat. Prod. 67 (2004) 2141–2153;
[d] H. Hoffmann, T. Lindel, Synthesis of the pyrrole-imidazole alkaloids, Synthesis (2003) 1753–1783.
[5] (a) C.W. Jefford, Q. Tang, A. Zaslona, Short, enantiogenic syntheses of (−)-indolizidine 167B and (+)-monomorine, J. Am. Chem. Soc. 113 (1991) 3513–3518;
(b) C.W. Jefford, F.V. Naide, K. Sienkiewicz, The synthesis of chiral 1-(1H-pyrrole) derivatives, Tetrahedron: Asymmetry 7 (1996) 1069–1076;
[c] C. Bird, G.W.H. Cheeseman, Comprehensive Heterocyclic Chemistry, vol. 4, Pergamon, Oxford, 1994.
[6] F. Palacios, D. Aparico, J.M.D.L. Santos, J. Vicario, Regioselective alkylation reactions of hydrazones derived from phosphine oxides and phosphonates.

Synthesis of phosphorus substituted 1-amino-pyrrolones, Pyridinones and pyrroles, Tetrahedron 57 (2001) 1961–1972.
[7] F. Berree, E. Marchand, G. Morel, Base mediated reactions in solid-liquid media. A 1, 3-dipolar cycloaddition route to pyrrolines and pyrroles from imino chlorosulfides, Tetrahedron Lett. 33 (1992) 6155–6158.
[8] A. Katritzky, J. Jiang, P.J. Steel, L-Aza-1, 3-bis(triphenylphosphorany-1idene)propane: A Novel =CHCHzN= Synthon, J. Org. Chem. 59 (1994) 4551–4556.
[9] A. Furstner, H. Weintritt, A. Hupperts, A new, titanium-mediated approach to pyrroles: first synthesis of Lukianol A and Lamellarin *O* dimethyl ether, J. Org. Chem. 60 (1995) 6637–6641.
[10] B. Ramanathan, A.J. Keith, D. Armstrong, A.L. Odom, Pyrrole syntheses based on Titanium-catalyzed hydroamination of diynes, Org. Lett. 6 (2004) 2957–2960.
[11] G. Balme, Pyrrole syntheses by multicomponent coupling reactions, Angew. Chem, Int. Ed. 43 (2004) 6238–6241.
[12] D.J. Shaw, W.F. Wood, Preparation of 2, 5-dimethyl-1-phenylpyrrole, J. Chem. Edu. 69 (1992) A313.
[13] S. Raghavan, K. Anuradha, Solid-phase synthesis of heterocycles from 1, 4-diketone synthons, Synlett (2003) 711–713.
[14] H.S. Broadbent, W.S. Burnham, R.K. Olsen, R.M. Sheeley, Sterically-crowded pyrroles, J. Heterocyclic Chem. 5 (1968) 757–767.
[15] S.E. Drewes, C.J. Hogan, Furan derivatives from cyclodehydratign of brackein-like 1, 4-dicarbonyl compounds, Synth.Commun. 19 (1989) 2101–2107.
[16] B.K. Banik, S. Samajdar, I. Banik, Simple synthesis of substituted pyrroles, J. Org. Chem. 69 (2004) 213–216.
[17] J. Chen, H. Wu, Z. Zheng, C. Jin, X. Zhang, W. Su, An approach to the Paal–Knorr pyrroles synthesis catalyzed by $Sc(OTf)_3$ under solvent-free conditions, Tetrahedron Lett. 47 (2006) 5383–5387.
[18] B. Temelli, C. Unaleroglu, A novel method for the synthesis of dipyrromethanes by metal triflate catalysis, Tetrahedron 62 (2006) 10130–10135.
[19] B.K. Banik, I. Banik, M. Renteria, S.K. Dasgupta, A straightforward highly efficient Paal–Knorr synthesis of pyrroles, Tetrahedron Lett. 46 (2005) 2643–2645.
[20] P. Armugam, P.T. Perumal, SnCl2 2H2O-An alternative to Lewis acidic ionic liquids, Chem. Lett. 35 (2006) 632–633.
[21] J.S. Yadav, B.V.S. Reddy, B. Eeshwaraiah, M.K. Gupta, $Bi(OTf)_3$/[bmim]$BF_4$ as novel and reusable catalytic system for the synthesis of furan, pyrrole and thiophene derivatives, Tetrahedron Lett. 45 (2004) 5873–5876.
[22] M. Curini, F. Montanari, O. Rosati, E. Lioy, R. Margarita, Layered zirconium phosphate and phosphonate as heterogeneous catalyst in the preparation of pyrroles, Tetrahedron Lett. 44 (2003) 3923–3925.
[23] S.-X. Yu, P.W.L. Quesne, Quararibea metabolites. 3. Total synthesis of (±) – funebral, a rotationally restricted pyrrole alkaloid, using a novel Paal–Knorr reaction, Tetrahedron Lett. 36 (1995) 6205–6208.
[24] R. Sreekumar, R. Padmakumar, Simple, efficient and convenient synthesis of pyrroles and pyrazoles using zeolites, Synth. Commun. 28 (1998) 1661–1665.
[25] F. Texier-Boullet, B. Klein, J. Hamelin, Pyrrole and pyrazole ring closure in heterogeneous media, Synthesis (1986) 409–411.
[26] M. Kidwai, K. Singhal, S. Rastogi, Paal knorr reaction for novel pyrrolo [2, 3-d] pyrimidines, J. Heterocyclic Chem. 43 (2006) 1231–1236.
[27] G. Song, B. Wang, G. Wang, Y. Kang, T. Yang, L. Yang, $Fe^3$-Montmorillonite as effective, recyclable catalyst for Paal–Knorr pyrrole synthesis under mild conditions, Synth. Commun. 35 (2005) 1051–1057.
[28] K.D. Surya, Ruthenium (III) chloride as a novel and efficient catalyst for the synthesis of substituted pyrroles under solvent-free conditions, Catal. Lett. 124 (2008) 174–177.
[29] C.R. Brindaban, G. Sudip, D. Arijit, Zinc tetrafluoroborate-catalysed synthesis of highly substituted pyrroles by a solvent-free reaction, Mendeleev Commun. 16 (2006) 220–221.
[30] J.-X. Chen, M.-C. Liu, X.-L. Yang, J.-C. Ding, H.-Y. Wu, Indium(III)-catalyzed synthesis of *N*-substituted pyrroles under solvent-free conditions, J. Braz. Chem. Soc. 19 (2008) 877–883.
[31] S. Samajdar, F.F. Becker, B.K. Banik, Montmorillonite KSF-mediated facile synthesis of pyrroles, Heterocycles 55 (2001) 1019–1022.
[32] M. Abid, Q. Spaeth, B. Torok, Solvent-free solid acid-catalyzed electrophilic annelations: a new green approach for the synthesis of substituted five-membered N-heterocycles, Adv. Synth. Catal. 348 (2006) 2191–2196.
[33] B. Wang, C. Gu, Y.L. Luo, T. Yang, L.M. Yang, J.S. Suo, Pyrrole synthesis in ionic liquids by Paal–Knorr condensation under mild conditions, Tetrahedron Lett. 45 (2004) 3417–3419.
[34] T.N. Danks, Microwave assisted synthesis of pyrroles, Tetrahedron Lett. 40 (1999) 3957–3960.
[35] Z.-H. Zhan, J.-J. Li, T.-S. Li, Ultrasound-assisted synthesis of pyrroles catalyzed by zirconium chloride under solvent-free conditions, Ultrason. Sonochem. 15 (2008) 673–676.
[36] H. Xu, W.-M. Liao, H.-F. Li, A mild and efficient ultrasound-assisted synthesis of diaryl ethers without any catalyst, Ultrason. Sonochem. 14 (2007) 779–782.
[37] K.P. Guzen, A.S. Guarezemini, A.T.G. Orfao, R. Cella, C.M.P. Pereiraa, H.A. Stefani, Eco-friendly synthesis of imines by ultrasound irradiation, Tetrahedron Lett. 48 (2007) 1845–1848.
[38] M.A. Hayat, Principles and Techniques of Electron Microscopy, Van Nostrand Reinhold, New York, 1970.
[39] T.J. Mason, J.P. Lorimer, B.P. Mistry, The effect of ultrasound on the solvolysis of 2-chloro-2-methylpropane in aqueous ethanol, Tetrahedron 41 (1985) 5201–5204.
[40] V.S.V. Satyanarayana, P. Sreevani, A. Sivakumar, V. Vijayakumar, Synthesis and antimicrobial activity of new Schiff bases containing coumarin moiety and their spectral characterization, ARKIVOC xvii (2008) 221–233.