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Synthesis of Functionalized Pyrroles by Reaction of 3,4-Diacetylhexane-2,5-dione with Primary Amines in Water

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Abstract: 3,4-Diacetylhexane-2,5-dione (tetra-acetylethane) undergoes a complex reaction with primary amines in boiling water to produce *N*-alkyl-3-acetyl-2,5-dimethylpyrroles, together with small quantities of *N*-alkyl-3,4-diacetyl-2,5-dimethylpyrroles and 2,5-dimethyl-1*H*-pyrrol-3-yl-vinyl-acetamides. When the reaction was carried out in methanol at room temperature, the yields of the latter products increased.

Keywords: cyclization, 3,4-diacetylhexane-2,5-dione, *N*-heterocycles, Paal–Knorr, primary amine, pyrrole synthesis, water

INTRODUCTION

Simple *N*-heterocycles receive considerable attention in the literature as a consequence of their exciting biological properties and their role as pharmacophores.[1] Of these heterocycles, the synthesis, reactions, and biological activities of pyrroles stand as an area of research in heteroaromatic chemistry, and this structural motif appears in a large number of pharmaceutical agents and natural products.[2] Accordingly, many strategies have been developed for the preparation of pyrroles.[3] Despite these new developments, the classical Paal–Knorr[4] reaction remains one of the most attractive methods for the synthesis of pyrroles.[5]

In recent years, there has been increasing recognition of water as an attractive medium for many organic reactions.[6,7] The aqueous medium

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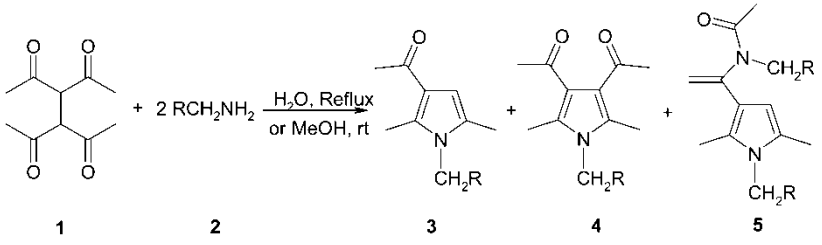
with respect to organic solvent is less expensive, less dangerous, and more environmentally friendly. Also, protection and deprotection processes in organic synthesis can be simplified in aqueous media. Water-soluble compounds can be reacted directly without the need of derivatization.

As a part of our current studies on the development of new reactions of organic compounds in water,[8] we report a convenient and facile synthesis of highly functionalized pyrrole derivatives **3**–**5** in moderate yields.

RESULTS AND DISCUSSION

The reaction between 3,4-diacetylhexane-2,5-dione (**1**) and primary amines in boiling water leads to *N*-alkyl-3,4-diacetyl-2,5-dimethylpyrroles **3**, together with variable amounts of *N*-alkyl-3-acetyl-2,5-dimethylpyrroles **4** and 2,5-dimethyl-1*H*-pyrrol-3-yl-vinyl-acetamide derivatives **5** (Scheme 1). Compound **1** is a readily available[9] polycarbonyl system, which is apparently completely enolized in solution, as indicated by NMR spectroscopy.

The reaction of **1** with primary amines **2** in boiling water was completed within 8 h. ^{1}H and ^{13}C NMR spectra of the crude reaction mixture indicated the presence of pyrrole derivatives **3**–**5**. This mixture was separated by column chromatography. The structures of compounds **3**–**5** were deduced from their elemental analyses, mass spectrometric data, and their ^{1}H NMR, ^{13}C NMR, and IR spectra. The ^{1}H NMR spectrum of **3a** exhibited five



2-5	R	%Yield of **3**	%Yield of **4**	%Yield of **5**
a	C_6H_5	71(32)	10 (48)	14(18)
b	4-Me-C_6H_4	81(28)	14(49)	12(17)
c	4-MeO-C_6H_4	81(32)	12(49)	17(16)
d	1-Naphthyl	60(28)	10(40)	— (—)
e	4-Cl-C_6H_4	80(31)	12(50)	7(18)
f	2-Cl-C_6H_4	79(20)	8(38)	5(17)
g	Me	82(35)	10(47)	4(17)

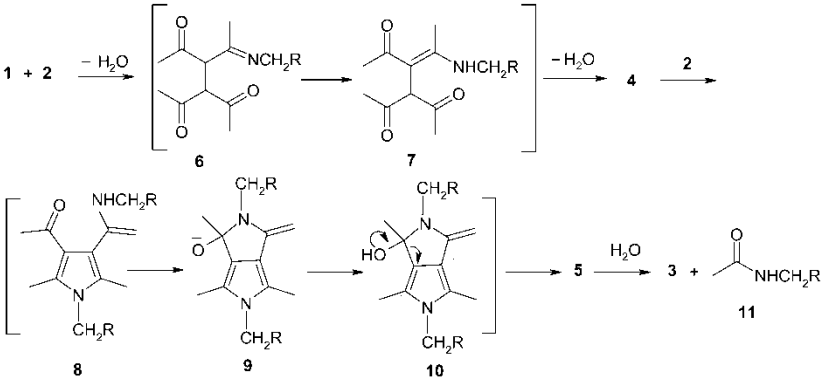
Scheme 1. Synthesis of pyrrole derivatives **3**–**5** in boiling water. The yields given in parentheses belong to the reactions performed in methanol at room temperature.

single resonances for methyl ($\delta = 2.13$, 2.40, and 2.48 ppm), methylene ($\delta = 5.04$ ppm), and methine ($\delta = 6.29$ ppm) protons. The ^{13}C NMR spectrum of **3a–g** show distinct resonances in agreement with the proposed structures. A synthesis of **3a** has been reported using a two-step sequence,[10] which involves the propargylation of secondary enaminones using *n*-BuLi and propargyl bromide, followed by intramolecular hydroamination catalyzed by silver nitrate.

The ^1H NMR spectrum of **4a** exhibited three sharp lines for CH_3 ($\delta = 2.42$ ppm), CH_3-CO ($\delta = 2.28$ ppm), and methylene ($\delta = 5.06$ ppm) protons. The phenyl moiety appeared as a multiplet at $\delta = 6.91–7.35$. The ^{13}C NMR spectrum of **4a** showed 10 signals in agreement with the proposed structure. Partial assignments of these resonances are given in the Experimental section. The ^1H NMR spectra of **4b–4g** are similar to those of **4a**. Observation of two characteristic doublets with ^2J of about 1.2 Hz in the ^1H NMR spectra of **5a–c** and **5e–g** is consistent with the presence of C=CH_2 protons. The ^{13}C NMR spectrum of **5a** exhibited 20 sharp lines in agreement with the proposed structure.

A plausible way for the formation of products **3–5** is proposed in Scheme 2. The reaction starts by formation of enaminone **7**, which is converted to pyrrole **4** by elimination of water. Compound **4** is attacked by another molecule of the amine to form enamine **8**, which undergoes intramolecular acyl-transfer reaction via **9** and **10** to produce **5**. Hydrolysis of **5** can produce **3**. In fact, the *N*-alkylacetamide derivatives **11** were isolated and characterized in some of these reactions.

In summary, the presented reactions of 3,4-diacetylhexane-2,5-dione with primary amines provide a simple entry into the synthesis of functionalized pyrroles of potential synthetic and pharmaceutical interest from readily available starting materials. The present procedure has the advantage that the reaction is performed under neutral conditions and the starting material



Scheme 2.

can be used without any activation or modification. The simplicity of the present procedure makes it an interesting alternative to complex multistep approaches.[2–5]

EXPERIMENTAL

General

Melting points were measured on a Electrothermal-9100 apparatus and are uncorrected. IR spectra were measured on a Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra were measured on a Bruker DRX-500 Avance instrument in $CDCl_3$ at 500.1 and 125.7 MHz, respectively δ in ppm, J in Hz. EI-MS (70 eV) was measured on a Finnigan-MAT-8430 mass spectrometer in m/z. Elemental analyses (C, H, N) were performed with a Heraeus CHN-O-Rapid analyzer. Primary amines were obtained from Fluka and were used without further purification. 3,4-Diacetyl-2,5-hexanedione was prepared by a known method.[9]

General Procedure for the Preparation of 3a, 4a, and 5a

To a stirred solution of 3,4-diacetyl-2,5-hexanedione (0.39 g, 2 mmol) in methanol (30 mL) the amine (4 mmol) was added dropwise and allowed to stand for 24 h. The solvent was removed under reduced pressure, and the mixture of products was obtained as yellow oil. The products were separated by silica-gel column chromatography (Merck 230–400 mesh) using *n*-hexane-EtOAc (4:1) as eluent to afford pure **4** and **5**. Compound **3** was eluted using a 7:3 mixture of *n*-hexane-EtOAc.

Typical Procedure for the Synthesis of 3a, 4a, 5a

To a stirred solution of **1** (0.39 g, 2 mmol) in water (30 mL), the amine (4 mmol) was added dropwise and refluxed for 24 h. The solvent was removed under reduced pressure, and the residue was purified by silica-gel column chromatography (Merck 230–400 mesh) using *n*-hexane-EtOAc (4:1) as eluent to afford pure **3** and **5**. Compound **4** was eluted using a 7:3 mixture of *n*-hexane–EtOAc.

Data

***N*-Benzyl-3-acetyl-2,5-dimethylpyrrole (3a).** Yellow oil,[10] yield 0.32 g, 71%. ^{1}H NMR: $\delta = 2.13$ (s, CH_3), 2.40 (s, CH_3), 2.48 (s, CH_3), 5.04 (s, CH_2), 6.29 (s, CH), 6.88–7.32 (m, 5CH). ^{13}C NMR: $\delta = 11.8$ (CH_3),

12.2 (CH_3), 28.6 (CH_3), 46.6 (CH_2), 108.4 (CH of pyrrole), 120.3, 127.8, and 135.1 (3 C of pyrrole), 125.6 (2CH), 127.5 (CH), 128.9 (2CH), 136.8 (C_{ipso}), 195.1 (C═O).

***N*-(4-Methylbenzyl)-3-acetyl-2,5-dimethylpyrrole (3b).** Cream powder, mp 58–59°C, yield 0.39 g, 81%. IR (KBr) (ν_{max}/cm^{-1}): 1635 (C═O), 1505 (C═C), 1364 (C-N). ^{1}H NMR: $\delta = 2.14$ (s, CH_3), 2.32 (s, CH_3), 2.40 (s, CH_3), 2.49 (s, CH_3), 5.00 (s, CH_2), 6.29 (s, CH), 6.7–7.1 (4H, 2d, $^3J = 7.8$, CH). ^{13}C NMR: $\delta = 11.8$ (CH_3), 12.2 (CH_3), 21.0 (CH_3), 28.6 (CH_3), 46.4 (CH_2), 108.4 (CH of pyrrole), 120.3, 127.9, and 133.8 (3C of pyrrole), 125.5 (2CH), 129.6 (2CH), 135.2 (C) 137.1 (C), 195.0 (C═O). EI-MS: 241(M^+, 5), 198 (54), 106 (40), 105 (100), 77 (20), 43 (14). Anal. calcd. for $C_{16}H_{19}NO$ (241.3): C, 79.63; H, 7.94; N, 5.80%. Found: C, 79.55; H, 7.90; N, 5.86%.

***N*-(4-Methoxybenzyl)-3-acetyl-2,5-dimethylpyrrole (3c).** Yellow oil, yield 0.42 g, 81%. IR (KBr) (ν_{max}/cm^{-1}): 1640 (C═O), 1605, 1568, and 1506 (C═C), 1367 (C-N), 1245 (C-O). ^{1}H NMR: $\delta = 2.13$ (s, CH_3), 2.39 (s, CH_3), 2.49 (s, CH_3), 3.76 (s, OCH_3), 4.96 (s, CH_2), 6.27 (s, CH), 6.82 (4H, m, 4CH). ^{13}C NMR: $\delta = 11.8$ (CH_3), 12.2 (CH_3), 28.9 (CH_3), 46.1 (CH_2), 55.2 (OCH_3), 108.4 (CH of pyrrole), 120.3, 127.8, and 130.9 (3 C of pyrrole), 126.8 (2CH), 128.7 (2CH), 132.5 (C), 159.0 (C), 194.9 (C═O). EI-MS: 257 (M^+, 6), 242 (23), 214 (43), 120 (87), 119 (100), 43 (27). Anal. calcd. for $C_{16}H_{19}NO_2$ (257.3): C, 74.68; H, 7.44; N, 5.44%. Found: C, 74.70; H, 7.53; N, 5.51%.

***N*-(1-Naphthylmethyl)-3-acetyl-2,5-dimethylpyrrole (3d).** Yellow crystals, mp 179–181°C, yield 0.33 g, 60%. IR (KBr) (ν_{max}/cm^{-1}): 1637 (C═O), 1518 (C═C), 1367 (C-N). ^{1}H NMR: $\delta = 2.13$ (s, CH_3), 2.47 (s, CH_3), 2.49 (s, CH_3), 5.49 (s, CH_2), 6.39 (s, CH), 7.32–8.02 (7H, m, 7 CH). ^{13}C NMR: $\delta = 11.6$ (CH_3), 12.0 (CH_3), 28.7 (CH_3), 44.5 (CH_2), 108.56 (CH of pyrrole), 120.6, 128.2, and 135.5 (3C of pyrrole), 121.9 (CH), 122.2 (CH), 125.8 (CH), 126.1 (CH), 126.6 (CH), 128.0 (CH), 129.1 (CH), 130.7 (C), 132.1 (C), 133.5 (C), 197.5 (C═O). EI-MS: 278 ($M^+ + 1$, 10), 277 (M^+, 8), 149 (100), 141 (92), 71 (80), 57 (54), 43 (21). Anal. calcd. for $C_{19}H_{19}NO$ (277.4): C, 82.28; H, 6.90; N, 5.05%. Found: C, 82.41; H, 6.98; N, 5.11%.

***N*-1-(4-Chlorobenzyl)-3-acetyl-2,5-dimethylpyrrole (3e).** Yellow crystals, mp 88–90°C, yield 0.42 g, 80%. IR (KBr) (ν_{max}/cm^{-1}): 1641 (C═O), 1565 and 1512 (C═C), 1347 (C-N). ^{1}H NMR: $\delta = 2.11$ (s, CH_3), 2.39 (s, CH_3), 2.46 (s, CH_3), 5.00 (s, CH_2), 6.29 (s, CH), 6.8–7.2 (4H, 2d, $^3J = 7.8$, CH). ^{13}C NMR: $\delta = 11.7$ (CH_3), 12.1 (CH_3), 28.6 (CH_3), 46.6 (CH_2), 108.6 (CH of pyrrole), 120.3, 127.7, and 135.4 (3C of pyrrole), 120.5 (C), 127.0 (2CH), 129.1 (2CH), 134.8 (C), 195.0 (C═O). EI-MS: 261 (M^+,

2), 247 (12), 219 (40), 127 (100), 43 (32). Anal. calcd. for $C_{15}H_{16}ClNO$ (261.7): C, 68.83; H, 6.16; N, 5.35%. Found: C, 68.94; H, 6.21; N, 5.41%.

***N*-1-(2-Chlorobenzyl)-3-acetyl-2,5-dimethylpyrrole (3f).** Cream powder, mp 65–70°C, yield 0.41 g, 79%. IR (KBr) (ν_{max}/cm^{-1}): 1642 (C=O), 1518 (C=C), 1340 (C-N). ^1H NMR: $\delta = 2.10$ (s, CH_3), 2.41 (s, CH_3), 2.44 (s, CH_3), 5.06 (s, CH_2), 6.32 (s, CH), 6.26 (1H, d, $^3J = 7.62$, CH), 7.12–7.40 (3H, m, 3CH). ^{13}C NMR: $\delta = 11.6$ (CH_3), 11.9 (CH_3), 28.6 (CH_3), 44.6 (CH_2), 108.6 (CH of pyrrole), 120.6, 127.8, 131.7 (3C of pyrrole), 126.4 (CH), 127.5 (CH) 128.7 (CH), 129.4 (CH), 134.4 (C), 135.1 (C), 195.0 (C=O). EI-MS: 261 (M^+, 4), 247 (18), 219 (51), 127 (100), 43 (22). Anal. calcd. for $C_{15}H_{16}ClNO$ (261.7): C, 68.83; H, 6.16; N, 5.35%. Found: C, 69.03; H, 6.21; N, 5.40%.

***N*-Ethyl-3-acetyl-2,5-dimethylpyrrole (3g).** Yellow oil, yield 0.27 g, 82%. IR (KBr) (ν_{max}/cm^{-1}): 1630 (C=O), 1563 and 1509 (C=C), 1370 (C-N). ^1H NMR: $\delta = 1.25$ (t, $^3J = 11.8$, CH_3), 2.22 (s, CH_3), 2.35 (s, CH_3), 2.54 (s, CH_3), 3.85 (2H, q, $^3J = 11.8$, CH_2), 6.20 (s, CH). ^{13}C NMR: $\delta = 11.6$ (CH_3), 12.0 (CH_3), 15.5 (CH_3), 28.4 (CH_3), 38.0 (CH_2), 108.2 (CH of pyrrole), 120.0, 126.8 and 134.2 (3C of pyrrole), 194.8 (C=O). EI-MS: 165 (M^+, 30), 150 (100), 122 (30), 43 (36). Anal. calcd. for $C_{10}H_{15}NO$ (165.2): C, 72.69; H, 9.15; N, 8.48. Found: C, 72.54; H, 9.12; N, 8.42%.

***N*-Benzyl-3,4-diacetyl-2,5-dimethylpyrrole (4a).** Brown crystals, mp 101–103°C, yield 0.05 g, 10%. IR (KBr) (ν_{max}/cm^{-1}): 1637 (C=O), 1516 (C=C), 1370 (C-N). ^1H NMR: $\delta = 2.28$ (s, $2CH_3$), 2.42 (s, $2CH_3$), 5.06 (s, CH_2), 6.91–7.35 (5H, m, 5CH). ^{13}C NMR: $\delta = 11.3$ ($2CH_3$), 31.3 ($2CH_3$), 46.9 (CH_2), 123.4 and 132.3 (4C of pyrrole), 125.5 (2CH), 127.8 (CH), 129.1 (2 CH), 135.8 (C_{ipso}), 197.6 (2C=O). EI-MS: 269 (M^+, 6), 254 (43), 226 (39), 183 (32), 91 (76), 90 (100), 43 (78). Anal. calcd. for $C_{17}H_{19}NO_2$ (269.3): C, 75.81; H, 7.11; N, 5.20. Found: C, 75.86; H, 7.08; N, 5.24%.

***N*-(4-Methylbenzyl)-3,4-diacetyl-2,5-dimethylpyrrole (4b).** Cream powder, mp 117–118°C, yield 0.08 g, 14%. IR (KBr) (ν_{max}/cm^{-1}): 1663 (C=O), 1628 and 1506 (C=C), 1347 (C-N). ^1H NMR: $\delta = 2.23$ (s, $2CH_3$), 2.28 (s, CH_3), 2.36 (s, $2CH_3$), 4.98 (s, CH_2), 6.77–7.08 (4H, 2d, $^3J = 7.7$, 4CH). ^{13}C NMR: $\delta = 11.3$ ($2CH_3$), 21.0 ($2CH_3$), 31.2 (CH_3), 46.7 (CH_2), 123.3 and 132.3 (4C of pyrrole), 132.9 (C), 137.4 (C), 125.5 (2CH), 129.7 (2CH), 197.4 (2C=O). EI-MS: 283 (M^+, 5), 268 (54), 240 (77), 198 (32), 105 (100), 43 (82). Anal. calcd. for $C_{18}H_{21}NO_2$ (283.4): C, 76.30; H, 7.47; N, 4.94. Found: C, 76.36; H, 7.54; N, 4.90%.

***N*-(4-Methoxybenzyl)-3,4-diacetyl-2,5-dimethylpyrrole (4c).** Yellow powder, mp 65–67°C, yield 0.07 g, 12%. IR (KBr) (ν_{max}/cm^{-1}): 1656 (C=O), 1631 and 1505 (C=C), 1347(C-N), 1243 (C-O). ^1H NMR:

$\delta = 2.23$ (s, $2CH_3$), 2.35 (s, $2CH_3$), 3.72 (s, OCH_3), 4.95 (s, CH_2), 6.80 (4H, m, 4CH). ^{13}C NMR: $\delta = 11.3$ ($2CH_3$), 31.2 ($2CH_3$), 46.4 (CH_2), 55.3 (OCH_3), 114.5 (2CH), 126.8 (2CH), 123.4 and 129.1 (4C of pyrrole), 132.3 (C), 159.1 (C), 197.5 (2C═O). EI-MS: 300 (M^++1, 10), 179 (60), 136 (100), 57 (84), 43 (80). Anal. calcd. for $C_{18}H_{21}NO_3$ (299.4): C, 72.22; H, 7.07; N, 4.68%. Found: C, 72.68; H, 7.00; N, 4.69%.

***N*-(1-Naphthylmethyl)-3,4-diacetyl-2,5-dimethylpyrrole (4d).** Yellow powder, mp 165–167°C, yield 0.06 g, 10%. IR (KBr) (ν_{max}/cm^{-1}): 1640 (C═O), 1517, 1405 (C═C), 1347 (C-N). ^{1}H NMR: $\delta = 2.27$ (s, $2CH_3$), 2.46 (s, $2CH_3$), 5.49 (s, CH_2), 7.34–8.00 (7 H, m, 7 CH) ^{13}C NMR: $\delta = 11.2$ ($2CH_3$), 31.3 ($2CH_3$), 44.8 (CH_2), 122.1 (CH), 125.8 (CH), 126.3 (CH), 126.8 (CH), 128.3 (CH), 129.2 (CH), 128.8 (C), 129.9 (C), 130.9 (CH), 131.1 (C), 121.8 and 131.07 (4C of pyrrole), 197.5 (2C═O). EI-MS: 319 (M^+, 5), 141 (100), 115 (78), 43 (45). Anal. calcd. for $C_{21}H_{21}NO_2$ (319.4): C, 78.97; H, 6.63; N, 4.39%. Found: C, 78.86; H, 6.72; N, 4.37%.

***N*-1-(4-Chlorobenzyl)-3-acetyl-2,5-dimethylpyrrole (4e).** Yellow crystals, mp 65–67°C, yield 0.07 g, 12%. IR (KBr) (ν_{max}/cm^{-1}): 1641 (C═O), 1600 (C═C), 1380 (C-N). ^{1}H NMR: $\delta = 2.27$ (s, $2CH_3$), 2.41 (s, $2CH_3$), 5.03 (s, CH_2), 6.8–7.3 (4H, 2d, 2CH). ^{13}C NMR: $\delta = 11.3$ ($2CH_3$), 31.2 ($2CH_3$), 46.3 (CH_2), 123.6 and 134.5 (4C of pyrrole), 127 and 129.3 (4CH), 132.0 (C), 133.7 (C), 197.5 (2C═O). EI-MS: 304 (M^+, 9), 289 (67), 261 (67), 219 (45), 126 (100), 43 (53). Anal. calcd. for $C_{17}H_{18}$ $ClNO_2$ (303.8): C, 67.21; H, 5.97; N, 4.61%. Found: C, 67.41; H, 6.04; N, 4.73%.

***N*-1-(2-Chlorobenzyl)-3,4-diacetyl-2,5-dimethylpyrrole (4f).** White powder, mp 143–147°C, yield 0.05 g, 8%. IR (KBr) (ν_{max}/cm^1): 1676 (C═O), 1629 and 1507 (C═C), 1346 (C-N). ^{1}H NMR: $\delta = 2.25$ (s, 2 CH_3), 2.43 (s, $2CH_3$), 5.09 (s, CH_2), 6.35 (d, $^3J = 7.6$, CH,), 7.18–7.43 (3H, m, 3CH). ^{13}C NMR: $\delta = 11.2$ ($2CH_3$), 31.3 ($2CH_3$), 44.8 (CH_2), 123.6 and 132.2 (4C of pyrrole), 126.3 (CH), 127.7 (CH), 129.1 (CH), 129.6 (CH), 131.1 (C), 133.4 (C), 197.5 (2C═O). EI-MS: 304 (M^+, 7), 289 (60), 261 (56), 219 (41), 126 (100), 43 (58). Anal. calcd. for $C_{17}H_{18}$ $ClNO_2$ (303.8): C, 67.21; H, 5.97; N, 4.61%. Found: C, 67.44; H, 6.03; N, 4.72%.

***N*-Ethyl-3,4-diacetyl-2,5-dimethylpyrrole (4g).** White powder, mp 85–90°C, yield 0.04 g, 10%. IR (KBr) (ν_{max}/cm^{-1}): 1659 (C═O), 1629 and 1589 (C═C), 1390 (C-N). ^{1}H NMR: $\delta = 1.27$ (t, $^3J = 7.3$ Hz, CH_3), 2.35 (s, $2CH_3$), 2.38 (s, $2CH_3$), 3.85 (q, $^3J = 7.3$, CH_2). ^{13}C NMR: $\delta = 11.1$ ($2CH_3$), 15.4 ($2CH_3$), 31.3 (CH_3), 38.38 (CH_2), 123.2 and 131.3 (4C of pyrrole), 197.6 (2 C═O). EI-MS: 208 ($M^+ + 1$, 5), 207 (M^+, 10), 192 (100), 164 (70), 122 (50), 43 (90). Anal. calcd. for $C_{12}H_{17}NO_2$ (207.3): C, 69.54; H, 8.27; N, 6.76%. Found: C, 69.60; H, 8.30; N, 6.78%.

N^1-Benzyl-N^1-[1-(1-benzyl-2,5-dimethyl-1H-pyrrol-3-yl)vinyl]acetamide (5a). Yellow oil, yield 0.14 g, 14%. IR (KBr) (ν_{max}/cm^{-1}): 1637 (C=O), 1600 shoulder (C=C), 1386 (C-N). ^{1}H NMR: $\delta = 2.10$ (s, CH_3), 2.14 (s, CH_3), 2.18 (s, CH_3), 4.64 (s, CH_2), 5.03 (s, CH_2), 4.66 (d, $^2J = 1.2$, =CH), 5.00 (d, $^2J = 1.2$, =CH), 5.84 (s, CH of pyrrole), 6.80–7.30 (10H, m, 10 CH). ^{13}C NMR: $\delta = 10.9$ (CH_3), 12.2 (CH_3), 22.3 (CH_3), 46.6 (CH_2), 49.5 (CH_2), 105.7 (CH of pyrrole), 108.5 (C=*C*H_2), 116.3, 126.9. and 128.3 (3C of pyrrole), 125.5 (2CH), 127.0 (CH), 127.3 (2CH), 128.1 (2CH), 128.9 (2CH), 129.0 (CH), 138.1 (C_{ipso}), 137.8 (C_{ipso}), 142.9 (CH_2=*C*), 170.7 (C=O). EI-MS: 359 ($M^+ + 1$, 7), 344 (17), 316 (38), 273 (36), 268 (40), 91 (87), 90 (100), 43 (52). Anal. calcd. for $C_{24}H_{26}N_2O$ (358.5): C, 80.41; H, 7.31; N, 7.81%. Found: C, 80.50; H, 7.33; N, 7.86%.

N^1-{1-[2,5-Dimethyl-1-(4-methylbenzyl)-1H-pyrrole-3-yl]vinyl}-N^1-(4-methylbenzyl)acetamide (5b). Yellow oil; yield 0.13 g, 12%. IR (KBr) (ν_{max}/cm): 1643 (C=O), 1507 (C=C), 1367 (C-N). ^{1}H NMR: $\delta = 2.10$ (s, CH_3), 2.14 (s, CH_3), 2.18 (s, CH_3), 2.40 (s, CH_3), 2.49 (s, CH_3), 4.60 (s, CH_2), 5.03 (s, CH_2), 4.66 (d, $^2J = 1.2$, =CH), 5.00 (d, $^2J = 1.2$, =CH), 5.84 (s, CH of pyrrole), 6.8–7.3 (8H, m, 8CH). ^{13}C NMR: $\delta = 11.8$ (CH_3), 12.2 (CH_3), 21.1 (CH_3), 23.3 (CH_3), 28.6 (CH_3), 43.6 (CH_2), 46.4 (CH_2), 108.3 (CH of pyrrole), 108.5 (C=*C*H_2), 120.1, 127.9 and 129.01 (3C of pyrrole), 125.5 (2CH), 127.9 (2CH), 129.4 (2CH), 129.5 (2CH), 135.2 (C), 133.7 (C), 137.2 (C), 137.3 (C), 148 (CH_2=*C*), 170.0 (C=O). EI-MS: 387 ($M^+ + 1$, 6), 372 (14), 344 (32), 302 (28), 282 (21), 177 (18), 105 (100), 43 (67). Anal. calcd. for $C_{26}H_{30}N_2O$ (386.5): C, 80.79; H, 7.82; N, 7.25%. Found: C, 80.85; H, 7.76; N, 7.31%.

N^1-(4-Methoxybenzyl)-N^1-{1-[1-(4-methoxybenzyl)-2,5-dimethyl-1*H*-pyrrol]vinyl}acetamide (5c). Yellow oil, yield 0.13 g, 17%. IR (KBr) (ν_{max}/cm^{-1}): 1637 (C=O), 1610 and 1504 (C=C), 1375 (C-N), 1244 (C-O). ^{1}H NMR: $\delta = 2.10$(s, CH_3), 2.14 (s, CH_3), 2.15 (s, CH_3), 3.77 (s, OCH_3), 3.78 (s, OCH_3), 4.62 (s, CH_2), 5.00 (s, CH_2), 4.57 (d, $^2J = 1.2$, =CH), 4.97 (d, $^2J = 1.2$, =CH), 5.83 (s, CH), 6.78–6.86 (m, 8CH). ^{13}C NMR: $\delta = 11.0$ (CH_3), 12.3 (CH_3), 22.3 (CH_3), 55.2 (OCH_3), 55.3 (OCH_3), 46.3 (CH_2), 49.5 (CH_2), 105.7 (CH of pyrrole), 111.1 (C=*C*H_2), 128, 129.8, and 129.9 (3C of pyrrole), 113 (2CH), 114.3 (2CH), 126.7 (2CH), 126.8 (2CH), 129.8 (C), 130.4 (C), 158.9, 158.7 (2CO), 142.0 (CH_2=*C*), 170.6 (C=O). EI-MS: 419 ($M^+ + 1$, 5), 404 (11), 376 (18), 334 (24), 179 (86), 149 (100), 136 (90), 121 (79), 57 (90), 43 (38). Anal. calcd. for $C_{26}H_{30}N_2O_3$ (418.5): C, 74.61; H, 7.22; N, 6.69%. Found: C, 74.43; H, 7.31; N, 6.72%.

N^1-(4-Chlorobenzyl)-N^1-{1-[1-(4-chlorobenzyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]vinyl}acetamide (5e). Yellow oil, yield 0.14 g, 7%. IR (KBr) (ν_{max}/cm^{-1}): 1648 (C=O), 1514 (C=C), 1349 (C-N). ^{1}H NMR: $\delta = 2.07$ (s, CH_3), 2.12 (s, CH_3), 2.17 (s, CH_3), 4.58 and 5.02 (2s, $2CH_2$), 4.65 (d, $^2J = 1.2$, =CH),

4.99 (d, $^2J = 1.2$, =CH), 5.83 (s, CH), 6.81–7.30 (8H, m, 8CH). ^{13}C NMR: $\delta = 11.0$ (CH_3), 12.2 (CH_3), 22.2 (CH_3), 46.3 (CH_2), 48.8 (CH_2), 105.9 (CH of pyrrole), 111.4 (*C*H_2=C), 116.3, 126.7, and 136.5 (3C of pyrrole), 126.7 (2CH), 126.9 (2CH), 128.3 (2CH), 129.1 (2CH), 130.4 (C), 132.9 (C), 133.3 (C), 136.3 (C), 142.7 (CH_2=*C*), 170.0 (C=O). EI-MS: 428 ($M^+ + 1$, 5), 413 (16), 385 (32), 343 (25), 127 (43), 125 (100), 57 (74), 43 (51). Anal. calcd. for $C_{24}H_{24}Cl_2N_2O$ (427.4): C, 67.45; H, 5.66; N, 6.55%. Found: C, 67.65; H, 5.72; N, 6.59%.

***N*^{1}-(2-Chlorobenzyl)-*N*^{1}-{1-[1-(2-chlorobenzyl)-2,5-dimethyl-1*H*-pyrrol-3-yl] vinyl} acetamide (5f).** Brown oil, yield 0.14 g, 5%. IR (KBr) (ν_{max}/cm^{-1}): 1644 (C=O), 1514 and 1427 (C=C), 1371 (C-N). ^{1}H NMR: $\delta = 2.04$ (s, CH_3), 2.10 (s, CH_3), 2.26 (s, CH_3), 4.84 (s, CH_2), 5.05 (s, CH_2), 4.82 (d, $^2J = 1.2$, =CH), 4.99 (d, $^2J = 1.2$, =CH), 5.87 (s, CH), 6.27 (d, CH, ^3J=7.5 Hz), 7.16–7.40 (7H, m, 7CH). ^{13}C NMR: $\delta = 11.6$ (CH_3), 11.9 (CH_3), 28.6 (CH_3), 41.6 (CH_2), 44.6 (CH_2), 108.6 (CH of pyrrole), 111.2 (*C*H_2=C), 115.3, 126.6, and 127.5 (3C of pyrrole), 127.2 (CH), 127.8 (CH), 128.3 (CH), 128.6 (CH), 128.7 (CH), 129.0 (CH), 129.3 (CH), 130.4 (CH), 129.2 (C), 129.4 (C), 129.5 (C), 134.4 (C), 142.0 (CH_2=*C*), 170.0 (C=O). EI-MS: 428 ($M^+ +$ 1, 6), 413 (13), 385 (45), 343 (23), 127 (51), 125 (100), 57 (47), 43 (60). Anal. calcd. for $C_{24}H_{24}Cl_2N_2O$ (427.4): C, 67.45; H, 5.66; N, 6.55%. Found: C, 67.54; H, 5.71; N, 6.63%.

***N*-Ethyl-*N*-[1-(1-ethyl-2,5-dimethyl-1*H*-pyrrol-3-yl)vinyl]-acetamide (5g).** Yellow oil, yield 0.08 g, 4%. IR (KBr) (ν_{max}/cm^{-1}): 1643 (C=O), 1610 and 1510 (C=C), 1380 shoulder (C-N). ^{1}H NMR: $\delta = 1.10$ (t, $^3J = 7.1$, CH_3), 1.25 (t, $^3J = 7.2$, CH_3), 2.10 (s, CH_3), 2.2 (s, CH_3), 2.25 (s, CH_3), 3.46 (q, $^2J = 7.1$, CH_2), 3.82 (q, $^2J = 3.27$, CH_2), 4.86 (d, $^2J = 1.2$, =CH), 5.12 (d, $^2J = 1.2$, =CH), 5.78 (s, CH). ^{13}C NMR: $\delta = 10.9$ (CH_3), 12.1 (CH_3), 12.9 (CH_3), 15.9 (CH_2), 22.3 (CH_2), 38.2 (CH_3), 40.6 (CH_3), 105.4 (CH of pyrrole), 109.5 (C=*C*H_2), 115.8, 125.6 and 127.2 (3C of pyrrole), 138.0 (CH_2=*C*), 170.3 (C=O). EI-MS: 235 ($M^+ + 1$, 8), 220 (32), 192 (43), 159 (21), 57 (65), 43 (100), 28 (54). Anal. calcd. for $C_{14}H_{22}N_2O$ (234.3): C, 71.76; H, 9.46; N, 11.95%. Found: C, 71.84; H, 9.60; N, 12.02%.

***N*^{1}-(Naphthylmethyl)acetamide (11d).** White powder, mp 155–157°C, yield 0.11 g, 30%. IR (KBr) (ν_{max}/cm^{-1}): 3440 (NH), 1622 (C=O), 1539 and 1501 (C=C). ^{1}H NMR (CD_3OD): $\delta = 1.9$ (s, CH_3), 4.6 (s, CH_2), 7.51–8.11 (m, 7CH).

***N*^{1}-(2-Chlorobenzyl)acetamide (11f).** Cream powder, mp 126–128°C, yield 0.07 g, 20%. IR (KBr) (ν_{max}/cm^{-1}): 3440 (NH), 1510, shoulder (C=O). ^{1}H NMR (CD_3OD): $\delta = 1.89$ (s, CH_3), 4.19 (s, CH_2), 7.37–7.53 (m, 4CH).

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