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FULL-LENGTH PAPER

Synthesis of new 1,5-diaryl-3-(arylamino)-1*H*-pyrrol-2(5*H*)-ones under catalyst-free and solvent-free conditions

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Abstract Several new 1,5-diaryl-3-(arylamino)-1*H*-pyrrol-2(5*H*)-ones were synthesized *via* the three-component condensation reaction of aldehydes, aromatic amines, and ethyl pyruvate under catalyst-free and solvent-free conditions. Also, 5-(4-hydroxyl-3-nitrophenyl)-1-(4-methoxy-phenyl)-3-(4-methoxyphenylamino)-1,5-dihydro-pyrrol-2-one was synthesized using oxime instead of aldehyde. The eco-friendly, simple procedure, green procedure, catalyst-free and solvent-free conditions, short reaction times, and high yields of the products are the advantages of this method.

Keywords 1*H*-Pyrrol-2(5*H*)-ones · Catalyst-free · Lactams · Solvent-free · MCRs · MCC · 4MCR

Introduction

Lactams, particularly pyrrole derivatives, are important structural motifs found in many natural products, synthetic pharmaceuticals, and molecular materials [1,2]. Among them, 3-arylaminopyrroline-2-one derivatives have shown biological activity, antimicrobial activity, and electroconvulsive shock (ECS)-induced amnesia reversing activity in mice [1–7].

3-Arylaminopyrroline-2-ones were synthesized *via* three-component condensation reaction of pyruvic acid derivatives, anilines, and aldehydes, in which sometimes processes and synthesies were preformed for imines or β, γ-unsaturated α-ketoesters [3,4,8]. Vaughan and Tripp synthesized 1,5-diary1-2,3-pyrrolidinediones by the condensation of anilines with pyrrolidine-2,3-diones or furan-2(5*H*)-ones [9]. Wu and co-workers reported a convenient preparation of 3-aryl-aminopyrroline-2-ones by the reaction between anilines and β, γ-unsaturated α-ketoesters in boiling dichloromethane [10]. Recently, the synthesis of 1,5-diaryl-3-(arylamino)-1*H*-pyrrol-2(5*H*)-ones was reported to take place by condensation reaction between anilines, aldehyde, and ethyl pyruvate using H_2SO_4 [11], different thioureas, phosphoric acid analogues [12], or SiO_2-$FeCl_3$ as catalysts [13]. However, all these methods suffer from long reaction times and the use of toluene, a solvent recognized for its toxicity. Therefore, there is still demand for more efficient synthetic strategies to provide these compounds.

We report here the synthesis of 1,5-diaryl-3-(arylamino)-1*H*-pyrrol-2(5*H*)-ones via three-component condensation reaction of aldehydes, amines, and ethyl pyruvate under catalyst- and solvent-free conditions (Scheme 1).

Results and discussion

The reaction of benzaldehyde, 4-methyl aniline, and ethyl pyruvate was studied as a model reaction, and the effects of solvents, catalyst loading, and reaction conditions were evaluated (Scheme 2; Tables 1, 2).

As shown in Table 1, different solvents [*n*-hexane (bp 69 °C), dichloromethane (bp 39 °C), chloroform (bp 61 °C), and ethanol (bp 78 °C)], and solvent-free conditions were studied under catalyst-free conditions. The best conditions were found to be solvent-free at 80 °C.

The effect of solid silica-supported acids and bases were investigated (Table 2; Scheme 3). Solid silica-supported

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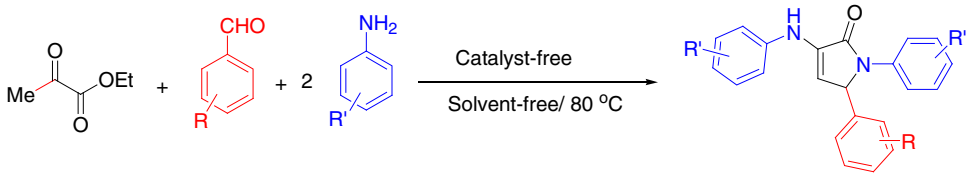
Scheme 1 Synthesis of 1,5-diaryl-3-(arylamino)-1*H*-pyrrol-2(5*H*)-one derivatives



Scheme 2 Preparation of 3-(*p*-toluidino)-5-phenyl-1-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one

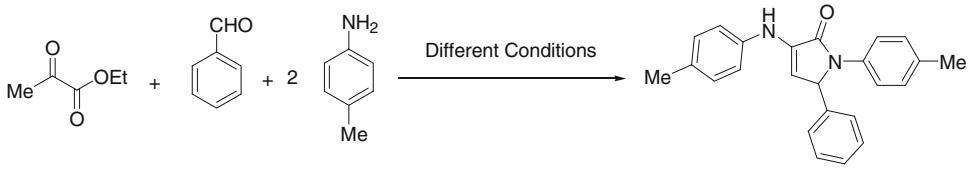


Table 1 Optimization of the reaction conditions for the synthesis of 3-(*p*-toluidino)-5-phenyl-1-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one under catalyst-free conditions

Entry	Solvent	Conditions	Time (min)	Yield (%)[a]
1	*n*-Hexane	Reflux (69 °C)	100	50
2	Chloroform	Reflux (61 °C)	160	35
3	Dichloromethane	Reflux (40 °C)	160	20
4	Ethanol	Reflux (78 °C)	90	20
5	Solvent-free	rt	120	–
6	Solvent-free	70 °C	40	80
7	Solvent-free	80 °C	20	91
8	Solvent-free	100 °C	17	91

Rection conditions ethyl pyruvate (1 mmol), *p*-toluidine (2 mmol), benzaldehyde (1 mmol), and solvent (4 mL)
[a] Isolated product

Table 2 Influence of solid silica-supported acids and bases on our solvent-free reaction

Entry	Catalyst	Amount of catalyst (g)	Time (min)	Yield (%)[b]
1	**1**	0.008	15	90
2	**1**	0.01	15	87
3	**1**	0.03	15	85
4	**2**	0.008	15	86
5	**4**	0.008	15	93
6	**3**	0.05	15	93
7	**5**	0.075	25	90
8	**6**	0.05	25	87
9	**7**	0.05	25	85
10	Catalyst-free	–	20	91

Rection conditions: ethyl pyruvate (1 mmol), *p*-toluidine (2 mmol), benzaldehyde (1 mmol), and solvent-free conditions at 100 °C
[b] Isolated product

bases such as silica-bonded *N*-propylpiperazine sodium *N*-propionate (**1**) [14], silica-bonded *N*-propylpiperazine (**2**) [15,16], silica-bonded *N*-propyl morpholine (**3**) [17], and silica-bonded *N*-propyl-triethylenetetramine (**4**) [18] were examined in the model reaction as catalyst. As shown in Table 2, the catalytic amounts of 0.008 g for catalysts **1**,**2**, and **4**; and 0.05 g for **3** at 100 °C gave the corresponding products in the range of 85–93 solvent-free conditions.

Solid silica-supported acids such as silica-bonded *N*-propyl-triethylenetetramine sulfamic acid (**5**) [19], silica-bonded *S*-sulfonic acid (**6**) [20], and silica-bonded *N*-propyl sulfamic acid (**7**) [21] were used as catalysts in model reaction. The catalytic amounts of 0.075 g of catalyst **5** and 0.05 g for catalysts **6** and **7** gave the corresponding products in 90, 87, and 85 % yields, respectively, at 100 °C and under solvent-free conditions (Table 2, entries 7–9). The optimum reaction condition is as follows: aldehyde (1 mmol), anilines (2 mmol), ethyl pyruvate (1 mmol), temperature = 80 °C, no catalyst, and solvent-free.

As shown in Table 3, this three-component condensation reaction proceeded with different substituted aromatic aldehydes and aniline derivatives under the optimized condition. Aromatic aldehydes containing electron-donating groups or electron-withdrawing groups gave corresponding products in high yields (Table 3). Butyraldehyde, the only aliphatic aldehyde tested, gives desired product in 90 % yield (Table 3, entry 12).

3-Pyridine carbaldehyde, the only heterocyclic aldehyde tested, also gave the required product in 90 % yield (Table 3, entry 13). As for anilines, those bearing electron-donating and electron-withdrawing groups gave products with high and lower yields, respectively (Table 3).

We would like to mention that when we used 4-hydroxy-3-nitro-benzyl oxime instead of the corresponding aldehyde and treated with ethyl pyruvate and 4-methoxy-aniline, the expected product 5-(hydroxyl-3-nitrophenyl)-1-(4-methoxy-phenyl)-3-(4-methox-yphenylamino)-1,5-dihydro-pyrrol-2-one was obtained after 25 min in 40 % yield. This confirms that aldehydes are the better substrates than the corresponding oximes in such a three-component condensation reactions.

In conclusion, we present, in this study, the synthesis of 1,5-diaryl-3-(arylamino)-1*H*-pyrrol-2(5*H*)-ones that

Scheme 3 The structures of solid bases and acids used as catalysts

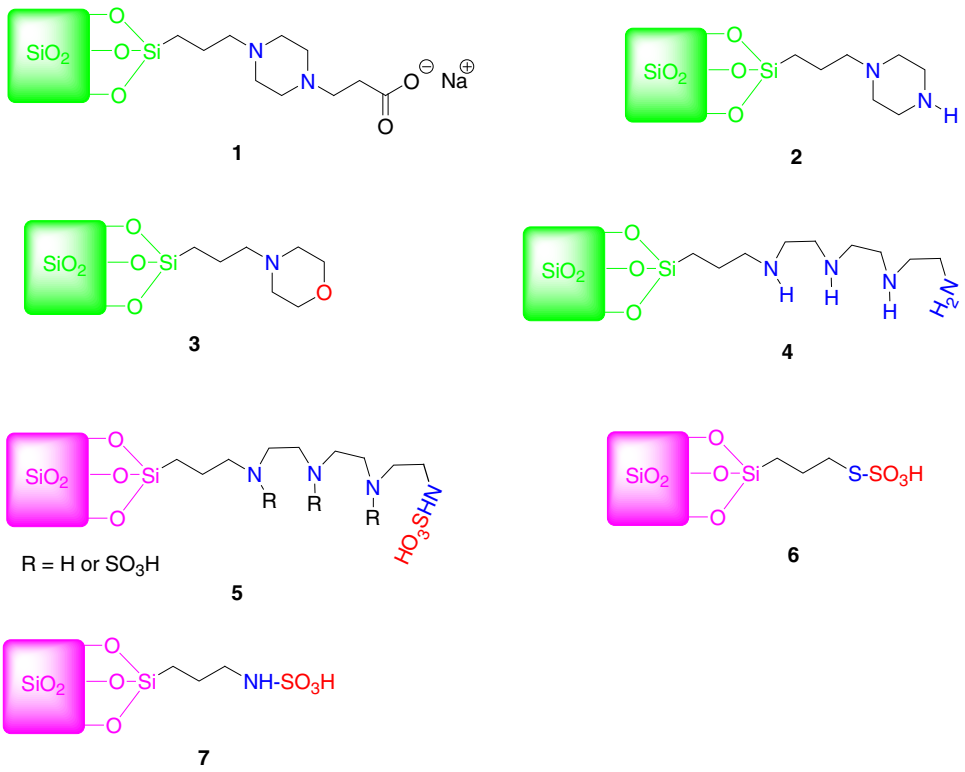


Table 3 Synthesis results using optimized reaction conditions

Entry	R-CHO	Ar-NH_2	Time (min)	Yield (%)[a]
1	C_6H_5–	C_6H_5–	20	90
2	3–Cl–C_6H_4–	4–MeO-C_6H_4–	15	93
3	4–Cl–C_6H_4–	4–MeO–C_6H_4–	30	67
4	4–Br–C_6H_4–	4–MeO–C_6H_4–	25	35
5	C_6H_5–	4–Me–C_6H_4–	20	91
6	4–MeO–C_6H_5–	4–Me–C_6H_4–	40	65
7	4–O_2N–C_6H_5–	4–Me-C_6H_4–	20	70
8	C_6H_5–	3–Cl–C_6H_4–	35	90
9	C_6H_5–	4-Cl–C_6H_4–	25	93
10	C_6H_5–	4–Br–C_6H_4–	27	95
11	4–MeO–C_6H_5–	3–O_2N–C_6H_5–	65	45
12	$CH_3CH_2CH_2$–	4–MeO–C_6H_4–	30	90
13	3–C_5H_4N–	4–MeO–C_6H_4–	15	90
14	C_6H_5–	3,4–$(Me)_2$–C_6H_3–	15	70
15	4–MeO–C_6H_5–	3,4–$(Me)_2$–C_6H_3–	45	68

[a] Isolated yield

were prepared by a three-component condensation reaction of aldehydes, aromatic amines, and ethyl pyruvate under catalyst-free and solvent-free conditions in good-to-high yields. This simple and green procedure, under catalyst-free and solvent-free conditions and much shorter reaction times, represents the advantages of this method.

Experimental

General

Chemicals were purchased from Fluka, Merck and Aldrich Chemical Companies and used as received. ^{1}H-NMR spectra were recorded on a Bruker Ultrashield (400 MHz) using $CDCl_3$ as deuterated solvent and with tetramethylsilane (TMS) as internal standard. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at 70 eV. Melting points were determined in open capillary tubes in a Barnstead Electrothermal 9100 BZ circulating oil melting point apparatus and uncorrected. Reactions were monitored by TLC using silica gel Poly Gram SILG/UV254 plates. All the products were characterized by IR, NMR, Mass spectra, and known compounds and compared to those reported in the literature [10–13]. Solid silica-supported bases such as silica-bonded *N*-propylpiperazine sodium *N*-propionate (**1**) [14], silica-bonded *N*-propylpiperazine (**2**) [15,16], silica-bonded *N*-propylmorpholine (**3**) [17], and silica-bonded *N*-propyl-triethylenetetramine (**4**) [18]; and solid silica-supported acids such as silica-bonded *N*-propyl-triethylenetetramine sulfamic acid (**5**) [19], silica-bonded *S*-sulfonic acid (**6**) [20], and silica-bonded *N*-propyl sulfamic acid (**7**) [21], were prepared according to our reported procedures.

General procedure for the synthesis of 1,5-diaryl-3-(arylamino)-1H -pyrrol-2(5H)-ones

A mixture of aldehyde (1 mmol), aromatic amine (2 mmol), and ethyl pyruvate (1 mmol) was heated with stirring in an oil bath at 80 °C under catalyst-free and solvent-free conditions. The progress of the reaction was monitored by TLC. After completion of the reaction, the crude products were purified by recrystallization from ethanol (95 %).

1,5-Diphenyl-3-phenylamino)-1,5-dihydro-1H-pyrrol-2 (5H)-one (Table 3, entry 1)

White solid; 0.29 g, 90 % yield; mp 227−229 °C. IR (KBr): 3,330 (N–H), 1,679 (cm^{-1}) (N–C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.72 (1H, d, J = 2.4 Hz, CH), 6.12 (1H, d, J = 2.4 Hz, = CH), 6.69 (1H, s, NH), 6.97 (1H, t, J = 8.4 Hz, Ar), 7.09–7.13 (3H, m, Ar), 7.23–7.28 (3H, m, Ar), 7.30–7.36 (6H, m, Ar), 7.56–7.58 (2H, m, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 64.2, 108.3, 116.7, 121.3, 121.6, 124.9, 126.7, 128.9, 129.0, 129.4, 131.9, 137.3, 137.5, 141.3, 167.3. Anal. Calcd for $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58; found: C, 80.69; H, 5.62; N, 8.36.

MS (EI, 70 eV): *m/z* (%) = 326 (M^+, base peak), 297 (28.7), 206 (97.5), 77 (85).

1-(4-Methoxyphenyl)-3-(4-methoxyphenyl-amino)-5-(3-chlorophenyl)-1H-pyrrol-2(5H)-one (Table 3, entry 2)

White cream solid; 0.41 g, 93 % yield; mp 192−194 °C, (Lit.: [13] 164−166 °C). IR (KBr): 3,313 (N–H), 1,672 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.78 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.57 (1H, d, J = 2.4 Hz, CH), 5.92 (1H, d, J = 2.4 Hz, = CH), 6.49 (1H, s, NH), 6.85-6.90 (4H, m, Ar), 7.05–7.10 (3H, m, Ar), 7.21–7.23 (3H, m, Ar), 7.36–7.39 (2H, m, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 55.4, 55.6, 64.2, 105.3, 114.1, 114.7, 118.6, 123.8, 125.1, 127.1, 128.4, 129.9, 130.2, 133.3, 134.6, 134.7, 140.0, 154.6, 157.1, 167.1.

MS (EI, 70 eV): *m/z* (%) = 422 (M^{+2}, 22), 420 (M^+, 54), 298 (21), 270 (base peak), 259 (22), 122 (27), 92 (20), 77 (25).

1-(4-Methoxyphenyl)-3-(4-methoxyphenyl-amino)-5-(4-chlorophenyl)-1H-pyrrol-2(5H)-one (Table 3, entry 3)

White cream solid; 0.29 g, 67 % yield; mp 195−197 °C, (Lit.: [13] 153−155 °C). IR (KBr): 3,313 (N–H), 1,674 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.78 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.57 (1H, d, J = 2.4 Hz, CH), 5.92 (1H, d, J = 2.4 Hz, = CH), 6.49 (1H, s, NH), 6.84-6.91 (4H, m, Ar), 7.05-7.07 (2H, m, Ar), 7.14–7.17 (2H, m, Ar), 7.25–7.28 (2H, m, Ar), 7.34–7.36 (2H, m, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm): 55.4, 55.6, 64.1, 105.5, 114.3, 114.7, 118.6, 123.9, 128.4, 129.1, 129.9, 133.3, 133.9, 134.7, 136.3, 154.5, 157.1, 167.0.

MS (EI, 70 eV): *m/z* (%) = 422 (M^{+2}, 0.8), 420 (M^+, 1.6), 264 (8), 122 (7.1), 97 (14.2), 69 (25.4), 57 (base peak).

1-(4-Methoxyphenyl)-3-(4-methoxyphenyl-amino)-5-(4-bromophenyl)-1H-pyrrol-2(5H)-one (Table 3, entry 4)

White solid; 0.16 g, 35 % yield; mp 213−215°C. IR (KBr): 3,309 (N–H), 1,672 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.78 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.56 (1H, d, J = 2.4 Hz, CH), 5.92 (1H, d, J = 2.4 Hz, = CH), 6.47 (1H, s, NH), 6.84–6.90 (4H, m, Ar), 7.02–7.10 (4H, m, Ar), 7.34–7.36 (2H, m, Ar), 7.41–7.50 (3H, m, Ar). ^{13}C NMR (100 MHz; $CDCl_3$) δ (ppm): 55.4, 55.6, 64.1, 105.4, 114.3, 114.7, 118.6, 121.9, 123.9, 128.7, 129.9, 132.1, 133.3, 134.7, 136.9, 154.6, 157.1, 167.0. Anal. Calcd for $C_{24}H_{21}BrN_2O_3$: C, 61.95; H, 4.55; Br, 17.17; N, 6.02; found: C, 61.73; H, 4.61; N, 5.84.

MS (EI, 70 eV): *m/z* (%) = 466 (M^++2, 36.8), 464 (M^+, 37.5), 323 (base peak), 77 (49.3).

5-Phenyl-1-p-tolyl-3-p-tolylamino-1,5-dihydro-1H-pyrrol-2 (5H)-one (Table 3, entry 5)

White cream solid; 0.32 g, 91 % yield; mp 215−217 °C, (Lit.: [10] 215−217 °C). IR (KBr): 3,311 (N–H), 1,675 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.28 (3H, s, CH_3), 2.32 (3H, s, CH_3), 5.66 (1H, d, J = 2.8 Hz, CH), 6.04 (1H, d, J = 2.8 Hz, = CH), 6.59 (1H, s, NH), 7.00 (2H, d, J = 8.4 Hz, Ar), 7.09–7.13 (4H, m, Ar), 7.22–7.7.32 (5H, m, Ar), 7.44 (2H, d, J = 7.6 Hz, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm): 20.7, 20.9, 64.4, 107.4, 116.8, 121.7, 126.8, 128.1, 128.9, 129.5, 129.9, 130.7, 132.4, 134.7, 134.7, 137.7, 138.9, 167.3.

MS (EI, 70 eV): *m/z* (%) = 354 (M^+, 3), 281 (8), 207 (16), 109 (16.5), 91 (69), 69 (56), 57 (92), 55 (base peak).

5-(4-Methoxy-phenyl)-1-p-tolyl-3-p-tolylamino-1,5-dihydro-1H-pyrrol-2(5H)-one (Table 3, entry 6)

White cream solid; 0.25 g, 65 % yield; mp 214−216 °C. IR (KBr): 3,313 (N–H), 1,672 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.29 (3H, s, CH_3), 2.32 (3H, s, CH_3), 3.77 (3H, s, OCH_3), 5.61 (1H, d, J = 2.4 Hz, CH), 6.02 (1H, d, J = 2.4 Hz, = CH), 6.58 (1H, s, NH), 6.81–6.84 (2H, m, Ar), 6.99–7.02 (2H, m, Ar), 7.10–7.16 (6H, m, Ar), 7.37–7.41 (2H, m, Ar). ^{13}C NMR (100 MHz; $CDCl_3$) δ (ppm): 20.7, 20.9, 55.2, 63.9, 107.6, 114.3, 116.8, 122.0, 128.1, 129.4, 129.5, 129.9, 130.6, 132.3, 134.7, 134.7, 138.9, 159.4, 167.2. Anal. Calcd for $C_{25}H_{24}N_2O_2$: C, 78.10; H, 6.29; N, 7.29; found: C, 77.84; H, 6.32; N, 7.10.

MS (EI, 70 eV): *m/z* (%) = 384 (M^+, 25.0), 291 (23.3), 250 (75.0), 91 (98.3), 77 (56.7), 57 (base peak).

5-(4-Nitro-phenyl)-1-p-tolyl-3-p-tolylamino-1,5-dihydro-1 H-pyrrol-2(5H)-one (Table 3, entry 7)

Yellow solid; 0.28 g, 70 % yield; mp 231−233 °C. IR (KBr): 3,313 (N–H), 1,682 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.29 (3H, s, CH_3), 2.32 (3H, s, CH_3), 5.78 (1H, d, J = 2.4 Hz, CH), 5.99 (1H, d, J = 2.4 Hz, = CH), 6.63 (1H, s, NH), 7.00 (2H, t, J = 8.4 Hz, Ar), 7.12–7.15 (4H, m, Ar), 7.31–7.42 (4H, m, Ar), 8.16 (2H, dd, J_1 = 6.8, J_2 = 1.6 Hz, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 20.7, 20.9, 63.5, 105.3, 117.1, 121.6, 124.3, 127.7, 129.8, 129.9, 131.3, 133.2, 134.1, 135.3, 138.4, 145.5, 147.7, 166.9. Anal. Calcd for $C_{24}H_{21}N_3O_3$: C, 72.16; H, 5.30; N, 10.52; found: C, 71.89; H, 5.34; N, 10.34.

MS (EI, 70 eV): *m/z* (%) = 399 (M^+, 2.2), 314 (15.5), 295 (26.7), 91 (86.7), 77 (55.6), 55 (base peak).

1-(3-Chloro-phenyl)-3-(3-chloro-phenylamino)-5-phenyl-1, 5-dihydro-1H-pyrrol-2(5H)-one (Table 3, entry 8)

White cream solid; 0.36 g, 90 % yield; mp 203−205 °C, (Lit.: [10] 207−209 °C). IR (KBr): 3,320 (N–H), 1,679 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.69 (1H, d, J = 2.4 Hz, CH), 6.14 (1H, d, J = 2.8 Hz, = CH), 6.72 (1H, s, NH), 6.94–6.97 (2H, m, Ar), 7.07–7.10 (2H, m, Ar), 7.20–7.26 (3H, m, Ar), 7.31–7.41 (5H, m, Ar), 7.73 (1H, t, J = 2.2 Hz, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 64.2, 109.5, 115.0, 116.4, 119.1, 121.4, 121.4, 125.0, 126.6, 128.5, 129.3, 129.9, 130.4, 131.4, 134.7, 135.1, 136.6, 138.3, 142.3, 167.

MS (EI, 70 eV): *m/z* (%) = 396 (M^{+2}, 50), 394 (M^+, 75), 268 (87), 240 (base peak), 229 (80), 204 (34), 75 (29).

1-(4-Chloro-phenyl)-3-(4-chloro-phenylamino)-5-phenyl-1, 5-dihydro-1H-pyrrol-2(5H)-one (Table 3, entry 9)

White solid; 0.37 g, 93 % yield; mp 208−210 °C, (Lit.: [10] 217−219 °C). IR (KBr): 3328 (N–H), 1,672 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.67 (1H, d, J = 2.8 Hz, CH), 6.08 (1H, d, J = 2.4 Hz, = CH), 6.68 (1H, s, NH), 7.00–7.04 (2H, m, Ar), 7.19–7.22 (2H, m, Ar), 7.28–7.37 (7H, m, Ar), 7.51–7.55 (2H, m, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm): 64.2, 108.6, 117.9, 122.5, 126.2, 126.7, 128.5, 129.1, 129.2, 129.4, 130.3, 131.8, 135.7, 136.8, 139.7, 167.0.

MS (EI, 70 eV): *m/z* (%) = 396 (M^{+2}, 31.5), 394 (M^+, 49), 268 (49), 240 (base peak), 229 (40), 204 (24), 75 (22.5).

1-(4-Bromo-phenyl)-3-(4-bromo-phenylamino)-5-phenyl-1, 5-dihydro-1H-pyrrol-2(5H)-one (Table 3, entry 10)

Cream solid; 0.46 g, 95 % yield; mp 226−228 °C, (Lit.: [12]). IR (KBr): 3,327 (N–H), 1,672 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.66 (1H, d, J = 2.4 Hz, CH), 6.08 (1H, d, J = 2.4 Hz, CH=), 6.68 (1H, s, NH), 6.95–7.01 (2H, m, Ar), 7.19–7.22 (2H, m, Ar), 7.30–7.35 (3H, m, Ar), 7.39–7.43 (4H, m, Ar), 7.46–7.49 (2H, m, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 64.1, 108.9, 113.5, 118.0, 118.3, 122.8, 126.6, 128.5, 129.2, 131.7, 132.0, 132.3, 136.2, 136.8, 140.2, 167.0.

MS (EI, 70 eV): *m/z* (%) = 486 (M^{+4}, 19), 484 (M^{+2}, 39), 480 (M^+, 20), 314 (43), 312 (45), 286 (88), 284 (base peak), 204 (79), 76 (28).

5-(4-Methoxy-phenyl)-1-(3-nitrophenyl)-3-(3-nitrophenyl-amino)-1,5-dihydro-1H-pyrrol-2(5H)-one (Table 3, entry 11)

Yellow solid; 0.20 g, 45 % yield; mp 184−186 °C. IR (KBr): 3,375 (N–H), 1,697 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.78 (3H, s, OCH_3), 5.80 (1H, s, CH), 6.30 (1H, s, = CH), 6.87 (2H, d, J = 8.4 Hz, Ar), 7.05 (1H, s, NH), 7.20 (2H, d, J = 8.4 Hz, Ar), 7.38–7.40 (1H, m, Ar), 7.46–7.51 (2H, m, Ar), 7.84 (1H, d, J = 7.6 Hz, Ar), 7.96–8.03 (3H, m, Ar), 8.49 (1H, s, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 55.3, 63.8, 110.4, 111.1, 114.9, 115.8, 116.1, 119.5, 122.7, 126.6, 127.1, 128.1, 129.8, 130.2, 130.9, 138.0, 142.1, 148.5, 149.2, 160.0, 166.9. Anal. Calcd for $C_{23}H_{18}N_4O_6$: C, 61.88; H, 4.06; N, 12.55; found: C, 61.69; H, 4.13; N, 12.39.

MS (EI, 70 eV): *m/z* (%) = 446 (M^+, 8.3), 382 (37.2), 262 (33.3), 234 (base peak), 77 (88.9), 57 (95.5).

1-(4-Methoxyphenyl)-3-(4-methoxyphenylamino)-5-propyl-1,5-dihydro-pyrrole-2(5H)-one (Table 3, entry 12)

Pale yellow solid; 0.32 g, 90 % yield; mp 201−203 °C. IR (KBr): 3,311 (N–H), 1,673 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.87 (3H, t, J = 7.2 Hz, CH_3), 1.26–1.46 (4H, m, 2 × CH_2), 3.83 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 4.65–4.68 (1H, m, CH), 5.98 (1H, d, J = 2.4 Hz, = CH), 6.40 (1H, s, NH), 6.90–6.94 (2H, m, Ar), 6.97–7.09 (4H, m, Ar), 7.37–7.41 (2H, m, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 14.1, 17.4, 34.1, 55.5, 55.6, 60.1, 104.4, 114.4, 114.7, 118.4, 124.8, 129.7, 133.9, 135.2, 154.3, 157.3, 166.3. Anal. Calcd for $C_{21}H_{24}N_2O_3$: C, 71.57; H, 6.86; N, 7.95; found: C, 71.38; H, 6.91; N, 7.79.

MS (EI, 70 eV): *m/z* (%) = 352 (M^+, 33.6), 309 (59.1), 202 (45.5), 77 (63.6), 69 (base peak), 55 (89.1).

1-(4-Methoxyphenyl)-3-(4-methoxyphenylamino)-5-pyridin-3-yl-1,5-dihydro-pyrrole-2(5H)-one (Table 3, entry 13)

Cream solid; 0.35 g, 90 % yield; mp 204−206 °C. IR (KBr): 3,310 (N–H), 1,665 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.77 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.68 (1H, s, CH), 5.93 (1H, s, =CH), 6.53 (1H, s, NH), 6.85–6.91 (4H, m, Ar), 7.07 (2H, d, J = 8.4 Hz, Ar), 7.29–7.35 (3H, m, Ar), 7.59 (1H, d, J = 8.0 Hz, Ar), 8.54 (1H, d, J = 4.4 Hz, Ar), 8.59 (1H, s, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 55.4, 55.6, 62.2, 104.6, 114.4, 114.8, 118.7, 124.1, 129.5, 133.8, 133.8, 134.5, 134.7, 148.6, 149.4, 154.7, 157.3, 166.9. Anal. Calcd for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85; found: C, 71.12; H, 5.51; N, 10.67.

MS (EI, 70 eV): *m/z* (%) = 387 (M^+, 10.0), 323 (7.7), 237 (24.6), 77 (35.4), 69 (70.8), 57 (base peak).

1-(3,4-Dimethylphenyl)-3-(3,4-dimethylphenylamino)-5-phenyl-1,5-dihydro-pyrrole-2(5H)-one (Table 3, entry 14)

White solid; 0.27 g, 70 % yield; mp 226 − 228 °C; (Lit.: [13] 220−222 °C). IR (KBr): 3,317 (N–H), 1,675 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.18 (3H, s, CH_3), 2.22 (6H, s, 2 × CH_3), 2.29 (3H, s, CH_3), 5.64 (1H, d, J = 2.8 Hz, CH), 6.03 (1H, d, J = 2.8 Hz, =CH), 6.54 (1H, s, NH), 6.84–6.89 (2H, m, Ar), 7.02–7.09 (2H, m, Ar), 7.13–7.16 (1H, m, Ar), 7.20–7.28 (3H, m, Ar), 7.30–7.38 (3H, m, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 19.0, 19.2, 20.1, 64.4, 107.2, 114.1, 118.3, 119.4, 123.4, 126.9, 128.1, 128.9, 129.4, 129.9, 130.3, 132.4, 133.6, 134.9, 137.2, 137.6, 137.8, 139.3, 167.3.

MS (EI, 70 eV): *m/z* (%) = 382 (M^+, 30), 262 (31), 234 (base peak), 222 (29), 105 (43), 77 (72).

1-(3,4-Dimethylphenyl)-3-(3,4-dimethylphenylamino)-5-(4-methoxyphenyl)-1,5-dihydro-pyrrole-2(5H)-one (Table 3, entry 15)

White solid; 0.28 g, 68 % yield; mp 212−214 °C. IR (KBr): 3,317 (N–H), 1,651 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.19 (3H, s, CH_3), 2.23 (6H, s, 2 × CH_3), 2.26 (3H, s, CH_3), 3.77 (3H, s, CH_3), 5.60 (1H, d, J = 2.8 Hz, CH), 6.01 (1H, d, J = 2.8 Hz, =CH), 6.55 (1H, s, NH), 6.81–6.90 (4H, m, Ar), 7.03–7.08 (2H, m, Ar), 7.12–7.17 (3H, m, Ar), 7.35 (1H, d, J = 2.0 Hz, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 19.0, 19.3, 20.1, 55.2, 63.9, 107.4, 114.1, 114.3, 118.3, 119.7, 123.7, 128.2, 129.3, 129.5, 129.9, 130.3, 132.3, 133.6, 134.8, 137.1, 137.6, 139.3, 159.3, 167.2. Anal. Calcd for $C_{27}H_{28}N_2O_2$: C, 78.61; H, 6.84; N, 6.79; found C, 78.39 H, 6.90; N, 6.62.

MS (EI, 70 eV): *m/z* (%) = 412 (M^+, 25.8), 292 (30.8), 264 (base peak), 77 (40.4).

5-(4-hydroxyl-3-nitrophenyl)-1-(4-methoxyphenyl)-3-(4-methoxyphenylamino)-1,5-dihydro-pyrrol-2-one

Orange solid; 0.18 g, 40 % yield; mp 196−202 °C. IR (KBr): 3,310 (OH), 3,304 (N–H), 1,683 (cm^{-1}) (N–C = O). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.78 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 5.61 (1H, s, CH), 5.90 (1H, s, =CH), 6.52 (1H, s, NH), 6.85–6.91 (4H, m, Ar), 7.03–7.10 (3H, m, Ar), 7.29-7.39 (3H, m, Ar), 8.00 (1H, s, Ar), 10.57 (1H, s, OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 55.4, 55.6, 63.5, 114.5, 114.8, 118.8, 121.0, 123.8, 124.1, 124.3, 130.4, 135.8, 155.0, 157.7. Anal. Calcd for $C_{24}H_{21}N_3O_6$: C, 64.42; H, 4.73; N, 9.39; found C, 64.12; H, 4.77; N, 9.12.

MS (EI, 70 eV): *m/z* (%) = 447 (M^+, 1.1), 384 (8.4), 250 (23.2), 147 (17.9), 119 (40.0), 105 (13.2), 91 (37.9), 70 (53.7), 57 (72.6), 55 (base peak).

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