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Efficient synthesis of highly substituted pyrroles based on the tandem reactions: intermolecular amination and Pd(II)-catalyzed intramolecular hydroamidation

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ABSTRACT

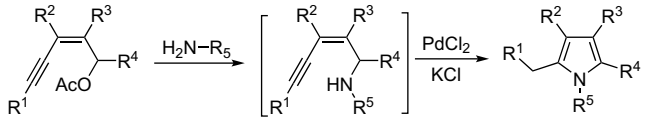
A novel and efficient method for construction of polysubstituted pyrroles, which included an intermolecular amination and Pd(II)-catalyzed intramolecular hydroamidation, was developed. It was found that the reactions gave high yields (55–92%).

1. Introduction

Pyrroles are important heterocycles broadly used in material science[1] and can be found in naturally occurring and biologically important molecules.[2] Accordingly, substantial attention has been paid to develop efficient methods for the synthesis of pyrroles. Recent strategies for the synthesis of pyrroles are based on metal-catalyzed[3] reactions and catalytic multicomponent coupling approaches,[3j,4] which can compensate for the classic synthetic approaches nicely. Most known methods for the construction of the pyrrole ring proceed via various types of cycloaddition and cycloisomerization of acyclic precursors. An economical approach to synthesize highly substituted pyrroles whose raw materials can be accessed in few steps is still challenging.

Very recently, we reported a gold catalyzed tandem process of 1-en-4-yn-3-ols to afford highly substituted pyrroles.[5] In order to further study this reaction, we chose (*Z*)-2-en-4-ynyl acetate as the raw substrate, which can be easily derived from 1-en-4-yn-3-ols[6] and could undergo an amination process efficiently. We also envisioned that this reaction could be applied in the synthesis of pyrroles by developing a domino process.

Herein, we aimed to report a novel and efficient method for the construction of polysubstituted pyrroles, which combined an intermolecular amination and Pd (II)-catalyzed[7] intramolecular hydroamidation (Scheme 1).

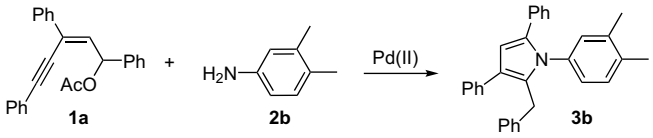


Scheme 1.

2. Results and discussion

We initially started our investigation by using 0.2 mmol of (*Z*)-1,3,5-triphenylpent-2-en-4-ynyl acetate **1a** and 0.8 mmol 3,4-dimethylaniline **2b**, and 5 mol % $PdCl_2$ and 10 mol % KCl in CH_3CN at room temperature, but no reaction was observed (Table 1, entry 1). To our delight, the desired product 1,2,3,5-tetraphenyl-1*H*-pyrrole **3b** was obtained in 55% yield in CH_3CN/H_2O (10:1) system at 60 °C (entry 4). Gratifyingly, when the reaction was carried out in

Table 1
Optimization of reaction conditions[a]



Entry	*T* (°C)	*t* (h)	Solvent	Yield[b] (%)
1	25	15	MeCN	0
2	60	15	MeCN	0
3	25	15	$MeCN/H_2O$ (10:1)	0
4	60	15	$MeCN/H_2O$ (10:1)	55
5	60	15	$MeCN/H_2O$ (6:1)	80
6	60	15	$MeCN/H_2O$ (2:1)	45
7	60	15	DMF/H_2O (6:1)	39
8	60	15	$DMSO/H_2O$ (6:1)	24

[a] Reactions were carried out in 0.2 mmol of **1a**, 0.8 mmol of 3,4-dimethylaniline **2b** using 5 mol % $PdCl_2$ and 10 mol % KCl.
[b] Isolated yields.

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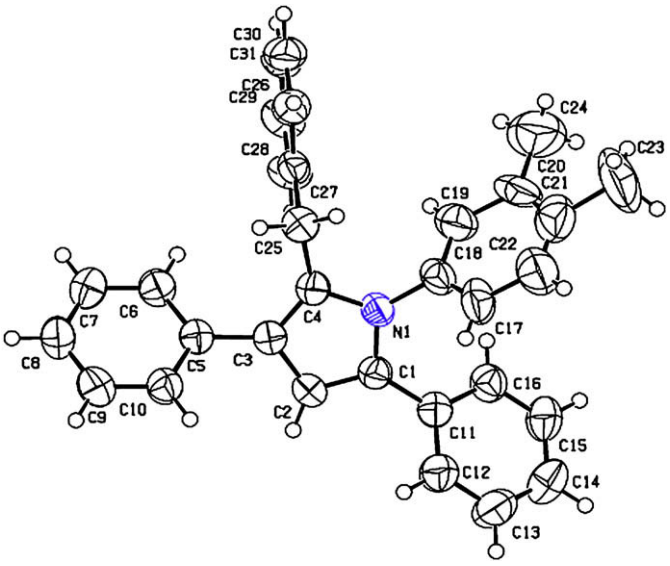


Figure 1. X-ray structure of **3b**.

MeCN/H_2O (6:1) at 60 °C, the desired product **3b** was obtained in 80% yield after 15 h (entry 5). On further decreasing the ratio of MeCN and H_2O to 2:1, the yield decreased dramatically. On the other hand, other mixed solvents were also investigated, but no superior results were obtained (entries 7 and 8). Thus, the reaction of (*Z*)-2-en-4-yn acetate **1a** with 3,4-dimethylaniline **2b** using 5 mol % $PdCl_2$ and 10 mol % KCl in MeCN/H_2O (6:1) at 60 °C was found to be the most effective and was utilized as the standard conditions. The structure of **3b** was further confirmed by its X-ray crystal structure analysis (Fig. 1).

Encouraged by our initial results, we sought to examine the scope and the generality of the method under the optimized reaction conditions. The reactions of **1a** with various primary amines **2a**–**j** were investigated. The results are summarized in Table 2. It was found that aniline **2a** showed good activity in this reaction (84%, entry 1). The reactions of **1a** with **2b**–**d** resulted in **3b**–**d** in good yields (entries 2–4). When an amine with electron-withdrawing substituent such as 3-chloroaniline **2e** was used, the yield was decreased (61%, entry 5). The alkylamines also showed good reaction activity (entries 6–10).

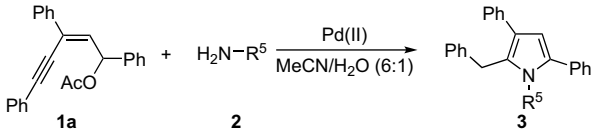
The reactions of different substituted (*Z*)-2-en-4-yn acetates were examined using aniline **2a** as the nucleophilic component (Table 3). It was found that the different substituted (*Z*)-2-en-4-ynyl acetate **1a**–**g** gave good yields (up to 93%).

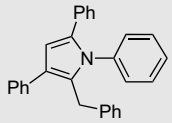
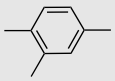
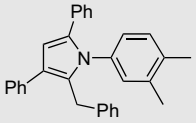
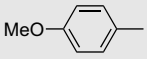
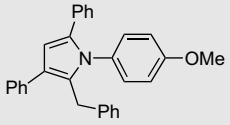
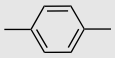
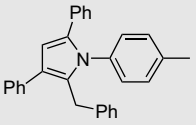
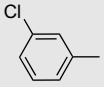
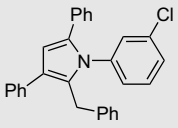
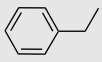
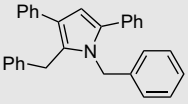
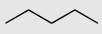
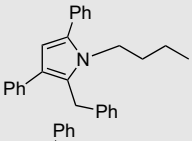
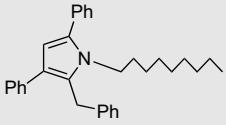
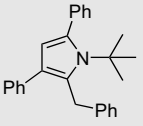
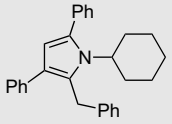
In order to confirm the mechanism for the one-pot reaction, we next conducted the reactions in two steps, as shown in Scheme 2. After the reaction was run with (*Z*)-1,3,5-triphenylpent-2-en-4-ynyl acetate **1a** and aniline **2a** in CH_3CN/H_2O (10:1) system for 10 h, an intermediate (*Z*)-*N*-(1,3,5-triphenyl-pent-2-en-4-ynyl)benzenamine **4a** was obtained in excellent yield (up to 93%). Subsequently, **4a** could be converted to **3a**[7b] in 80% yield under the optimized reaction conditions. These results strongly support our proposed two-step mechanism, one-pot procedure.

3. Conclusions

In summary, we have developed a simple, convenient, and efficient synthetic approach to synthesize highly substituted pyrroles utilizing a nucleophilic substitution forming (*Z*)-2-en-4-yn-1-amine, followed by Pd(II)-catalyzed intermolecular hydroamidation reaction.

Table 2
Test of amine scope[a]



Entry	R^5	Product
1		 15h 84% **3a**
2		 15h 80% **3b**
3		 12h 82% **3c**
4		 12h 77% **3d**
5		 12h 61% **3e**
6		 15h 76% **3f**
7		 20h 71% **3g**
8		 12h 81% **3h**
9		 20h 63% **3i**
10		 30h 55% **3j**

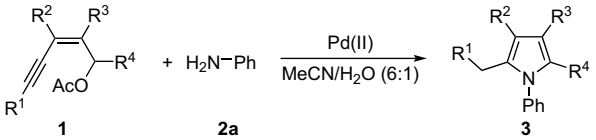
[a] Reactions were carried out in 0.2 mmol of **1a**, 0.8 mmol of amine **2** using 5 mol % $PdCl_2$ and 10 mol % KCl.

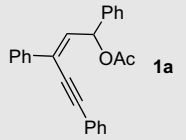
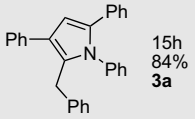
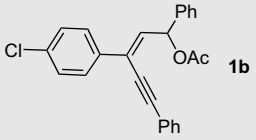
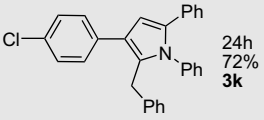
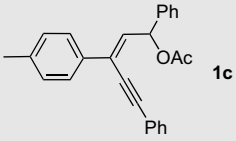
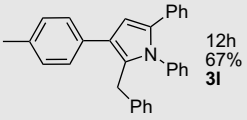
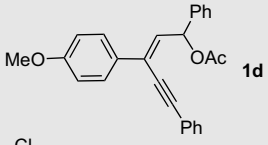
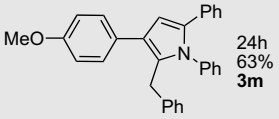
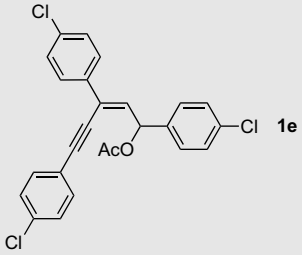
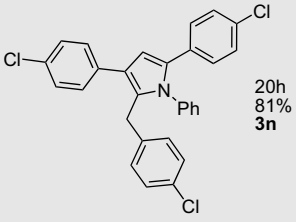
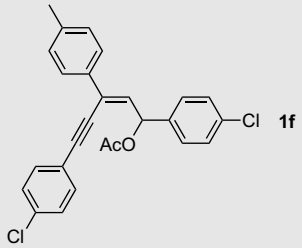
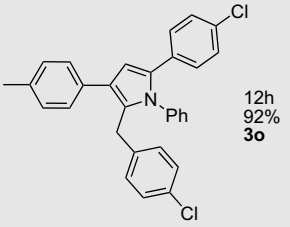
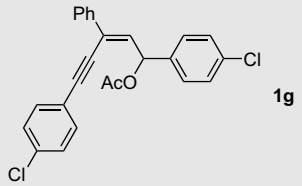
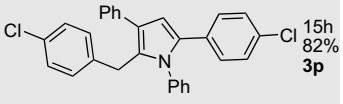
4. Experimental section

4.1. General

The materials were used as purchased. All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on silica gel GF_{254} plates. The silica gel (200–300 mesh) is used for column chromatography and the distillation range of

Table 3
Pd(II)-catalyzed synthesis of pyrroles[a]



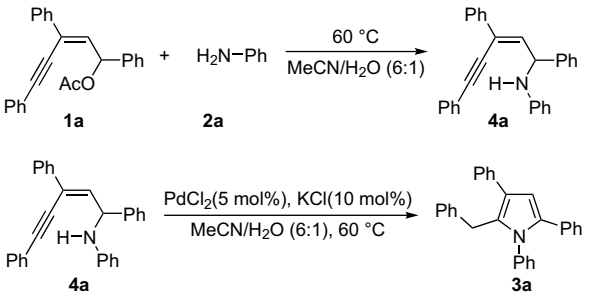
Entry	1	Product
1	 **1a**	 15h 84% **3a**
2	 **1b**	 24h 72% **3k**
3	 **1c**	 12h 67% **3l**
4	 **1d**	 24h 63% **3m**
5	 **1e**	 20h 81% **3n**
6	 **1f**	 12h 92% **3o**
7	 **1g**	 15h 82% **3p**

[a] Reactions were carried out in 0.2 mmol of **1**, 0.8 mmol aniline **2a** using 5 mol % $PdCl_2$ and 10 mol % KCl at 60 °C.

petroleum is 60–90 °C. ^1H and ^{13}C NMR spectra were recorded on the Varian Mercury-300 MHz or Varian Mercury-400 MHz instruments, using $CDCl_3$ as a solvent. The chemical shifts are reported in TM (ppm) values relative to $CHCl_3$ (TM 7.26 ppm for ^1H NMR and TM 77.0 ppm for ^{13}C NMR). IR spectra were obtained on Nicolet NEXUS 670 FT-IR instrument. Melting points were taken on an X-4 melting point apparatus and are uncorrected. Elemental analysis was performed using Germanic VARLIOLE instruments.

4.2. General procedure for preparation of (*Z*)-2-en-4-yn acetates 1a–g

Acetic anhydride (0.5 mmol) and triethylamine (1.2 mmol) were added to (*Z*)-2-en-4-yn-1-ol[6] (0.4 mmol) in CH_2Cl_2 (10 mL) at room temperature under argon atmosphere. After (*Z*)-2-en-4-yn-1-ol disappeared by TLC, HCl (2 M, 10 mL) was added to the resulting mixture, and the organic layer was separated followed by



Scheme 2.

extraction of the aqueous layer with Et_2O. The combined organic extracts were washed with H_2O and saturated solution of $NaHCO_3$, and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was purified by the column chromatography on silica gel (petroleum ether/ethyl acetate=16:1) to furnish the expected substrate.

4.3. Typical procedure for preparation of product 3b

(*Z*)-1,3,5-Triphenylpent-2-en-4-ynyl acetate **1a** (0.2 mmol), 3,4-dimethylaniline **2b** (0.8 mmol), MeCN/H_2O (6:1, 10 mL), 5 mol % $PdCl_2$, and 10 mol % KCl were placed in a 25 mL flask. The resulting mixture was then heated at 60 °C. When the reaction was completed as indicated by TLC analysis, water (10 mL) was added and the resulting reaction mixture was extracted with ethyl acetate. The extracts were concentrated to give a thick residue. The resulting residue was purified by column chromatography using 20:1 petroleum ether/ethyl acetate as an eluent to afford pure 1,2,3,5-tetraphenyl-1*H*-pyrrole **3b** (80%).

*4.3.1. 2-Benzyl-1,3,5-triphenyl-1H-pyrrole (**3a**)*

A yellow solid, mp: 139–140 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.51 (d, *J*=10.8 Hz, 2H), 7.33 (d, *J*=10.0 Hz, 2H), 7.05–7.23 (m, 12H), 6.87–6.95 (m, 4H), 6.67 (s, 1H), 4.03 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 140.3, 138.8, 136.6, 134.5, 132.9, 129.9, 128.7, 128.6, 128.4, 128.1, 128.0, 127.9, 127.7, 127.5, 125.9, 125.7, 124.2, 109.4, 31.2; IR (KBr, neat) cm^{-1}: 3397, 2922, 1600, 1493, 1453, 1072, 757, 698, 515. Anal. Calcd for $C_{29}H_{23}N$: C, 90.35; H, 6.01; N, 3.63. Found: C, 90.19; H, 6.20; N, 3.61.

*4.3.2. 2-Benzyl-1-(3,4-dimethylphenyl)-3,5-diphenyl-1H-pyrrole (**3b**)*

The molecular structure of the corresponding product **3a** was determined by X-ray crystallography (Fig. 1). X-ray data for compound **3a**: $C_{31}H_{27}N$, MW=413.54, *T*=294(2) K, λ=0.71073 Å, monoclinic space group, *P*21/*c*, *a*=18.967(3) Å, *b*=11.7217(16) Å, *c*=21.485(3) Å, α=90°, β=90°, γ=90°, *V*=4776.6(12) Å^3, *Z*=8, ρ_{cald}=1.150 mg m^{-3}, μ=0.066 mm^{-1}, *F*(000)=1760, crystal size 0.45×0.40×0.40 mm^3, independent reflections 3525 [*R*(int)=0.0505], reflections collected 19,583, refinement method, full-matrix least-squares on F^2, goodness-of-fit on F^2 0.983, final *R* indices [$I>2\sigma(I)$] R_1=0.0711, wR_2=0.1602, *R* indices (all date) R_1=0.0966, wR_2=0.1784, largest diff. peak and hole 0.734 and −0.290 e Å^{-3}. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic and allocated the deposition number CCDC 694218.

A white solid, mp: 140–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.51 (d, *J*=10.8 Hz, 2H), 7.33 (t, *J*=10.0 Hz, 2H), 7.04–7.22 (m, 9H), 6.92 (t, *J*=9.8 Hz, 3H), 6.65–6.69 (m, 3H), 4.00 (s, 2H), 2.18 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 140.7, 136.9, 136.8, 136.5, 136.0, 134.4, 133.2, 130.2, 129.8, 129.6, 128.5, 128.1, 128.0, 127.9, 127.7, 127.6, 126.0, 125.8, 125.7, 125.6, 123.9, 109.2, 31.3, 19.5, 19.4; IR (KBr, neat) cm^{-1}: 2921, 1601, 1496, 1451, 1024, 757, 697. Anal. Calcd for $C_{31}H_{27}N$: C, 90.03; H, 6.58; N, 3.39. Found: C, 90.13; H, 6.53; N, 3.34.

*4.3.3. 2-Benzyl-1-(4-methoxyphenyl)-3,5-diphenyl-1H-pyrrole (**3c**)*

A yellow solid, mp: 102–103 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.50 (d, *J*=7.8 Hz, 2H), 7.32 (t, *J*=7.5 Hz, 2H), 7.07–7.22 (m, 9H), 6.84–6.93 (m, 4H), 6.66–6.67 (m, 3H), 4.01 (s, 2H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 158.6, 140.4, 136.6, 134.6, 133.0, 131.6, 130.2, 129.7, 128.4, 128.1, 123.0, 127.9, 127.7, 127.6, 125.8, 125.7, 125.6, 123.9, 113.7, 109.9, 55.2, 31.2; IR (KBr, neat) cm^{-1}: 3055, 3926, 1512, 1250, 697, 529. Anal. Calcd for $C_{30}H_{25}NO$: C, 86.71; H, 6.06; N, 3.37. Found: C, 86.42; H, 6.01; N, 3.47.

*4.3.4. 2-Benzyl-3,5-diphenyl-1-p-tolyl-1H-pyrrole (**3d**)*

A yellow solid, mp: 166–168 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.50 (d, *J*=8.4 Hz, 2H), 7.32 (t, *J*=7.5 Hz, 2H), 7.06–7.22 (m, 9H), 6.81–6.97 (m, 6H), 6.66 (s, 1H), 4.02 (br s, 2H), 2.27 (br s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 140.5, 137.3, 136.7, 136.2, 134.5, 133.1, 130.1, 129.2, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 125.8, 125.0, 125.4, 124.0, 105.2, 31.2, 21.1; IR (KBr, neat) cm^{-1}: 3397, 2922, 1514, 1379, 1026, 757, 697, 520. Anal. Calcd for $C_{30}H_{25}N$: C, 90.19; H, 6.31; N, 3.51. Found: C, 90.09; H, 6.29; N, 3.62.

*4.3.5. 2-Benzyl-1-(3-chlorophenyl)-3,5-diphenyl-1H-pyrrole (**3e**)*

A yellow solid, mp: 141–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.51 (d, *J*=9.2 Hz, 2H), 7.35 (t, *J*=10.0 Hz, 2H), 7.01–7.28 (m, 11H), 6.94 (s, 1H), 6.78–6.90 (m, 3H), 6.64 (s, 1H), 4.02 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 140.1, 139.9, 136.3, 134.6, 134.0, 132.5, 130.1, 129.4, 129.0, 128.7, 128.5, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 127.1, 126.2, 125.9, 124.7, 109.8, 31.3; IR (KBr, neat) cm^{-1}: 3439, 3056, 1946, 1595, 1482, 1073, 761, 697. Anal. Calcd for $C_{29}H_{22}ClN$: C, 82.94; H, 5.28; N, 3.34. Found: C, 83.10; H, 5.44; N, 3.26.

*4.3.6. 1,2-Dibenzyl-3,5-diphenyl-1H-pyrrole (**3f**)*

A light yellow solid, mp: 130–131 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.44 (d, *J*=6.0 Hz, 2H), 7.18–7.36 (m, 14H), 7.09 (d, *J*=5.4 Hz, 2H), 6.86 (d, *J*=5.7 Hz, 2H), 6.54 (s, 1H), 4.94 (s, 2H), 3.98 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 139.9, 139.0, 136.9, 135.0, 133.3, 128.8, 128.7, 128.4, 128.3, 127.9, 127.8, 127.7, 127.0, 126.2, 125.5, 124.3, 108.9, 47.7, 30.9; IR (KBr, neat) cm^{-1}: 2922, 16.1, 1491, 1353, 1027, 732, 698. Anal. Calcd for $C_{30}H_{25}N$: C, 90.19; H, 6.31; N, 3.51. Found: C, 90.20; H, 6.21; N, 3.59.

*4.3.7. 2-Benzyl-1-butyl-3,5-diphenyl-1H-pyrrole (**3g**)*

A yellow solid, mp: 87–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.38–7.44 (m, 6H), 7.28–7.36 (m, 5H), 7.18–7.23 (m, 4H), 6.38 (s, 1H), 4.22 (s, 2H), 3.73 (t, *J*=7.8 Hz, 2H), 1.25–1.34 (m, 2H), 0.97–1.03 (m, 2H), 0.64 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 140.2, 137.0, 134.1, 134.0, 129.0, 128.6, 128.3, 128.2, 127.9, 127.7, 127.4, 126.8, 126.1, 125.4, 123.7, 108.9, 44.2, 33.2, 31.0, 19.8, 13.4; IR (KBr, neat) cm^{-1}: 3429, 2924, 1704, 1601, 1459, 1363, 1208, 1026, 760, 698, 521. Anal. Calcd for $C_{27}H_{27}N$: C, 88.72; H, 7.45; N, 3.83. Found: C, 88.90; H, 7.51; N, 3.59.

*4.3.8. 2-Benzyl-1-octyl-3,5-diphenyl-1H-pyrrole (**3h**)*

A yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.35–7.44 (m, 6H), 7.22–7.31 (m, 5H), 7.17–7.20 (m, 4H), 6.38 (s, 1H), 4.21 (s, 1H), 3.72 (t, *J*=8.0 Hz, 2H), 1.31–1.34 (m, 2H), 1.18–1.23 (m, 2H), 1.02–1.13 (m, 4H), 0.97–0.98 (m, 4H), 0.84 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 140.2, 137.1, 134.1, 134.0, 128.9, 128.6, 128.3, 127.9, 127.7, 127.4, 126.8, 126.1, 125.3, 123.7, 108.9, 44.4, 31.6, 31.0, 28.8, 28.7, 26.5, 22.5, 14.0; IR (neat) cm^{-1}: 3058, 2925, 1949, 1602, 1490, 1357, 1208, 1026, 758, 699, 509. Anal. Calcd for $C_{31}H_{35}N$: C, 88.31; H, 8.37; N, 3.32. Found: C, 88.40; H, 8.41; N, 3.19.

*4.3.9. 2-Benzyl-1-tert-butyl-3,5-diphenyl-1H-pyrrole (**3i**)*

A yellow solid, mp: 117–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.41–7.43 (m, 2H), 7.21–7.34 (m, 11H), 7.10–7.11 (m, 2H), 6.15 (s, 1H), 4.42 (s, 2H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 142.2, 139.2, 137.5, 136.0, 130.8, 128.5, 128.4, 128.1, 128.0, 127.4, 126.9, 126.0, 125.8, 125.5, 113.1, 59.5, 48.2, 34.4, 33.3; IR (KBr, neat) cm^{-1}: 3413, 2922, 1599, 1448, 1366, 1206, 1070, 699, 520. Anal. Calcd for $C_{27}H_{27}N$: C, 88.72; H, 7.45; N, 3.83. Found: C, 88.60; H, 7.41; N, 3.99.

*4.3.10. 2-Benzyl-1-hexamethylene-3,5-diphenyl-1H-pyrrole (**3j**)*

A yellow solid, mp: 140–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.19–7.44 (m, 11H), 7.14–7.17 (m, 4H), 6.27 (s, 1H), 4.27 (s, 2H), 3.91 (br s, 1H), 1.42–1.61 (m, 6H), 0.79–0.97 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 140.9, 137.2, 135.6, 134.2, 130.0, 128.4, 128.2, 128.0, 127.9, 127.7, 127.2, 126.9, 126.0, 125.3, 110.1, 57.9, 33.5, 31.8, 26.5, 25.2; IR (KBr, neat) cm^{-1}: 3440, 3055, 2934, 1954, 1600, 1448, 1361, 1206, 1026, 895, 757, 697, 505. Anal. Calcd for $C_{29}H_{29}N$: C, 88.96; H, 7.47; N, 3.58. Found: C, 88.95; H, 7.41; N, 3.64.

*4.3.11. 2-Benzyl-3-(4-chlorophenyl)-1,5-diphenyl-1H-pyrrole (**3k**)*

A yellow solid, mp: 134–135 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.39–7.43 (dd, *J*=5.7 Hz, 2H), 7.28–7.30 (d, *J*=8.4 Hz, 2H), 7.07–7.24 (m, 11H), 6.93–6.96 (dd, *J*=4.8 Hz, 2H), 6.87 (d, *J*=6.3 Hz, 2H), 6.62 (s, 1H), 4.00 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 140.4, 138.7, 135.1, 134.8, 132.7, 131.4, 130.0, 128.9, 128.7, 128.6, 128.5, 128.2, 128.0, 127.9, 127.8, 127.6, 126.0, 125.8, 123.0, 109.2, 31.2; IR (KBr, neat) cm^{-1}: 3029, 2923, 1948, 1599, 1492, 1122, 984, 813, 759, 695, 465. Anal. Calcd for $C_{29}H_{22}ClN$: C, 82.94; H, 5.28; N, 3.34. Found: C, 83.01; H, 5.32; N, 3.34.

*4.3.12. 2-Benzyl-3-(4-methylphenyl)-1,5-diphenyl-1H-pyrrole (**3l**)*

A yellow solid, mp: 134–136 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.41 (d, *J*=8.1 Hz, 2H), 7.04–7.18 (m, 13H), 6.92–6.95 (m, 2H), 6.88 (d, *J*=6.3 Hz, 2H), 6.64 (s, 1H), 4.02 (s, 2H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 140.4, 138.9, 135.2, 134.4, 133.6, 133.0, 129.8, 129.2, 128.7, 128.5, 128.1, 128.0, 127.9, 127.7, 127.6, 127.4, 125.8, 125.6, 124.1, 109.4, 31.2, 21.0; IR (KBr, neat) cm^{-1}: 3369, 3029, 2967, 1949, 1598, 1491, 1379, 1091, 912, 761, 697, 518. Anal. Calcd for $C_{30}H_{25}N$: C, 90.19; H, 6.31; N, 3.51. Found: C, 90.22; H, 6.32; N, 3.46.

*4.3.13. 2-Benzyl-3-(4-methoxyphenyl)-1,5-diphenyl-1H-pyrrole (**3m**)*

A white solid, mp: 102–103 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.49 (d, *J*=8.7 Hz, 2H), 7.14–7.25 (m, 11H), 6.94–7.02 (m, 6H), 6.68 (s, 1H), 4.07 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 157.8, 140.4, 138.9, 134.3, 132.9, 129.5, 129.1, 128.8, 128.7, 128.5, 128.1, 127.9, 127.8, 127.7, 127.4, 125.8, 125.6, 123.8, 113.9, 109.4, 55.1, 31.2; IR (KBr, neat) cm^{-1}: 3397, 3027, 2919, 1949, 1599, 1496, 1027, 760, 696, 19. Anal. Calcd for $C_{30}H_{25}NO$: C, 86.71; H, 6.06; N, 3.37. Found: C, 86.72; H, 6.12; N, 3.41.

*4.3.14. 2-(4-Chlorobenzyl)-3,5-bis(4-chlorophenyl)-1-phenyl-1H-pyrrole (**3n**)*

A yellow solid, mp: 108–109 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.03–7.43 (m, 13H), 6.97 (d, *J*=8.1 Hz, 2H), 6.80 (d, *J*=8.7 Hz, 2H), 6.63 (s, 1H), 3.99 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 138.7, 138.6, 135.1, 134.0, 132.4, 132.1, 132.0, 131.4, 130.2, 129.5, 129.3, 129.1, 128.9, 128.7, 128.6, 128.4, 123.7, 109.4, 30.9; IR (KBr, neat) cm^{-1}: 3392, 3059, 2926, 1952, 1600, 1498, 1379, 1246, 1178, 1033, 835, 761, 697, 533. Anal. Calcd for $C_{29}H_{20}Cl_3N$: C, 71.25; H, 4.12; N, 2.87. Found: C, 71.11; H, 4.09; N, 2.90.

*4.3.15. 2-(4-Chlorobenzyl)-3-(4-chlorophenyl)-1-phenyl-5-p-tolyl-1H-pyrrole (**3o**)*

A yellow solid, mp: 113–135 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.36 (d, *J*=7.8 Hz, 2H), 6.89–7.20 (m, 11H), 6.75 (d, *J*=8.1 Hz, 2H), 6.60 (s, 1H), 3.96 (s, 2H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 138.6, 138.5, 135.5, 133.3, 133.2, 131.7, 131.4, 131.3, 129.6, 129.3, 129.2, 128.8, 128.6, 128.2, 128.1, 127.8, 127.8, 124.4, 109.7, 30.6, 21.0; IR (KBr, neat) cm^{-1}: 3410, 3402, 2923, 2852, 1899, 1713, 1595, 1490, 1426, 1375, 1221, 1092, 1012, 823, 698, 527. Anal. Calcd for $C_{30}H_{23}Cl_2N$: C, 76.92; H, 4.95; N, 2.99. Found: C, 77.01; H, 4.99; N, 2.95.

*4.3.16. 2-(4-Chlorobenzyl)-3-(4-chlorophenyl)-1,5-diphenyl-1H-pyrrole (**3p**)*

A yellow solid, mp: 119–120 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.46 (d, *J*=7.8 Hz, 2H), 7.36 (t, *J*=8.1 Hz, 2H), 7.80–7.23 (m, 12H), 6.77 (d, *J*=8.1 Hz, 2H), 6.63 (s, 1H), 3.98 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 138.6, 138.5, 136.2, 133.5, 131.8, 131.5, 131.2, 129.8, 129.2, 128.9, 128.6, 128.5, 128.2, 128.1, 127.9, 127.8, 126.0, 124.5, 109.7, 30.6; IR (neat) cm^{-1}: 3411, 2922, 1955, 1713, 1595, 1495, 1375, 1222, 1092, 1013, 801, 697, 517. Anal. Calcd for $C_{29}H_{21}Cl_2N$: C, 76.65; H, 4.66; N, 3.08. Found: C, 76.61; H, 4.60; N, 2.98.

4.4. Procedure for preparation of the intermediate 4a

(*Z*)-1,3,5-Triphenylpent-2-en-4-ynyl acetate **1a** (0.2 mmol), aniline **2a** (0.8 mmol), and MeCN/H_2O (6:1, 10 mL) were placed in a 25 mL flask. The resulting mixture was then heated at 60 °C. When the reaction was completed as indicated by TLC analysis, water (10 mL) was added and the resulting reaction mixture was extracted with ethyl acetate. The extracts were concentrated to give a thick residue. The resulting residue was purified by column chromatography using 20:1 petroleum ether/ethyl acetate as an eluent to afford pure (*Z*)-*N*-(1,3,5-triphenyl-pent-2-en-4-ynyl)-benzenamine **4a** (93%).

*4.4.1. (Z)-N-(1,3,5-Triphenylpent-2-en-4-ynyl)benzenamine (**4a**)*

A yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.66–7.80 (m, 21H), 5.88 (d, *J*=9.0 Hz, 1H), 4.31 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 147.4, 142.0, 138.7, 137.0, 131.5, 129.2, 128.8, 128.6, 128.4, 128.1, 127.5, 126.8, 126.2, 124.7, 122.8, 117.8, 113.6, 97.3, 86.0, 59.0; IR (neat) cm^{-1}: 3406, 3055, 1600, 1498, 1413, 909, 754, 693, 511. Anal. Calcd for $C_{29}H_{23}N$: C, 90.35; H, 6.01; N, 3.63. Found: C, 90.33; H, 6.0; N, 3.67.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.12.018.

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