AgOTf-catalyzed cyclization of enynals or enynones with amines: an efficient synthesis of 1,2,4-trisubstituted pyrroles and 2,3,5-trisubstituted furans

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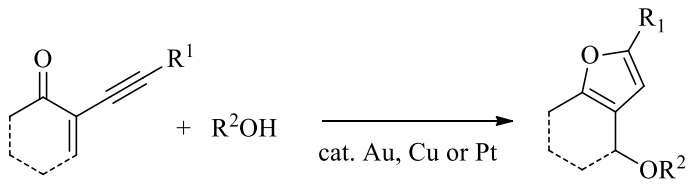
Abstract
AgOTf-catalyzed amino-cyclization of 2-(1-alkynyl)-2-alken-1-als or 2-(1-alkynyl)-2-alken-1-ones is presented, providing an efficient method for synthesis of 1,2,4-trisubstituted pyrroles or 2,3,5-trisubstituted furans with an arylamino-group function respectively under mild conditions in moderate yields.

Keywords: AgOTf, amino-cyclization, 1,2,4-trisubstituted pyrroles, 2,3,5-trisubstituted furans, enynones, enynals

Introduction

Pyrroles and furans, two classes of the most important heterocyclic compounds, are not only important building blocks in the synthesis of natural products but also key structural units in compounds with interesting biological activities.[1,2] Recently it was also found that pyrroles have broad application in the field of materials chemistry and as structural elements in molecular recognition studies.[3] As a result, development of new and efficient methodologies for the synthesis of pyrroles and furans with different substituent groups from simple, readily available starting materials remains an important research theme in organic chemistry though many strategies already existed.[4,5] Recently, an interesting Au(III), Cu(I) or Pt(II) catalyzed alkoxy-cyclization of 2-(1-alkynyl)-2-alken-1-ones leading to substituted furans with a remote C-O bond has been described (Scheme 1).[6] In the reaction, alcohol as the nucleophile assists the

cyclization. We envisioned if amines as the nucleophile were involved, an amino-function group would be introduced. With these considerations in mind and in our ongoing efforts to explore the synthesis of heterocyclic compounds,[7] herein we present our results in the amino-cyclization of 2-(1-alkynyl)-2-alken-1-als or 2-(1-alkynyl)-2-alken-1-ones using AgOTf as catalyst to afford an efficient synthesis of substituted pyrroles and furans with an amino-group function, which would be useful intermediates for access to other heterocyclic derivatives since they could be further elaborated to amplify complexity via a variety of carbon-carbon or carbon- heteroatom bond formation reactions.[8]



Scheme 1

Results and Discussion

Effect of catalysts

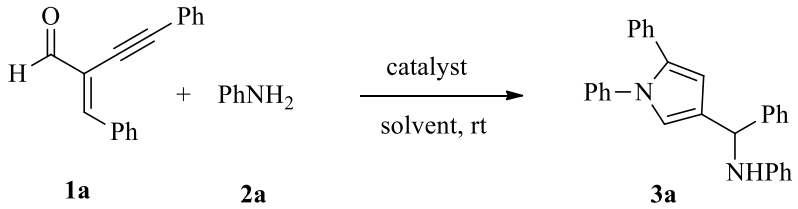
In order to find the most efficient catalyst, we initially examined the reaction of (*E*)-2-phenylethynyl-3-phenylpropen-1-al **1a** with phenylamine **2a** under different reaction conditions and the results are summarized in Table 1.

Soft metal salts such as copper, zinc, or silver with mild Lewis acidity were examined for the reaction. Gratifyingly, in an initial experiment, we observed the formation of the pyrrole product **3a** with a remote C-N bond when the reaction was performed in EtOH catalyzed by $Cu(OTf)_2$ (5 mol %) (Table 1, entry 1). Further screening of metal salts revealed that the yield could be dramatically improved when AgOTf was utilized in the reaction (Table 1, entries 5). Next, we examined the effect of solvent choice on this reaction (Table 1, entries 6-9). A better yield was obtained when CH_2Cl_2 was used as the solvent. An inferior result was found when L-proline was added as the co-catalyst in the reaction (Table 1, entry 10).

AgOTf-Catalyzed cyclization of 2-(1-alkynyl)-2-alken-1-als 1 with amines (2)

With the optimized reaction conditions in hand (Table 1, entry 5), the scope and the limitation of this reaction were examined. The results in Table 2 demonstrated that the reaction could proceed smoothly using arylamines as the nucleophiles to afford pyrroles in moderate yields (Table 2, entries 1-7, 9-10). However, when an aliphatic amine was used, only a trace amount of the product **3h** was formed (Table 2, entry 7).[10]

Table 1. Optimization of reaction conditions for the cyclization of **1a** with **2a**[a]



1a **2a** **3a**

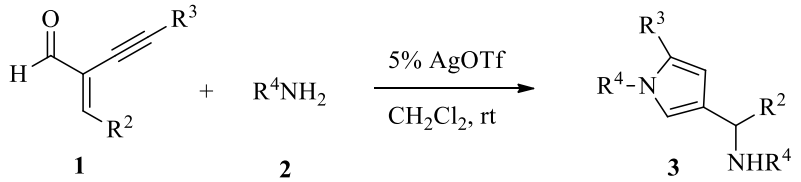
Entry	Catalyst	Solvent	Time(h)	Yield (%)[b]
1	$Cu(OTf)_2$	C_2H_5OH	16	20
2	$Cu(OTf)_2$	CH_2Cl_2	16	48
3	$Zn(OTf)_2$	CH_2Cl_2	16	42
4	CuBr	CH_2Cl_2	16	36
5	**AgOTf**	**CH_2Cl_2**	**0.5**	**88(75)**
6	AgOTf	C_2H_5OH	16	22
7	AgOTf	$PhCH_3$	2	78
8	AgOTf	CH_3CN	1.5	48
9	AgOTf	THF	0.5	82
10[c]	AgOTf	CH_2Cl_2	0.5	84

[a]The reaction was carried out using **1a** (0.258 mmol), **2a** (2.2 equiv) and catalyst (5 mol %) at room temperature in solvent (2 mL). [b]Yields were determined by ^{1}H NMR spectroscopy using CH_2Br_2 as an internal standard;[9] yields of isolated product are shown in parentheses. [c] 10 mol % L-proline was added.

AgOTf-Catalyzed cyclization of 2-(1-alkynyl)-2-alken-1-ones 1 with amines (2)

However, when (*E*)-3-phenylethynyl-4-phenylbut-3-en-2-one **1d** was used as the substrate under the above reaction conditions, we only observed that the reaction proceeded to afford furan **4a.**[11] Further screening demonstrated that THF as the solvent and elevated reaction temperature with 1.2 equivalent amine were more suitable conditions for the reaction and the yield of **4a** could be improved up to 85%. Using the optimal reaction conditions, we then carried out the reactions with various 2-(1-alkynyl)-2-alken-1-ones **1** and amines **2**, and the results are listed in Table 3. Acyclic enynone **1d-1f** and cyclic enynone **1g** were also effective for this reaction when arylamines was used as the nucleophiles, and the corresponding furans incorporating an arylamino-group function **4** were obtained in moderate yields (Table 3, entries 1-5, 7-9). However, when aliphatic amine was used as nucleophile, only a trace amount of the product **4f** was formed (Table 3, entry 6).

Table 2. AgOTf-Catalyzed cyclization of 2-(1-alkynyl)-2-alken-1-als **1** with amines **2**

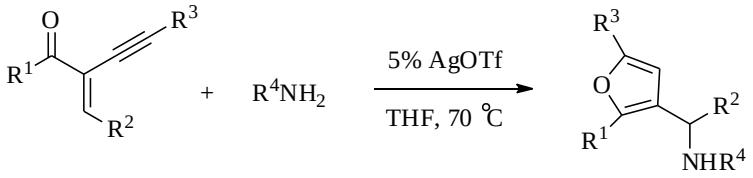


1 **2** **3**

Entry	R^2/ R^3	R^4	Product	Yield (%)[a]
1	C_6H_5/C_6H_5, **1a**	C_6H_5, **2a**	**3a**	75
2	**1a**	*p*-ClC_6H_4, **2b**	**3b**	81
3	**1a**	*o*-ClC_6H_4, **2c**	**3c**	83
4	**1a**	*p*-$CH_3C_6H_4$, **2d**	**3d**	84
5	**1a**	*o*-$CH_3C_6H_4$, **2e**	**3e**	86
6	**1a**	*m*-$CH_3C_6H_4$, **2f**	**3f**	30
7	**1a**	*p*-$CH_3OC_6H_4$, **2g**	**3g**	70
8	**1a**	$C_6H_5CH_2$, **2h**	**3h**	trace
9	C_6H_5/C_4H_9, **1b**	**2a**	**3i**	43
10	C_6H_5/CH_2OH,**1c**	**2a**	**3j**	53

[a] Isolated yield based on **1**.

Table 3. AgOTf-Catalyzed cyclization of 2-(1-alkynyl)-2-alken-1-ones **1** with amines **2**



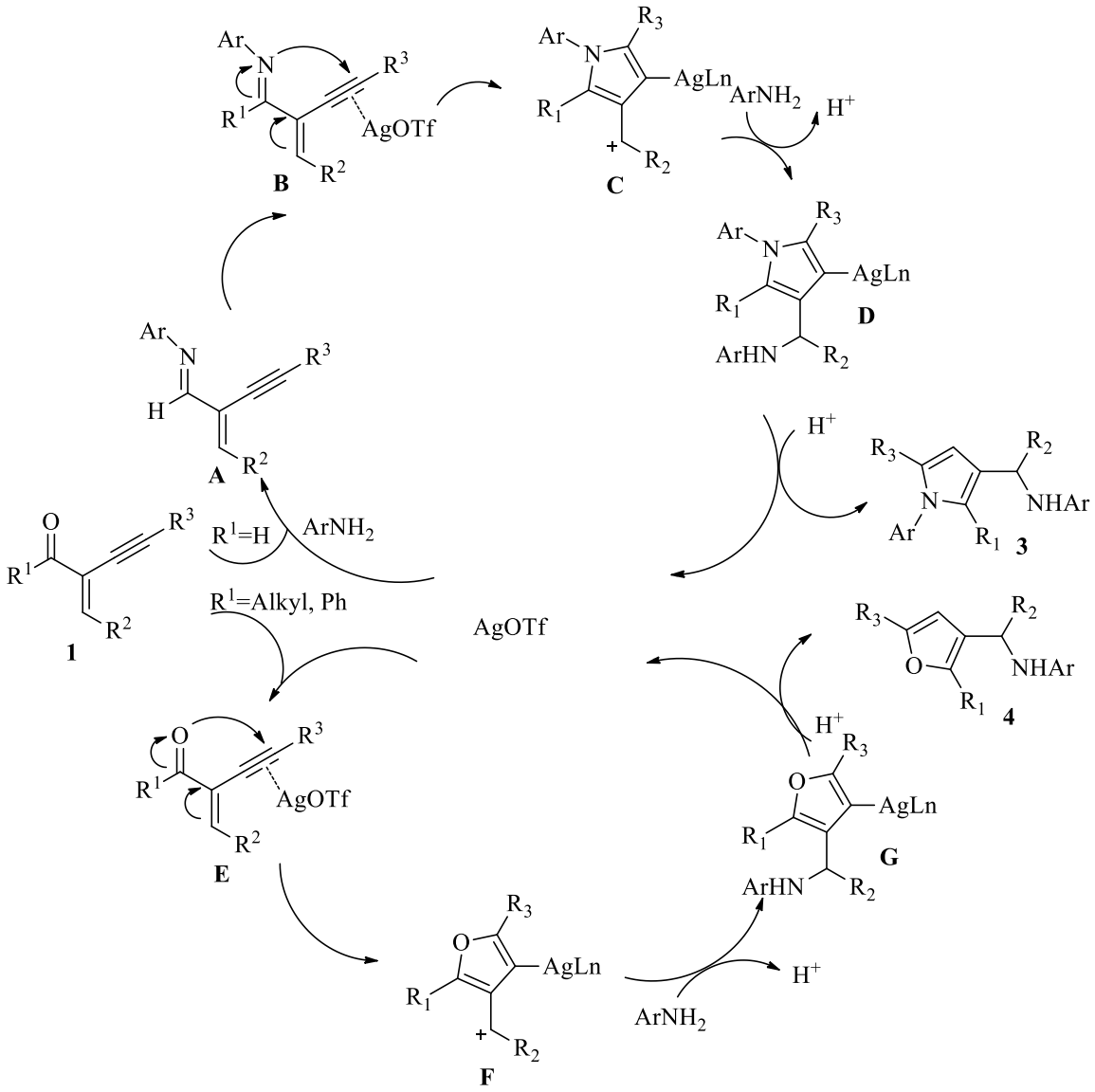
1 **2** **4**

Entry	R^1/R^2/ R^3	R^4	Product	Yield (%)[a]
1	CH_3/C_6H_5/C_6H_5, **1d**	**C_6H_5, 2a**	**4a**	85
2	**1d**	***p*-ClC_6H_4, 2b**	**4b**	89
3	**1d**	***o*-ClC_6H_4, 2c**	**4c**	71
4	**1d**	***p*-$CH_3C_6H_4$, 2d**	**4d**	72
5	**1d**	***o*-$CH_3C_6H_4$, 2e**	**4e**	80
6	**1d**	**$C_6H_5CH_2$, 2h**	**4f**	trace
7	CH_3/C_6H_5/C_4H_9, **1e**	**2a**	**4g**	68
8	C_6H_5/C_6H_5/C_4H_9, **1f**	**2a**	**4h**	87
9	-$(CH_2)_3$-/C_6H_5, **1g**	**2a**	**4i**	90

[a]Isolated yield based on 1.

Plausible reaction mechanism

On the basis of the above results and previous investigations on the Au(III) or Cu(I) catalyzed alkoxy-cyclization of 2-(1-alkynyl)-2-alken-1-ones,[6] a plausible mechanism for the AgOTf-catalyzed cyclization of enynals or enynones with amines is outlined in Scheme 2. When the reaction substrate has an aldehyde group (R^1 = H), an initial condensation reaction with arylamine affords the imine intermediate **A**. Subsequent coordination of the alkynyl moiety of the substrate to AgOTf induces a cyclization of the oxygen or nitrogen onto the triple bond to afford **C** or **F**, then elimination of a proton and protonation of the resulting organosilver intermediate to afford pyrrole **3** or furan **4** and simultaneously regenerate the catalyst AgOTf.



Scheme 2

Conclusions

In summary, we have developed an efficient method for 1,2,4-trisubstituted pyrroles or 2,3,5-trisubstitued furans with an arylamino-group respectively in moderate to good yields under mild conditions. Theses pyrroles and furans compounds bearing arylamino functional groups may be converted to other interesting and useful structural units in organic synthesis. Further studies into the scope and synthetic applications of this transformation are being carried out in our laboratory.

Experimental Section

General. All ^{1}H- and ^{13}C- NMR spectra were measured in $CDCl_3$ and recorded on Bruker Avance III 500 MHz (125 MHz) spectrometer spectra with TMS as the internal standard. Chemical shifts are expressed in ppm and *J* values are given in Hz. IR spectra were run on a Thermo Nicolet 6700 spectrometer. EIMS were determined with a Thermo ITQ 1100 mass spectrometer. HRMS were performed on a Waters GCT Premier instrument. Melting points were measured using CRC-1 melting point instrument and are uncorrected. Solvents were obtained from commercial sources and used as received. Enynones and enynals were prepared as previously described.[6]

General procedure for the synthesis of (3)

To a solution of (*E*)-2-phenylethynyl-3-phenylpropen-1-al **1a** (60 mg, 0.259 mmol) and phenylamine **2a** (52.9 mg, 0.569 mmol) in 2 mL of CH_2Cl_2 was added AgOTf (3.3 mg, 0.0129 mmol). The resulting mixture was stirred at room temperature for 0.5h. Then the reaction mixture was quenched with 10 mL of H_2O and extracted with Et_2O (15 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration and removal of the solvent *in vacuo*, the residues were purified with flash chromatography (silica/ petroleum ether-ethyl acetate 40:1 to 3:1 v/v) to afford **3**.

1,2-Diphenyl-4-[(phenylamino)(phenyl)methyl]pyrrole (3a). Solid. Mp 62-64 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.38-7.11 (m, 15H, Ar-H), 6.69 (t, 1H, *J* = 7.5 Hz, Ar-H), 6.63-6.61 (m, 3H, Ar-H, 5-pyrrole-H), 6.40 (d, 1H, *J* = 2.0 Hz, 3-pyrrole-H), 5.57 (s, 1H, -CH), 4.43 (br, 1H, -NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.49, 143.26, 140.29, 134.16, 132.64, 129.07, 128.95, 128.52, 128.14, 128.05, 127.00, 126.98, 126.59, 126.40, 125.59, 122.63, 117.26, 113.33, 110.02, 56.55. MS (EI), *m/z* (%) 400 (M^+, 1.1). HRMS-EI Calcd. for $C_{29}H_{24}N_2$ 400.1939, Found 400.1956. IR (cm^{-1}) 3413, 3050, 3025, 1600, 1499, 763, 697.

1-(4-Chlorophenyl)-2-phenyl-4-[(4-chlorophenylamino)(phenyl)methyl]pyrrole (3b). Solid, m.p. 76-78 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.35 (t, 2H, *J* = 7.5 Hz, Ar-H), 7.28-7.01 (m, 12H, Ar-H), 6.57 (d, 1H, *J* = 1.5 Hz, 5-pyrrole-H), 6.50 (d, 2H, *J* = 9.0 Hz, Ar-H), 6.35 (d, 1H, *J* = 1.5 Hz, 3-pyrrole-H), 5.48 (s, 1H, -CH), 4.39 (br, 1H, -NH). ^{13}C

NMR (125 MHz, $CDCl_3$) δ 145.96, 142.73, 138.83, 134.43, 132.41, 132.33, 129.17, 128.94, 128.66, 128.25, 128.09, 127.26, 126.98, 126.75, 126.72, 122.35, 122.07, 114.51, 110.27, 56.69. MS (EI), *m/z* (%) 468 (M^+, 1.5). HRMS-EI Calcd. for $C_{29}H_{22}Cl_2N_2$ 468.1160, Found 468.1144. IR (cm^{-1}) 3419, 3060, 1598, 1494.

1-(2-Chlorophenyl)-2-phenyl-4-[(2-chlorophenylamino)(phenyl)methyl]pyrrole (3c). Oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, 2H, *J* = 7.0 Hz, Ar-H), 7.38-6.96 (m, 14H, Ar-H), 6.41-6.58 (m, 4H, Ar-H, pyrrole-H), 5.61 (s, 1H, -CH), 5.08 (br, 1H, -NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.24, 142.60, 138.11, 135.53, 132.47, 131.91, 130.31, 129.88, 128.95, 128.90, 128.56, 128.07, 127.59, 127.44, 127.40, 127.25, 127.16, 127.04, 126.46, 122.95, 119.08, 117.19, 112.60, 108.63, 56.33. MS (EI), *m/z* (%) 468 (M^+, 0.4). HRMS-EI Calcd. for $C_{29}H_{22}Cl_2N_2$ 468.1160, Found 468.1137. IR (cm^{-1}) 3421, 3064, 3027, 1595, 1491, 760, 697.

1-(4-Methylphenyl)-2-phenyl-4-[(4-methylphenylamino)(phenyl)methyl]pyrrole (3d). Solid, m.p. 64-66 ºC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.32 (t, 2H *J* = 7.0 Hz, Ar-H), 7.24-7.05 (m, 8H, Ar-H), 6.97 (d, 2H, *J* = 8.0 Hz, Ar-H), 6.91 (d, 2H, *J* = 8.5 Hz, Ar-H), 6.57 (d, 1H, *J* = 1.5 Hz, 5-pyrrole-H), 6.50 (d, 2H, *J* = 8.5 Hz, Ar-H), 6.34 (d, *J* = 2.0 Hz, 1H, 3-pyrrole-H), 5.49 (s, 1H, -CH), 4.28 (br, 1H, -NH), 2.31 (s, 3H, $-CH_3$), 2.19 (s, 3H, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.30, 143.52, 137.85, 136.38, 134.05, 132.78, 129.55, 129.51, 128.46, 128.10, 128.00, 127.00, 126.86, 126.33, 126.28, 125.40, 122.65, 113.43, 109.75, 56.81, 20.93, 20.33. MS (EI), *m/z* (%) 428 (M^+, 2.1). HRMS-EI Calcd. for $C_{31}H_{28}N_2$: 428.2252, Found 428.2268. IR (cm^{-1}) 3411, 3058, 3025, 2917, 1614, 515, 808, 762, 699.

1-(2-Methylphenyl)-2-phenyl-4-[(2-methylphenylamino)(phenyl)methyl]pyrrole (3e). Oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, 2H, *J* = 7.0 Hz, Ar-H), 7.31 (t, 2H, *J* = 7.0 Hz, Ar-H), 7.23-6.96 (m, 12H, Ar-H), 6.60 (dt, 1H, J_1 = 7.5 Hz, J_2 = 0.5 Hz, Ar-H), 6.52 (d, 1H, *J* = 8.0 Hz, Ar-H), 6.44-6.38 (m, 2H, pyrrole-H), 5.60 (s, 1H, -CH), 4.23 (br, 1H, -NH), 2.21 (s, 3H, $-CH_3$), 1.86 (s, 3H, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.45, 143.41, 139.79, 135.42, 135.16, 132.84, 130.79, 129.84, 128.43, 128.04, 127.97, 127.01, 126.98, 126.93, 126.90, 126.45, 126.17, 122.84, 121.67, 116.81, 111.10, 108.07, 56.49, 17.73, 17.54. MS (EI), *m/z* (%) 428 (M^+, 1.6). HRMS-EI Calcd. for $C_{31}H_{28}N_2$: 428.2252, Found 428.2268. IR (cm^{-1}) 3436, 3060, 3027, 2921, 1602, 1499, 750, 698.

1-(3-Methylphenyl)-2-phenyl-4-[(3-methylphenylamino)(phenyl)methyl]pyrrole (3f). Solid. Mp 58-60 ºC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, 2H, *J* = 7.0 Hz, Ar-H), 7.33 (t, 2H, *J* = 7.5 Hz, Ar-H), 7.22-6.96 (m, 10H, Ar-H), 6.84 (d, 1H, *J* = 8.0Hz, Ar-H), 6.57 (d, 1H, *J* = 2.0 Hz, 5-pyrrole-H), 6.48 (d, 1H, *J* = 7.5Hz, Ar-H), 6.43 (s, 1H, 3-pyrrole-H), 6.40-6.35 (m, 2H, Ar-H), 5.52 (s, 1H, -CH), 4.33 (br, 1H, -NH), 2.27 (s, 3H, $-CH_3$), 2.21 (s, 3H, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.58, 143.43, 140.23, 138.97, 138.75, 134.09, 132.72, 128.97, 128.63, 128.47, 128.08, 128.05, 127.98, 127.34, 127.00, 126.88, 126.30, 126.07, 122.86, 122.63, 118.21, 114.19, 110.30, 109.88, 56.54, 21.59, 21.22. MS (EI), *m/z* (%) 428 (M^+, 1.6). HRMS-EI Calcd. for $C_{31}H_{28}N_2$: 428.2252, Found 428.2267. IR (cm^{-1}) 3413, 3035, 2923, 1601, 1492, 762, 698.

1-(4-Methoxylphenyl)-2-phenyl-4-[(4-methoxylphenylamino)(phenyl)methyl]pyrrole (3g). Oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, 2H, *J* = 7.0Hz, Ar-H), 7.31 (t, 2H, *J* = 7.5 Hz, Ar-

H), 7.23-7.07 (m, 6H, Ar-H), 7.00 (d, 2H, *J* = 8.5Hz, Ar-H), 6.76 (d, 2H, *J* = 9.0Hz, Ar-H), 6.69 (d, 2H, *J* = 9.0Hz, Ar-H), 6.55-6.52 (m, 3H, Ar-H, 5-pyrrole-H), 6.34 (d, 1H, *J* = 2.0Hz, 3-pyrrole-H), 5.45 (s, 1H, -CH), 4.15 (br, 1H, -NH), 3.73 (s, 3H, $-CH_3$), 3.66 (s, 3H, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.14, 151.87, 143.62, 141.87, 134.09, 133.46, 132.70, 128.43, 128.01, 127.98, 127.95, 126.98, 126.84, 126.77, 126.20, 122.65, 114.73, 114.46, 114.06, 109.38, 57.31, 55.68, 55.33. MS (EI), *m/z* (%) 460 (M^+, 4). HRMS-EI Calcd. for $C_{31}H_{28}N_2O_2$ 460.2151, Found 460.2165. IR (cm^{-1}) 3405, 3058, 3012, 2942, 1511, 1242, 1037, 759.

1-Phenyl-2-butyl-4-[(phenylamino)(phenyl)methyl]pyrrole (3i). Oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, 2H, *J* = 7.5Hz, Ar-H), 7.43 (t, 2H, *J* = 7.5 Hz, Ar-H), 7.39-7.14 (m, 8H, Ar-H), 6.70 (t, 1H, *J* = 7.0Hz, Ar-H), 6.62 (d, 2H, *J* = 7.5Hz, Ar-H), 6.40 (d, 1H, *J* = 1.5 Hz, 5-pyrrole-H), 6.07 (s, 1H, 3-pyrrole-H), 5.53 (s, 1H, -CH), 4.43 (br, 1H, -NH), 2.53 (t, 2H, *J* = 7.5Hz, $-CH_2$), 1.56-1.50 (m, 2H, $-CH_2$), 1.35-1.30 (m, 2H, $-CH_2$), 0.88 (t, 3H, *J* = 7.5Hz, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.58, 143.53, 140.18, 134.82, 129.02, 128.96, 128.38, 126.96, 126.94, 126.77, 126.01, 119.74, 117.06, 113.26, 106.12, 56.61, 31.13, 26.50, 22.43, 13.80. MS (EI), *m/z* (%) 380 (M^+, 0.2). HRMS-EI Calcd. for $C_{27}H_{28}N_2$ 380.2252, Found 380.2267. IR (cm^{-1}) 3417, 3053, 2956, 2928, 1600, 1500, 750, 697.

1-Phenyl-2-(1-hydroxylmethyl)-4-[(phenylamino)(phenyl)methyl]pyrrole (3j). Oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, 2H, *J* = 7.5Hz, Ar-H), 7.45-7.27 (m, 8H, Ar-H), 7.17-7.14 (m, 2H, Ar-H), 6.71 (t, 1H, *J* = 7.5Hz, Ar-H), 6.63-6.61 (m, 3H, Ar-H, 5-pyrrole-H), 6.29 (d, 1H, *J* = 2.0 Hz, 3-pyrrole-H), 5.53 (s, 1H, -CH), 4.48 (s, 2H, $-CH_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.38, 143.27, 139.48, 132.92, 129.14, 129.01, 128.47, 127.16, 127.10, 126.91, 126.88, 125.26, 121.29, 117.20, 113.26, 109.84, 56.40, 56.15. MS (EI), *m/z* (%) 354 (M^+, 1.2). HRMS-EI Calcd. for $C_{24}H_{22}N_2O$ 354.1732, Found 354.1756. IR (cm^{-1}) 3406, 3053, 2928, 1600, 1500.

General procedure for the synthesis of (4)

To a solution of (*E*)-3-phenylethynyl-4-phenylbut-3-en-2-one **1d** (60 mg, 0.244 mmol) and phenylamine **2a** (27.2 mg, 0.293 mmol) in 2 mL of THF was added AgOTf (3.1 mg, 0.0122 mmol). The resulting mixture was stirred at 70°C for 1h. Then the reaction mixture was quenched with 10 mL of H_2O and extracted with Et_2O (15 mL×3). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration and removal of the solvent in vacuo, the residues were purified with flash chromatography (silica/ petroleum ether-ethyl acetate 30:1 v/v) to afford **4**.

2-Methyl-3-[(phenylamino)(phenyl)methyl]-5-phenylfuran (4a). Solid. Mp 114-116 ºC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, 2H, *J* = 8.5Hz, Ar-H), 7.52 (d, 2H, *J* = 7.0Hz Ar-H), 7.44-7.02 (m, 8H, Ar-H), 6.80 (t, 1H, *J* = 7.5Hz,), 6.66 (d, 2H, *J* = 8.0Hz, Ar-H), 6.54 (s, 1H, Furan-H), 5.49 (s, 1H, -CH), 4.25 (br, 1H,-NH), 2.43 (s, 3H, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.76, 147.70, 147.35, 142.51, 130.70, 129.10, 128.69, 128.50, 127.22, 126.91, 126.77, 123.88, 123.26, 117.68, 113.40, 105.51, 54.87, 12.10. MS (EI), *m/z* (%) 339 (M^+, 11.5). HRMS-EI Calcd. for $C_{24}H_{21}NO$ 339.1623 Found 339.1611. IR (cm^{-1}) 3418, 2921, 1599, 1501, 756, 699.

2-Methyl-3-[(4-chlorophenylamino)(phenyl)methyl]-5-phenylfuran (4b). Solid. Mp 90-92 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, 2H, *J* = 8.0Hz, Ar-H), 7.39-7.25 (m, 7H, Ar-H), 7.18 (t, 1H, *J* = 7.5Hz, Ar-H), 7.05 (d, 2H, *J* = 9.0Hz, Ar-H), 6.46 (d, 2H, *J* = 9.0Hz, Ar-H), 6.41 (s, 1H, Furan-H), 5.33 (s, 1H, -CH), 4.16 (br, 1H, -NH), 2.32 (s, 3H, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.88, 147.78, 145.80, 142.01, 130.61, 128.94, 128.78, 128.54, 127.41, 127.02, 126.72, 123.49, 123.29, 122.34, 114.49, 105.35, 54.95, 12.12. MS (EI), *m/z* (%) 373 (M^+, 11). HRMS-EI Calcd. for $C_{24}H_{20}ClNO$ 373.1233 Found 373.1222. IR (cm^{-1}) 3423, 3029, 2919, 1597, 1494816, 756, 697.

2-Methyl-3-[(2-chlorophenylamino)(phenyl)methyl]-5-phenylfuran (4c). Solid. Mp 130-132 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.47 (d, 2H, *J* = 7.0 Hz, Ar-H), 7.42-7.22 (m, 7H, Ar-H), 7.08-7.04 (m, 1H, Ar-H), 6.67 (dt, 1H, J_1 = 7.5 Hz, J_2 = 1.5 Hz, Ar-H), 6.67 (dd, 1H, J_1 = 8.5 Hz, J_2 = 1.5 Hz, Ar-H), 6.49 (s, 1H, Furan-H), 5.50 (s, 1H, -CH), 4.88 (br, 1H, -NH), 2.40 (s, 3H, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.90, 147.89, 143.05, 141.86, 130.66, 129.01, 128.83, 128.55, 127.68, 127.46, 127.02, 126.73, 123.34, 119.27, 117.66, 112.50, 105.55, 54.62, 12.17. MS (EI), *m/z* (%) 373 (M^+, 12). HRMS-EI Calcd. for $C_{24}H_{20}ClNO$ 373.1233 Found 373.1232. IR (cm^{-1}) 3427, 3062, 3027, 1596, 1497, 755, 696.

2-Methyl-3-[(4-methylphenylamino)(phenyl)methyl]-5-phenylfuran (4d). Oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, 2H, *J* = 8.5Hz, Ar-H), 7.50 (d, 2H *J* = 7.5 Hz, Ar-H), 7.42-7.25 (m, 6H, Ar-H), 7.01 (d, 2H, *J* = 8.5 Hz, Ar-H), 6.57 (d, 2H, *J* = 8.5Hz, Ar-H), 6.53 (s, 1H, Furan-H), 5.44 (s, 1H, -CH), 4.10 (br, 1H, -NH), 2.41 (s, 3H, $-CH_3$), 2.29 (s, 3H, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.73, 147.66, 145.15, 142.73, 130.75, 129.61, 128.67, 128.51, 127.17, 126.90, 126.88, 126.78, 124.06, 123.27, 113.53, 105.54, 55.14, 20.34, 12.12. MS (EI), *m/z* (%) 353 (M^+, 26). HRMS-EI Calcd. for $C_{25}H_{23}NO$ 353.1780 Found 353.1779. IR (cm^{-1}) 3409, 3058, 3027, 2919, 1601, 1514, 1452, 808, 760, 697.

2-Methyl-3-[(2-methylphenylamino)(phenyl)methyl]-5-phenylfuran (4e). Solid; Mp 110-112 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.50 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.43-7.07 (m, 8H, Ar-H), 6.74 (dd, 1H, J_1 = 7.5 Hz, J_2 = 0.5 Hz, Ar-H), 6.55 (d, 1H, *J* = 8.0 Hz, Ar-H), 6.53 (s, 1H, Furan-H), 5.53 (s, 1H, -CH), 4.07 (br, 1H, -NH), 2.42 (s, 3H, $-CH_3$), 2.28 (s, 3H, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.78, 147.73, 145.21, 142.57, 130.70, 129.96, 128.72, 128.52, 127.23, 127.02, 126.94, 126.74, 124.04, 123.29, 121.99, 117.33, 111.11, 105.54, 54.71, 17.65, 12.14. MS (EI), *m/z* (%) 353 (M^+, 23). HRMS-EI Calcd. for $C_{25}H_{23}NO$ 353.1780 Found 353.1788. IR (cm^{-1}) 3435, 3056, 3020, 2919, 1603, 1502, 1447, 1306, 747, 697.

2-Methyl-3-[(phenylamino)(phenyl)methyl]-5-butylfuran (4g). Oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.40 (t, 2H, *J* = 7.5 Hz, Ar-H), 7.31 (t, 1H, *J* = 7.5 Hz, Ar-H), 7.21-7.17 (m, 2H, Ar-H), 6.76 (t, 1H, *J* = 7.5 Hz, Ar-H), 6.62 (d, 2H, *J* = 7.5Hz, Ar-H), 5.84 (s, 1H, Furan-H), 5.40 (s, 1H, -CH), 4.21 (br, 1H, -NH), 2.57 (t, 2H, *J* = 7.5 Hz, $-CH_2$), 2.31 (s, 3H, $-CH_3$), 1.67-1.61 (m, 2H, $-CH_2$), 1.46-1.39 (m, 2H, $-CH_2$), 0.99 (t, 3H, *J* = 7.5 Hz, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.44, 147.47, 145.64, 142.93, 129.04, 128.57, 126.97, 126.65, 122.00, 117.46, 113.34, 104.80, 54.88, 30.06, 27.72, 22.31, 13.78, 11.86. MS (EI), *m/z* (%) 319

(M^+, 9.5). HRMS-EI Calcd. for $C_{22}H_{25}NO$ 319.1936 Found 319.1939. IR (cm^{-1}) 3413, 3053, 3023, 2956, 2927, 1602, 1500, 749, 697.

2-Phenyl-3-[(phenylamino)(phenyl)methyl]-5-butylfuran (4h). Solid; Mp 108-110 ºC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.46 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.41-7.28 (m, 6H, Ar-H), 7.14 (t, 2H, *J* = 7.5 Hz, Ar-H), 6.72 (d, 1H, *J* = 7.5 Hz, Ar-H), 6.55 (d, 2H, *J* = 8.0 Hz, Ar-H), 5.90 (s, 1H, Furan-H), 5.73 (s, 1H, -CH), 4.34 (br, 1H, -NH), 2.63 (t, 2H, *J* = 7.5 Hz, $-CH_2$), 1.67-1.63 (m, 2H, $-CH_2$), 1.43-1.39 (m, 2H, $-CH_2$), 0.96 (t, 3H, $-CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.86, 147.58, 147.00, 142.38, 131.06, 129.12, 128.68, 128.65, 127.23, 127.14, 125.82, 123.76, 117.54, 113.31, 107.20, 54.48, 30.04, 27.85, 22.33, 13.79. MS (EI), *m/z* (%) 381 (M^+, 15). HRMS-EI Calcd. for $C_{27}H_{27}NO$ 381.2093 Found 381.2102. IR (cm^{-1}) 3411, 3052, 2956, 2928, 1601, 1498, 745, 697.

2-Phenyl-4-phenylamino-4,5,6,7-tetrahydrobenzofuran (4i). Solid; Mp 74-76 ºC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 7.5 Hz, Ar-H), 7.41 (t, 2H, *J* = 7.5 Hz, Ar-H), 7.28 (t, 3H, *J* = 7.5 Hz, Ar-H), 6.81 (d, 1H, *J* = 7.5 Hz, Ar-H), 6.75 (d, 2H, *J* = 7.0 Hz, Ar-H), 6.66 (s, 1H, Furan-H), 4.62 (s, 1H, -CH), 3.86 (br, 1H, -NH), 2.81-2.67 (m, 2H, $-CH_2$), 2.05-2.03 (m, 2H, $-CH_2$), 1.92-1.87 (m, 2H, $-CH_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.25, 152.05, 147.18, 130.94, 129.32, 128.54, 126.87, 123.28, 121.40, 117.23, 113.05, 104.83, 46.72, 29.20, 23.07, 19.62. MS (EI), *m/z* (%) 289 (M^+, 18). HRMS-EI Calcd. for $C_{20}H_{19}NO$ 289.1467, Found 289.1463 IR (cm^{-1}) 3407, 3051, 2938, 1601, 1503, 1313, 755, 692.

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