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Silver-Catalyzed One-Pot Cyclization Reaction of Electron-Deficient Alkynes and 2-Yn-1-ols: An Efficient Domino Process to Polysubstituted Furans

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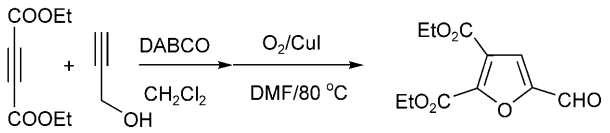
Abstract: Transition metal-catalyzed domino reactions have been used as powerful tools for the preparation of polysubstituted furans in a one-pot manner. In this paper, an efficient synthetic method was developed for the construction of tri- or tetrasubstituted furans from electron-deficient alkynes and 2-yn-1-ols by a silver-catalyzed domino reaction. It is especially noteworthy that a 2,3,5-trisubstituted 4-ynylfuran was formally obtained in an extremely direct manner without tedious stepwise synthesis. In addition, regio-isomeric furans were observed when substituted aryl alkynyl ketones were employed. This methodology represents a highly efficient synthetic route to electron-deficient furans for which catalytic approaches are scarce. The reaction proceeds efficiently under mild conditions with commercially available catalysts and materials.

Keywords: cyclization; domino process; furans; homogeneous catalysis; one-pot reaction; silver

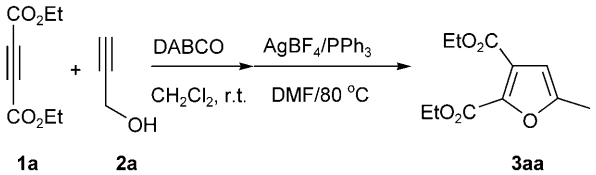
Introduction

The rapid synthesis of elaborate and diverse organic molecules in one single operation without isolation of intermediates is one of the current concerns of the chemical community[1] that attracts increasing interest. To this end, transition metal-catalyzed domino reactions[2] have been used as powerful tools for the preparation of various compounds in a one-pot manner. Furan derivatives are important targets of these metal-catalyzed methods,[3] because functionalized furans have exhibited a broad range of biological activities[4] and been found as key structural units in many natural products.[5] They have also been extensively used as building blocks for the synthesis of more elaborate heterocyclic compounds[6] and as communicating moieties in molecular materials.[7] Thus, the search for efficient transition metal-catalyzed syntheses of polysubstituted furans continues to attract the interest of synthetic chemists. In spite of several methodologies that were developed during the last decade,[8] there is still an intrinsic need for improved routes for the expedient synthesis of more diverse furans under mild conditions and with a simple catalytic system.[9]

Very recently, our group has reported a one-pot, copper-catalyzed domino process for the synthesis of highly functionalized polysubstituted furans (Scheme 1).[10] During our further investigation of different metal catalysts in this sequential system, we were delighted to find that the product diethyl 5-methylfuran-2,3-dicarboxylate (**3aa**) can be detected with the $AgBF_4$/DMF catalytic system at 80 °C (Scheme 2). Herein we report a one-pot, Ag-catalyzed



Scheme 1. One-pot copper-catalyzed synthesis of diethyl 5-formylfuran-2,3-dicarboxylate.



Scheme 2. $AgBF_4$-catalyzed synthesis of diethyl 5-methylfuran-2,3-dicarboxylate.

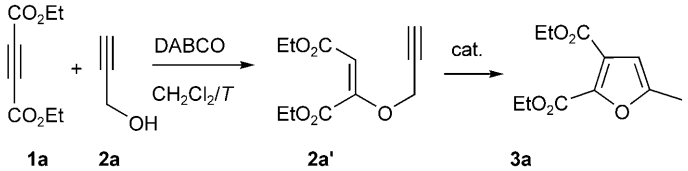
atom-economical domino process synthesis of polysubstituted furans from electron-deficient alkynes and alkynols without the aid of traditional catalysts such as Au and Pt. This methodology represents a highly efficient synthetic route to electron-deficient furans for which catalytic approaches are scarce.

Results and Discussion

Initial efforts were focused on searching for potential catalysts and suitable reaction conditions, and substrates **1a** and **2a** were used as the starting materials. In a typical procedure, **1a** (0.5 mmol), **2a** (0.5 mmol) and DABCO in CH_2Cl_2 were stirred for 10 min at room temperature.[11] Then the solution was evaporated to dryness under reduced pressure. Subsequently, various silver catalysts were added. Based on the experience of our previous work, we first examined the reaction in the presence of 5 mol% of $AgBF_4$ and 10 mol% PPh_3. The desired product was obtained after stirring at 100 °C in DMF (Table 1, entry 1). Other Ag(I) catalysts, such as 5 mol% AgOAc, 5 mol% $AgNO_3$, 5 mol% Ag_2CO_3 were next examined (Table 1, entries 2–4). Interestingly, AgOAc was found to catalyze the reaction more effectively. Other transition metal salts, such as $PdCl_2$, $Pd(OAc)_2$, $Pd(dba)_2$ and $Ru_3(CO)_{12}$ (Table 1, entries 5–8), were employed, no conversion was observed in the above cases due to the complete recovery of compound **2a′**. Treatment of **2a′** with 3 mol% of $AuCl_3$ or 3 mol% of $AuCl_3$ with 5 mol% of PPh_3 gave the desired furan **3aa** in 11% and 13% yields, respectively (Table 1, entries 9 and 10). To our surprise, when toluene was used as the solvent, it was found that the yield of **3aa** was increased to 76% (Table 1, entry 11). Other solvents, such as 1,2-dichloroethane, 1,4-dioxane, which were employed, led to moderate yields (Table 1, entries 12 and 13). Different temperatures were scanned, and 50 °C was found the most optimal one for the domino reaction (Table 1, entries 14 and 15). After systematically tuning the different conditions, the optimized conditions were found as indicated in entry 14 in Table 1.

On the basis of the above optimization, we proceeded to probe the scope of the AgOAc/PPh_3-catalyzed conversion of propargyl vinyl ethers to a variety of polysubstituted furans in Table 2. It was pleasing to find that all the reactions proceeded efficiently and afforded the desired products in good to excellent yields. To examine the scope of this cyclization, we first investigated reactions of **1a** with prop-2-yn-1-ol (**2a**) or but-2-yn-1-ol (**2b**) or pent-2-yn-1-ol (**2c**), as depicted in Table 2. Tetrasubstituted furans (**3aa**–**3ac**) were obtained in 64–71% yields (Table 2, entries 1–3). The furan products were formed in good yields (entries 4–13), when **2a**–**2c** were replaced by **2d**–**2m**. These results showed that aliphatic groups could work as well as aryl groups. Both electron-rich aryl groups and electron-withdrawing groups furnished good yields in this reaction. Subsequently, ethyl 3-phenylpropiolate was examined and the product (**3bh**) was

Table 1. Optimization of reaction conditions.

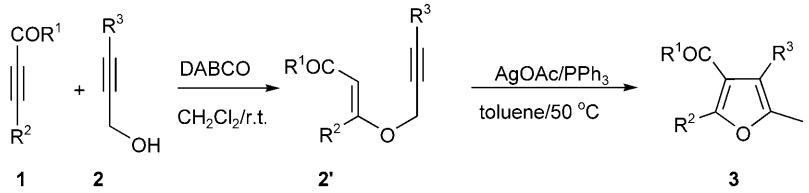


1a **2a** **2a'** **3a**

Entry	Catalyst	Solvent	Temperature [°C]	Yield [%][a]
1	5 mol% $AgBF_4$/10% PPh_3	DMF	100	37
2	5 mol% AgOAc/10% PPh_3	DMF	100	68
3	5 mol% $AgNO_3$/10% PPh_3	DMF	100	32
4	5 mol% $AgCO_3$/10% PPh_3	DMF	100	trace
5	5 mol% $PdCl_2$/10% PPh_3	CH_2Cl_2	50	–
6	5 mol% $Pd(OAc)_2$/10% PPh_3	DMF	100	–
7	5 mol% $Pd(dba)_2$	DMF	100	–
8	5 mol% $Ru_3(CO)_{12}$	DMF	100	–
9	3 mol% $AuCl_3$	DMF	100	11
10	3 mol% $AuCl_3$/5 mol% PPh_3	DMF	100	13
11	5 mol% AgOAc/10 mol% PPh_3	toluene	100	76
12	5 mol% AgOAc/10 mol% PPh_3	1,2-dichloroethane	100	40
13	5 mol% AgOAc/10 mol% PPh_3	1,4-dioxane	100	46
14	5 mol% AgOAc/10 mol% PPh_3	toluene	50	79
15	5 mol% AgOAc/10 mol% PPh_3	toluene	r.t.	–

[a] Yield determined by GC.

Table 2. Ag(I)-catalyzed formation of polysubstituted furans.



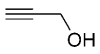
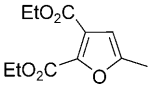
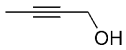
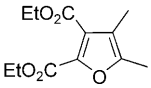
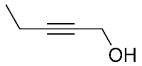
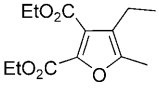
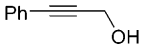
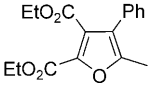
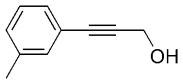
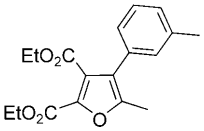
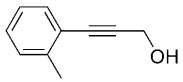
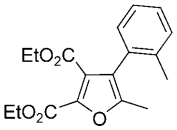
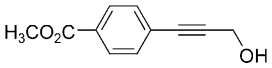
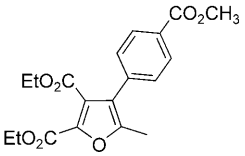
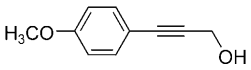
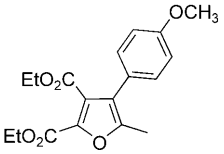
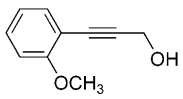
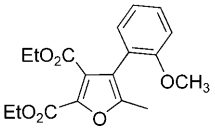
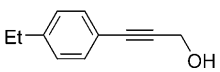
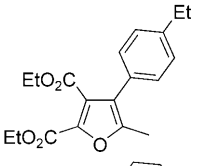
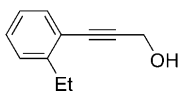
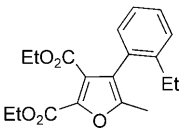
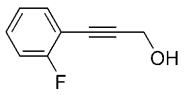
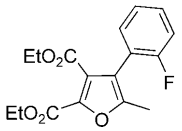
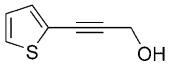
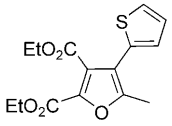
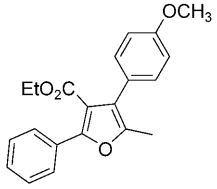
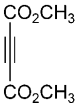
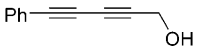
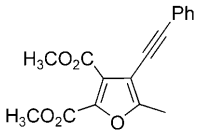
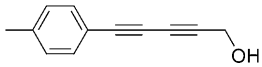
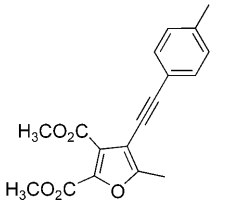
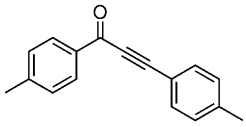
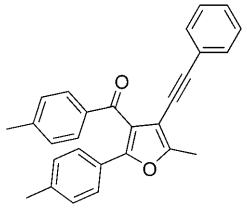
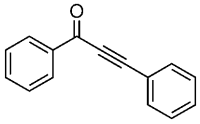
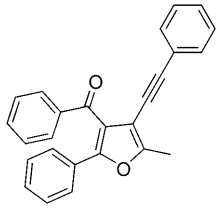
Entry	Electron-deficient alkyne	2-Yn-1-ol	Product	Yield [%][a]
1	**1a**	**2a** 	**3aa** 	71
2	**1a**	**2b** 	**3ab** 	70
3	**1a**	**2c** 	**3ac** 	64
4	**1a**	**2d** 	**3ad** 	68
5	**1a**	**2e** 	**3ae** 	68
6	**1a**	**2f** 	**3af** 	59
7	**1a**	**2g** 	**3ag** 	69
8	**1a**	**2h** 	**3ah** 	66
9	**1a**	**2i** 	**3ai** 	55
10	**1a**	**2j** 	**3aj** 	67
11	**1a**	**2k** 	**3ak** 	53

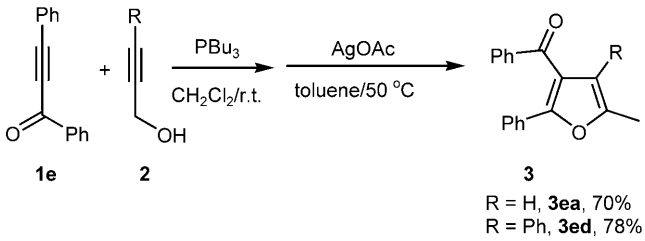
Table 2. (Continued)

Entry	Electron-deficient alkyne	2-Yn-1-ol	Product	Yield [%][a]
12	**1a**	**2l** 	**3al** 	62
13	**1a**	**2m** 	**3am** 	64
14[b]	**1b** 	**2h**	**3bh** 	79
15	**1c** 	**2n** 	**3cn** 	70
16	**1c**	**2o** 	**3co** 	68
17[b]	**1d** 	**2n**	**3dn** 	75
18[b]	**1e** 	**2n**	**3en** 	72

[a] Isolated yields.
[b] PBu_3 substituted DABCO as a catalyst.

obtained in 79% yield (entry 14). Furthermore, 5-phenylpenta-2,4-diyn-1-ol (**2n**) and 5-*p*-tolylpenta-2,4-diyn-1-ol (**2o**) were tested. Interestingly, the desired products **3cn**, **3co**, **3dn** and **3en** were formed in 70%, 68%, 75%, 72% yields, respectively (entries 15–18), when **1c, 1d**, and **1e** were reacted with **2n** or **2o**. No formation of other regioisomers was observed by GC/MS. It is especially noteworthy that a novel 2,3,5-trisubstituted 4-ynylfuran was formally formed in an extremely direct manner without tedious stepwise synthesis.[13]

The above studies dealt with **1a**, **1b**, **1c**, **1d**, and **1e** as the starting materials. As an extension of the above study (Table 2), we devised other electronic-deficient compounds, such as substituted aryl alkynyl ketones (**1e–1h**), to investigate the possibility of this transformation. In contrast to but-2-ynedioates, phenyl alkynyl ketone (**1e**) gave the corresponding rearrangement products (**3ea**, **3ed**) with good yields only upon the initiation of tributylphosphine (Bu_3P)[12] (Scheme 3) since the DABCO-catalyzed reaction of **1e** with **2a** could not take place. Interestingly, substrates bearing

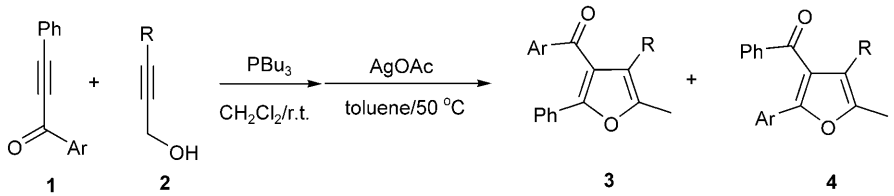


Scheme 3. Formation of the desired products **3** from **1e** and **2**.

different substituents gave a pair of regioisomers. As summarized in Table 3, we examined the domino reaction of alkynyl ketones bearing different aryl groups with 2-yn-1-ols. The rearrangement products (**3fa–3hd**) and their regioisomers (**4fa–4hd**) were obtained in reasonable yields. To the best of our knowledge, this transformation had not been reported in previous work.[14] The molecular structure of representative product **4fd** was confirmed by an X-ray diffraction study (Figure 1).

On the basis of these experimental results and previous reports,[14–16] a plausible reaction mechanism is shown in Scheme 4. The PBu_3-promoted nucleoaddition of propargyl alcohol to electron-deficient alkynes formed enyne adduct **A**. Alkyne-coordinated silver **B** was generated from the intermediate **A** and Ag(I). The complex **C** which underwent rearrangement to form complex **D**, was then formed *via* 5-*endo* cyclization. Since two carbonyl groups in complex **D** were both active in the following cyclization reaction, regioisomers would be produced in an around 1:1 ratio by different attack directions (Paths **I** and **II**).

Table 3. Cyclization of alkynyl ketones with 2-yn-1-ol.



Entry	Electron-deficient alkyne	2-Yn-1-ol	Product	Yield [%][a]
1	**1f**	**2a**	**3fa + 4fa**	73 (50:50)[b]
2	**1f**	**2d**	**3fd + 4fd**	64(45:55)[b]
3	**1g**	**2a**	**3ga + 4ga**	72 (50:50)[b]
4	**1h**	**2a**	**3ha + 4ha**	83 (53:47)[c]
5	**1h**	**2d**	**3hd + 4hd**	40 (50:50)[c]

[a] Isolated yields.
[b] The ratio was determined by HPLC.
[c] Ratio was determined by ^{1}H NMR.

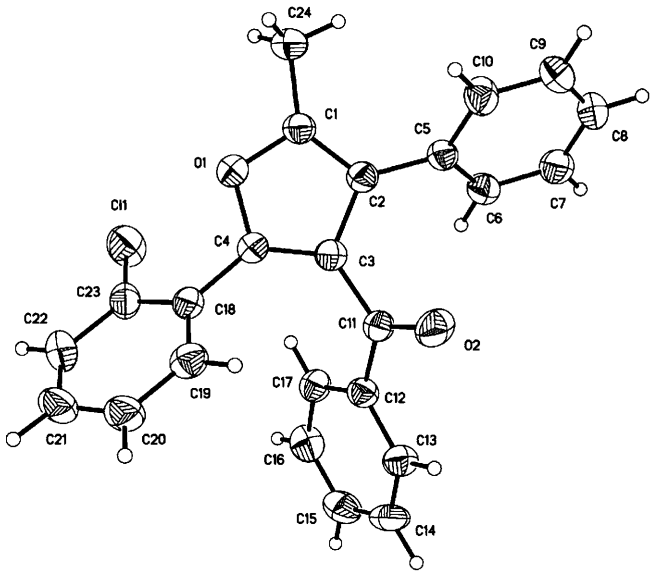


Figure 1. X-ray structure of compound **4fd**.

Conclusions

We have developed a facile one-pot, Ag-catalyzed atom-economical domino reaction which provides efficient access to highly substituted furans from electron-deficient alkynes and alkynols. Different from previous work,[13] the 2,3,5-trisubstituted 4-ynyl-furan was obtained from electron-deficient alkynes (**1c–1e**) and **2n** or **2o** in a one-pot manner. The reaction proceeds efficiently under mild conditions with commercially available catalysts. Further studies and applications of the domino reactions are ongoing in our laboratory.

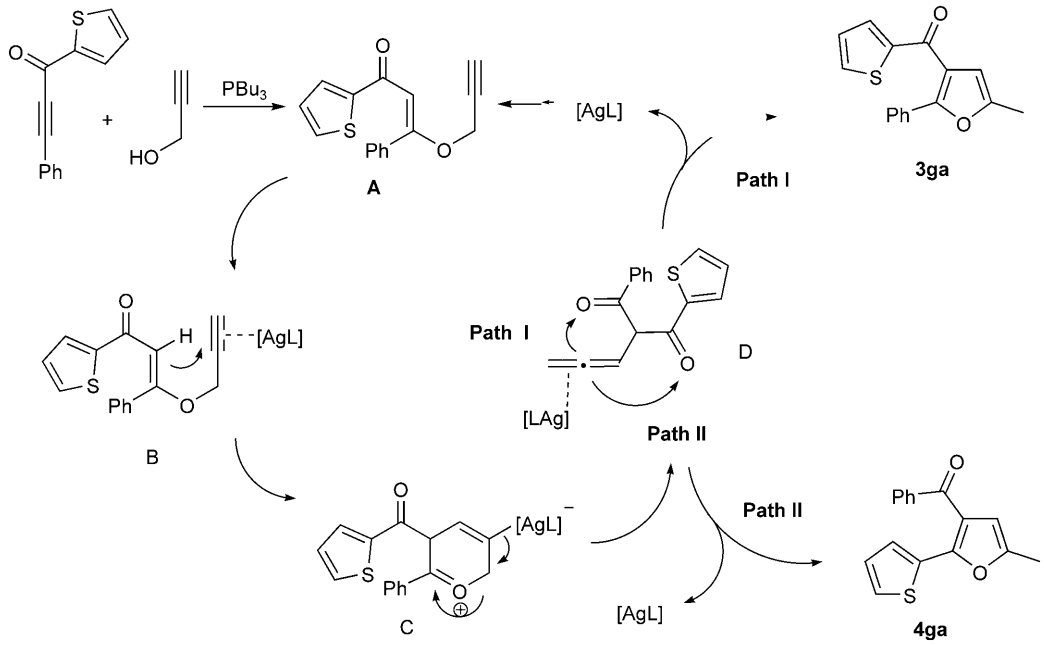
Experimental Section

General Remarks

All reactions were performed at the room temperature under air atmosphere in a round-bottom flask equipped with a magnetic stir bar. ^{1}H NMR spectra and ^{13}H NMR spectra were recorded using a Bruker Avance 400 MHz NMR spectrometer and referenced to 7.24 ppm and 77.0 ppm for chloroform solvent, respectively, with TMS as internal standard. IR spectra were obtained as potassium bromide pellets or as liquid films between two potassium bromide pellets with a Brucker Vector 22 spectrometer. Mass spectra were recorded on a Shimadzu GCMS-QP5050 A at an ionization voltage of 70 eV equipped with a DB-WAX capillary column (internal diameter = 0.25 mm, length = 30 m). Elemental analysis was performed on a Vario EL elemental analyzer. TLC was performed using commercially prepared 100–400 mesh silica gel plates (GF254), and visualization was effected at 254 nm. All the other chemicals were purchased from Aldrich Chemicals.

General Procedure for the Synthesis of Diethyl 5-Methylfuran-2,3-dicarboxylate (3aa)

Diethyl acetylenedicarboxylate (**1a** 0.5 mmol), prop-2-yn-1-ol (**2a** 0.5 mmol), DABCO (0.05 mmol) in CH_2Cl_2 were stirred for 10 min at room temperature. And then the solution was evaporated to dryness under reduced pressure. Subsequently, AgOAc/PPh_3 and toluene were added at 50 °C. After completion of the reaction (as monitored by TLC), the solution was evaporated to dryness under reduced pres-



Scheme 4. Plausible reaction mechanism.

sure and then water (8 mL) was added. The aqueous solution was extracted with diethyl ether (3×8 mL) and the combined extract was dried with anhydrous $MgSO_4$. The solvent was removed and the crude product was separated by column chromatography to give a pure sample of **3aa**.

General Procedure for the Synthesis of (5-Methyl-2-phenylfuran-3-yl)(phenyl)methanone (3ea)

1,3-Diphenylprop-2-yn-1-one (**1c** 0.5 mmol), prop-2-yn-1-ol (**2a** 0.5 mmol), and PBu_3 (0.1 mmol) in CH_2Cl_2 were stirred for 30 min at room temperature. And then the solution was evaporated to dryness under reduced pressure. Subsequently, AgOAc and toluene were added at 50 °C. After completion of the reaction (as monitored by TLC), the solution was evaporated to dryness under reduced pressure and then water (8 mL) was added. The aqueous solution was extracted with diethyl ether (3×8 mL) and the combined extract was dried with anhydrous $MgSO_4$. The solvent was removed and the crude product was separated by column chromatography to give a pure sample of **3ea**.

Diethyl 5-methylfuran-2,3-dicarboxylate (3aa): Yellowish viscous oil; IR (KBr): ν = 2980, 1725, 1603, 1581, 1138 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 6.30 (s, 1H), 4.25–4.31 (m, 4H), 2.30 (s, 3H), 1.26–1.32 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 162.7, 157.8, 155.4, 142.0, 125.1, 109.2, 61.2, 14.1, 14.0, 13.5; MS (EI): *m/z* (%) = 226, 198, 181, 153, 126, 109; anal. calcd. for $C_{11}H_{14}O_5$: C 58.40, H 6.24; found: C 58.26, H 6.32.

Diethyl 4,5-dimethylfuran-2,3-dicarboxylate (3ab): Yellowish viscous oil; IR (KBr): ν = 2983, 1722, 1556,1092 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 4.27–4.35 (m, 4H), 2.25 (s, 3H), 1.96 (s, 3H), 1.29–1.35 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 163.9, 157.9, 152.0, 140.0, 126.5, 116.5, 61.3, 61.0, 14.2, 14.1, 11.7, 8.50; MS (EI): *m/z* (%) = 240, 229, 194, 166, 137; anal. calcd. for $C_{12}H_{16}O_5$: C 59.99, H 6.71, found: C 60.24, H 6.63.

Diethyl 4-ethyl-5-methylfuran-2,3-dicarboxylate (3ac): Yellowish viscous oil; IR (KBr): ν = 2981, 1730, 1603, 1528, 1105 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 4.28–4.36 (m, 4H), 2.39 (d, *J* = 7.6 Hz, 2H), 2.27 (s, 3H), 1.29–1.36 (m, 6H), 1.07 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 164.1, 157.9, 151.8, 139.7, 122.8, 110.8, 61.4, 61.0, 16.9, 14.7, 14.1, 14.0, 11.7; MS (EI): *m/z* (%) = 254, 208, 179, 162, 135, 108; anal. calcd. for $C_{13}H_{18}O_5$: C 61.40, H 7.14; found: C 61.16, H 7.20.

Diethyl 5-methyl-4-phenylfuran-2,3-dicarboxylate (3ad): Yellowish viscous oil; IR (KBr): ν = 3059, 2984, 1732, 1558, 1177, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 7.22–7.34 (m, 5H), 4.29 (q, *J* = 7.2 Hz, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 2.34 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.14 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 163.9, 157.8, 152.6, 139.5, 131.7, 130.7, 128.8, 128.3, 127.7, 126.6, 122.6, 111.4, 61.6, 61.2, 14.2, 13.9, 12.6; MS (EI): *m/z* (%) = 302, 257, 229, 202, 185, 128, 77; anal. calcd. for $C_{17}H_{18}O_5$: C 67.54, H 6.00; found: C 67.30, H 6.14.

Diethyl 5-methyl-4-*m*-tolylfuran-2,3-dicarboxylate (3ae): Yellowish viscous oil; IR (KBr): ν = 3052, 2984, 2935, 1733, 1610, 1557, 1096, 789 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 7.19–7.21 (m, 1H), 7.02–7.09 (m, 3H), 4.31 (q, *J* = 7.2 Hz, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 2.34 (s, 3H), 2.30 (s, 3H), 1.29 (t, *J* = 6.8 Hz, 3H), 1.16 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 164.0, 157.8, 152.6, 139.4, 138.1, 130.6, 129.4, 128.5, 128.4, 126.7, 125.8, 122.7, 61.6, 61.2, 21.3, 14.1, 13.9, 12.6; MS (EI): *m/z* (%) = 316, 271, 243, 199, 91; anal. calcd. for $C_{18}H_{20}O_5$: C 68.34, H 6.37; found: C 68.13, H 6.45.

Diethyl 5-methyl-4-*o*-tolylfuran-2,3-dicarboxylate (3af): Yellowish viscous oil; IR (KBr): ν = 3048, 2983, 1732, 1560, 1450, 1177, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 7.11–7.26 (m, 4H), 4.39 (q, *J* = 8.0 Hz, 2H), 4.14 (q, *J* = 8.0 Hz, 2H), 2.21 (s, 3H), 2.15 (s, 3H), 1.37 (t, *J* = 8.0 Hz, 3H), 1.08 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 163.3, 157.9, 152.7, 140.0, 137.4, 130.4, 129.9, 128.3, 126.9, 125.5, 122.4, 111.3, 61.2, 60.6, 19.7, 14.2, 13.7, 12.3; MS (EI): *m/z* (%) = 316, 270, 242, 198, 170, 115, 91; anal. calcd. for $C_{18}H_{20}O_5$: C 68.34, H 6.37; found: C 68.25, H 6.44.

Diethyl 4-(4-acetylphenyl)-5-methylfuran-2,3-dicarboxylate (3ag): Yellowish viscous oil; IR (KBr): ν = 3046, 2983, 1729, 1612, 1573, 1046 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 8.05 (d, *J* = 8.0 Hz, 2H), 7.34 (t, *J* = 8.0 Hz, 2H), 4.37 (q, *J* = 8.0 Hz, 2H), 4.26 (q, *J* = 8.0 Hz, 2H), 3.90 (s, 3H), 2.39 (s, 3H), 1.33 (t, *J* = 8.0 Hz, 3H), 1.19 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 166.6, 163.6, 157.6, 153.0, 152.9, 140.0, 135.5, 129.8, 128.8, 126.1, 121.8, 61.8, 61.4, 52.1, 14.1, 13.9, 12.7; MS (EI): *m/z* (%) = 360, 329, 315, 288, 211, 143, 128, 58; anal. calcd. for $C_{19}H_{20}O_7$: C 63.33, H 5.59; found: C 63.02 H 5.63.

Diethyl 4-(4-methoxyphenyl)-5-methylfuran-2,3-dicarboxylate (3ah): Yellowish viscous oil; IR (KBr): ν = 3041, 2983, 1737, 1606, 1560, 773 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 7.22 (d, *J* = 8.0 Hz, 2H), 6.94 (t, *J* = 9.6 Hz, 2H), 4.39 (q, *J* = 8.0 Hz, 2H), 4.27 (q, *J* = 8.0 Hz, 2H), 3.82 (s, 3H), 2.39 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 164.0, 159.1, 157.8, 152.4, 139.3, 130.0, 126.7, 122.9, 122.2, 114.0, 61.6, 61.2, 55.2, 14.1, 13.9, 12.5; MS (EI): *m/z* (%) = 332, 304, 287, 259, 232, 187, 115; anal. calcd. for $C_{18}H_{20}O_6$: C 65.05, H 6.07; found: C 65.22, H 5.93.

Diethyl 4-(2-methoxyphenyl)-5-methylfuran-2,3-dicarboxylate (3ai): Yellowish viscous oil; IR (KBr): ν = 3044, 2971, 1731, 1609, 1561, 1156 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 7.97 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 4.36 (q, *J* = 6.8 Hz, 2H), 4.09 (q, *J* = 6.8 Hz, 2H), 3.72 (s, 3H), 2.20 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H), 1.03 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 167.1, 162.8, 158.0, 152.2, 140.4, 131.9, 131.6, 131.1, 130.5, 128.2, 126.1, 122.7, 61.2, 61.1, 52.1, 14.1, 13.6, 12.2; MS (EI): *m/z* (%) = 332, 314, 242, 226; anal. calcd. for $C_{18}H_{20}O_6$: C 65.05, H 6.07; found: C 65.20, H 5.95.

Diethyl 4-(4-ethylphenyl)-5-methylfuran-2,3-dicarboxylate (3aj): Yellowish viscous oil; IR (KBr): ν = 3039, 2975, 1728, 1600, 1577, 765 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 7.19 (s, 4H), 4.35 (q, *J* = 7.2 Hz, 2H), 4.25 (q, *J* = 7.2 Hz, 2H), 2.63 (q, *J* = 7.6 Hz, 2H), 2.38 (s, 3H), 1.33 (t, *J* = 6.8 Hz, 3H), 1.18–1.25 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 164.0, 157.8, 152.5, 143.8, 139.4, 128.7, 128.0, 127.9, 126.7, 122.6, 61.6, 61.2, 28.5, 15.3, 14.2, 13.9, 12.6; MS (EI): *m/z* = (%): 330, 315, 285, 258, 77; anal. calcd. for $C_{19}H_{22}O_5$: C 69.07, H 6.71; found: C 69.29, H 6.57.

Diethyl 4-(2-ethylphenyl)-5-methylfuran-2,3-dicarboxylate (3ak): Yellowish viscous oil; IR (KBr): ν = 3042, 2985, 1727, 1608, 1562, 763 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 7.25–7.33 (m, 2H), 7.06–7.15 (m, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 4.18 (q, *J* = 8.0 Hz, 2H), 2.50 (q, *J* = 7.6 Hz, 2H), 2.30 (s,

3H), 1.33 (t, $J=7.2$ Hz, 3H), 1.14 (t, $J=7.2$ Hz, 3H), 0.99 (t, $J=7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=163.1$, 157.7, 153.6, 140.5, 131.3, 129.9, 126.3, 124.0, 118.6, 116.8, 115.8, 61.4, 61.3, 46.2, 14.1, 13.7, 12.6, 11.5; MS (EI): m/z (%)= 330, 315, 285, 257, 77; anal. calcd. for $C_{19}H_{22}O_5$: C 69.07, H 6.71; found: C 70.42, H 6.65.

Diethyl 4-(2-fluorophenyl)-5-methylfuran-2,3-dicarboxylate (3al): Yellowish viscous oil; IR (KBr): $\nu=3057$, 2986, 1732, 1612, 1575, 1027 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=$ 7.30–7.33 (m, 2H), 7.07–7.15 (m, 2H), 4.36 (q, $J=7.2$ Hz, 2H), 4.21 (q, $J=8.0$ Hz, 2H), 2.31 (s, 3H), 1.32 (t, $J=$ 7.2 Hz, 3H), 1.15 (t, $J=7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=163.1$, 157.7, 153.6, 140.5, 131.3, 129.9, 129.8 126.3, 124.1, 118.6, 115.8, 115.6, 61.4, 61.3, 14.1, 13.8, 12.7; MS (EI): m/z (%)=320, 275, 247, 220, 203, 116; anal. calcd. for $C_{17}H_{17}FO_5$: C 63.74, H 5.35; found: C, 63.56, H 5.42.

Diethyl 5-methyl-4-(thiophen-2-yl)furan-2,3-dicarboxylate (3am): Yellowish viscous oil; IR (KBr): $\nu=3057$, 2986, 1732, 1612, 1575, 1027 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=7.33$–7.34 (m, 1H), 7.05–7.06 (m, 2H), 4.30–4.39 (m, 4H), 2.49 (s, 3H), 1.28–1.37 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=$ 163.7, 157.6, 153.2, 139.5, 132.9, 127.3 126.9, 125.9, 116.1, 111.6, 61.9, 61.4, 14.2, 13.9, 13.0; MS (EI): m/z (%)=308, 263, 235, 208, 163, 135, 91; anal. calcd. for $C_{15}H_{16}O_5S$: C 58.43, H 5.23; found: C 58.26, H 5.17.

Ethyl 4-(4-methoxyphenyl)-5-methyl-2-phenylfuran-3-carboxylate (3bh): white solid, mp 100.8–102.7 °C; IR (KBr): $\nu=3057$, 2986, 1732, 1612, 1575, 1027 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=7.83$ (d, $J=7.2$ Hz, 2H), 7.36–7.44 (m, 3H), 7.26 (d, $J=8.0$ Hz, 2H), 6.93 (d, $J=7.6$ Hz, 2H), 4.13 (q, $J=6.8$ Hz, 2H), 3.85 (s, 3H), 2.32 (s, 3H), 1.05 (t, $J=$ 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=164.6$, 158.7, 153.7, 148.2, 130.7, 130.2, 128.5, 128.0, 127.5, 125.2, 122.5, 115.0, 113.4, 60.3, 55.2, 13.6, 11.9; MS (EI): m/z (%)=336, 308, 291, 105, 77; anal. calcd. for $C_{21}H_{20}O_4$: C 74.98, H 5.99; found: C 74.76, H 6.02.

Dimethyl 5-methyl-4-(2-phenylethynyl)furan-2,3-dicarboxylate (3cn): IR (KBr): $\nu=3051$ 2969, 1730, 1647, 1582, 1027 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=7.45$–7.47 (m, 2H), 7.31–7.33 (m, 3H), 3.93 (s, 3H), 3.89 (s, 3H), 2.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=162.6$, 159.4, 157.8, 140.6, 131.6, 128.7, 128.5, 126.4, 122.7, 106.5, 94.9, 52.7, 52.5, 13.2; MS (EI): m/z (%)=298, 267, 211, 152, 59; anal. calcd. for $C_{17}H_{14}O_5$: C 68.45, H 4.73; found: C 68.59, H 4.69.

Dimethyl 5-methyl-4-(*p*-tolylethynyl)furan-2,3-dicarboxylate (3co): white solid, mp 123.9–125.4 °C; IR (KBr): $\nu=$ 3055 2973, 1728, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=$ 7.37 (d, $J=8.0$ Hz, 2H), 7.13 (d, $J=7.2$ Hz, 2H), 3.95 (s, 3H), 3.91 (s, 3H), 2.50 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=162.0$, 158.5, 157.2, 140.0, 138.3, 130.9, 128.6, 125.9, 119.1, 106.0, 94.5, 52.0, 51.8, 20.9, 12.5; MS (EI): m/z (%)=312, 297, 281, 167, 59; anal. calcd. for $C_{18}H_{16}O_5$: C 69.22, H 5.16; found: C 69.43, H 5.19.

[5-Methyl-4-(phenylethynyl)-2-*p*-tolylfuran-3-yl](p-tolyl)-methanone (3dn): white solid, mp 142.5–144.3 °C; IR (KBr): $\nu=3035$, 2950, 1742, 1645 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=7.84$ (d, $J=8.0$ Hz, 2H), 7.53 (d, $J=8.0$ Hz, 2H), 7.06–7.22 (m, 9H), 2.53 (s, 3H), 2.38 (s, 3H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=191.1$, 154.4, 151.8, 143.4, 138.2, 134.8, 130.6, 129.8, 128.6, 128.5, 127.5, 127.4, 126.2, 126.0, 122.7, 121.2, 105.6, 94.5, 79.6, 21.4, 20.7, 12.3; MS (EI): m/z (%)=390, 223, 207, 119, 105, 91, 77; anal. calcd. for $C_{28}H_{22}O_2$: C 86.13, H 5.68; found: C 85.90, H 5.70.

[5-Methyl-2-phenyl-4-(phenylethynyl)furan-3-yl]-(phenyl)methanone (3en): Yellowish viscous oil; IR (KBr): $\nu=3029$ 1738, 1632 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=7.94$ (d, $J=7.2$ Hz, 2H), 7.08–7.65 (m, 13H), 2.54 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=191.3$, 154.8, 151.9, 137.2, 132.7, 130.7, 129.6, 128.8, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.5, 126.7, 126.1, 122.5, 121.7, 105.7, 94.7, 79.4, 12.3; MS (EI): m/z (%)=390, 223, 207, 119, 105, 91, 77; anal. calcd. for $C_{26}H_{18}O_2$: C 86.16, H 5.01, found: C 86.41, H 4.97.

(5-Methyl-2-phenylfuran-3-yl)(phenyl)methanone (3ea): Yellowish viscous oil; IR (KBr): $\nu=3037$, 1746, 1612, 1582, 1031 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=7.81$ (d, $J=9.6$ Hz, 2H), 7.64–7.66 (m, 2H), 7.25–7.49 (m, 6H), 6.28 (s, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=191.9$, 154.4, 151.1, 138.2, 132.6,130.0, 129.6, 128.9, 128.6, 128.5, 128.4, 128.2, 127.2, 121.7, 109.7, 13.3; MS (EI): m/z (%)=262, 185, 105, 77; anal. calcd. for $C_{18}H_{14}O_2$: C 82.42, H 5.38; found: C 82.03, H 5.42.

(5-Methyl-2,4-diphenylfuran-3-yl)(phenyl)methanone (3ed): Yellowish viscous oil; IR (KBr): $\nu=3032$, 1749, 1604, 1576 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=7.81$ (d, $J=9.6$ Hz, 2H), 7.55–7.57 (d, $J=8.4$ Hz, 2H), 7.35–7.39 (m, 1H), 7.14–7.27 (m, 10H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=$ 193.7, 150.8, 148.1, 137.5, 133.1, 132.2, 130.0, 129.8, 129.7, 129.3, 129.0, 128.9, 128.7, 128.6, 128.4, 128.2, 128.0, 126.8, 126.2, 123.5, 121.7, 12.2; MS (EI): m/z (%)=262, 141, 105, 77; anal. calcd. for $C_{24}H_{18}O_2$: C 85.18, H 5.36; found: C 84.92, H 5.43.

(2-Chlorophenyl)(5-methyl-2-phenylfuran-3-yl)methanone (3fa): IR (KBr): $\nu=3027$, 1723, 1608, 1542 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=7.76$–7.78 (m, 2H), 7.20–7.36 (m, 7H), 6.23 (s, 1H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=$ 189.8, 156.9, 151.5, 139.7, 131.3, 130.9, 130.0, 129.7, 129.2, 129.1, 128.9, 128.0, 127.9, 126.3, 122.5, 109.0, 13.3; MS (EI): m/z (%)=296, 185, 139, 77; anal. calcd. for $C_{18}H_{13}ClO_2$: C 72.85, H 4.42; found: C 72.73, H 4.49.

(2-Chlorophenyl)(4-methyl-2-phenylfuran-3-yl)methanone (4fa): Yellowish viscous oil; IR (KBr): $\nu=3029$, 1720, 1600, 1537 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=7.74$ (d, $J=8.0$ Hz, 2H), 7.37–7.43 (m, 2H), 7.22–7.33 (m, 3H), 7.16–7.20 (m, 2H), 6.46 (s, 1H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=191.0$, 152.4, 138.0, 133.5, 132.2, 131.9, 130.1, 129.8, 129.7, 129.3, 127.8, 126.3, 124.3, 108.2, 13.4; MS (EI): m/z (%)= 296, 261, 130, 77; anal. calcd. for $C_{18}H_{13}ClO_2$: C 72.85, H 4.42; found: C 72.42, H 4.46.

(2-Chlorophenyl)(5-methyl-2,4-diphenylfuran-3-yl)methanone (3fd): Yellowish viscous oil; IR (KBr): $\nu=3018$, 1732 1609, 1561 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=7.71$–7.73 (m, 2H), 7.42–7.44 (m, 1H), 7.14–7.32 (m, 11H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=191.9$, 150.7, 149.1, 137.6, 133.4, 132.5, 132.1, 132.0, 130.1, 129.8, 129.6, 129.4, 129.3, 128.1, 127.7, 126.8, 126.4, 124.2, 122.8, 12.3; MS (EI): m/z (%)=372, 261, 139, 111, 105, 77; anal. calcd. for $C_{24}H_{17}ClO_2$: C 77.31, H 4.60; found: C 77.13, H 4.68.

[2-(2-Chlorophenyl)-5-methyl-4-phenylfuran-3-yl]-(phenyl)methanone (4fd): white solid, mp 121–123 °C IR (KBr): $\nu=3021$, 1730 1613, 1570 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz): $\delta=7.70$–7.73 (m, 2H), 7.29–7.35 (m, 5H), 7.16–7.25 (m, 7H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): $\delta=191.0$,

154.5, 148.4, 138.4, 132.6, 132.0, 131.7, 131.0, 129.6, 129.3, 128.9, 128.5, 128.1, 127.9, 127.7, 127.5, 126.8, 125.9, 123.3, 12.0; MS (EI): *m/z* (%) = 372, 337, 105, 77; anal. calcd. for $C_{24}H_{17}ClO_2$: C 77.31, H 4.60; found: C 77.54, H 4.51.

(5-Methyl-2-phenylfuran-3-yl)(thiophen-2-yl)methanone (3ga): Yellowish viscous oil; IR (KBr): ν = 3020, 1728 1610, 1540 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 7.78–7.80 (m, 2H), 7.63–7.66 (m, 2H), 7.30–7.39 (m, 3H), 7.06–7.08 (m, 1H), 6.44 (s, 1H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 183.4, 153.6, 151.3, 144.8, 134.2, 133.9, 133.0, 130.8, 130.0, 128.6, 128.3, 127.8, 127.0, 121.6, 109.3, 13.4; MS (EI): *m/z* (%) = 268, 235, 165, 111, 77; anal. calcd. for $C_{16}H_{12}O_2S$: C 71.62, H 4.51; found: C 71.84, H 4.14.

[5-Methyl-2-(thiophen-2-yl)furan-3-yl](phenyl)methanone (4ga): IR (KBr): ν = 3025, 1726, 1602, 1530 cm^{-1}; ^1H NMR ($CDCl_3$, 400 Hz): δ = 7.88–7.90 (m, 3H), 7.48–7.60 (m, 3H), 7.38–7.40 (m, 1H), 7.08–7.10 (m, 1H), 6.29 (s, 1H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 190.5, 150.4, 138.9, 132.2, 132.0, 129.3, 128.2, 127.6, 127.3, 127.1, 120.3, 109.7, 13.3; MS (EI): *m/z* (%) = 268, 191, 105, 77; anal. calcd. for $C_{16}H_{12}O_2S$: C 71.62, H 4.51; found: C 71.76, H 4.15.

(5-Methyl-2-phenylfuran-3-yl)(*p*-tolyl)methanone (3ha) and (5-methyl-2-*p*-tolylfuran-3-yl)(phenyl)methanone (4ha): ^1H NMR ($CDCl_3$, 400 Hz): δ = 7.87 (d, *J* = 8.0 Hz, 2H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.38–7.43 (m, 3H), 7.30–7.32 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.31 (s, 2H), 2.42 (s, 3H) , 2.41 (s, 3H) , 2.39 (s, 3H) , 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 191.9, 191.7, 154.9, 153.9, 151.0, 150.8, 143.5, 138.7, 138.4, 135.8, 132.5, 132.3, 130.1, 129.9, 129.6, 129.4, 129.0, 128.9, 128.6, 128.4, 128.3, 128.2, 128.1, 127.3, 127.2, 127.1, 127.1, 121.9, 121.1, 109.8, 109.7, 21.6, 21.3, 13.5, 13.4; MS (EI): *m/z* (%) = 276, 105, 91, 55; anal. calcd. for $C_{16}H_{12}O_2$: C 82.58, H 5.84; found: C 82.15, H 5.90.

(5-Methyl-2,4-diphenylfuran-3-yl)(*p*-tolyl)methanone (3hd) and (5-methyl-4-phenyl-2-*p*-tolylfuran-3-yl)(phenyl)-methanone (4hd): ^1H NMR ($CDCl_3$, 400 Hz): δ = 7.85 (d, *J* = 8.0 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.38–7.43 (m, 2H), 7.25–7.32 (m, 16H), 7.08–9.10 (m, 4H), 2.50 (s, 3H), 2.49 (s, 3H) , 2.32 (s, 3H) , 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz): δ = 194.0, 193,8, 148.3, 144.4, 138.3, 133.3, 132.6, 132.5, 130.2, 130.0, 129.4, 129.3, 128.7, 128.5, 128.4, 128.2, 127.1, 126.4, 126.2, 123.7, 21.8, 21.4, 12.6, 12.5; MS (EI): *m/z* (%) = 352, 105, 91, 77, 55; anal. calcd. for $C_{16}H_{12}O_2$: C 85.20, H 5.72; found: C 85.77, H 5.68.

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