JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

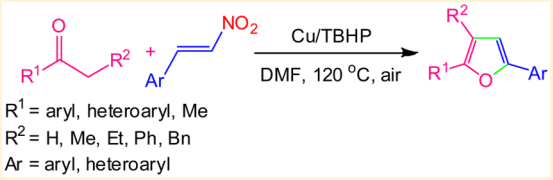
Regioselective Synthesis of Multisubstituted Furans via Copper-Mediated Coupling between Ketones and β-Nitrostyrenes

Monoranjan Ghosh, Subhajit Mishra, and Alakananda Hajra*

Department of Chemistry, Visva-Bharati (A Central University), Santiniketan 731235, India

Supporting Information

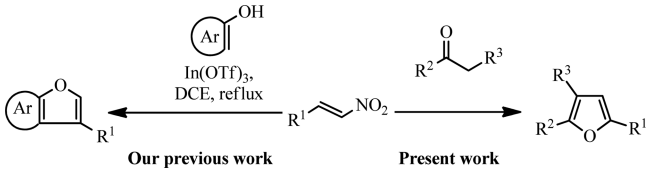
ABSTRACT: A copper-mediated intermolecular annulation of alkyl ketones and β-nitrostyrenes has been developed for the regioselective synthesis of multisubstituted furan derivatives in good yields. This protocol is applicable to both cyclic and acyclic ketones.



Polysubstituted furan derivatives represent an important class of five-membered heterocycles that are ubiquitous in a number of biologically active natural products. They are the constituents of numerous therapeutic agents and are also used as building blocks in organic synthesis.[1] Because of their versatile biological activities, extensive synthetic efforts have been devoted to the construction of polysubstituted furans. The classical methods such as the Paal–Knorr synthesis[2] and Feist–Benary synthesis[3] provide rapid access to substituted furans from dicarbonyl compounds. On the other hand, many excellent methods have also been developed for the synthesis of substituted furans from acyclic ketone precursors involving alkyne- or allene-assisted cyclizations.[4] During the past decades, transition-metal-catalyzed inter/intramolecular condensation reactions for the synthesis of furan derivatives have provided powerful means of access to diversely substituted furans that have been extensively studied.[5] In view of the great importance of furans in natural and synthetic substances, the development of new synthetic methods that allow more straightforward and environmentally accessible intermolecular approaches from simple and cheap chemical reagents is highly desirable. Although various dicarbonyl compounds and prefunctionalized ketones have been extensively utilized for the synthesis of furans, the use of commercially available simple alkyl ketones as precursors has been less explored.[6]

Conjugated nitroolefins are widely used as Michael acceptors in organic synthesis because of the high electrophilicity of the double bond. They have attracted attention as excellent building blocks for the synthesis of various types of heterocyclic and carbocyclic compounds.[7] In this context, reactive nitro-allylic acetates have also been explored for the synthesis of furans/benzofurans from dicarbonyl/phenol derivatives.[8] We recently described a simple and straightforward one-pot synthesis of benzofuran and naphthofuran derivatives from readily available nitroalkenes by coupling with phenols/naphthols via tandem Michael addition/denitration (Scheme 1).[9] More recently, we reported a copper-catalyzed regioselective synthesis of multisubstituted furans employing ketones and cinnamic acid as the coupling partners.[10] Coupling

Scheme 1. Synthesis of Multisubstituted Furans from Nitroalkenes



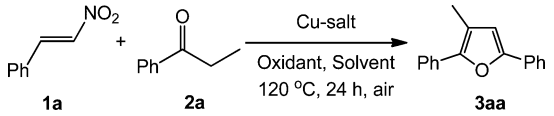
between simple alkyl ketones and nitrostyrenes has not been studied to date, but we envisioned that commercially available ketones and easily accessible nitrostyrenes would be a good choice for annulation to synthesize more structurally diverse furan derivatives. Herein we report a regioselective synthesis of 2,3,5-trisubstituted furans from readily available simple alkyl ketones and β-nitrostyrenes (Scheme 1).

We commenced our study with a mixture of β-nitrostyrene (**1a**) and propiophenone (**2a**) in a 1:2 molar ratio in the presence of 1 equiv of CuBr in DMF (Table 1, entry 1), which afforded a 20% yield of the corresponding furan **3aa** regioselectively. When CuBr was replaced by CuBr·SMe_2 (1 equiv), an improvement in the yield to 35% was observed (entry 2). Different solvents such as DMA, NMP, toluene, xylene, and DMSO (entries 3–7) were also screened; among them, DMF was found to be the best one. Next, we turned our attention to the effect of oxidants. When various oxidants such as O_2, TBHP, DTPB, $K_2S_2O_8$, and DDQ were scrutinized (entries 8–13), and TBHP (1 equiv) had the beneficial effect to give the best yield (67%; entry 10). However, the yield decreased when the amount of TBHP was lowered. The yield of the product decreased when the molar ratio of the reactants was changed (entries 14 and 15). The reaction did not proceed at all in the presence of other Cu salts, such as CuCl, CuI, $CuCl_2$, and $CuBr_2$ (entries 16–19). However, only a trace amount of product was obtained in the presence of $Cu(OAc)_2 \cdot H_2O$ (entry 20). The reaction did not occur in the absence of a

Received: March 31, 2015
Published: April 26, 2015

DOI: 10.1021/acs.joc.5b00704
J. Org. Chem. 2015, 80, 5364–5368

Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3aa

entry	[Cu]	oxidant	solvent	yield (%)
1	CuBr	–	DMF	20
2	$CuBr{\cdot}SMe_2$	–	DMF	35
3	$CuBr{\cdot}SMe_2$	–	DMA	32
4	$CuBr{\cdot}SMe_2$	–	NMP	9
5	$CuBr{\cdot}SMe_2$	–	toluene	N.R.
6	$CuBr{\cdot}SMe_2$	–	xylene	8
7	$CuBr{\cdot}SMe_2$	–	DMSO	29
8	$CuBr{\cdot}SMe_2$	O_2 (1 atm)	DMF	35
9	$CuBr{\cdot}SMe_2$	O_2 (5 atm)	DMF	37
10	$CuBr{\cdot}SMe_2$	TBHP	DMF	67
11	$CuBr{\cdot}SMe_2$	DTBP	DMF	48
12	$CuBr{\cdot}SMe_2$	$K_2S_2O_8$	DMF	12
13	$CuBr{\cdot}SMe_2$	DDQ	DMF	8
14	$CuBr{\cdot}SMe_2$	TBHP	DMF	35[b]
15	$CuBr{\cdot}SMe_2$	TBHP	DMF	36[c]
16	CuCl	TBHP	DMF	N.R.
17	CuI	TBHP	DMF	N.R.
18	$CuCl_2$	TBHP	DMF	N.R.
19	$CuBr_2$	TBHP	DMF	N.R.
20	$Cu(OAc)_2{\cdot}H_2O$	TBHP	DMF	10
21	–	TBHP	DMF	N.R.
22	$CuBr{\cdot}SMe_2$	TBHP	DMF	69[d]
23	$CuBr{\cdot}SMe_2$	TBHP	DMF	29[e]

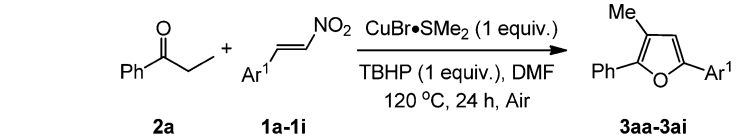
[a]Reaction conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), Cu salt (1 equiv), oxidant (1 equiv), solvent (1.5 mL), 120 °C, 24 h, air. [b]**1a**:**2a** = 2:1. [c]**1a**:**2a** = 1:1. [d]Cu salt (2 equiv). [e]Cu salt (0.5 equiv).

Cu salt (entry 21). Increasing the amount of Cu salt (2 equiv) did not improve the yield (entry 22), whereas decreasing the amount of Cu salt (50 mol %) decreased the yield (entry 23). Finally, the optimized reaction conditions were obtained using the combination of propiophenone and β-nitrostyrene (2:1) in the presence of 1 equiv of $CuBr{\cdot}SMe_2$ and TBHP (1 equiv) in DMF at 120 °C for 24 h under ambient air (entry 10). It is noteworthy that only one regioselective furan is obtained following this protocol.

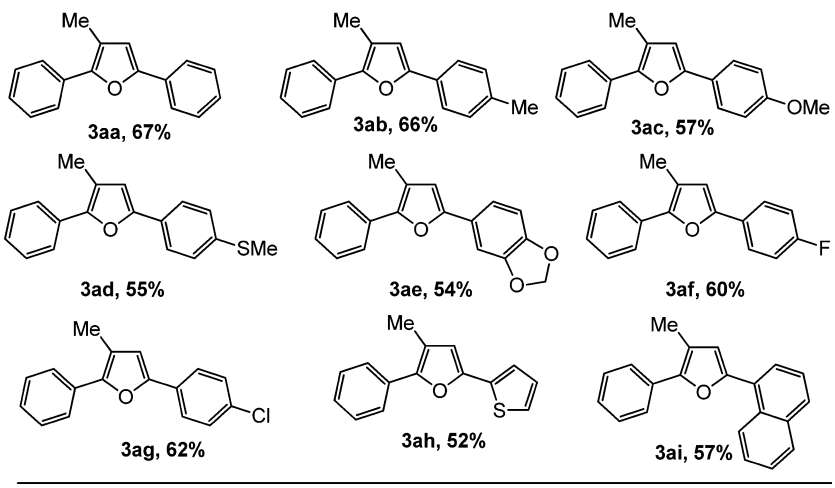
Under the optimized reaction conditions, we began to explore the scope of this annulation by employing various β-nitrostyrenes (**1a**–**i**) (Scheme 2). β-Nitrostyrenes bearing electron-donating groups such as −Me and −OMe on the phenyl ring successfully provided the corresponding furans in good yields (**3ab** and **3ac**), whereas halogen-substituted nitrostyrenes gave moderate yields (**3af** and **3ag**). Notably, the dioxole part in nitrostyrene **1e** was unaffected in the present reaction conditions, and the desired furan **3ae** was obtained in moderate yield. Moreover, a heteroaryl-substituted nitroalkene also produced the corresponding furan (**3ah**) in moderate yield. However, β-methyl-β-nitrostyrene did not give the desired furan under the present reaction conditions.

We then turned our attention to the scope of various alkyl aryl ketones to prove the general applicability of the reaction (Scheme 3). A diverse range of ketones such as 4′-methyl propiophenone (**2b**), butyrophenone (**2c**), acetophenones (**2d**–**h**), and 2′-phenylacetophenone (**2i**) were compatible with the reaction conditions and afforded the expected products with excellent regioselectivity. We also synthesized disubstituted furans (**3da**–**3hb**) from different acetophenone derivatives under the present reaction conditions. Moreover, 2-acetylthiophene (**2g**) underwent the reaction smoothly to give the corresponding furan (**3gc**). 4-Phenyl-2-butanone successfully produced the corrosponding furan (**3jb**) in 52% yield. Interestingly, the alicyclic ketone α-tetralone also produced the

Scheme 2. Annulation of Propiophenone with Various β-Nitrostyrenes[a]



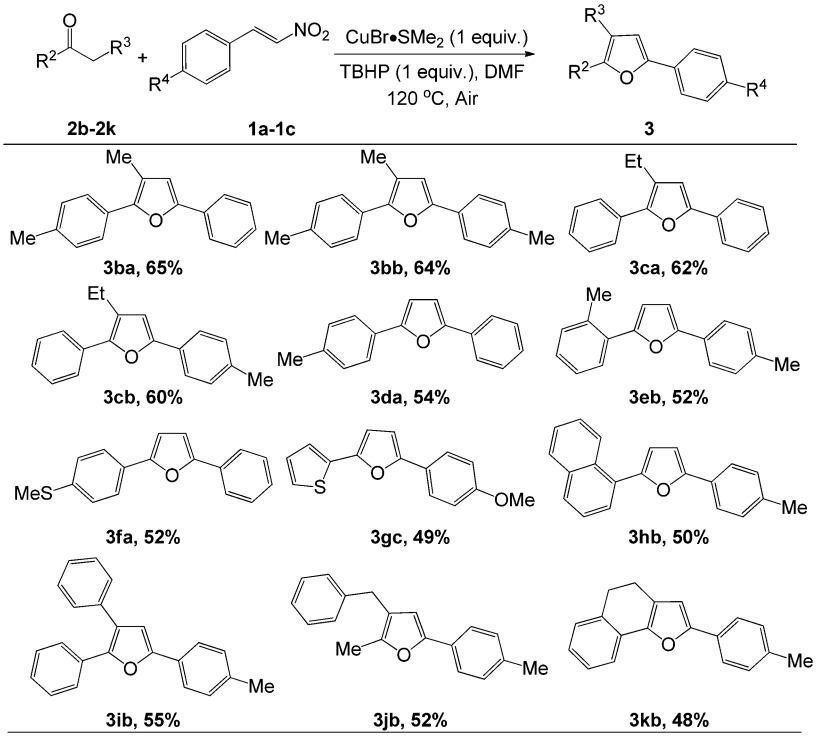
2a 1a-1i 3aa-3ai



[a]Reaction conditions: **2a** (1 mmol), β-nitrostyrene **1** (0.5 mmol), $CuBr{\cdot}SMe_2$ (0.5 mmol), TBHP (5–6 M) in decane (0.1 mL, 1 equiv), DMF (1.5 mL), 120 °C, 24 h, air.

DOI: 10.1021/acs.joc.5b00704
J. Org. Chem. 2015, 80, 5364–5368

Scheme 3. Annulations of Different Alkyl Aryl Ketones with β-Nitrostyrenes[a]

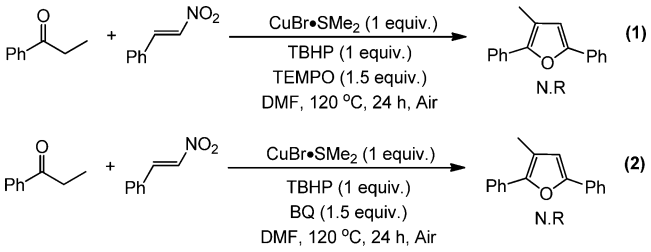


[a]Reaction conditions: ketone **2** (1 mmol), β-nitrostyrene **1** (0.5 mmol), CuBr·SMe_2 (0.5 mmol), TBHP (5−6 M) in decane (0.1 mL, 1 equiv), DMF (1.5 mL), 120 °C, 24 h, air.

desired furan (**3kb**) in moderate yield. However, no reaction occurred in the case of cyclohexanone and ethyl methyl ketone.

To gain insight into the possible mechanism of this reaction, a few control experiments were carried out (Scheme 4). It is noteworthy that the reaction did not proceed at all upon addition of a radical scavenger such as TEMPO (1.5 equiv) or BQ (1.5 equiv). These results indicate that the reaction possibly proceeds through a radical formation pathway.

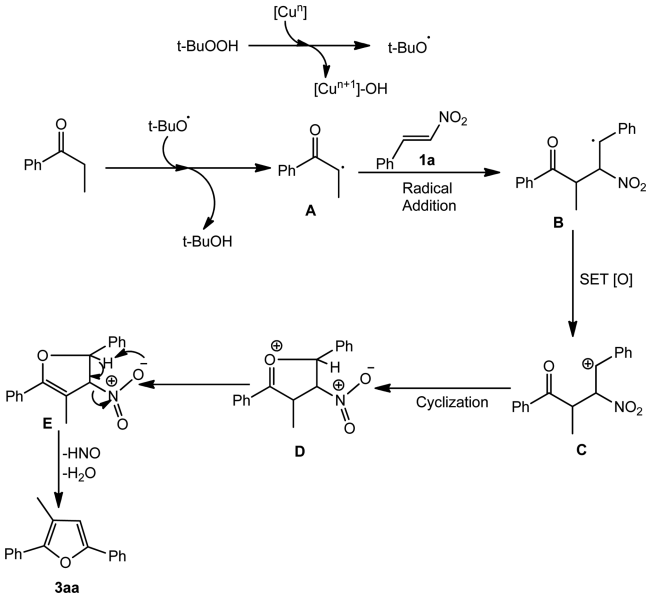
Scheme 4. Control Experiments



On the basis of the control experiments and literature reports,[11] a plausible mechanism is outlined in Scheme 5. The formation of *tert*-butylperoxy radical from TBHP is facilitated in the presence of the Cu(I) catalyst. Consequently, propiophenone is converted into the carbon-centered radical **A** in the presence of *tert*-butylperoxy radical. Intermediate **A** attacks at the β-position of the nitroalkene (**1a**) to form the radical intermediate **B**, which is further transformed to intermediate **C** through single-electron transfer (SET). Upon cyclization and successive elimination of HNO and H_2O,[9,12] **C** is consecutively converted to **3aa** via the intermediates **D** and **E**.

In summary, we have demonstrated a CuBr·SMe_2/TBHP-mediated regioselective direct synthesis of 2,3,5-trisubstituted furan derivatives by a SET radical pathway. The versatile method shows broad functional group tolerance and is applicable to a wide range of simple alkyl ketones and nitrostyrenes. Complete regioselectivity and widely available starting materials make this protocol synthetically useful to create a library of furan derivatives.

Scheme 5. Plausible Mechanism



EXPERIMENTAL SECTION

General Information. ^{1}H NMR spectra were determined on a 400 MHz spectrometer using solutions in $CDCl_3$. Chemical shifts (δ) are

DOI: 10.1021/acs.joc.5b00704
J. Org. Chem. 2015, 80, 5364−5368

expressed in parts per million and are referenced to tetramethylsilane (TMS) as an internal standard. The multiplicities of the signals are reported as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), or m (multiplet), and coupling constants (J) are given in hertz. Proton-decoupled $^{13}C\{^1H\}$ NMR spectra were recorded at 100 MHz. TLC was done on silica gel 60 F_{254} coated on aluminum sheets (Merck). Silica gel (60−120 mesh) was used for column chromatography. Petroleum ether refers to the fraction boiling in the range of 60−80 °C unless otherwise mentioned. All of the solvents were dried and distilled before use. Commercially available substrates were freshly distilled before the reaction. All of the reactions involving moisture-sensitive reactants were executed using oven-dried glassware.

General Experimental Procedure for the Synthesis of Multisubstituted Furans: Synthesis of 3aa. A mixture of propiophenone (**2a**) (1 mmol, 134 mg), β-nitrostyrene (**1a**) (0.5 mmol, 74 mg), and CuBr·SMe_2 (0.5 mmol, 102 mg) in DMF (1.5 mL) was placed in a reaction vessel, and TBHP (5−6 M in decane, 1 equiv, 0.1 mL) was added dropwise. Then the reaction mixture was stirred at 120 °C for 24 h under ambient air. After completion of the reaction (TLC), the reaction mixture was cooled to room temperature and extracted with ethyl acetate. The organic phase was dried over anhydrous Na_2SO_4. The crude residue was obtained after evaporation of the solvent in vacuum and was purified by column chromatography on silica gel (60−120 mesh) using petroleum ether as the eluent to afford pure **3aa** as a white solid (78 mg, 67% yield).

*3-Methyl-2,5-diphenylfuran (**3aa**).*[10] White solid (67%, 78 mg), mp 47−48 °C (lit. mp 45−46 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 4H), 7.61−7.54 (m, 4H), 7.44−7.43 (m, 2H), 6.73 (s, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.6, 148.2, 131.8, 130.8, 128.7, 128.6, 127.2, 126.6, 125.2, 123.7, 118.7, 110.9, 12.1.

*3-Methyl-2-phenyl-5-p-tolylfuran (**3ab**).*[10] White solid (66%, 81 mg), mp 81−83 °C (lit. mp 80−82 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.6 Hz, 2H), 7.67 (d, J = 8.0 Hz, 2H), 7.48 (t, J = 8.0 Hz, 2H), 7.32 (t, J = 7.2 Hz, 1H), 7.25 (d, J = 8.0 Hz, 2H), 6.60 (s, 1H), 2.42 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 147.9, 137.1, 132.0, 129.4, 128.6, 128.2, 126.6, 125.2, 123.7, 118.7, 110.2, 21.4, 12.2.

*5-(4-Methoxyphenyl)-3-methyl-2-phenylfuran (**3ac**).*[10] White solid (57%, 75 mg), mp 96−97 °C (lit. mp 97−98 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.8 Hz, 2H), 7.46 (t, J = 8.4 Hz, 2H), 7.31−7.28 (m, 1H), 6.97 (d, J = 8.8 Hz, 2H), 6.51 (s, 1H), 3.87 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 151.8, 147.6, 132.0, 128.6, 126.5, 125.2, 125.1, 124.0, 118.7, 114.2, 109.4, 55.4, 12.2.

*3-Methyl-5-(4-(methylthio)phenyl)-2-phenylfuran (**3ad**).* Colorless oil (55%, 77 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 9.2 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H), 7.35 (t, J = 8.0 Hz, 2H), 7.21−7.17 (m, 3H), 6.48 (s, 1H), 2.43 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 148.2, 137.4, 131.8, 128.7, 127.9, 126.9, 126.8, 125.3, 124.2, 118.8, 110.6, 16.0, 12.2. Anal. Calcd for $C_{18}H_{16}OS$: C, 77.11; H, 5.75%. Found: C, 77.13; H, 5.79%.

*5-(4-Methyl-5-phenylfuran-2-yl)benzo[1,3]dioxole (**3ae**).*[10] White solid (54%, 75 mg), mp 111−112 °C (lit. mp 110−112 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.6 Hz, 2H), 7.34 (t, J = 8.0 Hz, 2H), 7.19−7.10 (m, 3H), 6.75 (d, J = 8.0 Hz, 1H), 6.37 (s, 1H), 5.89 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.6, 148.1, 147.7, 147.0, 131.9, 128.6, 126.6, 125.4, 125.2, 118.7, 117.7, 109.9, 108.7, 104.6, 101.2, 12.2.

*5-(4-Fluorophenyl)-3-methyl-2-phenylfuran (**3af**).*[10] White solid (60%, 75 mg), mp 85−86 °C (lit. mp 85−86 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.63−7.57 (m, 4H), 7.35 (t, J = 8.0 Hz, 2H), 7.21−7.17 (m, 1H), 7.00 (d, J = 8.8 Hz, 2H), 6.46 (s, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2 (d, $^1J_{C-F}$ = 245 Hz), 150.9, 148.3, 131.8, 128.7, 127.2, 126.8, 125.5 (d, $^3J_{C-F}$ = 8 Hz), 125.3, 118.8, 115.8 (d, $^2J_{C-F}$ = 22 Hz), 110.6, 12.2.

*5-(4-Chlorophenyl)-3-methyl-2-phenylfuran (**3ag**).*[10] Colorless oil (62%, 83 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.8 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H), 7.35 (t, J = 8.0 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7.22−7.17 (m, 1H), 6.51 (s, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 148.6, 132.9, 131.9, 131.7, 129.4, 129.0, 128.7, 127.0, 125.4, 124.9, 118.8, 111.3, 12.2.

*3-Methyl-2-phenyl-5-(thiophen-2-yl)furan (**3ah**).*[10] Light-yellow oil (52%, 62 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 9.2 Hz, 2H), 7.35 (t, J = 8.0 Hz, 2H), 7.22−7.17 (m, 2H), 7.14 (d, J = 6.0 Hz, 1H), 6.97 (d, J = 8.0 Hz, 1H), 6.39 (s, 1H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 147.5, 131.6, 131.1, 129.3, 128.7, 127.8, 126.8, 125.3, 124.1, 122.4, 118.7, 110.8, 12.2.

*3-Methyl-5-(naphthalen-1-yl)-2-phenylfuran(**3ai**).*[6] Colorless oil (57%, 80 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.87−7.83 (m, 1H), 7.81−7.75 (m, 5H), 7.49−7.41 (m, 4H), 7.28 (t, J = 7.6 Hz, 1H), 6.71 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 148.7, 133.7, 132.8, 131.9, 128.7, 128.4, 128.2, 127.9, 126.9, 126.6, 125.9, 125.4, 122.4, 122.0, 118.9, 111.6, 12.3.

*3-Methyl-5-phenyl-2-p-tolylfuran (**3ba**).* White solid (65%, 80 mg), mp 95−96 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.8 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.46−7.43 (m, 2H), 7.32−7.29 (m, 3H), 6.65 (s, 1H), 2.45 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 148.5, 136.5, 131.0, 129.3, 129.1, 128.7, 127.1, 125.3, 123.7, 123.7, 118.0, 110.8, 21.3, 12.1. Anal. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49%. Found: C, 87.02; H, 6.55%.

*3-Methyl-2,5-di-p-tolylfuran (**3bb**).* White solid (64%, 83 mg), mp 98−99 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 8.0 Hz, 4H), 7.16−7.09 (m, 4H), 6.45 (s, 1H), 2.30 (s, 3H), 2.28 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 148.2 137.0, 136.4, 129.4, 129.3, 129.2, 128.3, 125.3, 125.0, 123.7, 117.9, 110.1, 21.4, 21.3, 12.2. Anal. Calcd for $C_{19}H_{18}O$: C, 86.99; H, 6.92%. Found: C, 87.02; H, 6.88%.

*3-Ethyl-2,5-diphenylfuran (**3ca**).*[10] Colorless oil (62%, 76 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.70−7.64 (m, 4H), 7.41−7.33 (m, 4H), 7.26−7.21 (m, 2H), 6.65 (s, 1H), 2.71 (q, J = 7.6 Hz, 2H), 1.27 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 147.7, 131.9, 130.9, 128.8, 128.7, 128.5, 127.3, 126.9, 125.6, 125.5, 125.3, 123.8, 108.8, 19.4, 14.5.

*3-Ethyl-2-phenyl-5-p-tolylfuran (**3cb**).* Colorless oil (60%, 78 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 9.2 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H), 7.36−7.32 (m, 2H), 7.21−7.17 (m, 1H), 7.12 (d, J = 8.0 Hz, 2H), 6.55 (s, 1H), 2.66 (q, J = 7.6 Hz, 2H), 2.29 (s, 3H), 1.22 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 147.3, 137.1, 131.9, 129.4, 128.6, 128.3, 126.8, 125.6, 125.5, 123.7, 108.0, 21.4, 19.4, 14.5. Anal. Calcd for $C_{19}H_{18}O$: C, 86.99; H, 6.92%. Found: C, 86.89; H, 6.97%.

*2-Phenyl-5-p-tolylfuran (**3da**).* Colorless oil (54%, 63 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 9.2 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 7.34−7.30 (m, 2H), 7.20−7.16 (m, 1H), 7.14 (d, J = 8.0 Hz, 2H), 6.66 (d, J = 3.6 Hz, 1H), 6.60 (d, J = 3.6 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.7, 153.1, 137.3, 131.0, 129.5, 128.8, 128.2, 127.3, 123.8, 123.7, 107.3, 106.6, 21.4. Anal. Calcd for $C_{17}H_{14}O$: C, 87.15; H, 6.02%. Found: C, 87.16; H, 6.05%.

*2-o-Tolyl-5-p-tolylfuran (**3eb**).* Colorless oil (52%, 64 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 7.6 Hz, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.27−7.24 (m, 3H), 7.21 (d, J = 8.0 Hz, 2H), 6.70 (d, J = 3.6 Hz, 1H), 6.62 (d, J = 3.6 Hz, 1H), 2.56 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 152.8, 137.3, 134.5, 131.4, 130.3, 129.5, 128.3, 127.4, 126.9, 126.1, 123.8, 110.7, 106.3, 22.2, 21.4. Anal. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49%. Found: C, 87.01; H, 6.56%.

*2-(4-(Methylthio)phenyl)-5-phenylfuran (**3fa**).* Colorless oil (52%, 69 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 9.2 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.38 (t, J = 8.0 Hz, 2H), 7.28−7.24 (m, 3H), 6.71 (d, J = 3.2 Hz, 1H), 6.67 (d, J = 3.6 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 153.1, 137.7, 130.8, 128.8, 127.9, 127.4, 126.9, 124.2, 123.8, 107.4, 107.0, 16.0. Anal. Calcd for $C_{17}H_{14}OS$: C, 76.66; H, 5.30%. Found: C, 76.68; H, 5.34%.

*2-(4-Methoxyphenyl)-5-(thiophen-2-yl)furan (**3gc**).* Colorless oil (49%, 62 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.8 Hz, 2H), 7.21 (d, J = 4.4 Hz, 1H), 7.14 (d, J = 6.4 Hz, 1H), 6.97 (d, J = 8.4 Hz, 1H), 6.85 (d, J = 7.2 Hz, 2H), 6.48 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 153.2, 148.8, 134.0, 127.7, 125.3, 123.9, 123.7, 122.3, 114.3, 107.3, 105.6, 55.4. Anal. Calcd for $C_{15}H_{12}O_2S$: C, 70.29; H, 4.72%. Found: C, 70.22; H, 4.76%.

DOI: 10.1021/acs.joc.5b00704
J. Org. Chem. 2015, 80, 5364−5368

*2-(Naphthalen-1-yl)-5-p-tolylfuran (**3hb**).*[6] Colorless oil (50%, 71 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, J = 8.0 Hz, 1H), 7.89 (d, J = 9.2 Hz, 1H), 7.84−7.81 (m, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.57−7.50 (m, 3H), 7.25−7.22 (m, 2H), 6.81−6.79 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 152.7, 137.4, 134.1, 130.4, 129.6, 128.7, 128.5, 128.3, 126.7, 126.0, 125.7, 125.5, 123.9, 111.5, 106.3, 21.4.

*2,3-Diphenyl-5-p-tolylfuran (**3ib**).*[10] White solid (55%, 85 mg), mp 99−101 °C (lit. mp 99−100 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.8 Hz, 2H), 7.37−7.34 (m, 2H), 7.29−7.25 (m, 2H), 7.23−7.17 (m, 3H), 7.14−7.10 (m, 3H), 6.65 (s, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.9, 147.6, 137.5, 134.5, 131.3, 129.5, 128.8, 128.7, 128.5, 127.9, 127.5, 127.3, 126.2, 124.6, 123.9, 108.9, 21.4.

*3-Benzyl-2-methyl-5-p-tolylfuran (**3jb**).* Colorless oil (52%, 68 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 2H), 7.30−7.24 (m, 2H), 7.21−7.17 (m, 3H), 7.12 (d, J = 8.0 Hz, 2H), 6.33 (s, 1H), 3.71 (s, 2H), 2.32 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 147.4, 140.9, 136.5, 129.3, 128.5, 126.1, 123.5, 123.3, 120.0, 106.9, 31.3, 21.3, 11.8. Anal. Calcd for $C_{19}H_{18}O$: C, 86.99; H, 6.92%. Found: C, 86.95; H, 6.96%.

*2-p-Tolyl-4,5-dihydronaphtho[1,2-b]furan (**3kb**).* Colorless oil (48%, 62 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.0 Hz, 1H), 7.25−7.21 (m, 1H), 7.13−7.11 (m, 3H), 7.10−7.09 (m, 1H), 6.57 (s, 1H), 2.99 (t, J = 8.0 Hz, 2H), 2.76 (t, J = 8.0 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 149.4, 137.1, 134.7, 129.5, 128.4, 128.0, 126.8, 126.3, 124.7, 123.7, 121.6, 119.1, 105.9, 29.2, 21.4, 21.2; Anal. Calcd for $C_{19}H_{16}O$: C, 87.66; H, 6.19%. Found: C, 87.65; H, 6.21%.

■ ASSOCIATED CONTENT

Supporting Information

Scanned copies of ^{1}H and ^{13}C NMR spectra of the synthesized compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00704.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: alakananda.hajra@visva-bharati.ac.in.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

A.H. acknowledges the financial support from CSIR, New Delhi (Grant 02(0168)/13/EMR-II). M.G. and S.M. thank UGC for their fellowships.

■ REFERENCES

(1) (a) Donnelly, D. M. X.; Meegan, M. J. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, U.K., 1984; Vol. *4*, p 657. (b) Lipshutz, B. H. *Chem. Rev.* **1986**, *86*, 795. (c) Keay, B. A.; Dibble, P. W. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Sciven, E. F. V., Eds.; Elsevier: Oxford, U.K., 1997; Vol. *2*, p 395. (d) Zanatta, N.; Alves, S. H.; Coelho, H. S.; Borchhardt, D. M.; Machado, P.; Flores, K. M.; Silva, F. M.; Spader, T. B.; Santurio, J. M.; Bonacorso, H. G.; Martins, M. A. P. *Bioorg. Med. Chem.* **2007**, *15*, 1947.

(2) Amarnath, V.; Amarnath, K. *J. Org. Chem.* **1995**, *60*, 301.

(3) (a) Feist, F. *Chem. Ber.* **1902**, *35*, 1537. (b) Benary, E. *Chem. Ber.* **1911**, *44*, 489.

(4) (a) Ma, S.; Zhang, J. *J. Am. Chem. Soc.* **2003**, *125*, 12386. (b) Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Milton, M. D.; Hidai, M.; Uemura, S. *Angew. Chem.* **2003**, *115*, 2785. (c) Kel'in, A. V.; Gevorgyan, V. *J. Org. Chem.* **2002**, *67*, 95. (d) Zhang, J.; Schmalz, H.-G. *Angew. Chem.* **2006**, *118*, 6856. (e) Sanz, R.; Miguel, D.; Martinez, A.; Alvarez-Gutierrez, J. M.; Rodriguez, F. *Org. Lett.* **2007**, *9*, 727. (f) Barluenga, J.; Riesgo, L.; Vicente, R.; Lopez, L. A.; Tomas, M. *J. Am. Chem. Soc.* **2008**, *130*, 13528. (g) Sydnes, L. K.; Holmelid, B.; Sengee, M.; Hanstein, M. *J. Org. Chem.* **2009**, *74*, 3430. (h) He, C.; Guo, S.; Ke, J.; Hao, J.; Xu, H.; Chen, H.; Lei, A. *J. Am. Chem. Soc.* **2012**, *134*, 5766. (i) Li, L.; Zhao, M.-N.; Ren, Z.-H.; Li, J.; Guan, Z.-H. *Synthesis* **2012**, *44*, 532.

(5) (a) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701. (b) Nakamura, M.; Ilies, L.; Otsubo, S.; Nakamura, E. *Angew. Chem.* **2006**, *118*, 958; *Angew. Chem., Int. Ed.* **2006**, *45*, 944. (c) Tsuji, H.; Mitsui, C.; Ilies, L.; Sato, Y.; Nakamura, E. *J. Am. Chem. Soc.* **2007**, *129*, 11902. (d) Sniady, A.; Durham, A.; Morreale, M. S.; Wheeler, K. A.; Dembinski, R. *Org. Lett.* **2007**, *9*, 1175. (e) Zhao, L.-B.; Guan, Z.-H.; Han, Y.; Xie, Y.-X.; He, S.; Liang, Y.-M. *J. Org. Chem.* **2007**, *72*, 10276. (f) Melzig, L.; Rauhut, C. B.; Knochel, P. *Chem. Commun.* **2009**, 3536. (g) Chen, Z.; Huang, G.; Jiang, H.; Huang, H.; Pan, X. *J. Org. Chem.* **2011**, *76*, 1134. (h) Kuram, M. R.; Bhanuchandra, M.; Sahoo, A. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 4607. (i) Sharma, U.; Naveen, T.; Maji, A.; Manna, S.; Maiti, D. *Angew. Chem., Int. Ed.* **2013**, *52*, 12669. (j) Tsuji, H.; Ilies, L.; Nakamura, E. *Synlett* **2014**, *25*, 2099. (k) Agasti, S.; Sharma, U.; Naveen, T.; Maiti, D. *Chem. Commun.* **2015**, *51*, 5375.

(6) Yang, Y.; Yao, J.; Zhang, Y. *Org. Lett.* **2013**, *15*, 3206.

(7) (a) Rosini, G.; Ballini, R. *Synthesis* **1988**, 833. (b) Ono, N. *The Nitro Group in Organic Synthesis*; Wiley-VCH: New York, 2001. (c) Ballini, R.; Bosica, G.; Fiorini, D.; Palmieri, A.; Petrini, M. *Chem. Rev.* **2005**, *105*, 933. (d) Maity, S.; Manna, S.; Rana, S.; Naveen, T.; Mallick, A.; Maiti, D. *J. Am. Chem. Soc.* **2013**, *135*, 3355. (e) Halimehjani, A. Z.; Namboothiri, I. N. N.; Hooshmand, S. E. *RSC Adv.* **2014**, *4*, 48022. (f) Halimehjani, A. Z.; Namboothiri, I. N. N.; Hooshmand, S. E. *RSC Adv.* **2014**, *4*, 31261. (g) Monir, K.; Bagdi, A. K.; Ghosh, M.; Hajra, A. *Org. Lett.* **2014**, *16*, 4630.

(8) (a) Nair, D. K.; Mobin, S. M.; Namboothiri, I. N. N. *Tetrahedron Lett.* **2012**, *53*, 3349. (b) Nair, D. K.; Mobin, S. M.; Namboothiri, I. N. N. *Org. Lett.* **2012**, *14*, 4580. (c) Huang, W. Y.; Chen, Y. C.; Chen, K. *Chem.—Asian J.* **2012**, *7*, 688. (d) Anwar, S.; Huang, W.-Y.; Chen, C.-H.; Cheng, Y.-S.; Chen, K. *Chem.—Eur. J.* **2013**, *19*, 4344.

(9) Kundu, D.; Samim, M.; Majee, A.; Hajra, A. *Chem.—Asian J.* **2011**, *6*, 406.

(10) Ghosh, M.; Mishra, S.; Monir, K.; Hajra, A. *Org. Biomol. Chem.* **2015**, *13*, 309.

(11) Liu, C.; Liu, D.; Lei, A. *Acc. Chem. Res.* **2014**, *47*, 3459.

(12) (a) Shiraishi, H.; Nishitani, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1998**, *63*, 6234. (b) Maiti, S.; Biswas, S.; Jana, U. *J. Org. Chem.* **2010**, *75*, 1674. (c) Santra, S.; Bagdi, A. K.; Majee, A.; Hajra, A. *Adv. Synth. Catal.* **2013**, *355*, 1065.

DOI: 10.1021/acs.joc.5b00704
J. Org. Chem. 2015, 80, 5364−5368