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Base- and Copper-Catalyzed Intramolecular Cyclization for the Direct Synthesis of Dihydrofurans

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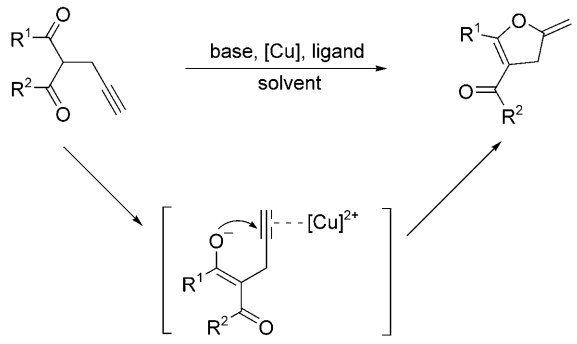
Abstract: A simple and convenient synthetic approach to dihydrofurans has been developed from the cyclization of 2-propynyl-1,3-dicarbonyl compounds catalyzed by potassium *tert*-butoxide, copper(II) trifluoromethanesulfonate and triphenylphosphine using methanol/dichloromethane as the solvent under very mild conditions. Moreover, dihydrofurans could be easily transformed into the corresponding furans in the presence of trifluoroacetic acid.

Keywords: alkynes; copper; cyclization; dihydrofurans; furans

Introduction

Dihydrofurans are an important class of oxygenated heterocycles with widespread occurrence in nature, and they are also useful building blocks in organic synthesis.[1a–k] Meanwhile, a vast number of bioactive natural and unnatural products based on the dihydrofuran ring are very useful in the area of pharmaceutical chemistry.[1l–p] So, the development of efficient synthetic approaches to dihydrofurans has attracted tremendous attention.[2,3] Several methods for cyclic ethers based on the metal-catalyzed cyclization reactions have been reported.[3] Trost and co-workers reported the cycloisomerization of 1-alkyn-4-ols to dihydrofurans catalyzed by Rh.[3a] McDonald and cowokers discovered that acyclic alkynols could be transformed to cyclic enol ethers promoted by $Mo(CO)_5$.[3b] The Pd-catalyzed cyclization of allenol was reported by Ma and Alcaide, respectively.[3c,d] The conversion of α-hydroxyallenes or (*Z*)-enynols to 2,5-dihydrofurans catalyzed by Au has been developed by Lee, Krause and Liu, respectively.[3e–g] However, few methodologies were reported for the synthesis of 5-methylene-4,5-dihydrofurans. Therefore, the investigation of new synthetic routes which allow the facile building of 5-methylene-4,5-dihydrofuran rings under the mild conditions would be a timely endeavor.

In recent years, copper-catalyzed reactions have received considerable attention owing to their efficiency, excellent selectivity and low costs.[4,5] Although many copper-catalyzed strategies have been successfully applied to the preparation of many heterocyclic compounds,[6] few applications in the synthesis of dihydrofurans were reported.[7] Based on our previous studies,[8] we hypothesize that the direct synthesis of 5-methylene-4,5-dihydrofurans could be achieved by using 2-propynyl-1,3-dicarbonyl compounds as starting materials (Scheme 1). It is anticipated that the rapid enolization of the dicarbonyl compounds under base catalysis followed by an intramolecular nucleophilic addition of the oxygen anion of an enol to a carbon-carbon triple bond activated by a copper salt

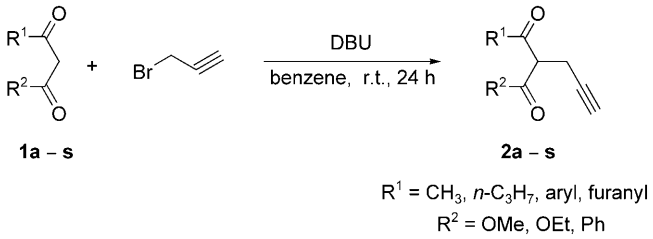


Scheme 1. The synthesis of dihydrofurans from 2-propynyl-1,3-dicarbonyl compounds by the intramolecular cyclization under the catalysis of base and copper.

might provide a facile route to the construction of substituted 5-methylene-4,5-dihydrofuran compounds. To the best of our knowledge, this is the first synthesis of 5-methylene-4,5-dihydrofurans from 2-propynyl-1,3-dicarbonyl compounds using the combination of base and copper salt as catalysts. Herein we present our findings on this reaction that provides a new approach to dihydrofurans in a direct, efficient and facile manner.

Results and Discussion

The starting 2-propynyl-1,3-dicarbonyl compounds (**2a**–**s**) were easily prepared from 1,3-dicarbonyl compounds (**1a**–**s**) (Scheme 2).[9]

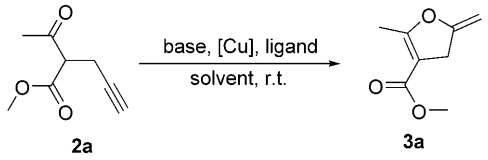


Scheme 2. Synthesis of the substrates.

Preliminary catalyst screening studies were performed using methyl 2-acetylpent-4-ynoate **2a** in methanol at room temperature as a model reaction (Table 1). No significant reaction was observed without the addition of either $Cu(OTf)_2$ or PPh_3 (Table 1, entries 1–3). The screenings of various assemblies of strong bases and copper salts revealed a combination of potassium *tert*-butoxide (10 mol%) and $Cu(OTf)_2$ (0.5 mol%) in the presence of triphenylphosphine (2 mol%) provided the best yield for the reaction (Table 1, entries 4–11). Further examination of various solvents showed that $MeOH/CH_2Cl_2$ (1/1 v/v) was the most effective solvent for the reaction (Table 1, entries 12–22). Although methanol was also a suitable solvent for the reaction, it was found that the product partly isomerized in it (Table 1, entry 4). Thus, the intramolecular cyclization reaction of methyl 2-acetylpent-4-ynoate (**2a**) could be completed smoothly within 30 min in the presence of KO-*t*-Bu (10 mol%), $Cu(OTf)_2$ (0.5 mol%) and PPh_3 (2 mol%) using $MeOH/CH_2Cl_2$ (1/1 v/v) as the solvent at room temperature in excellent yield.

Under these optimized conditions, the scope of reaction was then explored. Typical results are shown in Table 2. For the aliphatic 2-propynyl-1,3-dicarbonyl compounds, the reaction gave excellent yields (Table 2, entries 1 and 2). In general, the reaction for all aromatic 2-propynyl-1,3-dicarbonyl compounds afforded the corresponding 5-methylene-4,5-dihydrofurans in high yields. The results indicated that 2-propynyl-1,3-dicarbonyl compounds without substitution or with *para* or *meta* electron-withdrawing groups on the phenyl ring could be rapidly converted to corresponding 5-methylene-4,5-dihydrofurans in excellent yields (Table 2, entries 3, 6, 7, 8, 11, 12 and 17). The reaction was also efficient for 2-propynyl-1,3-dicarbonyl compounds with *para* or *meta* electron-donating groups on the phenyl ring (Table 2, entries 4, 5, 9 and 10). Meanwhile, substrates possessing *ortho* groups on the phenyl ring were also successfully employed to give 5-methylene-4,5-dihydrofuran compounds in good yields (Table 2, entries 13–16). For the heteroaromatic compound **2r**, the reaction was effectively carried out in excellent yield (Table 2, entry 18). However, the reaction of **2s** ($R^1 = R^2 =$ phenyl) provided a complex mixture under the optimized conditions. It was found

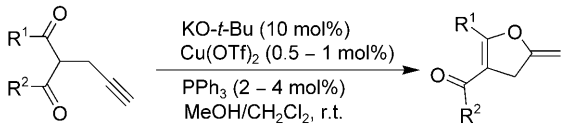
Table 1. Optimization of the catalytic conditions.[a]



Entry	[Cu]	Base	Ligand	Solvent	Yield [%][b]
1	–	KO-*t*-Bu	–	MeOH	0
2	$Cu(OTf)_2$	KO-*t*-Bu	–	MeOH	trace
3	–	KO-*t*-Bu	PPh_3	MeOH	0
4	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	MeOH	99[c]
5	$Cu(OTf)_2$	DABCO	PPh_3	MeOH	52
6	$Cu(OTf)_2$	DBU	PPh_3	MeOH	97
7	$Cu(OTf)_2$	KOH	PPh_3	MeOH	95
8	$Cu(OTf)_2$	K_2CO_3	PPh_3	MeOH	93
9	CuCl	KO-*t*-Bu	PPh_3	MeOH	24
10	$CuSO_4$	KO-*t*-Bu	PPh_3	MeOH	90
11	CuI	KO-*t*-Bu	PPh_3	MeOH	91
12	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	CH_3CN	51
13	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	CH_2Cl_2	51
14	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	benzene	37
15	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	$CHCl_3$	79
16	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	toluene	37
17	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	hexane	60
18	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	EtOH	77
19	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	Et_2O	28
20	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	THF	trace
21	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	dioxane	trace
22	$Cu(OTf)_2$	KO-*t*-Bu	PPh_3	MeOH-CH_2Cl_2	99[d]

[a] *Reaction conditions:* unless otherwise noted, [Cu] (0.5 mol%), PPh_3 (2 mol%), **2a** (0.2 mmol) and KO-*t*-Bu (10 mol%) stirred in solvent (0.2 mL) at room temperature for 0.5 h.
[b] Isolated yield after flash column chromatography.
[c] Product easily partly isomerized in MeOH.
[d] $MeOH/CH_2Cl_2 = 1/1$ (v/v).

Table 2. The synthesis of 5-methylene-4,5-dihydrofurans from various 2-propynyl-1,3-dicarbonyl compounds: the scope of substrates.



2a – s **3a – s**

Entry	R^1	R^2	Time [h]	**3**	Yield [%][d]
1	CH_3	OMe	0.5	**a**	99[a]
2	n-C_3H_7	OMe	0.5	**b**	99[a]
3	Ph	OMe	0.5	**c**	99[a]
4	p-CH_3-C_6H_5	OMe	2.0	**d**	95[b]
5	p-CH_3O-C_6H_5	OMe	5.0	**e**	83[b]
6	p-F-C_6H_5	OMe	0.5	**f**	99[a]
7	p-Cl-C_6H_5	OMe	0.5	**g**	99[a]
8	p-Br-C_6H_5	OMe	0.5	**h**	99[a]
9	m-CH_3-C_6H_5	OMe	2.0	**i**	95[b]
10	m-CH_3O-C_6H_5	OMe	2.0	**j**	90[b]
11	m-Cl-C_6H_5	OMe	1.5	**k**	99[a]
12	m-Br-C_6H_5	OMe	1.0	**l**	99[a]
13	o-CH_3-C_6H_5	OMe	2.0	**m**	88[b]
14	o-CH_3O-C_6H_5	OMe	2.0	**n**	85[b]
15	o-F-C_6H_5	OMe	1.0	**o**	95[b]
16	o-Cl-C_6H_5	OMe	1.5	**p**	91[b]
17	m-Cl-C_6H_5	OC_2H_5	1.0	**q**	99[a]
18	2-furyl	OMe	1.0	**r**	99[a]
19	Ph	Ph	2.0	**s**	90[c]

[a] $Cu(OTf)_2$ (0.5 mol%), PPh_3 (2 mol%), **2** (0.2 mmol) and KO-*t*-Bu (10 mol%) stirred in $MeOH/CH_2Cl_2$ (1/1, v/v, 0.2 mL) at room temperature.

[b] $Cu(OTf)_2$ (1 mol%), PPh_3 (4 mol%), **2** (0.2 mmol) and KO-*t*-Bu (10 mol%) stirred in $MeOH/CH_2Cl_2$ (1/1, v/v, 0.2 mL) at room temperature.

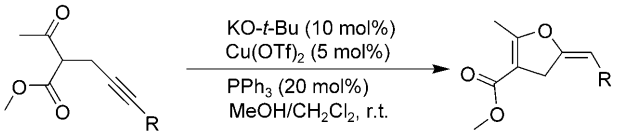
[c] $Cu(OTf)_2$ (0.5 mol%), PPh_3 (2 mol%), **2** (0.2 mmol) and KO-*t*-Bu (10 mol%) stirred in $MeOH/CH_2Cl_2$ (1/1, v/v, 0.2 mL) at 0 °C.

[d] Isolated yield after flash column chromatography.

later that the desired product **3s** could be obtained in good yield when the reaction temperature was decreased to 0 °C (Table 2, entry 19).

Next, in order to extend the generality of our method, the scope of this cyclization reaction was explored further with 1,3-dicarbonyl compounds bearing an internal alkyne. Firstly, the cyclization of methyl 2-acetyl-5-phenylpent-4-ynoate was studied (entry 1, Table 3). However, under the optimized conditions, the rate of the reaction was very slow. Fortunately, when the amount of catalysts was increased, the cyclization reaction could be smoothly carried out in good yield. For the 1,3-dicarbonyl compound with *para* electron-withdrawing groups on the phenyl ring, like a CH_3CO group, the reaction was effectively performed in good yield (entry 2, Table 3). The 1,3-dicarbonyl compound with a *para* electron-donating group

Table 3. The synthesis of substituted 5-methylene-4,5-dihydrofurans.[a]



2t – x **3t – x**

Entry	R	**2**	Time [h]	**3**	Yield [%]
1	phenyl	**2t**	6	**3t**	84
2	p-CH_3CO-C_6H_5	**2u**	3	**3u**	90
3	p-CH_3-C_6H_5	**2v**	12	**3v**	80
4	ethyl	**2w**	12	**3w**	trace
5	n-propyl	**2x**	12	**2x**	trace

[a] *Reaction conditions:* $Cu(OTf)_2$ (5 mol%), PPh_3 (20 mol%), **2** (0.2 mmol) and KO-*t*Bu (10 mol%) stirred in $MeOH/CH_2Cl_2$ (1/1, 0.2 mL) at room temperature.

on the phenyl ring, like a methyl group, could also be converted into the corresponding dihydrofuran with a longer time (entry 3, Table 3). However, for 1,3-dicarbonyl compounds bearing an internal alkyne with aliphatic substituted groups (ethyl and *n*-propyl), the reaction could not be carried out effectively under these catalytic conditions (entries 4 and 5, Table 3).

Referring to the related literature,[8] the proposed mechanism for the reaction is shown in Figure 1. First, under base catalysis, the enol anion is rapidly generated from **2**. Meanwhile, the coordination of the carbon-carbon triple bond of **2** to $[Cu]^{2+}$ activated by the ligand (PPh_3) enhances the electrophilicity of the alkyne. Subsequently, the intramolecular cyclization reaction proceeds through the nucleophilic addition of the enolate oxygen anion to the electron-deficient alkyne moiety to form a vinyl-copper adduct. Finally, the adduct undergoes protodemetallation to give the observed 5-methylene-4,5-dihydrofuran product **3**.

Additionally, in the process of the examination of various solvents for the reaction, we found that the product **3a** was partly isomerized to the substituted furan **4a** in methanol in a long reaction time. Furthermore, some substituted furans are also useful and versatile intermediates in synthetic organic chemistry.[10] As a consequence, many methodologies have been reported for the synthesis of furan derivatives.[11] The most important strategies involving metal-catalyzed cyclization of suitable precursors such as enynols, epoxyalkynes, ketoalkynes or ketoallenes, and others.[11a–e] Nishizawa reported the $Hg(OTf)_2$-catalyzed ketoalkyne cyclization leading to 2-methylfurans.[11x] Wipf, Dixneuf and co-workers reported a Pd-catalyzed cyclization reaction to afford substituted furans.[11f,i,w] Cadierno found a highly efficient ruthenium-catalyzed method for the preparation of substituted furans from secondary propargylic alcohols and

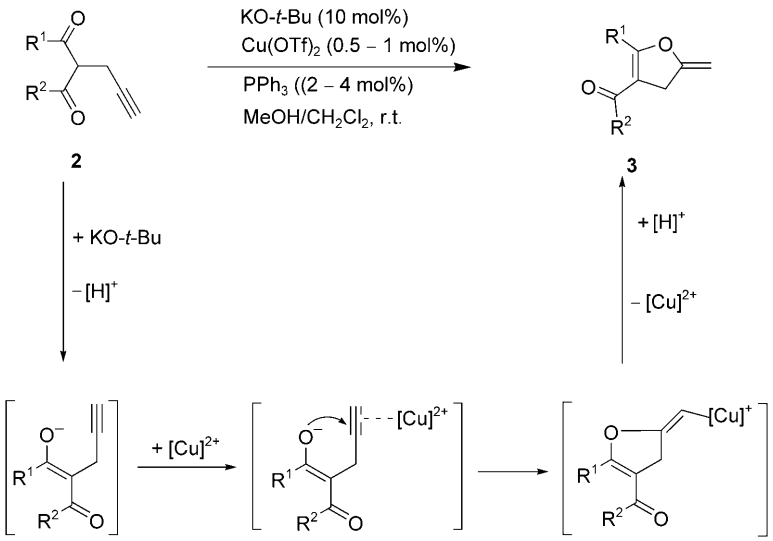
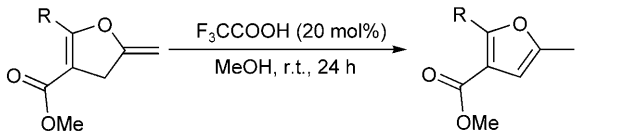


Figure 1. Proposed mechanistic pathway.

Table 4. Dihydrofuran isomerisation studies.[a]



3b, c, d, g — 4b, c, d, g

Entry	3	4	Yield [%]
1	**3b**	**b**	80
2	**3c**	**c**	85
3	**3d**	**d**	80
4	**3g**	**g**	88

[a] **3** (0.2 mmol) and F_3CCOOH (20 mol%) stirred in dry MeOH (3 mL) at room temperature for 24 h.

1,3-dicarbonyl compounds, etc.[12a] Encouraged by these results, we tried to transform 5-methylene-4,5-dihydrofurans into the corresponding furans *via* the addition of an acid.[12] To our delight, 5-methylene-4,5-dihydrofurans could be smoothly converted into the corresponding furans in the presence of CF_3COOH in dry MeOH at room temperature within 24 h in good yields (Table 4, entries 1–4).

Conclusions

In summary, a general and highly efficient synthetic method for substituted 5-methylene-4,5-dihydrofuran compounds has been developed. This intramolecular cyclization reaction was performed using readily available materials (2-propynyl-1,3-dicarbonyl compounds), an inexpensive catalyst (Cu^{2+} salt) and ligand (PPh_3) under very mild basic conditions in good to excellent yields. Furthermore, the reaction exhibited excellent functional group compatibility. Furthermore, 5-methylene-4,5-dihydrofurans could be easily converted into the corresponding furans under acidic conditions. Future studies will focus on the development of related transformations, and the application of this methodology towards the synthesis of natural products containing the dihydrofuran or furan moiety.

Experimental Section

General Remarks

All reactions were performed under an air atmosphere unless otherwise stated. All ^1H and ^{13}C NMR spectra were recorded using Bruker 400 MHz and 75 MHz spectrometers. Chemical shifts (δ) are given in ppm, and coupling constants (J) are given in Hertz (Hz). HR-MS were performed on a Bruker Apex II mass instrument (ESI). MS were measured on a VG-7070E spectrometer (EI at 70 eV); IR spectra were recorded using a Nicolet NEXUS 670 FT-IR instrument.

General Procedure for the Synthesis of Starting Materials 2a–x

Under an argon atmosphere, propargyl bromide (5.1 mmol) was added to a solution of **1** (5 mmol) and DBU (5.1 mmol) in benzene (15 mL) and the solution was stirred at room temperature for 24 h. After filtering off the DBU-HBr salt, the solvent was evaporated and the residue was purified by column chromatography (petroleum ether/ethyl acetate = 1/20, v/v) to afford the desired products **2**.

The product **2a** (70%) was isolated as a colourless oil after column chromatography. IR (KBr): $\nu = 3288$, 2957, 2926, 2122, 1745, 1718, 1435, 1361, 1154, 657 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.77$ (s, 3H), 3.73 (t, $J = 7.6$ Hz, 1H), 2.72 (m, 2H), 2.31 (s, 3H), 2.02 (t, $J = 2.8$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 200.85$, 168.47, 80.23, 70.26, 57.97, 52.65, 29.52, 17.38; MS (EI): *m/z* (rel. intensity, %) = 154 (0.44), 139 (33.80), 123 (1.27), 95 (1.83), 43 (100.00).

Compounds **2b**–**2s** could be synthesized *via* a similar method. The propargyl bromide was replaced by other substituted propargyl bromide, and **2t**–**2x** could be obtained.

The product **2t** (yield: 63%) was isolated as a colourless oil after column chromatography. IR (KBr): $\nu = 2954$, 1745, 1719, 1490, 1437, 1358, 1272, 1224, 1152, 759, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.37$ (m, 2H), 7.29 (m, 3H), 3.81 (t, $J = 7.6$ Hz, 1H), 3.80 (s, 3H), 2.96 (dd, $J = 7.6$, 2.0 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 201.33, 168.75, 131.60, 128.21, 128.03, 123.07, 85.59, 82.47, 58.28, 52.74, 29.69, 18.53.

General Procedure for the Synthesis of 5-Methylene-4,5-dihydrofuran Compounds 3a–s

A mixture of $Cu(OTf)_2$ (0.001 mmol) and PPh_3 (0.004 mmol) in dry $MeOH/CH_2Cl_2$ (1/1, v/v, 0.2 mL) was stirred for 10 min. Substrate **2** (0.2 mmol) and KO-*t*-Bu (0.02 mmol) were added and the reaction mixture was stirred at room temperature. After the completion of the reaction (monitored by TLC), the reaction mixture was directly loaded onto a silica gel column and eluted with petroleum ether/ethyl acetate/triethylamine (100:2:1) to afford the desired product **3**.

The product **3a** (yield: 99%) was isolated as a colourless oil after flash chromatography. IR (KBr): $\nu = 2925$, 2855, 1725, 1651, 1438, 1119, 1074, 1026, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 4.63$ (dd, $J = 5.6$, 3.2 Hz, 1H), 4.28 (dd, $J = 5.2$, 2.8 Hz, 1H), 3.74 (s, 3H), 3.57 (dt, $J = 2.8$, 2.0 Hz, 2H), 2.27 (t, $J = 2.0$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 166.04$, 165.15, 159.81, 103.72, 85.95, 51.06, 33.33, 13.60; MS (EI): *m/z* (rel. intensity, %) = 154 (M^+, 100.00), 139 (67.14), 123 (62.97), 95 (62.18); HR-MS (ESI): $m/z = 155.0703$, calcd. for $C_8H_{11}O_3$ $[M+H]^+$: 155.0701.

Typical Procedure for the Synthesis of Substituted 5-Methylene-4,5-dihydrofuran Compounds 3t–v

A mixture of $Cu(OTf)_2$ (0.01 mmol) and PPh_3 (0.04 mmol) in dry $MeOH/CH_2Cl_2$ (1/1, v/v, 0.2 mL) was stirred for 10 min. Substrate **2t** (0.2 mmol) and KO-*t*-Bu (0.02 mmol) were added and the reaction mixture was stirred at room temperature. After the completion of the reaction (monitored by TLC), the reaction mixture was directly loaded onto a silica gel column and eluted with petroleum ether/ethyl acetate/triethylamine (100/2/1, v/v) to afford the desired product **3t** (yield: 84%) as a white solid. IR (KBr): $\nu =$ 2952, 2924, 1717, 1695, 1656, 1442, 1232, 1086, 987, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.52$ (d, $J = 7.6$ Hz, 2H), 7.31 (dd, $J = 8.0$, 7.2 Hz, 2H), 7.16 (t, $J = 7.6$ Hz, 1H), 5.57 (s, 1H), 3.75 (s, 5H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.98$, 165.07, 153.11, 134.90, 128.32, 127.72, 125.94, 103.87, 102.59, 51.17, 35.12, 13.81; MS (EI, 70 eV): *m/z* (rel. intensity, %) = 230 (M^+, 5.95), 215 (4.05), 128 (12.43), 105 (21.66); HR-MS (ESI): $m/z = 253.0833$, calcd. for $C_{14}H_{14}O_3Na$ $[M+Na]^+$: 253.0835.

General Procedure for the Synthesis of 2,3,5-Trisubstituted Furan compounds 4b, c, d, g

The compound **3** (0.2 mmol) was dissolved in dry MeOH (3 mL). F_3CCOOH (20 mol%) was added to the solution and the reaction mixture was stirred at room temperature for 24 h. The reaction was quenched with saturated aqueous $NaHCO_3$ solution. The crude product was purified by flash column chromatography to afford the desired product **4**.

The product **4b** (yield: 80%) was isolated as a colourless oil after flash chromatography. IR (KBr): $\nu = 2960$, 1719, 1584, 1439, 1386, 1239, 1207, 1094, 1053, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.19$ (d, $J = 0.8$ Hz, 1H), 3.79 (s, 3H), 2.91 (t, $J = 7.6$ Hz, 2H), 2.24 (d, $J = 0.8$ Hz, 3H), 1.68 (m, 2H), 0.94 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 164.72$, 161.72, 149.96, 113.37, 106.05, 51.11, 29.43, 21.52, 13.73, 23.23; MS (EI): *m/z* (rel. intensity, %) = 182 (M^+, 29.79), 167 (9.49), 153 (82.74), 151 (13.39), 123 (23.87), 43 (100.00); HR-MS (ESI): $m/z = 183.1017$, calcd. for $C_{10}H_{15}O_3$ $[M+H]^+$: 183.1021; HR-MS (ESI): $m/z = 183.1016$, calcd. for $C_{10}H_{15}O_3$ $[M+H]^+$: 183.1017.

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References

[1] For selected examples, see: a) F. M. Dean, in: *Advances in Heterocyclic Chemistry*, (Ed.: A. R. Katritzky), Academic Press, New York, **1982**, Vol. 30, pp 167–238; b) F. M. Dean, M. V. Sargent, in: *Comprehensive Heterocyclic Chemistry*, (Eds.: C. W. Bird, G. W. H. Cheeseman), Pergamon Press, New York, **1984**, Vol. 4, part 3, pp 531–598; c) B. H. Lipshutz, *Chem. Rev.* **1986**, *86*, 795–819; d) J. Lee, J.-H. Li, S. Oya, J. K. Snyder, *J. Org. Chem.* **1992**, *57*, 5301–5312; e) P. A. Jacobi, H. G. Selnick, *J. Org. Chem.* **1990**, *55*, 202–209; f) S. Schabbert, E. Schaumann, *Eur. J. Org. Chem.* **1998**, 1873–1878; g) P. F. Schuda, *Top. Curr. Chem.* **1980**, *91*, 75–111; h) G. Hoffmann, R. K. Johnson, *J. Nat. Prod.* **1993**, *56*, 1500–1505; i) J. P. Michael, *Nat. Prod. Rep.* **2000**, *17*, 603–620; j) M. F. Grundon, *Nat. Prod. Rep.* **1990**, *7*, 131–138; k) J. P. Michael, *Nat. Prod. Rep.* **1997**, *14*, 605–618; l) T. G. Kilroy, T. P. O'Sullivan, P. J. Guiry, *Eur. J. Org. Chem.* **2005**, 4929–4949; m) D. A. Evans, Z. K. Sweeney, T. Rovis, J. S. Tedrow, *J. Am. Chem. Soc.* **2001**, *123*, 12095–12096; n) R. L. Danheiser, E. J. Stoner, H. Kojama, D. S. Yamashita, C. A. Klade, *J. Am. Chem. Soc.* **1989**, *111*, 4407–4413; o) B. M. Fraga, *Nat. Prod. Rep.* **1992**, *9*, 217–241; p) A. T. Merrit, S. V. Ley, *Nat. Prod. Rep.* **1992**, *9*, 243–287.

[2] For selected papers, see: a) A. Arcadi, S. D. Giuseppe, F. Marinelli, E. Rossi, *Adv. Synth. Catal.* **2001**, *343*, 443–446; b) X. Du, F. Song, Y. Lu, H. Chen, Y. Liu, *Tetrahedron* **2009**, *65*, 1839–1845; c) C.-P. Chuang, K.-P. Chen, Y.-L. Hsu, A.-I. Tsai, S.-T. Liu, *Tetrahedron* **2008**, *64*, 7511–7516; d) E. V. Burgaz, M. Yılmaz, A. T. Pekel, A. Öktemer, *Tetrahedron* **2007**, *63*, 7229–7239.

[3] For selected papers, see: a) B. M. Trost, Y. H. Rhee, *J. Am. Chem. Soc.* **2003**, *125*, 7482–7483; b) F. E. McDonald, C. B. Connolly, M. M. Gleason, T. B. Towne, K. D. Treiber, *J. Org. Chem.* **1993**, *58*, 6952–6953; c) Y. Deng, J. Li, S. Ma, *Chem. Eur. J.* **2008**, *14*, 4263–4266; d) B. Alcaide, P. Almendros, T. M. del Campo, *Angew. Chem.* **2006**, *118*, 4613–4616; *Angew. Chem. Int. Ed.* **2006**, *45*, 4501–4504; e) S. Kima, P. H. Lee, *Adv. Synth. Catal.* **2008**, *350*, 547–551; f) Ö. Aksın, N. Krause, *Adv. Synth. Catal.* **2008**, *350*, 1106–1112; g) Y. Liu, F. Song, M. Liu, B. Yan, *Org. Lett.* **2005**, *7*, 5409–5412; h) R. K. Bowman, J. S. Johnson, *Org. Lett.* **2006**, *8*, 573–576; i) Y. Nishibayashi, M. Yoshikawa, Y. Inada, M. Hidai, S. Uemura, *J. Org. Chem.* **2004**, *69*, 3408–3412.

[4] For selected papers, see: a) F. Himo, T. Lovell, R. Hilgraf, V. V. Rostovtsev, L. Noodleman, K. B. Sharpless, V. V. Fokin, *J. Am. Chem. Soc.* **2005**, *127*, 210–216; b) H. Isobe, K. Cho, N. Solin, D. B. Werz, P. H. Seeberger, E. Nakamura, *Org. Lett.* **2007**, *9*, 4611–4614; c) A. Klapars, S. Parris, K. W. Anderson, S. L. Buchwald, *J. Am. Chem. Soc.* **2004**, *126*, 3529–3533; d) L. Ackermann, H. K. Potukuchi, D. Landsberg, R. Vicente, *Org. Lett.* **2008**, *10*, 3081–3084; e) D. Ma, Q. Cai, *Acc. Chem. Res.* **2008**, *41*, 1450–1460; f) A. V. Kel'in, A. W. Sromek, V. Gevorgyan, *J. Am. Chem. Soc.* 2**001**, 123, 2074–2075.

[5] For selected papers, see: a) I. P. Beletskaya, A. V. Cheprakov, *Coord. Chem. Rev.* **2004**, *248*, 2337–2364; b) G. Evano, N. Blanchard, M. Toumi, *Chem. Rev.* **2008**, *108*, 3054–3131; c) F. Monnier, M. Taillefer, *Angew. Chem.* **2008**, *120*, 3140–3143; *Angew. Chem. Int. Ed.* **2008**, *47*, 3096–3099.

[6] For selected papers, see: a) J. Zhu, H. Xie, Z. Chen, S. Li, Y. Wu, *Chem. Commun.* **2009**, 2338–2340; b) L. Li, M. Wang, X. Zhang, Y. Jiang, D. Ma, *Org. Lett.* 2**009**, 11, 1309–1312; c) A. K. Verma, T. Kesharwani, J. Singh, V. Tandon, R. C. Larock, *Angew. Chem.* **2009**, *121*, 1158–1163; *Angew. Chem. Int. Ed.* **2009**, *48*, 1138–1143; d) Y. Ohta, H. Chiba, S. Oishi, N. Fujii, H. Ohno, *Org. Lett.* **2008**, *10*, 3535–3538; e) Y. , Chen, Y. Wang, Z. Sun, D. Ma, *Org. Lett.* **2008**, *10*, 625–628; f) R. D. Viirre, G. Evindar, R. A. Batey, *J. Org. Chem.* **2008**, *73*, 3452–3459; g) B. Zou, Q. Yuan, D. Ma, *Angew. Chem.* **2007**, *119*, 2652–2655; *Angew. Chem. Int. Ed.* **2007**, *46*, 2598–2601; h) R. Martin, A. Cuenca, S. L. Buchwald, *Org. Lett.* **2007**, *9*, 5521–5524; i) Zheng, Buchwald, S. L. , *Org. Lett.* **2007**, *9*, 4749–4751; j) N. B. Zou, Q. Yuan, D. Ma, *Org. Lett.* **2007**, *9*, 4291–4294; k) M. R. Rivero, S. L. Buchwald, *Org. Lett.* **2007**, *9*, 973–976; l) R. Martín, M. R. Rivero, S. L. Buchwald, *Angew. Chem.* **2006**, *118*, 7237–7240; *Angew. Chem. Int. Ed.* **2006**, *45*, 7079–7082; m) X. Lv, W. Bao, *J. Org. Chem.* **2009**, *74*, 5618–5621.

[7] a) Y. Fang, C. Li, *Chem. Commun.* **2005**, 3574–3576; b) S. Son, G. C. Fu, *J. Am. Chem. Soc.* **2007**, *129*, 1046–1047.

[8] H.-F. Wang, T. Yang, P.-F. Xu, D. Dixon, *Chem. Commun.* **2009**, 3916–3918.

[9] N. Ono, T. Yoshimura, R. Tanikaga, A. Kaji, *Chem. Lett.* **1977**, *6*, 871–872.

[10] For selected papers, see: a) X. L. Hou, Z. Yang, H. N. C. Wong, in: *Progress in Heterocyclic Chemistry*, (Eds.: C. W. Gribble, T. L. Gilchrist), Pergamon Press, Oxford, **2003**, Vol. 15, pp 167–205; b) W. Friedrichsen, in: *Comprehensive Heterocyclic Chemistry II*, (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Pergamon Press, Oxford, **1996**, Vol. 2, pp 351–393; c) R. Benassi, in: *Comprehensive Heterocyclic Chemistry II*, (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Pergamon Press, Oxford, **1996**, Vol. 2, pp 259–295.

[11] For selected papers, see: a) A. S. K. Hashmi, P. Sinha, *Adv. Synth. Catal.* **2004**, *346*, 432–438; b) J. A. Marshall, E. D. Robinson, *J. Org. Chem.* **1990**, *55*, 3450–3451; c) A. S. K. Hashmi, L. Schwarz, J. H. Choi, T. M. Frost, *Angew. Chem.* **2000**, *112*, 2382–2385; *Angew. Chem. Int. Ed.* **2000**, *39*, 2285–2288; d) Y. Fukuda, H. Shiragami, K. Utimoto, H. Nozaki, *J. Org. Chem.* **1991**, *56*, 5816–5819; e) B. Seiller, C. Bruneau, P. H. Dixneuf, *Tetrahedron* **1995**, *51*, 13089–13102; f) P. Wipf, M. J. Soth, *Org. Lett.* **2002**, *4*, 1787–1790; g) J. A. Marshall, D. Zou, *Tetrahedron Lett.* **2000**, *41*, 1347–1350; h) D. I. MaGee, J. D. Leach, *Tetrahedron Lett.* **1997**, *38*, 8129–8132; i) P. Wipf, L. T. Rahman, S. R. Rector, *J. Org. Chem.* **1998**, *63*, 7132–7133; j) B. Sieller, C. Bruneau, P. H. Dixneuf, *J. Chem. Soc. Chem. Commun.* **1994**, 493–494; k) B. Gabriele, G. Salerno, F. De Pascali, M. Costa, G. P. Chiusoli, *J. Org. Chem.* **1999**, *64*, 7693–7699; l) N. Asao, T. Nogami, K. Takahashi, Y. Yamamoto, *J. Am. Chem. Soc.* **2002**, *124*, 764–765; m) A. Arcadi, S. Cacchi, R. C. Laroek, F. Marinelli, *Tetrahedron Lett.* **1993**, *34*, 2813–2816; n) S. Cacchi, G. Fabrizi, L. Moro, *J. Org. Chem.* **1997**, *62*, 5327–5332; o) A. Arcadi, G. Cerichelli, M. Chiarini, S. D. Giuseppe, F. Marinelli, *Tetrahedron Lett.* **2000**, *41*, 9195–9198; p) A. Arcadi, G. Cerichelli, M. Chiarini, S. D. Giuseppe, F. Marinelli, *Tetrahedron Lett.* **2000**, *41*, 9195–9198; q) J. A. Marshall, X.-J. Wang, *J. Org. Chem.* **1991**, *56*, 960–969; r) J. A. Marshall, G. S. Bartley, *J. Org. Chem.* **1994**, *59*, 7169–7171; s) J. A. Marshall, X.-J. Wang, *J. Org. Chem.* **1992**, *57*, 3387–3396; t) S. M. Ma, J. L. Zhang, L. H. Lu, *Chem. Eur. J.* **2003**, *9*, 2447–2456; u) J. Tsuji, H. Watanabe, I. Minami, I. Shimizu, *J. Am. Chem. Soc.* **1985**, *107*, 2196–2198; v) X. H. Duan, X.-Y. Liu, L.-N. Guo, M.-N. Liao, W.-M. Liu, Y.-M. Liang, *J. Org. Chem.* **2005**, *70*, 6980–6983; w) M. Picquet, C. Bruneau, P. H. Dixneuf, *Tetrahedron* **1999**, *55*,3937–3948; x) H. Imagawa, T. Kurisaki, M. Nishizawa, *Org. Lett.* **2004**, *6*, 3679–3681.

[12] a) V. Cadierno, J. Gimeno, N. Nebra, *Adv. Synth. Catal.* **2007**, *349*, 382–394; b) B. Gabriele, G. Salerno, E. Lauria, *J. Org. Chem.* **1999**, *64*, 7687–7692; c) X. Han, R. A. Widenhoefer, *J. Org. Chem.* **2004**, *69*, 1738–1740.

