Tetrahedron Letters 51 (2010) 273–276

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Copper-catalyzed addition of water affording highly substituted furan and unusual formation of naphthofuran ring from 3-(1-alkenyl)-2-alkene-1-al

Rathin Jana, Sunanda Paul, Anup Biswas, Jayanta K. Ray *

Department of Chemistry, Indian Institute of Technology, Kharagpur 721302, India

ARTICLE INFO

Article history:
Received 4 September 2009
Revised 22 October 2009
Accepted 28 October 2009
Available online 30 October 2009

Keywords:
Furan
Naphthofuran
Copper catalyzed
Sonogashira coupling

ABSTRACT

We have developed a novel one-pot reaction to generate highly substituted furan through the addition of water followed by oxidation and unusual cyclization to naphthofuran ring under the same reaction condition.

1. Introduction

Highly substituted furans are an important class of heterocyclic compounds which are not only present as key structural unit in many natural products but also useful building blocks in synthetic chemistry.[1] One of the reliable approaches for their synthesis is the cyclization of allenyl ketones and 3-alkyn-1-ones[2] by use of transitional metals catalyst. Larock, Oh and Yamamoto have independently reported Au-, Pt- and Cu-catalyzed synthesis of substituted furans from the 2-alkenyl-1-one.[3] It has been suggested that a metal salt can facilitate the reaction by its dual function, that is, Lewis acid to activate the carbonyl group and co-ordination of metal with alkynes.

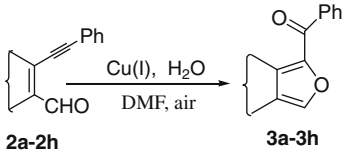
Herein, we report a synthetic approach towards the highly substituted furan[4] by a cuprous chloride-catalyzed sequential one-pot reaction of **2a–2h** through cyclization and 1,6-addition of water as a nucleophile followed by oxidation (Scheme 1).

The convergent approach involved the preparation of the precursors **2a–2o** which were efficiently synthesized from bromovinylaldehydes by Sonogashira coupling[5] as per Scheme 2.

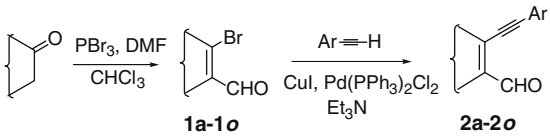
The initial experiment was carried out by heating the mixture of compound **2a**, H_2O (10 equiv) and CuCl in DMF at 95–100 °C in an open flask for 12–14 h (Table 1, entry 1). A furan ring resulted from the substrate **2a**. By shortening the reaction time to 6 h and lowering the temperature to 80 °C, very low yields were obtained (Table 1, entries 2–3). The reaction was then attempted by changing the catalyst and solvent to optimize the reaction conditions. The results are summarized in Table 1

Finally, we conclude that our optimization condition was CuCl (10 mol %), 10 equiv H_2O in 2–3 mL DMF, heated at 95–100 °C for 12–14 h. We next examined the scope of this reaction with different 3-(1-alkynyl)-2-alkene-1-als (**2a–2h**) to obtain the furan ring in moderate to good yield which are shown in Table 2.

The mechanism presumably involves copper-catalyzed 1,6-addition of water. In cycle A copper co-ordinates with carbonyl oxygen to activate the adjacent triple bond, followed by 5-exo-dig cyclization. Then 1,6-addition of water and consequently aerial



Scheme 1. Synthesis of substituted furan ring by copper-catalyzed reaction.

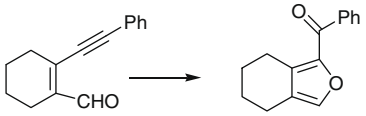


Scheme 2. Synthesis of starting materials.

* Corresponding author.
E-mail address: jkray@chem.iitkgp.ernet.in (J.K. Ray).

0040-4039/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2009.10.125

Table 1
Optimization studies[a]

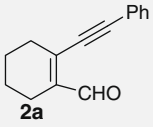
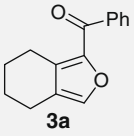
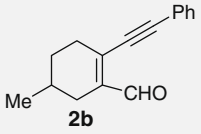
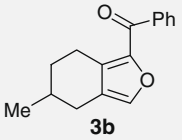
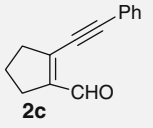
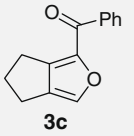
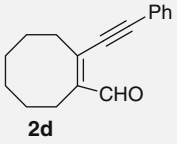
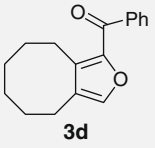
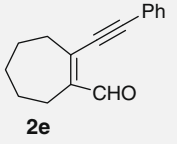
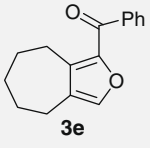
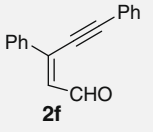
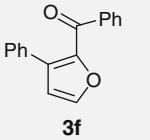
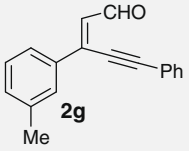
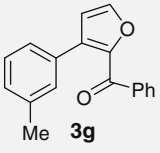
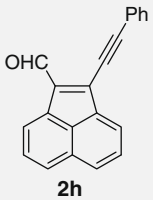
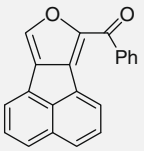


2a 3a

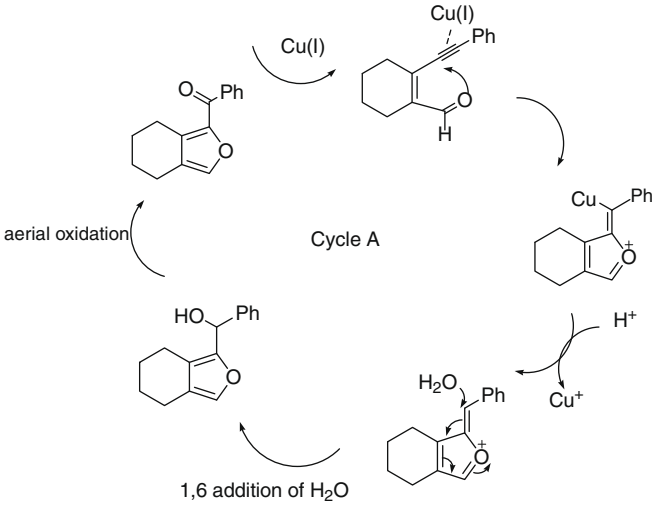
Entry	Catalyst	Solvent	Temp (°C)	Time (h)	Yield (%)
1	CuCl	DMF	95	12	68
2	CuCl	DMF	80	6	25
3	CuBr	DMF	80	6	20
4	CuBr	DMF	95	13	61
5	CuCl	CH_3CN	85	12	30
6	CuCl	Toluene	95	14	20
7	CuBr	CH_3CN	85	12	15

[a] All the reactions were carried out in the presence of 10 equiv H_2O, in open flask.

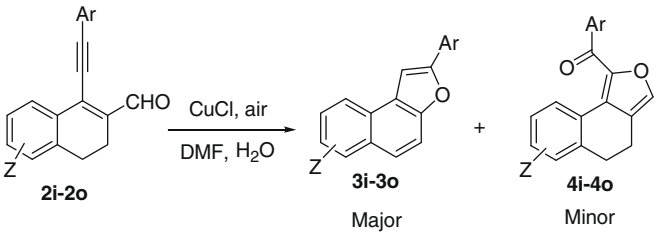
Table 2
Copper-catalyzed synthesis of furan[a]

Entry	Reactants	Products	Yield (%)
1	 2a	 3a	68
2	 2b	 3b	66
3	 2c	 3c	64
4	 2d	 3d	68
5	 2e	 3e	69
6	 2f	 3f	58
7	 2g	 3g	60
8	 2h	 3h	65

[a] Reagents and conditions: CuCl (10 mol %), H_2O (10 equiv) and DMF (2–3 mL), heated at 95–100 °C for 12–14 h.



Scheme 3. Proposed mechanism for the formation of furan ring.



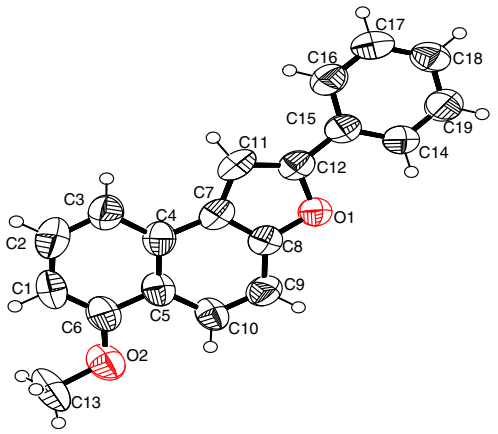
Scheme 4. Synthesis of substituted furan and naphthofuran ring.

oxidation of alcohols lead to furan ring. The plausible mechanism of this reaction is outlined below (Scheme 3).

During the course of our reaction an interesting result was obtained, when the reactants (**2i**–**2o**) were treated with cuprous chloride under the same reaction conditions to afford fused naphthofuran along with small amount of 1,6-addition product (Scheme 4). Then we generalized our reaction with different substituent and in every case we obtained the naphthofuran in moderate to good yield. The results are shown in Table 3.

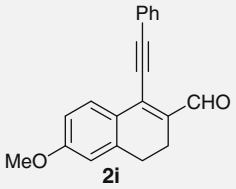
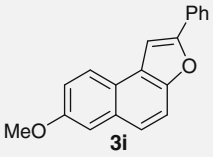
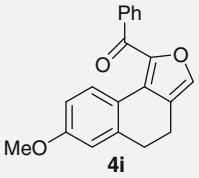
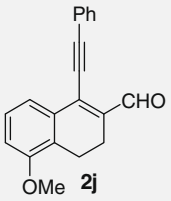
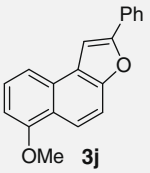
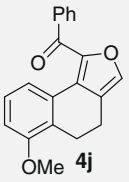
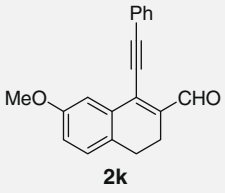
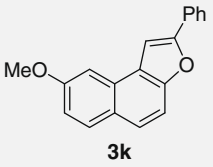
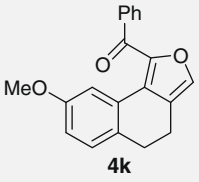
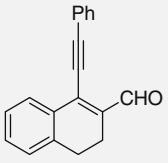
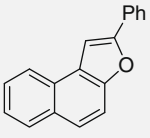
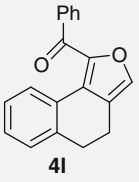
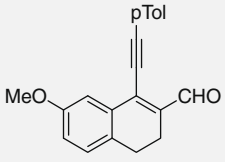
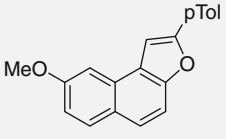
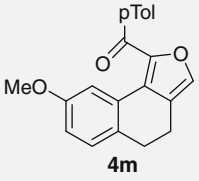
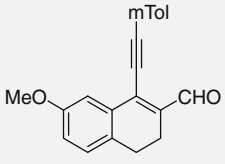
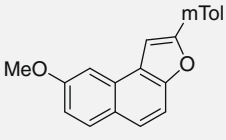
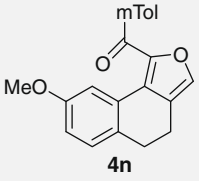
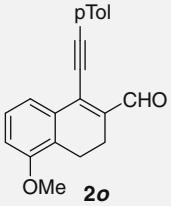
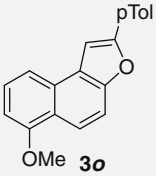
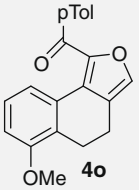
The ORTEP structure of naphthofuran of **3j** is shown below (Scheme 5).

The plausible mechanism of this reaction is described in Scheme 6**.** Cu(I) first co-ordinates with the triple bond to activate



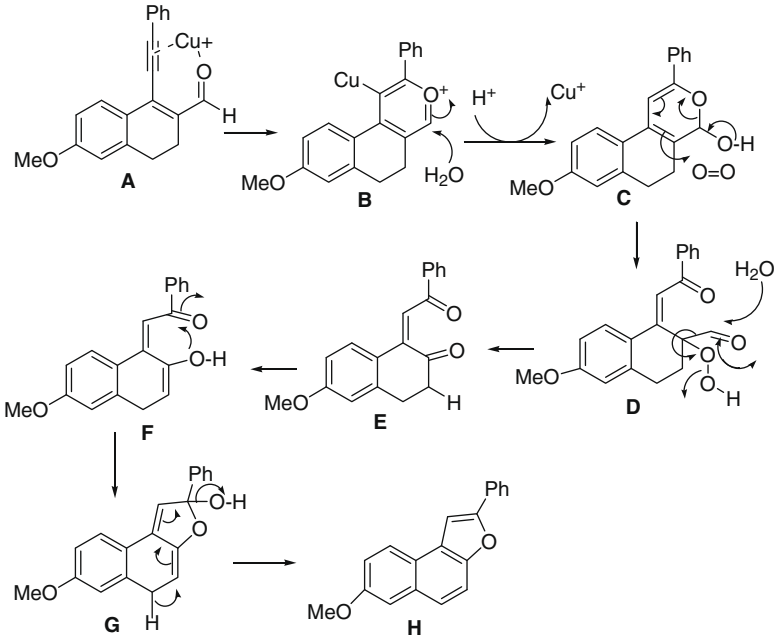
Scheme 5.

Table 3
Copper-catalyzed synthesis of furan and naphthofuran ring

Entry	Reactants	Products		Yield (%)
1	 **2i**	 **3i**	 **4i**	65 and 20
2	 **2j**	 **3j**	 **4j**	63 and 25
3	 **2k**	 **3k**	 **4k**	65 and 25
4	 **2l**	 **3l**	 **4l**	50 and 45
5	 **2m**	 **3m**	 **4m**	62 and 30
6	 **2n**	 **3n**	 **4n**	58 and 30
7	 **2o**	 **3o**	 **4o**	62 and 20

Reagents and conditions: CuCl (10 mol %), H_2O (10 equiv) and DMF (2–3 mL), heated at 95–100 °C for 12–14 h.

the carbonyl group to form oxonium complex B. Then water molecule attacks at the carbon atom adjacent to the oxygen atom to form intermediate C. Then ring opening followed by the reaction with the atmospheric oxygen molecule to form D, which undergoes rearrangement in the presence of water to afford 1,4-dicarbonyl compound E with the elimination of formic acid. This dicarbonyl



Scheme 6. Proposed mechanism for the formation of naphthofuran ring.

compound forms naphthofuran ring with the elimination of water molecule is shown in Scheme 6.

In conclusion, we have developed a new methodology for the synthesis of highly substituted furan ring by the addition of water and unusual formation of naphthofuran ring from 3-(1-alkynyl)-2-alkene-1-al derivatives at the same reaction condition. This reaction is also helpful for synthesis of some furoquinone-based natural products.

2. Typical experimental procedure for the synthesis of furan ring

Compounds **2a** (1 equiv), CuCl (10 mol %), H_2O (10 equiv) and DMF (2–3 mL) were placed in a two-necked round-bottomed flask. Then the mixture was heated to 95–100 °C for 12–14 h. After cooling, the reaction mixture was diluted with water, extracted with ether (20 mL × 3) and dried over anhydrous Na_2SO_4. The solvent was evaporated and the crude product was purified by preparative thin layer chromatography (petroleum ether/ethyl acetate 20:1).

3. Spectral data of representative compounds

3.1. Compound 4i

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 2.72 (m, 2H), 2.91 (m, 2H), 3.85 (s, 3H), 6.87 (m, 2H), 7.39 (s, 1H), 7.43–7.56 (m, 3H), 7.94 (dd, 2H, J = 8.4 Hz, J = 1.6 Hz), 8.60 (d, 1H, J = 8.4 Hz).

^{13}C NMR ($CDCl_3$, 50 MHz) δ: 19.02, 30.61, 55.31, 111.83, 114.08, 121.00, 125.28, 128.10 (2C), 129.64 (2C), 130.34, 131.51, 131.99, 138.78, 139.46, 140.21, 145.92, 160.11, 184.35.

HRMS: calcd for $C_{20}H_{17}O_3$ [M^++H]: 305.1178; found 305.1128.

3.2. Compound 3i

White solid, mp 156–158 °C ^{1}H NMR ($CDCl_3$, 400 MHz); 3.95 (s, 3H), 7.28 (m, 2H), 7.35 (t, 1H, J = 7.6 Hz), 7.47 (m, 3H), 7.64 (q, 2H, J = 8.8 Hz), 7.93 (d, 2H, J = 8 Hz), 8.07 (d, 1H, J = 8.8 Hz).

^{13}C NMR ($CDCl_3$, 100 MHz) δ: 55.32, 100.21, 107,57, 112.53, 118.21, 122.46, 123.97, 124.58, 124.65 (2C), 124.82, 128.17, 128.77 (2C), 130.63, 131.46, 151.33, 155.33, 156.70.

HRMS: calcd for $C_{19}H_{15}O_2$ [M^++H]: 275.1072; found 275.1073.

Acknowledgements

We thank CSIR, New Delhi, for the fellowships and we also thank D.S.T. for providing funds for the project and creating 400 MHz NMR facility under the IRPHA programme.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.10.125.

References and notes

1. (a) Maier, M. In *Organic Synthesis Highlights II*; Waldmann, H., Ed.; VCH: Weinheim, Germany, 1995; p 231; (b) Donnelly, D. M. X.; Meegan, M. J.. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: New York, 1984; Vol. 4, p 657.
2. (a) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285; (b) Marshall, J. A.; Bartley, G. S. *J. Org. Chem.* **1994**, *59*, 7169; (c) Marshall, J. A.; Wang, X.-J. *J. Org. Chem.* **1991**, *56*, 960; (d) Fukuda, Y.; Shiragami, H.; Utimoto, K.; Nozaki, H. *J. Org. Chem.* **1991**, *56*, 5816; (e) Kel'in, A. V.; Gevorgyan, V. *J. Org. Chem.* **2002**, *67*, 95; (f) Hou, X. L.; Yang, Z.; Wong, H. N. C.. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Gilchrist, T. L., Eds.; Pergamon Press: Oxford, UK, 2002; Vol. 14, p 139; (g) Cacchi, S. J. *Organomet. Chem.* **1999**, *576*, 42.
3. (a) Yao, T.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 11164; (b) Oh, C. H.; Reddy, V. R.; Kim, A.; Rhim, C. Y. *Tetrahedron Lett.* **2006**, *47*, 5307; (c) Patil, N. T.; Wu, H.; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 4531; (d) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285; (e) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Org. Lett.* **2001**, *3*, 3769.
4. (a) Cheng, G.; Hu, Y. *Chem. Commun.* **2007**, 3285; (b) Cheng, G.; Hu, Y. *J. Org. Chem.* **2008**, *73*, 4732.
5. (a) Liang, Y.; Xie, Y.-X.; Li, J.-H. *J. Org. Chem.* **2006**, *71*, 379; (b) Li, P.; Wang, L.; Li, H. *Tetrahedron* **2005**, *61*, 8633; (c) Gholap, A. R.; Venkatesan, K.; Pasricha, R.; Daniel, T.; Lahoti, R. J.; Srinivasan, K. V. *J. Org. Chem.* **2005**, *70*, 4869; (d) Yi, C.; Hua, R. *J. Org. Chem.* **2006**, *71*, 2535; (e) Gelman, D.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2003**, *42*, 5993; (f) Elangovan, A.; Wang, Y.-H.; Ho, T.-I. *Org. Lett.* **2003**, *5*, 1841.