ChemPubSoc Europe

DOI: 10.1002/chem.201501826

CHEMISTRY
A European Journal
Communication

Synthetic Methods

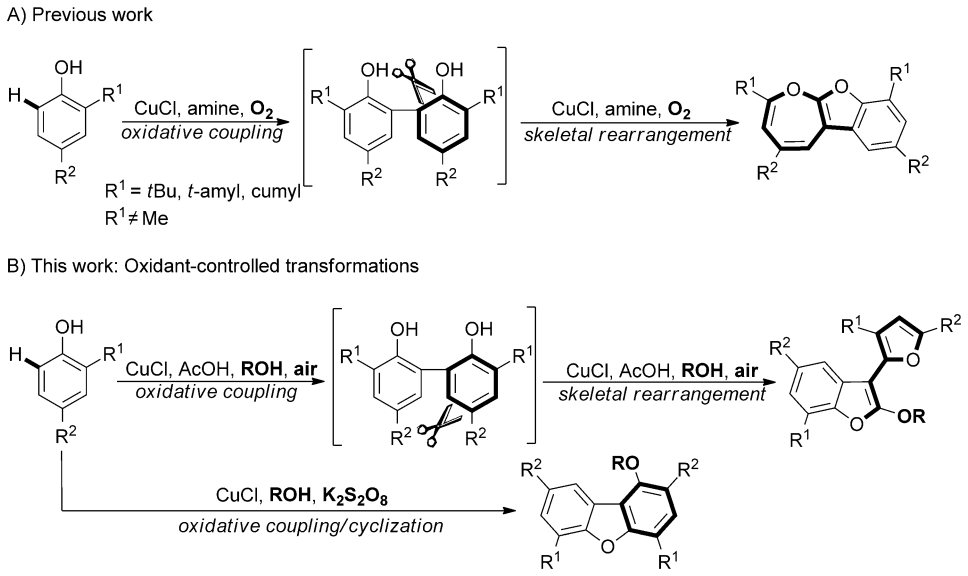
Oxidant-Controlled Catalytic Transformations of Phenols with Unexpected Cleavage of Aromatic Rings

Wei Li, Feijie Song, and Jingsong You*[a]

Abstract: Oxidative transformations of phenols have attracted significant attention of chemists due to their importance in biological process and organic synthesis. In contrast to the relatively well-developed oxygenation and coupling reactions of phenols, the highly efficient and selective oxidative ring cleavage of phenols is under-represented. This work describes a novel CuCl-catalyzed tandem homocoupling/skeletal rearrangement of phenols that realizes the cleavage of the phenol ring by using air or Ag_2CO_3 as the oxidant. Interestingly, simply changing the oxidant to $K_2S_2O_8$ results in the oxidative coupling/cyclization of phenols to give dibenzofurans. These results set an important precedent of oxidant-controlled catalytic transformations of phenols.

The oxidative transformations of phenols have attracted significant attention from chemists, due to their importance in biological process and organic synthesis.[1] These reactions include oxygenation,[2] cross- and homocoupling reactions,[3] and ring cleavage of phenol rings[4–8] depending on the substrates and the oxidants employed. In contrast to the relatively well-developed oxygenation and coupling reactions of phenols, the oxidative ring cleavage of phenols is under-represented. A pioneering study by Tsuji and Takayanagi accomplished the stoichiometric CuCl-promoted transformation of catechol to *cis*,*cis*-muconate in the presence of molecular oxygen.[5] The metallic copper-mediated ring contraction of phenol was realized by using high-pressure O_2 (3 atm) as the oxidant.[6] The copper-catalyzed ring expansion of phenols to benzoxepines was initially reported by Kushioka.[7] Unfortunately, these transformations often suffer from poor selectivity, limited substrate scope, and unsatisfactory yields. Thus, it is desirable to develop highly efficient and selective ring cleavage reactions of phenols under mild reaction conditions. To this end, Lumb and co-workers modified Kushioka's procedure and realized an elegant aerobic ring expansion of phenols by using CuCl as the catalyst alongside *N*,*N*′-di-*tert*-butylethylenediamine (DBED) as the ligand (Scheme 1 A).[8]

In an effort to realize the chemo- and regioselective aerobic oxidative coupling of phenols,[9] we observed an unprecedented tandem reaction under air atmosphere or with Ag_2CO_3 as oxidant, which involved the sequential homocoupling of phenols and skeletal rearrangement of in situ-formed biphenyldiols with the cleavage of a benzene ring (Scheme 1B).[10] Interestingly, an essentially different reaction occurred to afford dibenzofurans when using the inexpensive, stable, and easy-to-handle $K_2S_2O_8$ as the oxidant, which involved the tandem oxidative homocoupling/cyclization of phenols.

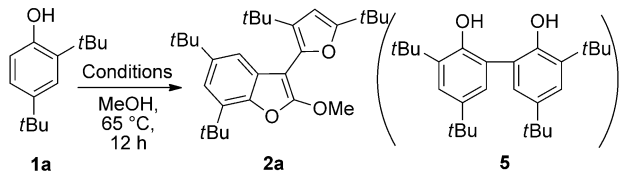


Scheme 1. Highly efficient and selective copper-catalyzed cleavage of phenol rings.

[a] *W. Li, Dr. F. Song, Prof. Dr. J. You*
Key Laboratory of Green Chemistry and Technology, Ministry of Education
College of Chemistry and State Key Laboratory of Biotherapy
West China Medical School, Sichuan University
29 Wangjiang Road, Chengdu 610064 (P. R. China)
E-mail: jsyou@scu.edu.cn

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201501826.

Table 1. Optimization of the Cu-catalyzed oxidative coupling/skeletal rearrangement of 2,4-di-*tert*-butylphenol **1a**.[a]



1a **2a** **5**

Entry	Catalyst (mol%)	Oxidant	Additive (equiv)	Yield [%][b]
1	CuCl (50)	air	none	33
2	none	air	none	0
3	CuCl (50)	dry air	none	32–60
4	CuCl (50)	dry air	K_2HPO_4 (1.0)	0
5	CuCl (50)	dry air	K_2CO_3 (1.0)	0 (49)
6	CuCl (50)	dry air	CF_3COOH (1.0)	0 (10)
7	CuCl (50)	dry air	AcOH (1.0)	40[c]
8	CuCl (50)	air	AcOH (1.0)	41
9	**CuCl (50)**	**air**	**AcOH (0.3)**	**59**
10	CuCl (50)	air	AcOH (0.3)	42[d]
11	CuCl (20)	air	AcOH (0.3)	45
12	CuCl (25)	air	AcOH (0.3)	47
13	CuCl (25)	O_2	AcOH (0.3)	40
14	CuBr (25)	air	AcOH (0.3)	0 (19)
15	CuI (25)	air	AcOH (0.3)	0
16	$CuCl_2$ (25)	air	AcOH (0.3)	0 (4)
17	$Cu(OAc)_2$ (25)	air	AcOH (0.3)	0 (9)
18	$Cu(NO_3)_2{\cdot}3H_2O$ (25)	air	AcOH (0.3)	0

[a] Reaction conditions: 2,4-Di-*tert*-butylphenol **1a** (1.0 mmol), catalyst, air or O_2 (bubbling), additive, and MeOH (10 mL) at 65 °C for 12 h. [b] Yield of isolated product. The yield of **5** is given in parenthesis. [c] An average of three runs. [d] 10.0 equivalents of H_2O were added.

Initially, we attempted to perform homocoupling of 2,4-di-*tert*-butylphenol **1a** in the presence of 50 mol% of CuCl in MeOH under air atmosphere. To our surprise, 3-furyl-2-methoxy benzofuran **2a** was obtained in 33% yield instead and the desired homocoupled product 3,3′,5,5′-tetra-*tert*-butyl-[1,1′-biphenyl]-2,2′-diol **5** was not observed (Table 1, entry 1). The structure of **2a** was confirmed by ^1H and ^{13}C NMR spectroscopy, high-resolution mass spectrometry (HRMS), and single crystal X-ray analysis (Figure 1).[11] A control experiment showed that no reaction happened in the absence of CuCl (Table 1, entry 2). When dry air was bubbled through the reaction mixture, **2a** was obtained in higher, albeit irreproducible yields (32–60%; Table 1, entry 3). Pleasingly, the addition of 1.0 equivalent of AcOH to the reaction mixture delivered **2a** in a reproducible yield of 40% (Table 1, entry 7). A similar result was obtained when undried air was directly bubbled into the solution (Table 1, entry 8). Further optimization showed that the yield of **2a** could be improved to 59% by employing 0.3 equivalents of AcOH as an additive (Table 1, entry 9). The competent enol or lactone derivative was not formed when 10.0 equivalents of H_2O was added to the reaction mixture (Table 1, entry 10). Decreasing the amount of CuCl to 25 mol% and changing the oxidant from air to molecular oxygen afforded **2a** in slightly lower yields of 47% and 40%, respectively (Table 1, entries 12 and 13). Using other copper(I) or copper(II) salts, such as CuBr, CuI, $CuCl_2$, $Cu(OAc)_2$, and $Cu(NO_3)_2{\cdot}3H_2O$, as the catalyst could not deliver **2a**, although the homocoupled product **5** was obtained in some cases (Table 1, entries 14–18). The final optimized reaction condition was as follows: 50 mol% of CuCl as the catalyst and 30 mol% of AcOH as the additive in MeOH solution with air bubbling through the reaction mixture.

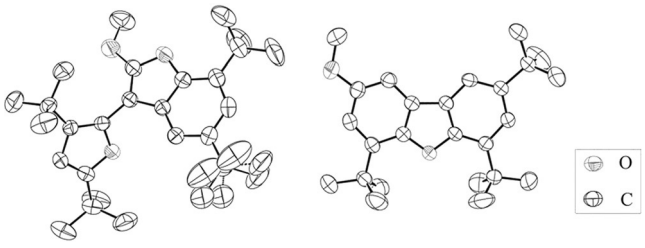
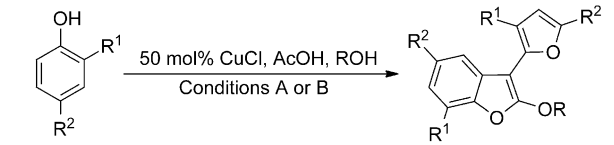


Figure 1. ORTEP representations of **2a** (left) and **4a** (right) with thermal ellipsoids drawn at 50% probability level. Hydrogen atoms were omitted for clarity.

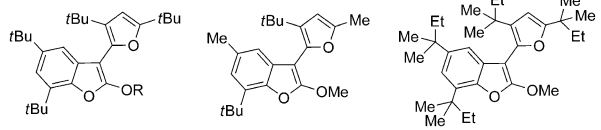
Benzofuran derivatives are frequently found in natural products,[12] bioactive molecules, pharmaceuticals,[13] and organic materials.[14] With the optimized reaction conditions in hand, we next investigated the substrate scope. As summarized in Table 2, phenols bearing alkyl substituents at the C2 and C4 positions reacted smoothly with methanol and ethanol to give the corresponding products **2** under the optimized reaction conditions (Table 2, **2a**–**d**). Other alcohols, such as isopropanol, benzyl alcohol, and allyl alcohol, only afforded the homocoupled product and the desired benzofurans were not formed. However, when the C4 position of phenols was substituted with an aryl group, the desired products were obtained, albeit in less than 20% yields. Consequently, other oxidants such as 1,4-benzoquinone (BQ), 4,5-dichloro-3,6-dioxocyclohexa-1,4-diene-1,2-dicarbonitrile (DDQ), 2-(*tert*-butylperoxy)-2-methylpropane (DTBP), 2-hydroperoxy-2-methylpropane (TBHP), Ag_2CO_3, and $K_2S_2O_8$ were screened to improve the product yields. Using 2.0 equivalents of Ag_2CO_3 as the oxidant was found to efficiently promote the reactions and the desired benzofuran products were obtained in 50–70% yields (Table 2, **2e**–**j**). Both electron-withdrawing and electron-donating groups on the phenyl ring could be tolerated (Table 2, **2f**–**i**). Notably, a bulky 2-alkyl group was crucial for the smooth occurrence of these reactions. Even the oxidative homocoupling reaction was not observed in the absence of such a bulky group.

Surprisingly, when $K_2S_2O_8$ was used as the oxidant, dibenzofurans instead of benzofurans were obtained. Considering that dibenzofuran derivatives are an important class of naturally occurring products and have wide applications in a variety of fields,[15,16] we then used **1b** as the model substrate to optimize the reaction conditions (see the Supporting Information, Table S1). The desired dibenzofuran **3a** was obtained in the highest yield of 65% by using 25 mol% CuCl as the catalyst and 2.0 equivalents of $K_2S_2O_8$ as the oxidant in MeOH at 80 °C for 24 h [Eq. (1)]. This catalytic reaction did not occur in the absence of CuCl, demonstrating the crucial role of CuCl for the smooth occurrence of the reaction (see the Supporting Information, Table S1, entry 3).

Table 2. CuCl-catalyzed oxidative coupling/skeletal rearrangement of phenols.[a]

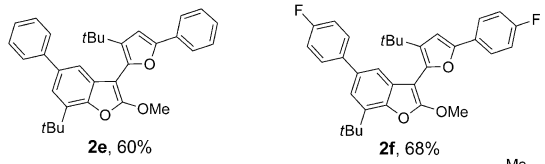


Conditions A



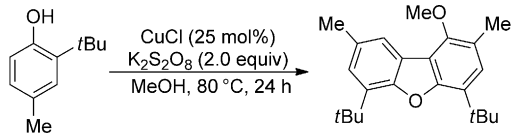
2a, R = Me, 59%
2b, R = Et, 41%
2c, 54%
2d, 63%

Conditions B



2e, 60%
2f, 68%
2g, 70%
2h, 50%
2i, 63%
2j, 54%

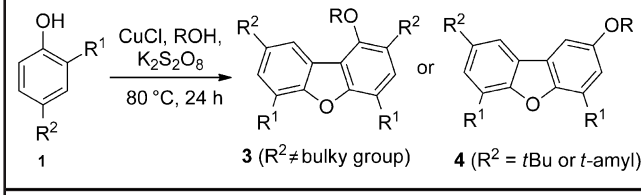
[a] Conditions A: phenol **1** (1.0 mmol), CuCl (50 mol%), air, AcOH (30 mol%), and ROH (10.0 mL) at 65 °C for 12 h; condition B: phenol **1** (0.5 mmol), CuCl (50 mol%), Ag_2CO_3 (2.0 equiv), and MeOH (1.5 mL) at 65 °C for 12 h; yields of isolated product are given.

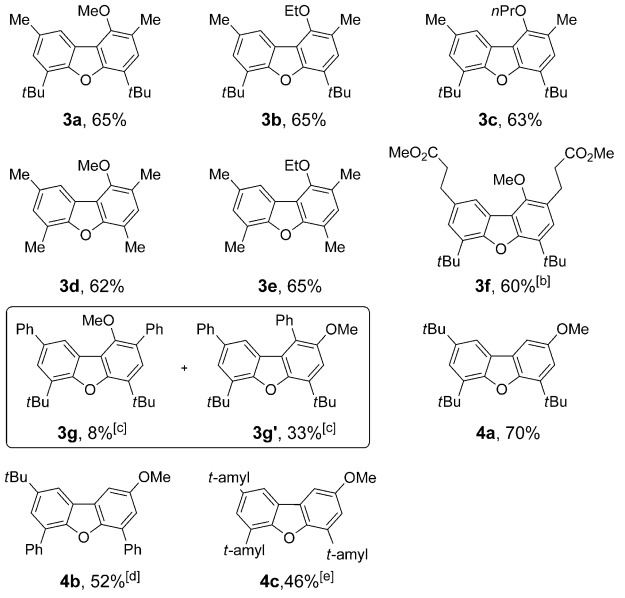


1b **3a**, 65% (1)

We then investigated the substrate scope of this dibenzofuran-forming reaction (Table 3). We found that various alkyl and aryl substituted phenols could react with alcohols to afford dibenzofurans in moderate to good yields, although the nature of the R^2 group had a significant effect on the subtle structure of the resultant dibenzofurans. When R^2 was a bulky substituent, such as *tert*-butyl or *tert*-amyl, it was easily removed to afford 8-alkoxydibenzofurans **4** (Table 3, **4a**–**c**; Figure 1).[17] When R^2 was a small alkyl group, 1-alkoxydibenzofurans **3** were obtained (Table 3, **3a**–**f**). When R^2 was a phenyl group, both 1-alkoxydibenzofuran **3g** and 2-alkoxydibenzofuran **3g′** were obtained in a 1:4 ratio. Besides methanol, other alcohols such as ethanol and *n*-propanol also participated in the reaction (Table 3, **3b**, **3c**, and **3e**). Notably, unlike the synthesis of benzofurans **2**, which requires the installation of a large alkyl group at the *ortho* position, phenols with a small methyl or a phenyl group at the *ortho* position were also suitable for the transformation (Table 3, **3d**, **3e**, and **4b**).

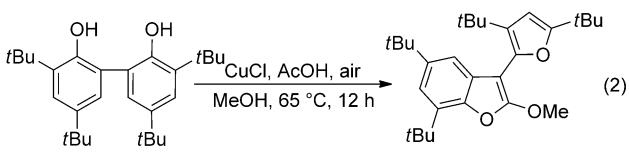
Table 3. CuCl-catalyzed oxidative coupling/cyclization of phenols.[a]



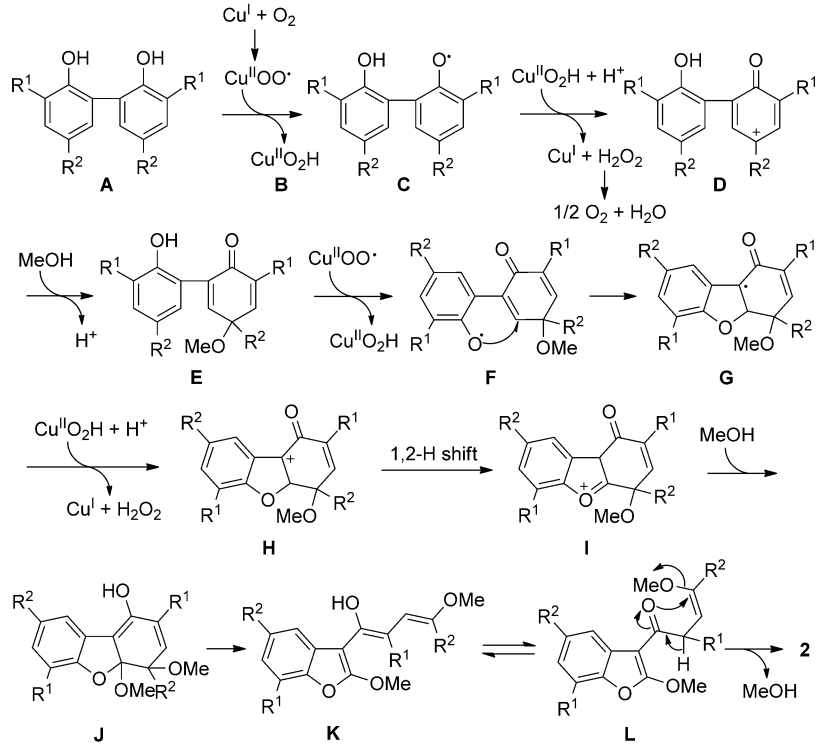


[a] Reactions conditions, unless otherwise stated: Phenol **1** (0.5 mmol), CuCl (25 mol%), $K_2S_2O_8$ (2.0 equiv), and ROH (1.5 mL) at 80 °C for 24 h; yields of isolated product are given. [b] CuCl (50 mol%) was used. [c] The reaction time was 48 h. [d] CuBr (50 mol%) was used. [e] 3.0 equivalents of $K_2S_2O_8$ were used.

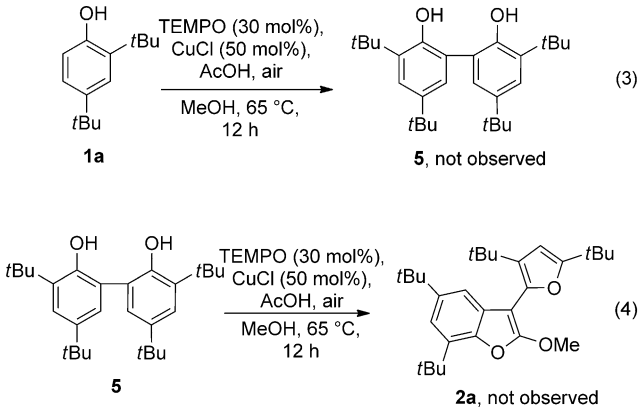
We next performed a series of control experiments to gain some insights into the mechanism of the benzofuran-forming reaction. Exposure of the independently synthesized biphenyldiol **5** to the CuCl/air reaction system delivered benzofuran **2a** in 54% yield [Eq. (2)], which clearly demonstrated the involvement of **5** as an intermediate. Upon addition of 30 mol% of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) to the reaction mixture, the reactions of **1a** and **5** were completely shut down [Eqs. (3) and (4)], which implied that both the oxidative homocoupling of phenols and the skeletal rearrangement of the in situ-formed biphenyldiols proceed through a free-radical pathway.



5 **2a**, 54% yield (2)

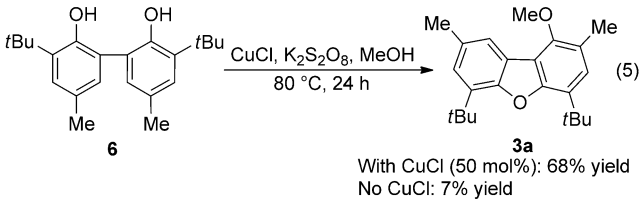


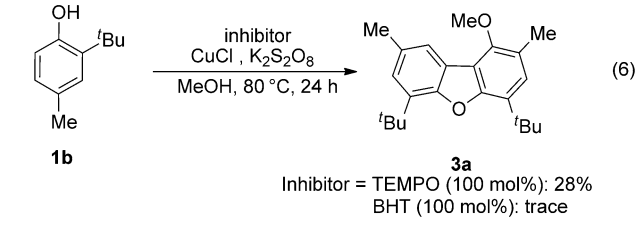
Scheme 2. Proposed mechanism for the conversion of biphenyldiols to benzofurans.

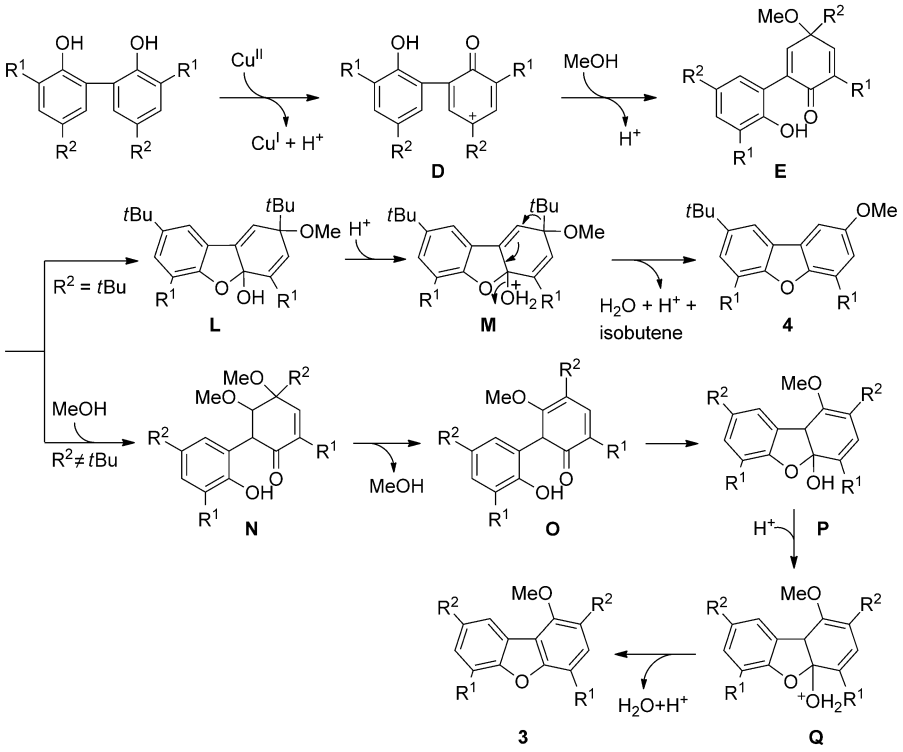


The copper-catalyzed oxidative homocoupling of phenols is well documented in literature.[18] Herein, a tentative mechanism of the ring cleavage of biphenyldiols is proposed on the basis of the above observations in combination with previous investigations (Scheme 2).[19] Initially, copper(I) is oxidized by dioxygen to afford the copper(II) peroxide radical, which then abstracts the hydrogen of biphenyldiol **A** to form the copper(II) hydroperoxo species **B** and the radical intermediate **C**. The electron transfer oxidation of **C** by **B** leads to the formation of cation **D**, which is attacked by MeOH to afford the intermediate **E**. Next, the sequential hydrogen abstraction from **E** by the copper(II) peroxide radical, intramolecular radical cyclization, electron transfer oxidation, and 1,2-hydrogen shift lead to the formation of cation **I**. **I** is then attacked by an additional methanol molecule to deliver intermediate **J**. The sequential electrocyclic ring opening of **J** and tautomerism of the resulting **K** afford the ketone intermediate **L**. Finally, an intramolecular cyclization of **L** gives **2** with the elimination of methanol.

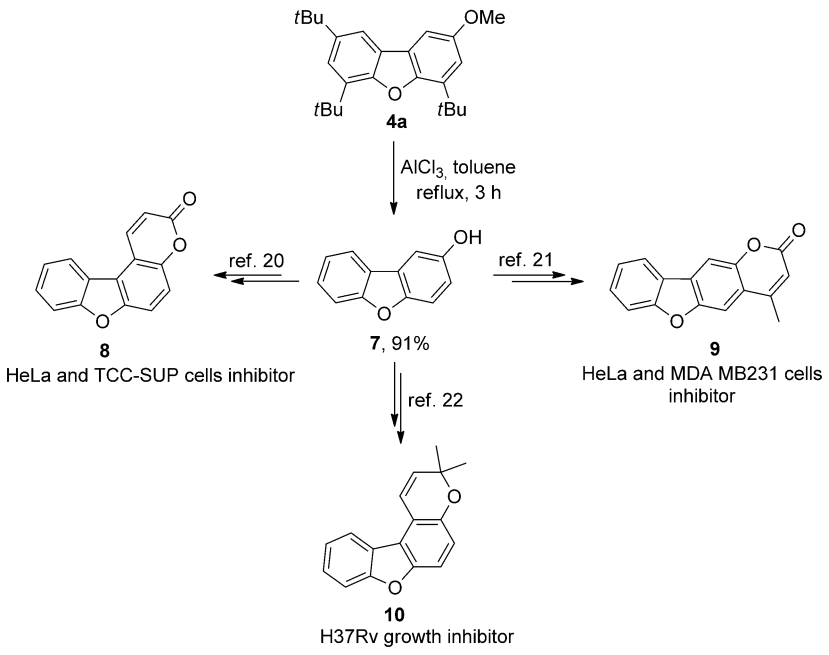
Subsequently, the mechanism of the $K_2S_2O_8$-promoted formation of dibenzofurans was investigated. The reaction of biphenyldiol **6** with MeOH afforded the desired dibenzofuran **3a** in 68% yield in the presence of 50 mol% of CuCl and $K_2S_2O_8$ [Eq. (5)]. However, only 7% yield of **3a** was obtained in the absence of CuCl. These results clearly showed that the dibenzofuran-forming reaction involved a biphenyldiol as the key intermediate and CuCl played a vital role in the cyclization step. In addition, the yield of **3a** dropped dramatically when 1.0 equivalent of TEMPO or 2,6-di-*tert*-butyl-4-methylphenol (BHT) was added to the reaction mixture of **1b** [Eq. (6)]. However, these radical scavengers had negligible effect on the cyclization of biphenyldiol **6** [Eq. (7)]. Thus, we concluded that the $K_2S_2O_8$-promoted homocoupling of phenols may go through a radical process,[9] and a radical pathway can be excluded in the subsequent cyclization reaction. Based on the above results, a plausible mechanism for the conversion of biphenyldiols to dibenzofurans **3** and **4** is proposed in Scheme 3. The product is dependent on the structure of substituent R^2: 1) When R^2 is a small group, the sequential conjugate addition of MeOH to intermediate **E** and elimination of MeOH afford **O**. Subsequent intramolecular cyclization, protonation of the hydroxy group, and elimination



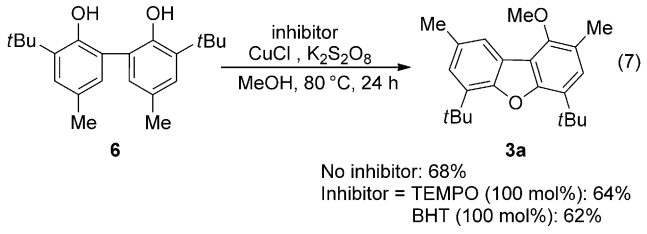




Scheme 3. Proposed mechanism for the formation of dibenzofurans **3** and **4**.



Scheme 4. Synthetic applications of the current methodology.



of water afford dibenzofuran **3**; 2) when R^2 is a bulky *tert*-butyl or *tert*-amyl group, **E** would first undergo intramolecular cyclization to afford **L**. Protonation of **L** and subsequent C–C bond cleavage of the resulting **M** with removal of water afford **4** and a tertiary carbenium ion, which then eliminates a hydrogen atom to deliver the corresponding alkene.

Finally, the synthetic applications of these protocols were demonstrated. As shown in Scheme 4, the *tert*-butyl and methyl groups of **4a** were easily removed by $AlCl_3$ in refluxing toluene, affording dibenzofuran-2-ol **7** in 91% yield. Compound **7** is an important intermediate for the synthesis of many bioactive substances, such as HeLa (cervix adenocarcinoma) and TCC-SUP (bladder transitional cell carcinoma) cells inhibitor **8**,[20] HeLa and MDA MB231 (breast adenocarcinoma) cells inhibitor **9**,[21] and H37Rv (mycobacterium tuberculosis) growth inhibitor **10**.[22]

In summary, a novel copper-catalyzed tandem oxidative homocoupling/skeletal rearrangement of phenols that involves the cleavage of a benzene ring under mild reaction conditions has been realized by using air or Ag_2CO_3 as the oxidant. Interestingly, simply changing the oxidant to cheap $K_2S_2O_8$ led to the tandem oxidative coupling/cyclization of phenols. These two transformations can offer structurally important benzofuran and dibenzofuran derivatives, respectively. Further studies to clarify the reaction mechanisms and to find more synthetic applications are currently underway in our laboratory.

Acknowledgements

This work was supported by grants from the National Basic Research Program of China (973 Program, 2011CB808600) and

the National Natural Science Foundation of China (Nos. 21432005, 21272160, and 21321061).

Keywords: benzofuran · C–C cleavage · copper · homogeneous catalysis · phenol

[1] a) S. Yamamura in *The Chemistry of Phenols*, (Ed. Z. Rappoport), Wiley, Hoboken, NJ, **2003**; pp. 1153 – 1346; b) T. D. H. Bugg, C. J. Winfield, *Nat. Prod. Rep.* **1998**, *15*, 513 – 530; c) L. B. Davin, M. Jourdes, A. M. Patten, K.-W. Kim, D. G. Vassão, N. G. Lewis, *Nat. Prod. Rep.* **2008**, *25*, 1015 – 1090.

[2] For selected examples, see: a) D. Magdziak, A. A. Rodriguez, R. W. Van De Water, T. R. R. Pettus, *Org. Lett.* **2002**, *4*, 285 – 288; b) K.-Q. Ling, Y. Lee, D. Macikenas, J. D. Protasiewicz, L. M. Sayre, *J. Org. Chem.* **2003**, *68*, 1358 – 1366; c) K. V. N. Esguerra, Y. Fall, J.-P. Lumb, *Angew. Chem. Int. Ed.* **2014**, *53*, 5877 – 5881; *Angew. Chem.* **2014**, *126*, 5987 – 5991.

[3] For a review on the copper-catalyzed oxidative coupling of phenols, see: a) S. E. Allen, R. R. Walvoord, R. Padilla-Salinas, M. C. Kozlowski, *Chem. Rev.* **2013**, *113*, 6234 – 6458. For selected examples, see: b) C. C. Price, K. Nakaoka, *Macromolecules* **1971**, *4*, 363 – 369; c) P. J. Baesjou, W. L. Driessen, G. Challa, J. Reedijk, *J. Am. Chem. Soc.* **1997**, *119*, 12590 – 12594.

[4] R. R. Grinstead, *Biochemistry* **1964**, *3*, 1308 – 1314.

[5] a) J. Tsuji, H. Takayanagi, *J. Am. Chem. Soc.* **1974**, *96*, 7349 – 7350; b) M. M. Rogic, T. R. Demmin, W. B. Hammond, *J. Am. Chem. Soc.* **1976**, *98*, 7441 – 7443.

[6] M. Lanfranchi, L. Prati, M. Rossi, A. Tiripicchio, *J. Mol. Catal. A* **1995**, *101*, 75 – 80.

[7] a) K. Kushioka, *J. Org. Chem.* **1983**, *48*, 4948 – 4950; b) K. Kushioka, *J. Org. Chem.* **1984**, *49*, 4456 – 4459.

[8] K. V. N. Esguerra, Y. Fall, L. Petitjean, J.-P. Lumb, *J. Am. Chem. Soc.* **2014**, *136*, 7662 – 7668.

[9] Y. E. Lee, T. Cao, C. Torruellas, M. C. Kozlowski, *J. Am. Chem. Soc.* **2014**, *136*, 6782 – 6785.

[10] a) D. Ellis, D. McKay, S. A. Macgregor, G. M. Rosair, A. J. Welch, *Angew. Chem. Int. Ed.* **2010**, *49*, 4943 – 4945; *Angew. Chem.* **2010**, *122*, 5063 – 5065; b) B. Szyszko, L. Latos-Grażyński, L. Szterenberg, *Angew. Chem. Int. Ed.* **2011**, *50*, 6587 – 6591; *Angew. Chem.* **2011**, *123*, 6717 – 6721; c) T. Matsuda, T. Goya, L. Liu, Y. Sakurai, S. Watanuki, N. Ishida, M. Murakami, *Angew. Chem. Int. Ed.* **2013**, *52*, 6492 – 6495; *Angew. Chem.* **2013**, *125*, 6620 – 6623; d) S. Hu, T. Shima, Z. Hou, *Nature* **2014**, *512*, 413 – 415.

[11] CCDC 1030958 and 1030966 (**2a** and **4a**, respectively) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[12] a) P. Cagniant, D. Cagniant, *Adv. Heterocycl. Chem.* **1975**, *18*, 337 – 482; b) D. E. Fuerst, B. M. Stoltz, J. L. Wood, *Org. Lett.* **2000**, *2*, 3521 – 3523.

[13] a) X.-L. Hou, Z. Yang, H. N. C. Wong in *Progress in Heterocyclic Chemistry*, (Eds.: G. W. Gribble, T. L. Gilchrist), Elsevier, Amsterdam, **2002**, vol. 14, pp. 139 – 179; b) I. A. Khan, M. V. Kulkarni, C.-M. Sun, *Eur. J. Med. Chem.* **2005**, *40*, 1168; c) S. Ansorge, U. Bank, K. Nordhoff, M. Täger, F. Striggow, WO 2005/037779A2, April 28, **2005**.

[14] B. Walker, A. B. Tamayo, X.-D. Dang, P. Zalar, J. H. Seo, A. Garcia, M. Tantiwiwat, T.-Q. Nguyen, *Adv. Funct. Mater.* **2009**, *19*, 3063 – 3069.

[15] a) J. R. Carney, J. M. Krenisky, R. T. Williamson, J. Luo, *J. Nat. Prod.* **2002**, *65*, 203 – 205; b) A. Momotake, N. Lindegger, E. Niggli, R. J. Barsotti, G. C. R. Ellis-Davies, *Nat. Methods* **2006**, *3*, 35 – 40; c) K. Kaniwa, T. Ohtsuki, Y. Yamamoto, M. Ishibashi, *Tetrahedron Lett.* **2006**, *47*, 1505 – 1508; d) Y. Q. Ye, H. Koshino, J. Onose, K. Yoshikawa, N. Abe, S. Takahashi, *Org. Lett.* **2009**, *11*, 5074 – 5077; e) C. W. Lee, K. S. Yook, J. Y. Lee, *Org. Electron.* **2013**, *14*, 1009 – 1014.

[16] For recent examples on the transition metal-catalyzed synthesis of dibenzofurans, see: a) C. Wang, I. Piel, F. Glorius, *J. Am. Chem. Soc.* **2009**, *131*, 4194 – 4195; b) B. Xiao, T.-J. Gong, Z.-J. Liu, J.-H. Liu, D.-F. Luo, J. Xu, L. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 9250 – 9253; c) J. Zhao, Y. Wang, Y. He, L. Liu, Q. Zhu, *Org. Lett.* **2012**, *14*, 1078 – 1081.

[17] H.-D. Becker, *J. Org. Chem.* **1969**, *34*, 1198 – 1203.

[18] a) P. P. Paul, Z. Tyeklár, R. R. Jacobson, K. D. Karlin, *J. Am. Chem. Soc.* **1991**, *113*, 5322 – 5332; b) T. Osako, K. Ohkubo, M. Taki, Y. Tachi, S. Fukuzumi, S. Itoh, *J. Am. Chem. Soc.* **2003**, *125*, 11027 – 11033; c) S. Itoh, S. Fukuzumi, *Acc. Chem. Res.* **2007**, *40*, 592 – 600.

[19] a) A. Crespo, M. A. Martí, A. E. Roitberg, L. M. Amzel, D. A. Estrin, *J. Am. Chem. Soc.* **2006**, *128*, 12817 – 12828; b) J. M. Hoover, B. L. Ryland, S. S. Stahl, *J. Am. Chem. Soc.* **2013**, *135*, 2357 – 2367; c) C. Huo, C. Wang, M. Wu, X. Jia, H. Xie, Y. Yuan, *Adv. Synth. Catal.* **2014**, *356*, 411 – 415.

[20] C. S. Francisco, L. R. Rodrigues, N. M. F. S. A. Cerqueira, A. M. F. Oliveira-Campos, L. M. Rodrigues, *Eur. J. Med. Chem.* **2012**, *47*, 370 – 376.

[21] C. S. Francisco, L. R. Rodrigues, N. M. F. S. A. Cerqueira, A. M. F. Oliveira-Campos, L. M. Rodrigues, A. P. Esteves, *Bioorg. Med. Chem.* **2013**, *21*, 5047 – 5053.

[22] a) S. Prado, H. Ledeit, S. Michel, M. Koch, J. C. Darbord, S. T. Cole, F. Tillequin, P. Brodin, *Bioorg. Med. Chem.* **2006**, *14*, 5423 – 5428; b) P. M. M. Brodin, S. Prado, S. T. Cole, M. Koch, F. Tillequin, S. Michel, EP 2007/1770089A1, April 4, **2007**.

Received: May 10, 2015
Published online on August 18, 2015

