

# Metal-Free Radical 5-*exo*-dig Cyclizations of Phenol-Linked 1,6-Enynes for the Synthesis of Carbonylated Benzofurans\*\*

Ming Hu, Ren-Jie Song, and Jin-Heng Li\*

**Abstract:** A new metal-free radical 5-*exo*-dig cyclization of phenol-linked 1,6-enynes with  $O_2$ , 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), and *t*BuONO is described. With this general method, carbonylated benzofurans can be accessed through incorporation of two oxygen atoms into the product from  $O_2$  and TEMPO through dioxygen activation and oxidative cleavage of the N–O bond, respectively.

**B**enzofurans, including carbonylated benzofurans (Figure 1), are pervasive structural motifs found in natural products and pharmaceutical compounds with powerful biological properties.<sup>[1–2]</sup> For example, brazanquinones show selective inhibitory activity against a series of cancer cell

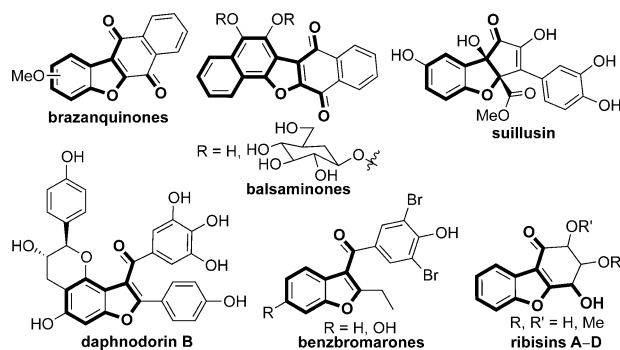
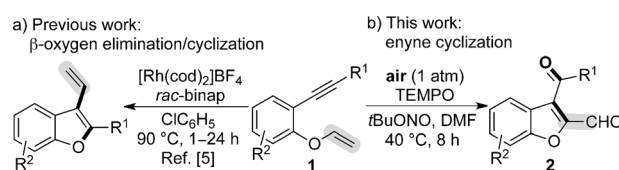


Figure 1. Examples of important carbonylated benzofurans.

lines.<sup>[2a–c]</sup> Balsaminones, which were isolated from the pericarp of the fruit *Impatiens balsamina* L., have significant antipruritic activity.<sup>[2d–f]</sup> Considerable efforts have thus been directed towards the discovery of efficient methods for their synthesis.<sup>[3–6]</sup> Despite remarkable advances in benzofuran synthesis, most of the traditional methods suffer from harsh

conditions, limited functional group tolerability, and/or the cost of the catalytic system.<sup>[3–6]</sup> Furthermore, the assembly of carbonylated benzofuran scaffolds remains a great challenge.<sup>[3,4]</sup> Therefore, the development of mild and efficient routes and especially metal-free strategies towards carbonylated benzofurans is desirable.<sup>[6]</sup>

The cyclization of 1,*n*-enynes has emerged as a powerful transformation that allows the rapid assembly of various complex ring systems in an atom- and step-economic manner.<sup>[7]</sup> Within the last years, many applications of the 1,*n*-enyn cyclization for the construction of various heterocycles, such as furans, pyrans, pyrroles, indoles, pyridines, quinolines, and other fused polyheterocycles, have been reported.<sup>[7,8]</sup> However, approaches using the real 1,*n*-enyn cyclization strategy to access benzofurans are lacking.<sup>[5]</sup> This is due to the fact that the intramolecular cyclization of phenol-linked 1,6-enynes in the presence of a rhodium catalyst leads to  $\beta$ -oxygen elimination/cyclization through cleavage and formation of the C(sp<sup>2</sup>)–O bonds rather than direct enyne cyclization (Scheme 1 a).<sup>[5]</sup> We reasoned that direct cycliza-



**Scheme 1.** Cyclization of phenol-linked 1,6-enynes into benzofurans. binap = 2,2'-bis(diphenylphosphanyl)-1,1'-binaphthyl, cod = cycloocta-1,5-diene.

tion reactions of phenol-linked 1,6-enynes might be realized under metal-free conditions. In the field of 1,*n*-enyn cyclization, radical strategies have played great roles and are now also shown to be useful for 1,*n*-enyn cyclizations.<sup>[7,8]</sup> However, the majority of radical cyclization reactions suffer from a requirement for precious and/or toxic metal complexes (often tin hydride reagents) and the difficult purification of the desired products from a large amount of unwanted side products and waste; therefore, they have received less attention over the past decade.<sup>[7,8]</sup> Herein, we report a novel metal-free radical 5-*exo*-dig cyclization of phenol-linked 1,6-enynes with air, 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), and *t*BuONO<sup>[9]</sup> for the formation of carbonylated benzofuran scaffolds (Scheme 1 b). In this transformation, the addition of TEMPO across the C=C bond, oxidative elimination through cleavage of the N–O bond with *t*BuONO, cyclization with an alkyne, and radical dioxygen activation are achieved.<sup>[10]</sup> It should be noted that the two oxygen atoms that

[\*] M. Hu, Dr. R.-J. Song, Prof. Dr. J.-H. Li  
State Key Laboratory of Chemo/Biosensing and Chemometrics  
College of Chemistry and Chemical Engineering, Hunan University  
Changsha 410082 (China)  
E-mail: jhli@hnu.edu.cn  
Prof. Dr. J.-H. Li  
State Key Laboratory of Applied Organic Chemistry  
Lanzhou University  
Lanzhou 730000 (China)

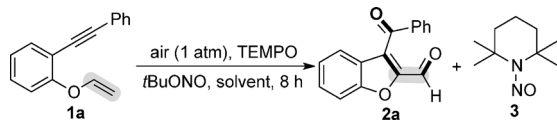
[\*\*] We thank the NSFC (21172060), the Specialized Research Fund for the Doctoral Program of Higher Education (20120161110041), and the Hunan Provincial Natural Science Foundation of China (13JJ2018) for financial support.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201408978>.

constitute the newly formed carbonyl groups of the benzofuran system originate from O<sub>2</sub> and TEMPO, respectively.

Our initial investigations began with the reaction of 1-(phenylethynyl)-2-(vinyl)oxybenzene (**1a**) with air, TEMPO, and *t*BuONO for reaction optimization (Table 1). Treatment

**Table 1:** Optimization of the reaction conditions.<sup>[a]</sup>



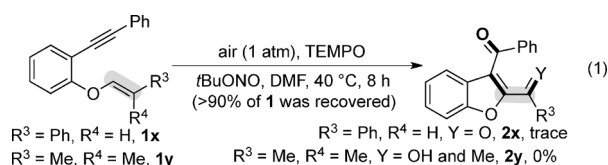
| Entry             | <i>t</i> BuONO [equiv] | TEMPO [equiv] | Solvent | T [°C] | Yield <sup>[b]</sup> [%] |
|-------------------|------------------------|---------------|---------|--------|--------------------------|
| 1                 | 3                      | 3             | DMF     | RT     | 65                       |
| 2                 | 0                      | 3             | DMF     | RT     | 0                        |
| 3 <sup>[c]</sup>  | 3                      | 0             | DMF     | RT     | 0                        |
| 4                 | 3                      | 3             | MeCN    | RT     | 48                       |
| 5                 | 3                      | 3             | EtOAc   | RT     | 38                       |
| 6                 | 3                      | 3             | toluene | RT     | 18                       |
| 7 <sup>[d]</sup>  | 3                      | 3             | DMF     | 40     | 73                       |
| 8                 | 3                      | 3             | DMF     | 60     | 71                       |
| 9 <sup>[e]</sup>  | 3                      | 3             | DMF     | 40     | 73                       |
| 10 <sup>[f]</sup> | 3                      | 3             | DMF     | 40     | trace                    |
| 11 <sup>[g]</sup> | 3                      | 3             | DMF     | 40     | 71                       |

[a] Reaction conditions: **1a** (0.3 mmol), *t*BuONO, TEMPO, air (1 atm), solvent (2 mL), 8 h. [b] Yield of isolated product. [c] Another product, (2-(nitromethyl)benzofuran-3-yl)(phenyl)methanone (**4a**), was isolated in 23 % yield together with > 50 % yield of **1a**. [d] Product **3** was isolated in 70 % yield based on the amount of TEMPO used. [e] Under O<sub>2</sub> atmosphere (1 atm). [f] Under argon atmosphere (1 atm) and in degassed solvent. [g] **1a** (1 g, 4.5 mmol), 24 h.

of 1,6-enyne **1a** with air, TEMPO, and *t*BuONO in DMF at room temperature for eight hours afforded the desired 3-benzoylbenzofuran-2-carbaldehyde (**2a**) in 65 % yield (entry 1). However, in the absence of either TEMPO or *t*BuONO, the reaction did not result in the formation of detectable amounts of **2a** (entries 2 and 3). Without TEMPO, the nitration/cyclization product (2-(nitromethyl)benzofuran-3-yl)(phenyl)methanone (**4a**) was isolated in 23 % yield (entry 3). Three other solvents, namely MeCN, EtOAc, and toluene, effected the reaction but were inferior to DMF (entries 4–6). Screening the effect of the reaction temperature revealed that higher temperatures were favorable, and 40 °C was found to be the preferred temperature (entries 1, 7, and 8). Notably, the reaction at 40 °C gave **2a** in 73 % yield, while TEMPO was converted into 2,2,6,6-tetramethyl-1-nitrosopiperidine (**3**) in 70 % yield (entry 7). When varying the amounts of TEMPO and *t*BuONO, we found that the reaction with three equivalents of TEMPO and *t*BuONO gave the best results (entry 7; see also the Supporting information, Table S1).<sup>[11]</sup> The yield under O<sub>2</sub> atmosphere was identical to that under air (entry 9), but the reaction was completely suppressed by using argon and degassed solvent (entry 10). The reaction with one gram of substrate **1a** gave the desired product in good yield (entry 11).

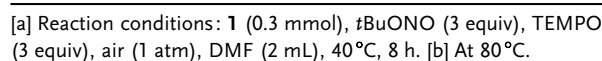
With the optimized reaction conditions in hand, we next investigated the generality of this metal-free cyclization

reaction with respect to a range of 1-ethynyl-2-(vinyl)oxybenzenes **1** (Table 2). Gratifyingly, both electron-donating (**2b–g** and **2o**) and electron-withdrawing (**2h–n**) aromatic substituents were tolerated at the terminal alkyne. Moreover, even with bulky *ortho*-substituted aryl groups, the carbonylated benzofurans were furnished in good yields (**2c**, **2f**, **2g**, and **2k**), although these substrates were less reactive than their *para*- or *meta*-substituted counterparts. For example, whereas *para*-methyl-substituted 1,6-enyne **1b** afforded **2b** in 76 % yield, *ortho*-methyl-substituted 1,6-enyne **1c** was converted into **2c** in 71 % yield. For methoxy-substituted 1,6-enynes **1d–f**, the reactivity decreased from *para* to *meta* to *ortho* substitution (**2d–f**). Notably, substrates with strongly electron-withdrawing cyano and acetyl groups also delivered the carbonylated benzofurans **2m** and **2n** in good yields. Halide substituents (I, Br, Cl, and F) were well tolerated under these oxidative conditions (**2h–l**), and may serve as handles for further synthetic manipulations. 1,6-Enyne **1o**, which bears two methyl groups, and 1,6-enyne **1p**, which features a naphthalen-1-yl group, afforded benzofurans **2o** and **2p** in 75 % and 59 % yield, respectively. We were pleased to find that heteroaryl-substituted alkynes **1q–s** were also suitable substrates and allowed the formation of **2q–s** in moderate to high yields. Furthermore, the optimized reaction conditions were applicable to 1,6-enyne **1t**, which bears an alkyl group at the terminal alkyne (**2t**). Subsequently, representative 1,6-enynes were selected to illustrate the tolerance for substituents on the aryl ring of the 1-(vinyl)oxybenzene moiety (**2u–w**). The substrate with an electron-donating methyl group afforded benzofuran **2u** in 57 % yield, whereas with an electron-withdrawing CN substituent, benzofuran **2v** was obtained in 80 % yield at 80 °C. We were pleased to find that **2w**, with a polycyclic ring system, was furnished in 75 % yield.<sup>[2d,e]</sup> However, internal alkenes **1x** and **1y** did not react under the current cyclization conditions [Eq. (1)].

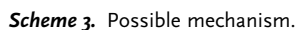


To elucidate the mechanism, some control experiments, including <sup>18</sup>O-labeling experiments, were conducted.<sup>[11]</sup> As expected, an <sup>18</sup>O atom was introduced into the ketonic carbonyl group under <sup>18</sup>O<sub>2</sub> atmosphere (1 atm) as determined by GC-MS and <sup>13</sup>C NMR analysis (Scheme 2a). However, according to GC-MS and <sup>13</sup>C NMR analysis, <sup>18</sup>O atoms were not incorporated into the carbonyl groups in the presence of H<sub>2</sub><sup>18</sup>O (5 equiv) and anhydrous DMF (Scheme 2a). Notably, the results in Table 1 show that during the reaction, TEMPO is converted into 2,2,6,6-tetramethyl-1-nitrosopiperidine (**3**). These results imply that the oxygen atom of the aldehydic carbonyl group originates from TEMPO. Substrate **5** was subjected to the reaction with air, TEMPO, and *t*BuONO, but the desired product **2a** was not observed (Scheme 2b).

**Table 2:** Substrate scope.<sup>[a]</sup>



Consequently, the mechanism outlined in Scheme 3 was proposed for this enyne radical cyclization reaction. Generally, *t*BuONO readily decomposes into HNO<sub>2</sub> and *t*BuOH in the presence of H<sub>2</sub>O, and HNO<sub>2</sub> is quickly converted into



In summary, we have developed the first metal-free 5-*exo*-dig cyclization of phenol-linked 1,6-enynes with O<sub>2</sub>, TEMPO, and *t*BuONO through a radical process for the synthesis of carbonylated benzofurans. Importantly, this transformation incorporates two oxygen atoms from O<sub>2</sub> and TEMPO, respectively into the benzofuran system. Owing to its metal-free nature, this reaction satisfies the particular purity requirements of biological and medicinal chemistry. This simple radical strategy will renew our interest into applications of 1,*n*-enyn radical cyclizations, and related studies are currently underway in our laboratory.

Published online: November 19, 2014

**Keywords:** benzofurans · cyclization · dioxygen activation · enynes · radical reactions

- [1] For selected reviews, see: a) "Furans and Their Benzo Derivatives": D. M. X. Donnelly, M. J. Meegan in *Comprehensive Heterocyclic Chemistry*, Vol. 4 (Ed.: A. R. Katritzky), Pergamon, New York, **1984**, pp. 657–712; b) P. Cagniant, D. Cagniant, *Adv. Heterocycl. Chem.* **1975**, 18, 337; c) K. M. Zareba, *Drugs Today* **2006**, 42, 75.
- [2] For studies on the brazanquinones, see: a) C. C. Cheng, Q. Dong, D.-F. Liu, Y.-L. Luo, L. F. Liu, A.-Y. Chen, C. Yu, N. Savaraj, T.-C. Chou, *J. Med. Chem.* **1993**, 36, 4108; b) P. W. Crawford, E. Carlos, J. C. Ellegood, C. C. Cheng, Q. Dong, D. F. Liu, Y. L. Luo, *Electrochim. Acta* **1996**, 41, 2399; c) H.-X. Chang, T.-C. Chou, N. Savaraj, L. F. Liu, C. Yu, C. C. Cheng, *J. Med. Chem.* **1999**, 42, 405; for studies on the balsaminones, see: d) K. Ishiguro, Y. Ohira, H. Oku, *J. Nat. Prod.* **1998**, 61, 1126; e) I. Y. Park, B.-K. Kim, Y. B. Kim, *Arch. Pharmacol. Res.* **1992**, 15, 52; for studies on suillusin, see: f) B.-S. Yun, H.-C. Kang, H. Koshino, S.-H. Yu, I.-D. Yoo, *J. Nat. Prod.* **2001**, 64, 1230; for studies on daphnodorin B, see: g) K. Baba, K. Takeuchi, F.

- Hamasaki, M. Kozawa, *Chem. Pharm. Bull.* **1985**, *33*, 416; h) K. Baba, K. Takeuchi, F. Hamasaki, M. Kozawa, *Chem. Pharm. Bull.* **1986**, *34*, 595; i) K. Baba, K. Takeuchi, M. Dio, M. Inoue, M. Kozawa, *Chem. Pharm. Bull.* **1986**, *34*, 1540; j) S. Takai, M. Sakaguchi, D. Jin, K. Baba, M. Miyazaki, *Life Sci.* **1999**, *64*, 1889; k) W.-F. Zheng, X.-W. Gao, C.-F. Chen, R.-X. Tian, *Int. Immunopharmacol.* **2007**, *7*, 117; for a study on the benzobromarones, see: l) G. Kremmliotis, A. F. Leske, T. C. Lavranos, D. Beaumont, J. Gasic, A. Hall, M. O'Callaghan, C. A. Matthews, B. L. Flynn, *Mol. Cancer Ther.* **2010**, *9*, 1562; for a study on the ribisins, see: m) Y. Liu, M. Kubo, Y. Fukuyama, *J. Nat. Prod.* **2012**, *75*, 2152.
- [3] For selected reviews on the synthesis of benzofurans, see: a) "Furans and Benzofurans": X.-L. Hou, Z. Yang, H. N. C. Wong in *Progress in Heterocyclic Chemistry*, Vol. 14 (Eds.: G. W. Gribble, T. L. Gilchrist), Pergamon, Oxford, **2002**, pp. 139–179; b) *Comprehensive Heterocyclic Chemistry*, Vol. 4 (Eds.: A. R. Katritzky, C. W. Rees), Pergamon, Oxford, **1984**, p. 531; c) *Comprehensive Heterocyclic Chemistry II*, Vol. 2 (Eds.: A. R. Katritzky, C. W. Rees, E. F. V. Scriven), Pergamon, Oxford, **1996**, p. 259; d) M. G. Kadieva, É. T. Oganessian, *Chem. Heterocycl. Compd.* **1997**, *33*, 1245; e) G. D. McCallion, *Curr. Org. Synth.* **1999**, *3*, 67; f) D. A. Horton, G. T. Bourne, M. L. Smythe, *Chem. Rev.* **2003**, *103*, 893; g) F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2004**, *104*, 3079; h) R. E. Ziegert, J. Toräng, K. Knepper, S. Bräse, *J. Comb. Chem.* **2005**, *7*, 147; i) G. Zeni, R. C. Larock, *Chem. Rev.* **2006**, *106*, 4644; j) R. Chinchilla, C. Nájera, *Chem. Rev.* **2007**, *107*, 874; k) H. Kwiecien, M. Smist, M. Kowalewska, *Curr. Org. Synth.* **2012**, *9*, 529.
- [4] For important examples of the synthesis of 3-carbonylated benzofurans, see: a) Y. Nan, H. Miao, Z. Yang, *Org. Lett.* **2000**, *2*, 297; b) E. Bellur, P. Langer, *J. Org. Chem.* **2005**, *70*, 7686; c) M. E. Dudley, M. M. Morshed, M. M. Hossain, *Synthesis* **2006**, 1711; d) B. Lu, B. Wang, Y. Zhang, D. Ma, *J. Org. Chem.* **2007**, *72*, 5337; e) X.-M. Cheng, X.-W. Liu, *J. Comb. Chem.* **2007**, *9*, 906; f) X.-C. Huang, Y.-L. Liu, Y. Liang, S.-F. Pi, F. Wang, J.-H. Li, *Org. Lett.* **2008**, *10*, 1525; g) X. Guo, R. Yu, H. Li, Z. Li, *J. Am. Chem. Soc.* **2009**, *131*, 17387; h) S. R. Mothe, D. Susanti, P. W. H. Chan, *Tetrahedron Lett.* **2010**, *51*, 2136; i) Y. Liu, J. Qian, S. Lou, Z. Xu, *J. Org. Chem.* **2010**, *75*, 6300; j) C. Li, Y. Zhang, P. Li, L. Wang, *J. Org. Chem.* **2011**, *76*, 4692; for examples of the synthesis of 2-carbonylated benzofurans, see: k) N. P. Buu-Hoi, G. Saintruf, T. B. Loc, N. D. Xuong, *J. Chem. Soc.* **1957**, 2593; l) A. Carrër, D. Brinet, J.-C. Florent, P. Rousselle, E. Bertounesque, *J. Org. Chem.* **2012**, *77*, 1316; m) F. Schevenels, I. E. Markó, *Org. Lett.* **2012**, *14*, 1298; n) F. Schevenels, B. Tinant, J.-P. Declercq, I. E. Markó, *Chem. Eur. J.* **2013**, *19*, 4335; o) P. Lan, M. G. Banwell, J. S. Ward, A. C. Willis, *Org. Lett.* **2014**, *16*, 228; for the synthesis of ribisins A, B, and D, see: p) P. Lan, M. G. Banwell, A. C. Willis, *J. Org. Chem.* **2014**, *79*, 2829; q) Z. Huang, L. Jin, Y. Feng, P. Peng, H. Yi, A. Lei, *Angew. Chem. Int. Ed.* **2013**, *52*, 7151; *Angew. Chem.* **2013**, *125*, 7292.
- [5] N. Sakiyama, K. Noguchi, K. Tanaka, *Angew. Chem. Int. Ed.* **2012**, *51*, 5976; *Angew. Chem.* **2012**, *124*, 6078.
- [6] For representative examples of the metal-free synthesis of benzofurans by [3,3] sigmatropic rearrangements, see: a) N. Takeda, O. Miyata, T. Naito, *Eur. J. Org. Chem.* **2007**, 1491; by Wittig reactions: b) S. Ghosh, J. Das, *Tetrahedron Lett.* **2011**, *52*, 1112; c) S.-e. Syu, Y.-T. Lee, Y.-J. Jang, W. Lin, *Org. Lett.* **2011**, *13*, 2970; by  $\text{PhI}(\text{OAc})_2$ -mediated cyclizations of *ortho*-hydroxystilbenes: d) F. V. Singh, T. Wirth, *Synthesis* **2012**, 1171; by electrophilic iodocyclization: e) D. Yue, T. Yao, R. C. Larock, *J. Org. Chem.* **2005**, *70*, 10292; by  $\text{TfOH}$ -catalyzed oxidative C–H transformations of quinones with alkenes: f) L. Meng, G. Zhang, C. Liu, K. Wu, A. Lei, *Angew. Chem. Int. Ed.* **2013**, *52*, 10195; *Angew. Chem.* **2013**, *125*, 10385.
- [7] For selected reviews, see: a) B. M. Trost, *Acc. Chem. Res.* **1990**, *23*, 34; b) B. M. Trost, M. J. Krische, *Synlett* **1998**, 1; c) B. M. Trost, *Chem. Eur. J.* **1998**, *4*, 2405; d) C. Aubert, O. Buisine, M. Malacria, *Chem. Rev.* **2002**, *102*, 813; e) C. Bruneau, *Angew. Chem. Int. Ed.* **2005**, *44*, 2328; *Angew. Chem.* **2005**, *117*, 2380; f) L. Zhang, J. Sun, S. Kozmin, *Adv. Synth. Catal.* **2006**, *348*, 2271; g) J. Marco-Contelles, E. Soriano, *Chem. Eur. J.* **2007**, *13*, 1350; h) A. Fürstner, P. W. Davies, *Angew. Chem. Int. Ed.* **2007**, *46*, 3410; *Angew. Chem.* **2007**, *119*, 3478; i) V. Michelet, P. Y. Toullec, J.-P. Genêt, *Angew. Chem. Int. Ed.* **2008**, *47*, 4268; *Angew. Chem.* **2008**, *120*, 4338; j) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326; k) S. I. Lee, N. Chatani, *Chem. Commun.* **2009**, 371; l) U. Wille, *Chem. Rev.* **2013**, *113*, 813.
- [8] Generally, the radical cyclization of 1,*n*-enynes proceeds through a trig cyclization; see: a) E. Lee, J. S. Tae, C. Lee, C. M. Park, *Tetrahedron Lett.* **1993**, *34*, 4831; b) D. L. J. Clive, S. R. Magnusson, H. W. Manning, D. L. Mayhew, *J. Org. Chem.* **1996**, *61*, 2095; c) M. A. Leeuwenburgh, R. E. J. N. Litjens, J. D. C. Codée, H. S. Overkleeft, G. A. van der Marel, J. H. van Boom, *Org. Lett.* **2000**, *2*, 1275; d) I. Ryu, H. Miyazato, H. Kuriyama, K. Matsu, M. Tojino, T. Fukuyama, S. Minakata, M. Komatsu, *J. Am. Chem. Soc.* **2003**, *125*, 5632; e) H. M. Ko, C. W. Lee, H. K. Kwon, H. S. Chung, S. Y. Choi, Y. K. Chung, E. Lee, *Angew. Chem. Int. Ed.* **2009**, *48*, 2364; *Angew. Chem.* **2009**, *121*, 2400; f) S. Mondal, R. K. Mohamed, M. Manoharan, H. Phan, I. V. Alabugin, *Org. Lett.* **2013**, *15*, 5650; g) S. Mondal, B. Gold, R. K. Mohamed, I. V. Alabugin, *Chem. Eur. J.* **2014**, *20*, 8664; h) P. C. Montevecchi, M. L. Navacchia, *J. Org. Chem.* **1997**, *62*, 5600; i) N. Hayashi, I. Shibata, A. Baba, *Org. Lett.* **2004**, *6*, 4981; j) J.-Y. Luo, H.-L. Hua, Z.-S. Chen, Z.-Z. Zhou, Y.-F. Yang, P.-X. Zhou, Y.-T. He, X.-Y. Liu, Y.-M. Liang, *Chem. Commun.* **2014**, *50*, 1564; for examples of dig cyclizations, see: k) L. Zhang, Z. Li, Z.-Q. Liu, *Org. Lett.* **2014**, *16*, 3688; l) Y.-T. He, L.-H. Li, Z.-Z. Zhou, H.-L. Hua, Y.-F. Qiu, X.-Y. Liu, Y.-M. Liang, *Org. Lett.* **2014**, *16*, 3896; for other cyclization reactions, see: m) A. Lei, M. He, S. Wu, X. Zhang, *Angew. Chem. Int. Ed.* **2002**, *41*, 3457; *Angew. Chem.* **2002**, *114*, 3607; n) A. Lei, J. P. Walckirch, M. He, X. Zhang, *Angew. Chem. Int. Ed.* **2002**, *41*, 4526; *Angew. Chem.* **2002**, *114*, 4708; o) A. Lei, M. He, X. Zhang, *J. Am. Chem. Soc.* **2002**, *124*, 8198; p) M. Chen, Y. Weng, M. Guo, H. Zhang, A. Lei, *Angew. Chem. Int. Ed.* **2008**, *47*, 2279; *Angew. Chem.* **2008**, *120*, 2311.
- [9] For selected reviews and papers on the use of *t*BuONO in synthesis, see: a) D. Fang, Q.-r. Shi, K. Gong, Z.-l. Lu, C.-x. Lü, *Chin. J. Energ. Mater.* **2008**, *16*, 103; b) J. Song, Z. Zhou, *Sci.-Tech. Rev.* **2013**, *31*, 69; c) D. Koley, O. C. Colón, S. N. Savinov, *Org. Lett.* **2009**, *11*, 4172; d) T. Taniguchi, A. Yajima, H. Ishibashi, *Adv. Synth. Catal.* **2011**, *353*, 2643; e) B. Kilpatrick, S. Arns, *Chem. Commun.* **2013**, *49*, 514; f) S. Manna, S. Jana, T. Saboo, A. Maji, D. Maiti, *Chem. Commun.* **2013**, *49*, 5286; g) S. Maity, T. Naveen, U. Sharma, D. Maiti, *Org. Lett.* **2013**, *15*, 3384; h) T. Shen, Y. Yuan, N. Jiao, *Chem. Commun.* **2014**, *50*, 554; i) Y. Liu, J.-L. Zhang, R.-J. Song, P.-C. Qian, J.-H. Li, *Angew. Chem. Int. Ed.* **2014**, *53*, 9017; *Angew. Chem.* **2014**, *126*, 9163; j) F. Chen, X. Huang, X. Li, T. Shen, M. Zou, N. Jiao, *Angew. Chem. Int. Ed.* **2014**, *53*, 10495; *Angew. Chem.* **2014**, *126*, 10663.
- [10] For selected reviews and papers, see: a) *Dioxygen Activation and Homogeneous Catalytic Oxidation* (Ed.: L. I. Simándi), Elsevier, Amsterdam, **1991**; b) *The Activation of Dioxygen and Homogeneous Catalytic Oxidation* (Eds.: D. H. R. Barton, A. E. Martell, D. T. Sawyer), Plenum, New York, **1993**; c) S. S. Stahl, *Angew. Chem. Int. Ed.* **2004**, *43*, 3400; *Angew. Chem.* **2004**, *116*, 3480; d) T. Punniyamurthy, S. Velusamy, J. Iqbal, *Chem. Rev.* **2005**, *105*, 2329; e) J. Muzart, *Chem. Asian J.* **2006**, *1*, 508; f) E. M. Beccalli, G. Broggini, M. Martinelli, S. Sottocornola, *Chem. Rev.* **2007**, *107*, 5318; g) J. Piera, J. E. Bäckvall, *Angew. Chem. Int. Ed.* **2008**, *47*, 3506; *Angew. Chem.* **2008**, *120*, 3558; h) S. S. Stahl, *Science* **2005**, *309*, 1824; i) W. Wu, H. Jiang, *Acc. Chem. Res.* **2012**, *45*,

- 1736; j) Z. Shi, C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3381; k) Q. Liu, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2013**, *52*, 13871; *Angew. Chem.* **2013**, *125*, 14115; l) A. Wang, H. Jiang, *J. Am. Chem. Soc.* **2008**, *130*, 5030; m) C. Zhang, N. Jiao, *J. Am. Chem. Soc.* **2010**, *132*, 28; n) Z.-Q. Wang, W.-W. Zhang, L.-B. Gong, R.-Y. Tang, X.-H. Yang, Y. Liu, J.-H. Li, *Angew. Chem. Int. Ed.* **2011**, *50*, 8968; *Angew. Chem.* **2011**, *123*, 9130; o) Q. Lu, J. Zhang, G. Zhao, Y. Qi, H. Wang, A. Lei, *J. Am. Chem. Soc.* **2013**, *135*, 11481; p) S. Handa, J. C. Fennelwald, B. H. Lipshutz, *Angew. Chem. Int. Ed.* **2014**, *53*, 3432; *Angew. Chem.* **2014**, *126*, 3500; q) Q. Lu, J. Zhang, F. Wei, Y. Qi, H. Wang, Z. Liu, A. Lei, *Angew. Chem. Int. Ed.* **2013**, *52*, 7156; *Angew. Chem.* **2013**, *125*, 7297; r) Q. Lu, C. Liu, Z. Huang, Y. Ma, J. Zhang, A. Lei, *Chem. Commun.* **2014**, *50*, 14101; s) T. Wang, N. Jiao, *J. Am. Chem. Soc.* **2013**, *135*, 11692; t) Z. Xu, C. Zhang, N. Jiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 11367; *Angew. Chem.* **2012**, *124*, 11529; u) Y. Su, X. Sun, G. Wu, N. Jiao, *Angew. Chem. Int. Ed.* **2013**, *52*, 9808; *Angew. Chem.* **2013**, *125*, 9990; v) Y. Su, L. Zhang, N. Jiao, *Org. Lett.* **2011**, *13*, 2168; w) R. Lin, F. Chen, N. Jiao, *Org. Lett.* **2012**, *14*, 4058; x) C. Zhang, P. Feng, N. Jiao, *J. Am. Chem. Soc.* **2013**, *135*, 15257; y) Y.-F. Liang, N. Jiao, *Angew. Chem. Int. Ed.* **2014**, *53*, 548; *Angew. Chem.* **2014**, *126*, 558.
- [11] Detailed data, including for the optimization of the reaction conditions (Table S1) and the  $^{18}\text{O}$ -labeling experiment (Figure S1), are provided in the Supporting Information.
- [12] a) M. P. Doyle, J. W. Terpstra, R. A. Pickering, D. M. LePoire, *J. Org. Chem.* **1983**, *48*, 3379; b) J.-Y. Park, Y.-N. Lee, *J. Phy. Chem.* **1988**, *92*, 6294; c) S. Ranganathan, S. K. Kar, *J. Org. Chem.* **1970**, *35*, 3962.